KHUFO 2024 YEOSU

JUNE 25TUE – JUNE 27THUR, 2024
YEOSU Expo Convention Center

여수시
YEOSU CITY

PROUD

PROTEOMICS
UNLIMITED DESIRE

Pioneering Proteomics

SomaScan® Assay Services Options

High-plex protein profiling for biomarker discovery and development.
Deepen your molecular insights of new biomarkers and therapeutic targets.

SomaScan Assay - now available in 11K and 7K formats.

NEW SomaScan 11K Assay

EXPLORE THE POWER OF MORE

More proteins. More pathways. More pQTLs.

Profile 11,000 protein measurements simultaneously in 55-µL

Recommended for new studies to get the greatest coverage of the proteome

Sample types: Human and non-human serum and plasma

SomaScan 7K Assay

DISCOVERY, VALIDATION, AND DEVELOPMENT

Available in a single proteomics platform

Profile 7,000 protein measurements simultaneously in 55-µL

Recommended for continuation of existing projects, use in a broader range of sample types and access to specialized proteomic panels and tests

Sample types: Human and non-human serum and plasma, tissue, CSF, urine, and more

Additional product services available with the SomaScan 7K Assay

Projects performed at the SomaLogic CLIA lab includes dedicated project managment. All services sites also provide comprehensive data and analysis tools with additional resources available at the SomaLogic customer portal (somalogic.com/life-sciences-portal/)

Now Available on SomaScan 11K Assay

SomaScan Panels

Custom Panels:
Design your own panel with up to 100 or 1,500 protein measurements from our 11K menu.

Disease Specific Panels:
Choose from panels that meaure proteins associated with therapeutic areas.

Learn more: somalogic.com/somascan-panels

SomaSignal® Tests

Powerful proteomic profiling provides multiple clinical assessments from a single blood draw.

Learn more: somalogic.com/somasignal-tests-for-research-use

SomaScan Assay Services are available at:

SomaLogic's CLIA certified laboratory in Colorado, USA

Worldwide Authorized Sites (somalogic.com/authorized-sites-worldwide)

Learn more at **somalogic.com/somascan-assay-services/**

SCIEX

The Power of Precision

Intabio ZT system

Be unstoppable with comprehensive charge variant analysis on a single system

The Intabio ZT system couples icIEF separation and UV detection with high-resolution mass spectrometry for peak identification.

> Achieve comprehensive proteoform ID in minutes

> Leverage key analytical functions with microfluidic chip-based integrated icIEF-UV/MS technology

> Eliminate the guess work with the ZenoTOF 7600 system

Comprehensive charge variant analysis made simple!

The SCIEX clinical diagnostic portfolio is For In Vitro Diagnostic Use. Rx Only. Product(s) not available in all countries. For information on availability, please contact your local sales representative or refer to www.sciex.com/diagnostics. All other products are For Research Use Only. Not for use in Diagnostic Procedures. Trademarks and/or registered trademarks mentioned herein, including associated logos, are the property of AB Sciex Pte. Ltd. or their respective owners in the United States and/or certain other countries (see www.sciex.com/trademarks). Intabio is being used under license.

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Framingham, MA 01701 USA
Phone 508-383-7700
sciex.com

맞춤형 펩타이드 합성을 위한 합리적인 솔루션

PEPS PRO

베르티스는 세계 수준의 단백질 분석, 동정, 정량 및 해석 기술로 프로테오믹스(Proteomics, 단백질체학) 기술의 상용화에 성공한 정밀의료 기술 기업입니다. PEPS PRO는 GMP 생산 체계를 구축해 수 만종의 단백질에서 유래한 펩타이드를 제작한 경험을 토대로 우수한 품질의 펩타이드를 합리적인 가격에 공급합니다.

Facility

GMP 생산 체계 구축으로 신뢰도 높은
고품질의 펩타이드 합성 서비스 제공

Expertise

수만 종의 펩타이드 합성 경험과
인체 유래 펩타이드 라이브러리 보유를 통한
비용 효율적 합성 노하우 구축

다품종 펩타이드 합성

마커 발굴용, 기능성 펩타이드,
스크리닝 및 기타 연구용 (mg 단위)

대용량 제품용 펩타이드 합성

화장품, 식품 및
의약품 원료 (g~kg 단위)

펩타이드 Modification

100여 종 이상의
modification

**PEPS PRO는 펩타이드 합성에 대한 최적화된 기술을 이용하며,
다양한 종류의 고품질 펩타이드를 신속하게 제공합니다.**

PEPS PRO
서비스 신청 바로가기

서비스 문의
pepspro@bertis.com

BERTIS

Panomics Analysis Service & Solution

질량분석 기반 오믹스 분석 서비스

PASS

신뢰성 높은 프로테오믹스 분석 결과를 얻기 위해서는 다양한 분석 경험이 필요합니다.
베르티스는 질량 분석 기반의 암 및 각종 주요질환에 대한 바이오마커 개발 및 상업화 노하우와
최고 사양의 질량 분석 장비를 기반으로 고객 맞춤형 단백체 분석 서비스를 제공합니다.

ESSENTIAL SERVICE

Biomarker discovery
Target quantification
Single cell analysis
Lipid analysis
Phospho analysis

BIOPHARMACEUTICAL SOLUTION

Drug target discovery
Protein characterization
Subtyping
Manufacture QC
Exosome
Targeted protein degradation (TPD)

INTEGRATED PROTEOMICS

Label free (DIA), labeling (DDA)법을 적용한
전체 단백체에 대한 정성 및 정량 분석

TARGETED PROTEOMICS

MRM/PRM법을 적용한
타겟 단백질에 대한 정량 분석

LIPIDOMICS

20종의 lipid 표준물질을 이용한 lipid 정성 및
정량 분석

SINGLE CELL PROTEOMICS

단일 세포에서의 단백질 정성 및 정량 분석

BIOINFORMATICS

생물정보학 기반 단백체 데이터 분석 및 해석

PASS
서비스 신청 바로가기

서비스 문의
pass@bertis.com

BERTIS

timsTOF Ultra 2

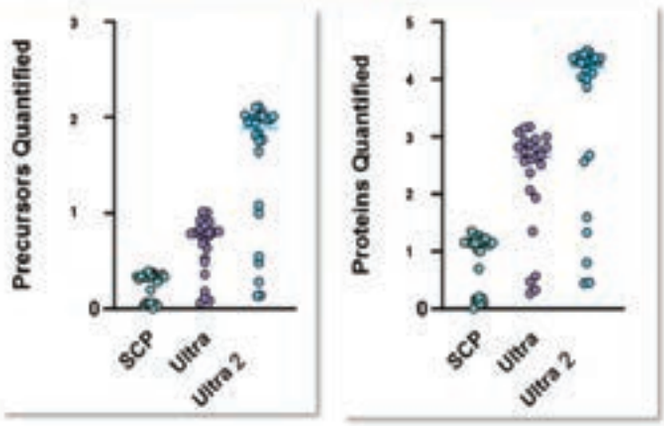
Move Forward for Deeper Single Cell Proteomics

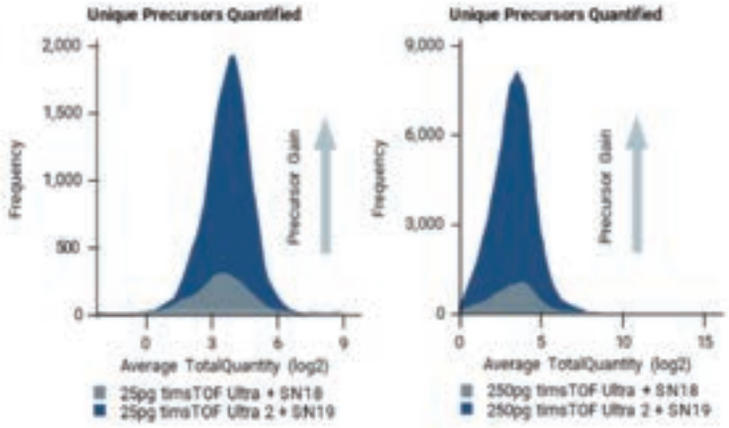
Redefining sensitivity

- Maximum ion transfer
  새로운 CaptiveSpray Ultra 2 (CSI Ultra 2)를 통한 안정적이고 최적화된 이온화 효율
- Enhanced specificity
  수 pg부터 수백 ng까지 폭 넓은 분석 범위
  300 Hz TIMS PASEF® 를 통한 빠른 시료 분석
- Increased confidence
  Single cell 분석에서 증가한 감도와 CCS 분석을 활용한 정확하고 효율적인 단백체 분석

Brochure : timsTOF Ultra 2

timsTOF Ultra 2 : Real single cell data





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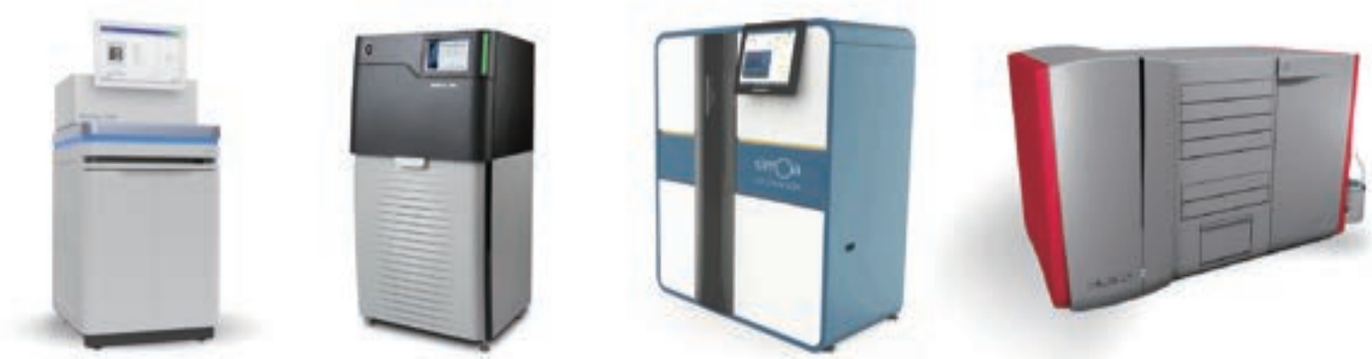
"Precision Genomics"
DNA LINK



Illumina
Novaseq6000
Hiseq2500
Nextseq500

Pacific Biosciences
Pacbio RSII
Pacbio Sequel
Pacbio Sequel2

Affymetrix Axiom
Genetitan

Quanterix
Simoa HD-X

10X Genomics
Single cell RNA
Immune Profiling
Single cell ATACseq
Multiome

Oxford NANOPORE
MinION
PromethION

illumina CSPro
PACBIO CERTIFIED SERVICE PROVIDER
affymetrix Authorized Service Provider
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(주)디엔에이링크는 지난 10여 년간 축적된 연구결과물과 노하우를 바탕으로 융합분석체계를 구축하여 유전체분석 서비스를 상용화한 유전체기반 생명공학 전문기업입니다.

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KBSI, a government-funded research institution established in 1988, conducts research and development, research support and joint research, related to high-tech research equipment as well as advanced analytical science technology.

USE Research equipment joint utilization service

use.kbsi.re.kr

TOTAL NUMBER OF EQUIPMENT

177

1 Equipment Search

Search by equipment search tool, and counsel about analytical approach with expert

2 Join & Login

After joining, proceed with discounts and reservations

3 Application

Reserve the equipment after check the schedule to use through consultation with

4 Monitoring Analysis

Monitoring the progress analysis in 'equipment use inquiry' tab

5 Payment

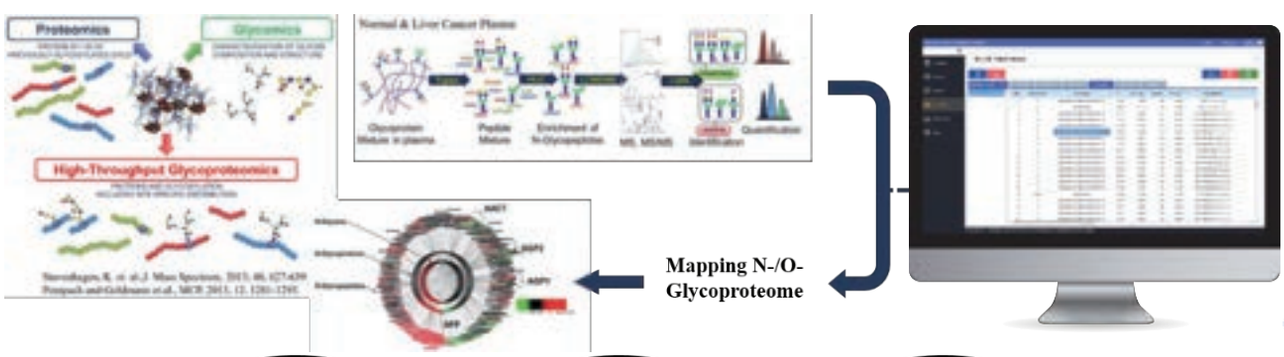
Payment by credit card or deposit without a bankbook : Visit, on-line payment available

6 Receive Result

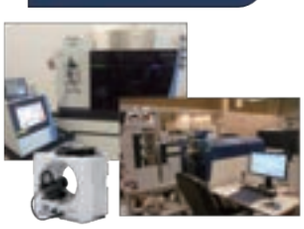
Receive the results (direct printing possible) after payment completed

IQGPA Identification and Quantification for GlycoProteome Analysis

IQGPA has been designed to easily handle high-throughput glycoproteomic data with graphical user interfaces and users enable to quickly provision on-demand infrastructures for high-performance gylcoproteome analysis using Microsoft Azure cloud platforms



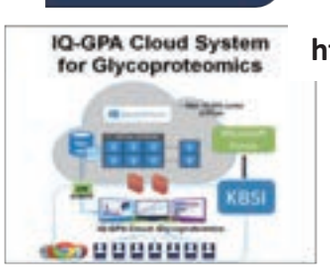
HARDWARE | SOFTWARE | CLOUD COMPUTE | WEBSITE



10~15 MS2 (CID/HCD/EThcD) scans/sec @R>30,000

GPA GlycoProteomeAnalyzer

python

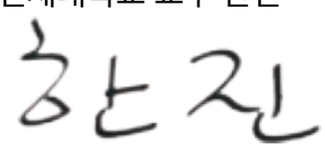


http://www.iqgpa.org

Contents

Welcome Message

한국단백체학회 12기 회장
인제대학교 교수 한진



존경하는 한국단백체학회 회원 여러분께,

프로테오믹스를 통한 제약 바이오 분야의 연구, 협업, 기술 혁신의 미래를 향한 도전과 도약에 동참하게 되어 영광이고 참 설레입니다.
우리 학회는 생명의 기본 과정을 좌우하는 다양하고 광범위한 단백질의 집합체인 인간 단백체의 신비를 풀고 인류를 위해 새로운 과학의 지평을 넓히려는 열정으로 결속되어 있습니다.

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6월 여수에서 직접 뵙고 인사드리겠습니다.

고맙습니다.

Organizing Committee

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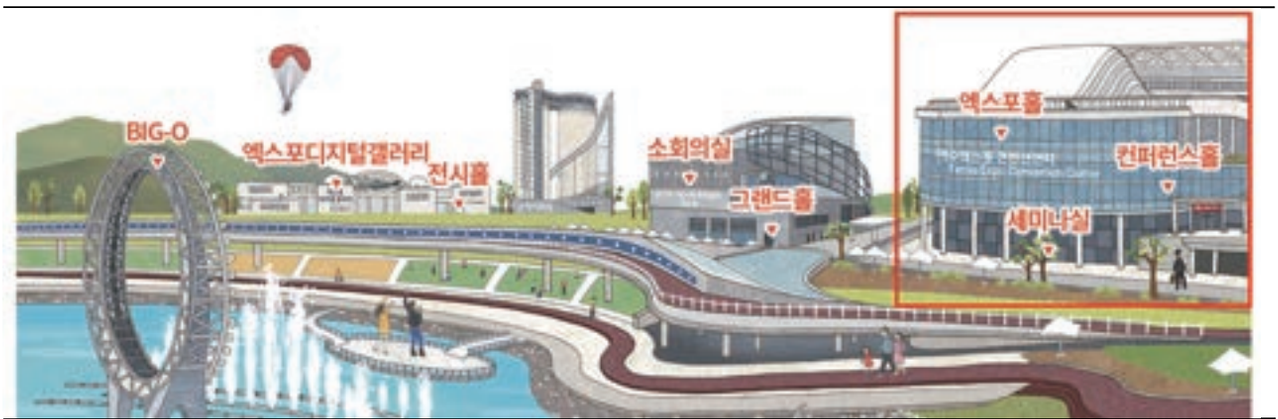
General Information

Overview

Title	The 22nd Annual International Proteomics Conference (KHUPO 2024)
Date	June 25 (Tue) - June 27 (Thur), 2024
Organized by	The Korean Human Proteome Organization (KHUPO)

Venue



B1F-2F, YEOSU Expo Convention Center

Program at a Glance

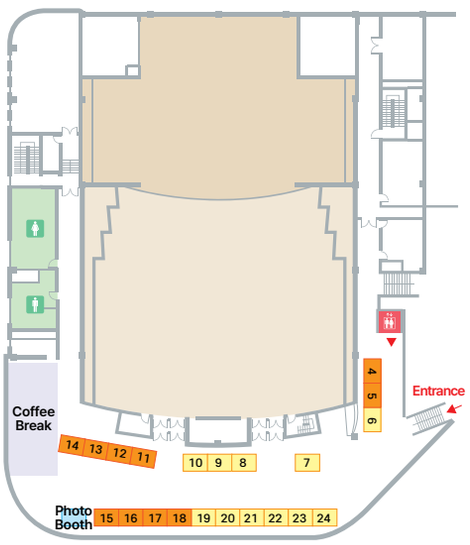
June 25 (Tue)	Education Session 1, Education Session 2, Corporate Workshop 1, Opening Ceremony, PL1, SYM A1, SYM B1, SYM A2, SYM B2, PL2, Reception
June 26 (Wed)	Education Session 3, Education Session 4, Satellite Session 1, SYM A3, SYM B3, Poster Session 1 (Odd Numbers), Corporate Workshop 2, Corporate Workshop 3, Corporate Workshop 4, 3 Minutes Talk, Poster Session 2 (Even Numbers), SYM A4, SYM B4, Satellite Session 2, Satellite Session 3, SYM A5, SYM B5, PL3
June 27 (Thur)	SYM A6, SYM B6, PL4, Poster Session 1 (Odd Numbers), Corporate Workshop 5, 3 Minutes Talk, Poster Session 2 (Even Numbers), SYM A7, SYM B7, PL5, General Assembly, Closing Ceremony

Secretariat (The PlanB Co., Ltd.)

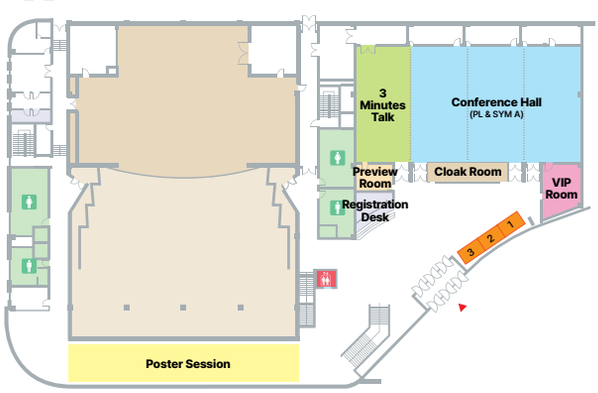
Address	#360, 55 APEC-ro, Haeundae-gu, Busan, Republic of Korea
Tel	82-2-393-8328
E-mail	admin@khupo.org
Website	http://khupo.org

Exhibition Information

2F



1F



B1F

NO.	Booth
1	Bertis
2	
3	Agilent Technologies
4	Thermo Fisher Scientific
5	
6	Waters Korea
7	Somalogic (St andard BioTools)
8	Bru ker Korea Co., Ltd.
9	SCIEX
10	SHIMADZU
11	Bio-Rad
12	Sartorius Korea Biotech
13	Revvity
14	SeouLin Bioscience
15	SIG
16	Bio-Medical Science Co., Ltd.
17	INTERFACE Co., Ltd.
18	
19	EliHighTech
20	Korea Ba sic Science Institute
21	University of Ulsan College of Medicine Digestive Diseases Research Center
22	KIM & FRIENDS
23	MDxK
24	DNALINK, Inc.

Program at a Glance

Time	Day 1 (6.25 Tue)		Day 2 (6.26 Wed)				Day 3 (6.27 Thu)	
Room	1F	B1	1F	B1			1F	B1
	Conference Hall	Seminar Room 4	Conference Hall	Seminar Room 4	Seminar Room 1	Seminar Room 2	Conference Hall	Seminar A
	Registration (09:00 - 18:00) Lobby (1F)		Registration (08:00 - 17:00) Lobby (1F)				Registration (08:00 - 15:00) Lobby (1F)	
09:00 - 10:00			ES 3 (Proteomics meets AI)	ES 4 (Public MS Data Repository)	Satellite Session 1 다중오믹스기반 정밀의료기술 개발산업성보고회		SYM-A6 (Young Scientists) (09:00 - 10:10)	SYM-B6 (New Role of HPP: Protein Function Annotation)
10:00 - 10:15								
10:15 - 10:30	ES 1 (Introduction to Proteomics)	ES 2 (Targeted Proteomics)	Coffee Break Lobby (1-2F)				Coffee Break Lobby (1-2F)	
10:30 - 11:00			SYM-A3 (Biomarker Discovery for Clinical Proteomics)	SYM-B3 (PTM in disease)			PL 4 (Charles Pineau)	
11:00 - 11:10								
11:10 - 11:30							Break	
11:30 - 11:45	Break (11:30 - 11:40)						Poster Session 1 -Odd Numbers Lobby (1F)	
11:45 - 12:00	CW ThermoFisher SCIENTIFIC (11:40 - 12:40) Conference Hall (1F)		Poster Session 1 -Odd Numbers Lobby (1F)					
12:00 - 12:30								
12:30 - 12:40			CW SCIEX	CW Agilent			CW BRUKER Conference Hall (1F)	
12:40 - 12:50	Break							
12:50 - 13:00	Opening Ceremony Conference Hall (1F)				Break			
13:00 - 13:30	PL 1 (John R. Yates III) Conference Hall (1F)		CW somalogic	3 Minutes Talk Rear of Conference Hall (1F)			3 Minutes Talk Rear of Conference Hall (1F)	
13:30 - 13:40			Poster Session 2 -Even Numbers Lobby (1F)				Poster Session 2 -Even Numbers Lobby (1F)	
13:40 - 14:00	Break							
14:00 - 14:30	SYM-A1 (New Technologies in Proteomics I)	SYM-B1 (Disease Models)			Satellite Session 2 국가암데이터센터 소개 및 단백유전체 사업 결합을 통한 데이터 활용법	Satellite Session 3 세포배양식품 개발 기술 워크샵		
14:30 - 14:45			Break				Break	
14:45 - 15:15			SYM-A4 (New Technologies in Proteomics II)	SYM-B4 (Glycoproteomics and Glycomics)			SYM-A7 (Degenerative Disease)	SYM-B7 (Chemical proteomics and drug development)
15:15 - 15:30	Coffee Break Lobby (1-2F)							
15:30 - 16:00	SYM-A2 (Tumor Microenvironment)	SYM-B2 (Proteogenomics in Translation) (15:30 - 16:45)	Coffee Break Lobby (1-2F)				Coffee Break Lobby (1-2F)	
16:00 - 16:15								
16:15 - 16:20			SYM-A5 (AI Driven Drug Development)	SYM-B5 (Immunothera Peutics)				
16:20 - 16:50							PL 5 (Youngsoo Kim) Conference Hall (1F)	
16:50 - 17:00	Break							
17:00 - 17:10	PL 2 (Woong-Yang Park) Conference Hall (1F)						General Assembly Conference Hall (1F)	
17:10 - 17:30							Closing Ceremony Conference Hall (1F)	
17:30 - 17:40								
17:40 - 17:45	Break		Break					
17:45 - 18:00			PL 3 (Naoyuki Taniguchi) Conference Hall (1F) (17:45 - 18:25)					
18:00 -	Reception Lobby (2F)							

Program by Date

Day 1 (6.25 Tue)		
09:00 - 18:00	1F, Lobby	Registration
10:15 - 11:30	1F, Conference Hall	Education Session 1: Introduction to proteomics - Basics and biological insights
	B1, Seminar Room 4	Education Session 2: Targeted proteomics - techniques, tools, and applications
11:30 - 11:40		Break
11:40 - 12:40	1F, Conference Hall	CW-1 (Thermo Fisher Scientific)
12:40 - 12:50		Break
12:50 - 13:00	1F, Conference Hall	Opening Ceremony
13:00 - 13:40	1F, Conference Hall	PL1: How A Single Mutation in CFTR Causes the Systemic Disease Cystic Fibrosis: Interactions, PTMs, And Structure
13:40 - 14:00		Break
14:00 - 15:15	1F, Conference Hall	Symposium A1: New Technologies in Proteomics I
	B1, Seminar Room 4	Symposium B1: Disease Models
15:15 - 15:30	1-2F, Lobby	Coffee Break
15:30 - 16:50	1F, Conference Hall	Symposium A2: Tumor Microenvironment
	B1, Seminar Room 4	Symposium B2: Proteogenomics in translation (15:30 - 16:45)
16:50 - 17:00		Break
17:00 - 17:40	1F, Conference Hall	PL2: Utility of Spatial Landscape of Cellular and Molecular Interactions in Precision Medicine
17:40 - 18:00		Break
18:00 - 20:00	2F, Lobby	Reception

Program by Date

Day 2 (6.26 Wed)		
08:00 - 17:00	1F, Looby	Registration
09:00 - 10:15	1F, Conference Hall	Education Session 3: Proteomics meets AI
	B1, Seminar Room 4	Education Session 4: Public MS Data Repository
09:00 - 12:30	B1, Seminar Room 1	Satellite Session 1 다중오믹스기반 정밀의료기술 개발산업 성과보고회
10:15 - 10:30	1-2F, Lobby	Coffee Break
10:30 - 11:45	1F, Conference Hall	Symposium A3: Biomarker discovery for Clinical Proteomics
	B1, Seminar Room 4	Symposium B3: PTMs in diseases
11:45 - 12:30	1F, Lobby	Poster Session 1 - Odd Numbers
12:30 - 13:00	B1, Seminar Room 4	CW-2 (SCIEX)
12:30 - 13:00	B1, Seminar Room 1	CW-3 (Agilent)
13:00 - 13:30	B1, Seminar Room 4	CW-4 (Somalogic)
13:00 - 13:30	1F, Rear of Conference Hall	3 Minutes Talk
13:30 - 14:30	1F, Lobby	Poster Session 2 - Even Numbers
14:00 - 17:00	B1, Seminar Room 1	Satellite Session 2 국가암데이터센터 소개 및 단백유전체 사업 결합을 통한 데이터 활용법
14:00 - 17:00	B1, Seminar Room 2	Satellite Session 3 세포배양식품 개발 기술 워크샵
14:30 - 14:45	1-2F, Lobby	Coffee Break
14:45 - 16:00	1F, Conference Hall	Symposium A4: New Technologies in Proteomics II
	B1, Seminar Room 4	Symposium B4: Glycoproteomics and Glycomics
16:00 - 16:15	1-2F, Lobby	Coffee break
16:15 - 17:30	1F, Conference Hall	Symposium A5: AI Driven Drug Development
	B1, Seminar Room 4	Symposium B5: Immunotherapeutics
17:30 - 17:45		Break
17:45 - 18:25	1F, Conference Hall	PL3: Glyco-redox and its Role in EMT/MET and Cancer

Program by Date

Day 3 (6.27 Thu)		
08:00 - 15:00	1F, Looby	Registration
09:00 - 10:15	1F, Conference Hall	Symposium A6: Young Scientist (09:00 - 10:10)
	B1, Seminar Room 4	Symposium B6: Protein Function Annotation or HPP
10:15 - 10:30	1-2F, Lobby	Coffee Break
10:30 - 11:10	1F, Conference Hall	PL4: The Human Proteome Project “Grand Challenge” - A function for every Human protein
11:10 - 11:30		Break
11:30 - 12:30	1F, Lobby	Poster Session 1 - Odd Numbers
12:30 - 13:00	1F, Conference Hall	CW-5 (Bruker)
13:00 - 13:30	1F, Rear of Conference Hall	3 Minutes Talk
13:30 - 14:30	1F, Lobby	Poster Session 2 - Even Numbers
14:30 - 14:45		Break
14:45 - 16:00	1F, Conference Hall	Symposium A7: Degenerative Disease
	B1, Seminar Room 4	Symposium B7: Chemical Proteomics and Drug Development
16:00 - 16:20	1-2F, Lobby	Coffee Break
16:20 - 17:00	1F, Conference Hall	PL5: A Road to Develop MRM-MS as a Diagnostic Platform: Surveillance Diagnosis for Hepatocellular Carcinoma (HCC)
17:00 - 17:10	1F, Conference Hall	General Assembly
17:10 - 17:40	1F, Conference Hall	Closing Ceremony

SCIENTIFIC PROGRAM

PLENARY LECTURES
EDUCATION SESSION
SYMPOSIA-A
SYMPOSIA-B
SATELLITE SESSION
CORPORATE WORKSHOP

PLENARY LECTURES

PLENARY LECTURES

PL-1

6.25 (Tue) 13:00 - 13:40

Chair: Jin Young Kim / Korea Basic Science Institute (KBSI)

How A Single Mutation in CFTR Causes the Systemic Disease Cystic Fibrosis: Interactions, PTMs, And Structure

John R. Yates III
Scripps Research Institute

PL-2

6.25 (Tue) 17:00 - 17:40

Chair: Jong Hoon Park / Sookmyung Women's University

Utility of Spatial Landscape of Cellular and Molecular Interactions in Precision Medicine

Woong-Yang Park
Samsung Medical Center

PL-3

6.26 (Wed) 17:45 - 18:25

Chair: Jeong Heon Ko / Korea Research Institute of Bioscience and Biotechnology (KRIBB)

Glyco-redox and its Role in EMT/MET and Cancer

Naoyuki Taniguchi
Osaka International Cancer Institute

PL-4

6.27 (Thu) 10:30 - 11:10

Chair: Ho Jeong Kwon / Yonsei University

The Human Proteome Project “Grand Challenge” - A function for every Human protein

Charles Pineau
French National Institute of Health and Medical Research (Inserm)

PL-5

6.27 (Thu) 16:20 - 17:00

Chair: Je-Yoel Cho / Seoul National University

A Road to Develop MRM-MS as a Diagnostic Platform: Surveillance Diagnosis for Hepatocellular Carcinoma (HCC)

Youngsoo Kim
CHA University

PLENARY LECTURES

John Robert Yates III, Ph.D

Position: Ernest W. Hahn Professor
Affiliation: Departments of Molecular Medicine and Neuroscience
Office: Scripps Research Institute, La Jolla, CA
E-mail: JYATES@SCRIPPS.EDU
Homepage: www.ncbi.nlm.nih.gov/sites/myncbi/john.yates.1/bibliography/40512487/public/?sort=date&direction=descending

Education

1987.05	Ph.D.	University of Virginia, Charlottesville, VA
1983.05	M.S.	University of Maine, Orono, ME
1980.05	B.A.	University of Maine, Orono, ME

Professional Experience

2001.12 - Present	Professor	Molecular Medicine & Neurology, Scripps Research Institute, La Jolla, CA
2017.06 - 2023.06	Adjunct Professor	The Salk Institute, La Jolla, CA
2012.01 - 2013.01	Visiting Professor	Department of Chemistry, University of Hong Kong
2003.03 - 2004.04	Sr. Research Fellow	Protein & Metabolite Dynamics, Diversa, La Jolla, CA

Publications

1. My laboratory has been a pioneer in the development of mass spectrometry technology for proteomics and the study of biology and diseases using these tools. A number of critical developments for proteomics were developed in my laboratory. My laboratory developed the concept of database searching using tandem mass spectra to identify protein sequences [a]. This was a critical development for large-scale protein analysis. In addition, these methods were extended to the analysis of post translational modifications and to the identification of proteins from nucleotide databases, which is now known as proteogenomics [b, c].

a. Eng J., McCormack A.L., Yates J.R. (1994) An approach to correlate tandem mass spectral data of peptides with amino acid sequences in a protein database. **J Am Soc Mass Spectrom.** (11):976-89. doi: 10.1016/1044-0305(94)80016-2 PMID: 24226387

b. Yates III J.R., Eng J.K., McCormack A.L. (1995) Mining Genomes: Correlating tandem mass spectra of modified and unmodified peptides to nucleotide sequences. **Anal Chem.** 67(18):3202-10 PMID: 8686885

c. Yates III J.R., Eng J.K., McCormack A.L., Schieltz D.M. (1995) Method to correlate tandem mass spectra of modified peptides to amino acid sequences in the protein database. **Anal Chem.** 67(8) pp 1426-1436. PMID: 7741214

Complete list of Published Work in My Bibliography

www.ncbi.nlm.nih.gov/sites/myncbi/john.yates.1/bibliography/40512487/public/?sort=date&direction=descending

PL-1

How A Single Mutation in CFTR Causes the Systemic Disease Cystic Fibrosis: Interactions, PTMs, And Structure

Sandra Pankow[1], Casimir Bamberger[1], Salvador Martínez-Bartolomé[2], Sung-Kyu Park[1,3], John R. Yates III[1]

[1] Department of Molecular Medicine, The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, CA 92037, USA; [2]Yatari Biotherapeutics, San Diego, CA; [3]Chaparral Labs, San Diego, CA

Protein conformation is dynamic as it is influenced by post-translational modifications (PTMs) and interactions with other proteins, small molecules or RNA, for example. However, in vivo characterization of protein structures and protein structural changes after perturbation is a major challenge. Therefore, experiments to characterize protein structures are typically performed in vitro and with highly purified proteins or protein complexes, revealing a static picture of the protein. To identify the true conformational space occupied by proteins in vivo, we developed a novel low-resolution method named Covalent Protein Painting (CPP) that allows the characterization of protein conformations in vivo. Here, we report how an ion channel, the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR), is conformationally changed during biogenesis and channel opening in the cell. Our study led to the identification of a novel opening mechanism for CFTR by revealing that the interaction of the intracellular loop 2 (ICL2) with the nucleotide binding domain 2 (NDB2) of CFTR is needed for channel gating, and this interaction occurs concomitantly with changes to the narrow part of the pore and the walker A lysine in NBD1 for wt CFTR. However, the ICL2:NBD2 interface, which forms a “ball-in-a-socket” motif, is uncoupled during biogenesis, likely to prevent inadvertent channel activation during transport. Mutation of K273 in the ICL2 loop severely impaired CFTR biogenesis and led to accumulation of CFTR in the Golgi and TGN. CPP further revealed that, even upon treatment with current approved drugs such as Trikafta or at permissive temperature, the uncoupled state of ICL2 is a prominent feature of the misfolded CFTR mutants ΔF508 and N1303K that cause Cystic Fibrosis (CF). Although Trikafta treatment reduced the amount of uncoupled ICL2:NBD2 interfaces, more than 75% of F508 CFTR remained in the uncoupled state, suggesting that stabilization of this interface could produce a more efficient CF drug. CPP can characterize a protein in its native environment and measure the effect of complex PTMs and protein interactions on protein structure, making it broadly applicable and valuable for the development of new therapies.

PLENARY LECTURES

Woong-Yang Park, Ph.D.

Position: Director / Professor
Affiliation:
1.Samsung Genome Institute, Samsung Medical Center
2. Sungkyunkwan University School of Medicine Office
: Samsung Genome Institute, Samsung Medical Center, Sungkyunkwan University
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E-mail: woongyang@skku.edu

Education

1998	Postdoctoral Fellow	Rockefeller University, New York, USA
1995	Ph.D.	Seoul National University Graduate School
1988	M.D.	Seoul National University College of Medicine

Professional Experience

2014 - Present	Editorial Board	Genome Biology
2017 - Present	Steering committee	Human Cell atlas Asia
2020 - Present	Independent Advisory Board	ICGC-ARGO
2023 - 2023	President	Korea Genome organization

Publications

1. Kim HS, Park S, Han KY, et al. Clonal expansion of resident memory T cells in peripheral blood of patients with non-small cell lung cancer during immune checkpoint inhibitor treatment. Journal for Immunotherapy of Cancer, 2023 Feb;11(2):e005509

2. Kim R, An M, Lee H et al. Early Tumor-Immune Microenvironmental Remodeling Underlies Response to Frontline Fluoropyrimidine and Oxaliplatin in Advanced Gastric Cancer. Cancer Discovery. 2022 Apr 1;12(4):984-1001.

3. Kwon M, Kim G, Kim R et al. Phase II study of ceralasertib (AZD6738) in combination with durvalumab in patients with advanced gastric cancer. Journal for Immunotherapy of Cancer. 2022 Jul;10(7):e005041.

4. Hong TH, Cha H, Shim JH et al. Clinical advantage of targeted sequencing for unbiased tumor mutational burden estimation in samples with low tumor purity. Journal for Immunotherapy of Cancer 2020 Oct;8(2):e001199. doi: 10.1136/jitc-2020-001199.

5. Lee HW, Chung W, Lee HO et al. Single-cell RNA sequencing reveals the tumor microenvironment and facilitates strategic choices to circumvent treatment failure in a chemorefractory bladder cancer patient. Genome Medicine 2020 May 27;12(1):47.

6. Yun JW, Yang L, Park HY et al. Dysregulation of cancer genes by recurrent intergenic fusions. Genome Biology 2020 Jul 6;21(1):166.

7. Lee HO, Hong Y, Etlioglu HE et al. Genetic triggers and microenvironmental signal amplification determine the immune landscape of colorectal cancer. Nature Genetics 2020 Jun;52(6):594-603.

8. Shim JH, Kim HS, Cha H et al. Corrected tumor mutation burden and homologous recombination deficiency for the prediction of response to PD-(L)1 blockade in non-small cell lung cancer patients. Annals of Oncology 2020 Apr 19:S0923-7534(20)39295-4.

PL-2

Utility of Spatial Landscape of Cellular and Molecular Interactions in Precision Medicine

Woong-Yang Park

Samsung Genome Institute, Samsung Medical Center, Sungkyunkwan University, and Geninus Inc., Seoul, Korea

The field of single-cell transcriptomics applied to paraffin-fixed tissue slides is experiencing rapid advancement. Spatial transcriptome analysis, a technique capable of simultaneously assessing gene expression and cellular localization at the genomic level within tissue slides, offers a comprehensive approach to studying the functional attributes of individual cells within the cancer microenvironment. By scrutinizing the transcriptome at the single-cell level across all cells present on a cancer tissue slide, this methodology provides insights into the intricate tumor microenvironment (TME), which plays a significant role in cancer progression and often exhibits patient-specific variability. The cellular composition of the TME profoundly impacts the clinical trajectory of the disease. Spatial transcriptome analysis facilitates the elucidation of vital information regarding the spatial arrangement of cells and their intercellular interactions within the TME. Future research endeavors focusing on investigating the relationship between the spatial cellular architecture of the TME and the response to immunotherapy will yield critical insights for identifying novel therapeutic targets and elucidating mechanisms of action.

PLENARY LECTURES

Naoyuki Taniguchi, Ph.D.

Position / Affiliation:
Director of Research Center, Osaka International Cancer Institute,
& Head, Department of Glyco-Oncology and Medical Biochemistry,
Professor Emeritus, Osaka University,
Honorable research scientist, RIKEN
E-mail: glycotani@mc.pref.osaka.jp or tani52@wd5.so-net.ne.jp

Education

1972	Ph.D.	Hokkaido University Graduate School of Medicine, Japan
1967	MD	Hokkaido University, Japan

Professional Experience

2019.04 - Presnet	Director of Research Center	Osaka International Cancer Institute & Head, Department of Glyco-Oncology and Medical Biochemistry
2018.04 - 2019.03	Department Head	Department of Glyco-Oncology, Osaka International Cancer Institute, Osaka, Japan
2007.10 - 2018.03	Goupr Director	Systems Glycobiology Research Group, RIKEN
2011.03 - 2017.03	Team Leader	Disease Glycomics Probe team, RIKEN-Max Planck Joint Research Center for Chemical Biology, RIKEN Advanced Science Institute, Saitama, Japan

Publications

1. Total citations 55723 h-index, 118, i10 710 (as of April 15, ,2024)

PL-3

Glyco-redox and its Role in EMT/MET and Cancer

[1]Naoyuki Taniguchi

[1]Department of Glyco-Oncology and Medical Biochemistry, Research Center, Osaka International Cancer Center

Glycans are biosynthesized by a specific glycosyltransferase and each glycosyltransferase is either directly or indirectly regulated via transcriptional factors, epigenetic modification, chaperon, availability of donor and acceptor substrates including sugar nucleotides, and competitive enzyme activity under oxidative stress. Therefore, glycomics is also one of the important research fields in human proteome. We proposed previously the concept of Glyco-redox which explains the interaction of reduction/oxidation (redox) and glycosylation (1) and involved in the endothelial mesenchymal transition (EMT) and mesenchymal epithelial transition (MET) processes that are highly associated with the onset of various diseases such as cancer and fibrosis (2).

The present studies introduce a typical example of Glyco-redox. One of the antioxidative enzyme SOD3 (extracellular SOD) has N-glycans with sialic acid and core fucose glycans that play important roles in secretion and in the ability to suppress the growth of cancer cell lines.

Recently several papers have described deep insight to describe the concept of Glyco-redox. This mini review describes the significance of Glyco-redox in EMT/MET and the roles of major N-glycan glycosyltransferases GnT-III, GnT-V, ST6Gal1, and Fut8. Herein, we also identify their target proteins and discuss the significance of their products. A clear-cut understanding of the significance of Glyco-redox in relation to the EMT/MET process is essential to develop biomarker discovery and treatments for these diseases.

References

1) Taniguchi N. et al. Arch Biochem Biophys. 2016 Apr 1;595:72-80.
2) Taniguchi N, Kizuka Y. Adv Cancer Res. 2015;126:11-51.

PLENARY LECTURES

Charles PINEAU, Ph.D.

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Team COCOON & PROTIM Core Facility
Campus Santé, Rennes University, 35000 Rennes, France
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Education

2005	Authorization to conduct research	University Rennes I
1990	Ph.D.	University Rennes I

Professional Experience

2019.12 - Present	Director Biosit, UAR 3480 CNRS US18 Inserm, Rennes
2007 - Presnet	Research Director Inserm 1st class, Team leader, U.1085, Rennes
2001 - Present	Director Protim core facility (IBiSA, ISO9001, NFX50-900)
1993 - 2006	Senior scientist Inserm, U.435 & U.625, Rennes

Academic Society

2001 - Present	Member Scientific Council Biogenouest
2007 - Present	Member of the board of directors Bretagne Santé Biotech

PL-4

The Human Proteome Project “Grand Challenge” - A function for every Human protein

Charles Pineau

Inserm U1085, IRSET, Rennes, France

The Human Proteome Project (HPP) is the flagship project of the Human Proteome Organization (www.hupo.org). Its mission is to characterize all of the proteins encoded by the human genome. To date, the HPP has identified a mass spectrometry signature for one product per gene for 93.1% of the genes in the human genome. There currently remain nearly 1400 proteins corresponding to coding genes which have still not been characterized by mass spectrometry. These proteins are either weakly expressed, expressed only at key times in development or in difficult-to-access tissues or cells. The characterization of these so-called Missing proteins continues.

As the HPP draws near to completion of its first goal of achieving confident detections of all entries in the human proteome parts list, the HPP has embarked on a more audacious Grand Challenge Project of determining at least one molecular function of each protein. This project requires the involvement of biologists and clinicians in all fields, who are specialists for example of a biological function, an organ, a pathology, etc. and most of whom are often far removed from the world of proteomics. The results of their work can be used by the HPP to achieve its objectives. All approaches and methods are possible, among which, those of chemical biology. The example of the French National Chemical Library (ChemBioFrance; https://chembiofrance.cn.cnrs.fr/en/) will be given. ChemBioFrance has joined forces with the HPP as part of its Grand Challenge. Ongoing work involves characterizing the effect of biologically active molecules on the global proteome of cells. The selected molecules must act on an identified target in order to determine the signaling pathways downstream of this target, and thus make it possible to better characterize the function(s) of the target in cells. The first results will be presented here.

The HPP now sets as its goal that we achieve a solid understanding of at least one function of each protein at the molecular level, ideally via at least two orthogonal methods. In order to track the progress in this goal, a metric is being developed since there is currently no suitable metric with which to measure the distance from our goal. The PE score, developed by Swiss-Prot decades ago, has served the HPP well in measuring its progress in its first goal, detection of each protein and information about where it is found. An analogous FE (“function evidence”) score was therefore developed. As PE1 is the ultimate goal for detection, FE1 is the ultimate goal for each protein for function, denoting a good understanding of its molecular function, which, as noted above, is not to imply that nothing more can be learned about an FE1 protein. FE5 represents the lowest category, meaning that essentially nothing is known. A draft of the FE score, how it is computed, will be presented.

In this presentation, we will discuss the progress of the HPP in pursuit of achieving a solid understanding of at least one function of each protein in the human proteome at the molecular level.

References

Adhikari et al., A high-stringency blueprint of the human proteome. Nat Commun 2020. Doi: 10.1038/s41467-020-19045-9 HPP Grand Challenge White paper

PLENARY LECTURES

Youngsoo Kim, Ph.D.

Position: Distinguished Professor
Department: Department of Biomedical Science, School of Medicine
Affiliation:
CHA University and Director, Advanced Omics Research Center,
CHA Future Medicine Research Institute, Bundang CHA Hospital,
Seongnam-si, Korea
E-mail: biolab@cha.ac.kr

Education

1992	Ph.D.	The University of Texas at Austin
1984	Master	The Korea Advanced Institute of Science and Technology

Professional Experience

2023 - Present	Distinguished Professor	CHA University
2002.03 - 2023.02	Professor	Seoul National University Fred Hutchinson Cancer Research Center, Seattle, WA USA
2010.09 - 2011.08	Visiting Principle Investigator	Seoul National University Fred Hutchinson Cancer Research Center, Seattle, WA USA
1991.03 - 2001.01	Academic Staff Scientist	University of Washington School of Medicine Department of Biological Structure, Seattle, WA USA

Academic Society

2010 - Present	Member of Board of Directors, President, Vice President & Auditor, The Korean Human Proteome Organization (KHUPO)
2015 - 2017	Editorial Board Member, Scientific Reports, Nature Journal Publishing
2008 - 2010	Editorial Board Member, BMB Reports, Journal of Korean Society for Biochemistry and Molecular Biology

PL-5

A Road to Develop MRM-MS as a Diagnostic Platform: Surveillance Diagnosis for Hepatocellular Carcinoma (HCC)

Youngsoo KIM, Ph.D.

Advanced Omics Research Center, CHA Future Medicine Research Institute, Bundang CHA Hospital and Department of Biomedical Science, School of Medicine, CHA University, Republic of Korea

Conventional methods for hepatocellular carcinoma (HCC) surveillance, including imaging and serum tumor markers (AFP and PIVKA-II), have limited accuracy. To improve diagnostic performance, we explored three approaches using mass spectrometry techniques.

Firstly, we aimed to develop an analytically sensitive multiple reaction monitoring-mass spectrometry (MRM-MS) assay to quantify AFP-L3 in serum. The performance of the MRM-MS assay was compared with that of LiBA (liquid-phase binding assay using capillary electrophoresis) in human serum samples. Integrated multinational guidelines were followed to validate the assay for clinical implementation. Secondly, we aimed to develop assays for protein induced by vitamin K absence or antagonist-II (PIVKA-II, DCP) using MRM-MS instead of antibody assays. We tried to improve the DCP measurement assay by applying a mass-spectrometry (MS)-based approach for a more inclusive quantification of various DCP proteoforms. We developed a multiple reaction monitoring-MS (MRM-MS) assay to quantify multiple non-carboxylated peptides included in the various des-carboxylation states of DCP. The quantitative DCP assay using the MRM-MS method is superior to antibody-based quantification, with equivalent performance. Thirdly, we aimed to develop a serum multi-protein marker panel using MRM-MS, aiming to improve diagnostic accuracy. We have developed and validated a reliable serum biomarker panel for the early detection of HCC. Finally, we developed a multiple reaction monitoring-mass spectrometry (MRM-MS) multi-marker panel using marker proteins from the sera of patients.

Collectively, these three approaches would have the potential to enhance Surveillance Diagnosis for Hepatocellular Carcinoma (HCC).

SYM-A1

New Technologies in Proteomics I

SYM-A1

New Technologies in Proteomics I

6.25 (Tue) 14:00 - 15:15

Chair: Cheolju Lee / Korea Institute of Science and Technology (KIST)

SYM-A1-1 6.25 (Tue) 14:00 - 14:25

Rethink what is possible

Yue Xuan
Thermo Fisher Scientific

SYM-A1-2 6.25 (Tue) 14:25 - 14:50

Mass cytometry, or cytometry by time-of-flight (CyTOF) ; its principle, applications, and prospects in single cell proteomics

Tae Hyun Yoon
Hanyang University

SYM-A1-3 6.25 (Tue) 14:50 - 15:15

Establishment of a universal label-free proteomic method for spatial proteomics

Jungho Park
CHA Universtiy

SYM-A1

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Education

2001 – 2004	Master of Science (MS) Chemistry	Free University Berlin
2004 – 2007	Dr.rer.nat Chemistry	TU Dortmund University
2019 – 2021	Executive Master of Business Administration (MBA)	ESMT Berlin

Professional Experience

2007.04 – 2017.06	Product Speialist FT-MS	Thermo Fisher Scientific
2017.09 - present	Sr. Global Product Marketing Manager, Precision Medicine	Thermo Fisher Scientific

Publications

1. Xuan, Y. et al. Standardization and harmonization of distributed multi-center proteotype analysis supporting precision medicine studies. Nat. Commun. 11, 5248 (2020).

2. Martínez-Val, A., Fort, K., Koenig, C. et al. Hybrid-DIA: intelligent data acquisition integrates targeted and discovery proteomics to analyze phospho-signaling in single spheroids. Nat Commun 14, 3599 (2023).

3. Guzman, U.H., Martinez-Val, A., Ye, Z. et al. Ultra-fast label-free quantification and comprehensive proteome coverage with narrow-window data-independent acquisition. Nat Biotechnol (2024)

4.Goetze, S., van Drogen, A., Albinus, J.B. et al. Simultaneous targeted and discovery-driven clinical proteotyping using hybrid-PRM/DIA. Clin Proteom 21, 26 (2024).

5. Zhu, T. et al. DPHL: A DIA Pan-human Protein Mass Spectrometry Library for Robust Biomarker Discovery. Genomics Proteomics Bioinformatics 18, 104–119 (2020).

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7.Bennike, T. B. et al. A Cost-Effective High-Throughput Plasma and Serum Proteomics Workflow Enables Mapping of the Molecular Impact of Total Pancreatectomy with Islet Autotransplantation. J. Proteome Res. 17, 1983–1992 (2018).

8. Bruderer, R. et al. Optimization of Experimental Parameters in Data-Independent Mass Spectrometry Significantly Increases Depth and Reproducibility of Results. Mol. Cell. Proteomics MCP 16, 2296–2309 (2017).

9. Muntel, J. et al. Advancing Urinary Protein Biomarker Discovery by Data-Independent Acquisition on a Quadrupole-Orbitrap Mass Spectrometer. J. Proteome Res. 14, 4752–4762 (2015).

10.Egertson, J. D., MacLean, B., Johnson, R., Xuan, Y. & MacCoss, M. J. Multiplexed peptide analysis using data-independent acquisition and Skyline. Nat. Protoc. 10, 887–903 (2015).

SYM-A1-1

Rethink what is possible

Yue Xuan

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Science isn't limited by ideas but by the ability to realize them. That is the inspiration behind the novel technology of the Thermo Scientific Orbitrap Astral Mass Spectrometer: to redefine what is possible for discovery and translational research. Faster throughput, deeper coverage, and higher sensitivity with accurate and precise quantitation to empower you to accomplish your aspirations.

Powered by the synergy of a high-resolution quadrupole mass filter, the Thermo Scientific™ Orbitrap™ mass analyzer and the novel Thermo Scientific™ Astral™ mass analyzer, this revolutionary new instrument achieves unsurpassed performance and experimental flexibility. The combination of the three mass analyzers enables the rapid acquisition of exceptional quality high resolution accurate mass (HRAM) spectra with high sensitivity and dynamic range. The new performance characteristics of the Thermo Scientific™ Orbitrap™ Astral™ mass spectrometer make it ideally suited for accurate and precise quantitation at an unprecedented depth of coverage and throughput for samples from single cells to body fluids to bulk tissues.

In this study, we evaluate the performance of the Orbitrap Astral mass spectrometer for single cell proteomics analysis, whole proteome analysis, and plasma proteomics. In addition, to address the large-cohort analysis needs, we consistently profile approximately 9000 proteins from human cell lines and around 800 proteins from undepleted plasma across multiple instruments over a period of more than 10 consecutive days in a 24/7 operating mode, demonstrating that the Orbitrap Astral mass platform can sensitively, robustly and reproducibly analyze the proteome of thousands of samples in a high-throughput manner.

SYM-A1

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Education

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Professional Experience

2019.11 - Present	Director	Institute of Next Generation Material Design, Hanyang University
2017.11 - Present	Director	Center for Next Generation Cytometry, Hanyang University
2005.09 - Present	Professor	Dept. of Chemistry, College of Natural Sciences, Dept. of Medical & Digital Engineering, College of Engineering, Hanyang University, Seoul, South Korea

Publications

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SYM-A1-2

Mass cytometry, or cytometry by time-of-flight (CyTOF) ; its principle, applications, and prospects in single cell proteomics

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Mass cytometry, also known as cytometry by time-of-flight (CyTOF), is a modern technique that enables multiparametric analysis of individual cells using numerous metal-tagged cellular markers with minimal signal overlap, thereby addressing the limitations in dimensionality faced by conventional flow cytometry in studies of phenotyping heterogeneous cellular systems and understanding complex biological pathways. This approach utilizes antibodies labeled with lanthanide metal isotope ions (with atomic weights between 75 and 209) to concurrently assess approximately 50 markers (both surface and intracellular proteins) at a single-cell level. As a novel technology with capability of multiparametric protein analysis at a single cell level, it enables a detailed exploration of cellular responses, with broad applications currently in progress in both clinical and basic research settings. This innovative technology offers potential applications across various biomedical research areas, including in-depth phenotyping of diverse cells, tracking cell differentiation and disease progression, creating detailed cell cycle profiles, examining variations in cytokine expression, and investigating signaling responses. In this presentation, drawing from four years of hands-on experience, I will explain the principles of single-cell mass cytometry, and its application in diverse clinical and basic research studies, discuss its future potential in single-cell proteomics.

SYM-A1

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Education

2014.03-2019.08	Ph.D.	Seoul National University
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Professional Experience

2022.04-present	Assistant Professor	CHA University
2021.08-2022.04	Postdoctoral researcher	Pacific Northwest National Laboratory
2021.02-2021.08	Associate research scientist	Columbia University Medical Center
2020.04-2020.12	Postdoctoral researcher	Seoul National University

Academic Society

2023.01-present	Member of Scientific Committee	KHUPO

Publications

1. J Park, F Yu, J Fulcher, S Williams, K Engbrecht, R Moore, G Clair, V Petyuk, A Nesvizhskii, and Y Zhu; Evaluating linear ion trap for MS3-based multiplexed single-cell proteomics. Analytical Chemistry, 2023

2. D Kim*, J Park*, D Han*, J Yang, A Kim, J Woo, Y Kim, I Mook-Jung; Molecular and functional signatures in a novel Alzheimer's disease mouse model assessed by quantitative proteomics. Molecular Neurodegeneration, 2018

3. J Park*, H Oh*, D Han, I Park, J Wang, H Ryu, Y Kim; Parallel Reaction Monitoring-Mass Spectrometry (PRM-MS)-Based Targeted Proteomic Surrogates for Intrinsic Subtypes in Breast Cancer: Comparative Analysis with Immunohistochemical Phenotypes. Journal of Proteome Research, 2019

SYM-A1-3

Establishment of a universal label-free proteomic method for spatial proteomics

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Advancements in mass spectrometry (MS)-based proteomics has revolutionized the study of archived tissue slides, enabling observation of the proteome within regions of interest (ROI) and facilitating a deeper understanding of spatially distinct pathophysiology. However, the inherent challenge of limited protein amounts in tissue slides often compromises data quality, even with minimal sample loss. Consequently, the acquired proteomic information frequently falls short of investigating the biological context in many studies. To overcome this limitation, we have developed a label-free Data-Independent Acquisition (DIA)-based proteomic method, which minimizes sample loss through optimization of entire experimental procedures from sample preparation to MS analysis. Remarkably, utilizing 40 ng of peptide as a starting input of this procedure—equivalent to 200 cells—we quantified approximately 7000 proteins. Inspired by these results, we extended this method to analyze regions of interest (ROIs) as small as 0.25 mm2, encompassing an estimated 300 cells, isolated from formalin-fixed, paraffin-embedded (FFPE) breast cancer tissue using spatial laser-assisted cell sorting (SLACS). Analysis of over 2000 protein expressions, coupled with bioinformatics analyses, revealed heterogeneity within the tissue. The primary advantage of our proposed workflow is its universal applicability. This method enables in-depth proteomic analysis of sub-microscale pieces of tissue without necessitating expensive equipment frequently used in single-cell analysis. In conclusion, our study underscores the utility of an accessible proteomic framework in delineating the heterogeneity of molecular phenotypes across the tissue.

SYM-A2

Tumor Microenvironment

SYM-A2

Tumor Microenvironment

6.25 (Tue) 15:30 - 16:50

Chair: Jong Bae Park / National Cancer Center (NCC)

SYM-A2-1 6.25 (Tue) 15:30 - 15:50

Differential cellular origins of the extracellular matrix of tumor and normal tissues according to colorectal cancer subtypes

Plinam Kim
Korea Advanced Institute of Science and Technology (KAIST)

SYM-A2-2 6.25 (Tue) 15:50 - 16:10

Role of Interleukin-33 in inflammatory disease and its mediated cancer development

Jong Ho Park
Keimyung University

SYM-A2-3 6.25 (Tue) 16:10 - 16:30

Involvement of Skeletal Muscle-Infiltrating Immune Cells in Cancer Cachexia

Na-Young Song
Yonsei University College of Dentistry

SYM-A2-4 6.25 (Tue) 16:30 - 16:50

Selenium Metabolites and Selenoproteins: Two Layers of Anti-Ferroptosis Mechanisms

Namgyu Lee
Dankook University

SYM-A2

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Professional Experience

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Publications

1. S. Mun, H.J. Lee, and P. Kim*, "Rebuilding the Microenvironment of Human Primary Tumors: A Focus on Stroma", EMM, 56, 527–548 (2024, 03)

2. S. W. Oh and P. Kim*, "Hydrogel-based strategies to enhance T-cell performance for solid tumor immunotherapy" Advanced Therapeutics., 2300094 (2023, 04)

3. MBD. Aldonza, J. Cha, I. Yong, J. Ku, D. Lee, P. Sinitcyn, R. Cho, R.D. Delos Reyes, D. Kim , H.-J. Sung , S. Kim , M. Kang, Y. Ku , G. Park , H.S. 4. Ryu, S. Cho , T.M. Kim , P. Kim *, J.Y. Cho *, Y. Kim *. "Widespread multi-targeted therapy resistance via drug-induced secretome fucosylation", eLife,12:e75191 (2023, 04)

4.H. M. Kim, S. Kim, J. Sim, B. S. Ma, I. Yong, Y. Jo, T.-S. Kim, J.-B. Chang, S.-H. Park, Y. Jeong* and P. Kim*,"Glycation-mediated tissue-level remodeling of brain meningeal membrane by aging", Aging Cell , 22:e138 (2023, 2)

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6. M. Jang, J. An, S. W. Oh, J. Y. Lim, J. Kim, J. K. Choi*, J.-H. Cheong*, P. Kim*, "Matrix stiffness epigenetically regulates the oncogenic activation of the Yes-associated protein in gastric cancer", Nature Biomedical Engineering, 5, 114–123(2021, 01)

SYM-A2-1

Differential cellular origins of the extracellular matrix of tumor and normal tissues according to colorectal cancer subtypes

Hyun Jin Lee[1†], Sang Woo Park[2†], Jun Hyeong Lee[1], Shin Young Chang[3], Sang Mi Oh[3], Siwon Mun[1], Junho Kang[4], Jong-Eun Park[4], Jung Kyoon Choi[1], Tae Il Kim[3*], Jin Young Kim[2*], Pilnam Kim[1*]

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Understanding the proteomic-level heterogeneity of the tumor microenvironment (TME) in colorectal cancer (CRC) is crucial due to its well-known heterogeneity. While heterogenous CRC has been extensively characterized at the molecular subtype level, research into the functional heterogeneity of fibroblasts, particularly their relationship with extracellular matrix (ECM) alterations, remains limited. Addressing this gap is essential for a comprehensive understanding of CRC progression and the development of targeted therapies. 24 tissue samples from 21 CRC patients, along with adjacent normal tissues (NAT), were collected and decellularized using a detergent-based method to enrich the ECM component. We conducted an extracellular matrix (ECM)-focused profiling of the TME by integrating quantitative proteomics with single-cell RNA sequencing (scRNA-seq) data from CRC patients. We identified the ECM proteins of normal adjacent to tumor (NAT) and tumor tissue, and established a cell-matrisome database. We defined mesenchymal subtype-specific molecules associated with specific fibroblast subtypes showing a significant association with poorer survival in patients with CRC. Our ECM-focused profiling of tumor stroma provides new insights as indicators for biological processes and clinical endpoints.

SYM-A2

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Education

2016.08	Ph.D.	Department of Biological Science, Seoul National University
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Professional Experience

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2018.03 - 2023.02	Postdoctoral Fellow	Harvard Medical School and Mass General Hospital (Cancer Center), USA
2016.09 - 2018.01	Research Associate	MOGAM Institute for Biomedical Research

Publications

1. Lee SW, Lee MH, Park JH, Kang SH, Yoo HM, Ka SH, Oh YM, Jeon YJ and Chung CH (2012) SUMOylation of hnRNP-K is required for p53-mediated cell-cycle arrest in response to DNAdamage. EMBO J. 2012 Nov 28;31(23):4441-4452.

2. Park JH*, Lee SW*, Yang SW, Yoo HM, Park JM, Seong MW, Ka SH, Oh KH, Jeon YJ and Chung CH (2014) Modification of DBC1 by SUMO2/3 is crucial for p53-mediated apoptosis in response to DNA damage. Nat. Commun. 2014 Nov 18;5:5483.

3. Seoung MW, Ka SH, Park JH, Park JH, Yoo HM, Yang SW, Seol JH and Chung CH (2015) Deleterious c-Cbl Exon Skipping Contributes to Human Glioma. Neoplasia. 2015 Jun;17(6):518-524

4. Yoo HM, Park JH, Jeon YJ and Chung CH (2015) Ubiquitin-fold modifier 1 acts as a positive regulator of breast cancer. Front Endocrinol. 2015 Mar 20;6:36.

5. Park JH*, Yang SW*, Park JM, Ka SH, JH Kim, YY Kong, Jeon YJ, Seol JH and Chung CH (2016) Positive feedback regulation of p53 transactivity by DNA damage-induced ISG15 modification. Nat. Commun. 2016 Aug 22;7:12513.

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7. Yoo KY, Jung SY, Hwang SH, Lee SM, Park JH, Nam HJ (2018) Global hemostatic assay of different target procoagulant activities of factor VIII and factor IX. Blood Res. 2018 Mar;53(1):41-48.

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SYM-A2-2

Role of Interleukin-33 in inflammatory disease and its mediated cancer development

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Chronic inflammation is a major cause of cancer worldwide. It has been regarded as the tumor-promoting environment, which are major driver of sporadic cancers by supporting tumor growth, metastasis and angiogenesis while blocking antitumor immunity. Interleukin 33 (IL-33) is a critical initiator of cancer-prone chronic inflammation; however, its induction and regulation mechanism by the environmental causes of chronic inflammation is unknown. Herein, we demonstrate that Toll-like receptor (TLR)3/4-TBK1-IRF3 pathway activation links environmental insults to IL-33 induction in the inflamed tissues. FDA-approved drug library screen identified pitavastatin as an effective IL-33 inhibitor by blocking TBK1 membrane recruitment/activation through the mevalonate pathway inhibition. Moreover, we also find that IL-33 promotes liver chronic inflammation by regulating regulatory T cells (Treg). Mice that lacked IL-33 receptor specifically on regulatory T cell had lower tumor in chronic inflammation mediated cancer development compared with wild-type mice. Interestingly, pitavastatin use correlated with a significantly reduced risk of the chronic hepatitis and hepatocellular carcinoma patients. Our findings demonstrate that blocking IL-33 expression suppresses both chronic inflammation and its mediated cancer development.

Keywords: Cancer, Chronic inflammation, Immunosuppressive environment, IL-33, Regulatory T cell.

SYM-A2

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Education

2012	Ph.D.	Seoul National University, College of Pharmacy
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Professional Experience

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2012 - 2018	Visiting Fellow	Cancer and Inflammation Program, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Frederick, MD, USA

Publications

1. Li X#, Song NY#, Singh AK#, Badger JH, Sun Z, Shi G, Willette-Brown J, Zhu F, Jiang C, Zhang P, Ferré EMN, Seyedmousavi S, Banerjee S, Chan K, Andersson T, O'hUigin C, Wu X, Lionakis MS, Trinchieri G, Hu Y. Oral Mucosal Fungal Infection Promotes an Acidic Oral Microenvironment, Dysbiosis, and Tumorigenesis via STAT3-Induced Metabolic and Oncogenic Activation. under revision (#Co-first author)

2. Kim DH#, Song NY#, Yim H. Targeting dysregulated lipid metabolism in the tumor microenvironment. Arch Pharm Res. 46(11-12):855-881. 2023. (#Co-first author)Park SY, Hwang BO, Song NY*. The role of myokines in cancer: crosstalk between skeletal muscle and tumor. BMB Rep. 56(7):365-373, 2023. (*Corresponding author)

3. Song NY#, Li X#, Ma B, Willette-Brown J, Zhu F, Jiang C, Su L, Shetty J, Zhao Y, Shi G, Banerjee S, Wu X, Tran B, Nussinov R, Karin M, Hu Y. IKKα-deficient lung adenocarcinomas generate an immunosuppressive microenvironment by overproducing Treg-inducing cytokines. Proc Natl Acad Sci USA. 119(6), 2022 (#Co-first author)

4. Park SY, Lee SK, Lim M, Kim B, Hwang BO, Cho ES, Zhang X, Chun KS, Chung WY, Song NY*. Direct Contact with Platelets Induces Podoplanin Expression and Invasion in Human Oral Squamous Cell Carcinoma Cells. Biomol Ther. 30(3):284-290, 2022. (*Corresponding author)

5. Hwang BO, Park SY, Cho ES, Zhang X, Lee SK, Ahn HJ, Chun KS, Chung WY, Song NY*. Platelet CLEC2-Podoplanin Axis as a Promising Target for Oral Cancer Treatment. Front Immunol. 12:807600, 2021 (*Corresponding author)

6. Lee YH, Kim SJ, Fang X, Song NY, Kim DH, Suh J, Na HK, Kim KO, Baek JH, Surh YJ. JNK-mediated Ser27 phosphorylation and stabilization of SIRT1 promote growth and progression of colon cancer through deacetylation-dependent activation of Snail. Mol Oncol. 16(7):1555-1571, 2021.

SYM-A2-3

Involvement of Skeletal Muscle-Infiltrating Immune Cells in Cancer Cachexia

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Cancer cachexia (CAC) is a multi-organ syndrome characterized by body weight loss and muscle wasting. Distinct from malnutrition and starvation, CAC cannot be reversed by adequate nutrient supplementation and finally accounts for approximately 20% of cancer-related deaths. Notably, CAC is a well-known poor prognostic factor in immunotherapy. On the contrary, we found that anti-PD-L1 blockade, a representative immune checkpoint inhibitor (ICI), exacerbated cachectic features in a syngeneic orthotopic lung cancer mouse model. This prompted us to investigate the involvement of immune cells in CAC. First, we established a syngeneic CAC mouse model through orthotopic transplantation of murine lung cancer cells. At 7 weeks post-injection, these mice developed CAC, displaying over 20 % body weight loss, almost total loss of epididymal fats, and profound skeletal muscle wasting. Then, we explored the immune cell profiles infiltrated into skeletal muscle of CAC mice by single cell RNA sequencing and observed the enrichment of cytotoxic cells. Depletion of these cytotoxic cells effectively prevent skeletal muscle wasting in CAC mice, supporting the cytotoxic immune cells as prominent drivers of CAC. Based on the RNA sequencing analysis, we identified a promising target that can simultaneously inhibit tumorigenesis as well as cachexia. Taken together, our study suggests that the skeletal muscle-infiltrating cytotoxic immune cells are crucial for pathogenesis of CAC, particularly in the immunotherapy. Therefore, the treatment with ICIs requires combination therapies dual-targeting both cancer and cachexia.

SYM-A2

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Education

2010.02 - 2016.08	Ph.D.	Pohang University of Science and Technology
2008.09 - 2010.02	Exhange Student	Bonn Rhein-Sieg University of Applied Sciences, Germany
2006.02 - 2010.02	B.S.	Kyungpook National University

Professional Experience

2023.09 - Present	Assistant Professor	Dankook University, Department of Biomedical Science & Engineering
2016.09 - 2023.08	Post-doctoral Fellow	University of Massachusetts Medical School, Department of Molecular, Cell and Cancer Biology, USA

Publications

1. **Namgyu Lee***[#], et al., Selenium reduction of ubiquinone via SQOR suppresses ferroptosis. *Nature Metabolism*, 2024, 6, 343–358 (#, co-corresponding; *, co-first)

2. Sung Jin Park, Paul L. Greer, **Namgyu Lee**[#]. From odor to oncology: Non-canonical olfactory receptors in cancer. *Oncogene*, 2024 Jan;43(5):304-318. (corresponding author)

3. Mihir B. Doshi, **Namgyu Lee**, et al. Disruption of sugar nucleotide clearance is a therapeutic vulnerability of cancer cells. *Nature*, 623(7987):625-632, 2023 Nov

4. Meghan E Spears, **Namgyu Lee**, et al., De novo sphingolipid biosynthesis necessitates detoxification in cancer cells. *Cell Reports*, 40(13):111415, 2022 Sep 27

5. **Namgyu Lee**, et al., Endogenous toxic metabolites and implications in cancer therapy. *Oncogene*, 39(35):5709-5720, 2020 July 24 (first author)

6. Anne E. Carlisle*, **Namgyu Lee***, et al., Selenium detoxification is required for cancer cell survival. Nature Metabolism, 2(7):603-611, 2020 Jul 06 (*, co-first)

SYM-A2-4

Selenium Metabolites and Selenoproteins: Two Layers of Anti-Ferroptosis Mechanisms

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Ferroptosis, an iron-dependent form of programmed cell death, is closely intertwined with cellular metabolism. Selenium metabolism plays a critical role in preventing cells from undergoing ferroptosis. The canonical biological function of selenium involves the production of selenocysteine residues within selenoproteins, forming the basis for its role as an essential antioxidant and cytoprotective micronutrient.

By examining selenium through the lens of cellular metabolism, we have elucidated that, via its metabolic intermediate hydrogen selenide, selenium reduces ubiquinone in the mitochondria through catalysis by sulfide quinone oxidoreductase (SQOR). Through this mechanism, selenium rapidly protects against lipid peroxidation and ferroptosis on a timescale that precedes selenoprotein production, even when selenoprotein production has been eliminated. Our findings unveil the initial layer of selenium's anti-ferroptosis mechanism, occurring before its incorporation into selenoproteins.

SYM-A3

Biomarker discovery for Clinical Proteomics

SYM-A3

Biomarker discovery for Clinical Proteomics

6.26 (Wed) 10:30 - 11:45

Chair: Un-Beom Kang / Bertis Inc.

SYM-A3-1 6.26 (Wed) 10:30 - 10:55

Proteogenomics-Driven Precision Oncology: Pancreatic Ductal Adenocarcinoma Subtype Identification Technology

Sang-Won Lee
Korea University

SYM-A3-2 6.26 (Wed) 10:55 - 11:20

Proteomic discovery of prognostic protein biomarkers for persisting problems after cerebral concussion

Byung-Mo Oh
Seoul National University Hospital

SYM-A3-3 6.26 (Wed) 11:20 - 11:45

Inhibitor of TBR1-RKIP binding is new drug target for NF2 syndrome

Bum-Joon Park
Pusan Natioanl University

SYM-A3

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Education

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2000 - 2002	Postdoctoral Fellow	Pacific Northwest National Laboratory
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2006 - 2011	Associate Professor	Korea University
2011 - current	Professor	Korea University
2019 - current	Director	Center for Proteogenome Research
2022 - current	Director	Proteome Data Curation Center

Academic Society

2015	Dir. General Affair	IUPAC-2015
2018 - 2019	Vice President	Korean Chemical Society

Publications

1. Hyeon DY et al. Proteogenomic landscape of human pancreatic ductal adenocarcinoma in an Asian population reveals tumor cell-enriched and immune-rich subtypes, Nature Cancer 2023; 4, 290-307.

2. Kang C et al. Novel Online Three-Dimensional Separation Expands the Detectable Functional Landscape of Cellular Phosphoproteome, Anal. Chem. 2022; 94, 2146-2159

3. Kim HK et al. Blockers of Wnt3a, Wnt10a, or β-Catenin Prevent Chemotherapy-Induced Neuropathic Pain in Vivo Neurotherapeutics. Neurotherapeutics 2021; 18: 601-614.

4. Mun DG et al. PASS-DIA: A data-independent acquisition approach for discovery studies. Anal Chem 2020; 92(21):14466-14475.

5. Mun DG et al. Proteogenomic Characterization of Human Early-Onset Gastric Cancer. Cancer Cell 2019; 35:111-124.

SYM-A3-1

Proteogenomics-Driven Precision Oncology: Pancreatic Ductal Adenocarcinoma Subtype Identification Technology

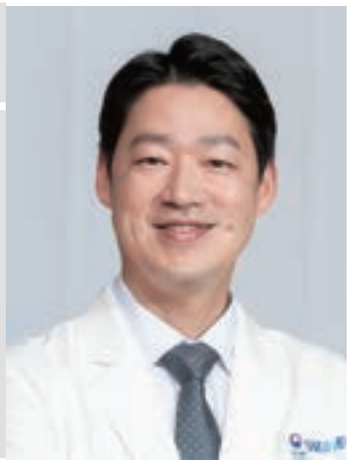
Sang-Won Lee

Center for ProteoGenome Research, Department of Chemistry, Korea University

Despite the significant advancements in genomics and proteomics technologies, and the keen interest in leveraging these tools for precision oncology, the number of new protein drugs and prognostic markers approved by the FDA in the last decade has fallen short of expectations. Several factors contribute to this gap between the efforts in precision oncology and FDA approvals. Technological challenges include the need for proteome measurements that are not only sensitive and extensive but also quantitative and capable of high throughput to ensure statistical reliability. Additionally, issues rooted in cancer biology, such as human variability, necessitate the analysis of large sample sets. Moreover, integrating multiple types of omics data—like genomics, transcriptomics, and proteomics—and correlating these data with clinical outcomes poses further complexities. We are developing and refining an advanced proteomics analysis platform that integrates cutting-edge proteome technologies and provides significantly improved sensitivity, throughput, and robustness of proteome profiling. Here we discuss our efforts to develop pancreatic ductal adenocarcinoma Subtype Identification Technology (PDAC-SIT) technology, a precision medicine strategy, based on comprehensive proteogenomics analysis of PDAC.

SYM-A3

Byung-Mo Oh, MD, PhD



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Education

2005-2009	Ph.D.	Medical Science, Seoul National University College of Medicine, Seoul, South Korea
2002-2004	M.S.	Medical Science, Seoul National University College of Medicine, Seoul, South Korea
1993-1999	B.S.	Seoul National University College of Medicine, Seoul, South Korea

Professional Experience

2021.Sep – current	Clinical Professor	Seoul National University College of Medicine, Seoul National University Hospital, Seoul, South Korea
2019.Oct – 2020. Jun	Director	National Traffic Injury Rehabilitation Research Institute, Yangpyung, South Korea
2016.Sep – 2020. Jun	Associate Clinical Professor	Seoul National University College of Medicine, Seoul National University Hospital, Seoul, South Korea
2014.Dec – 2016.Jun	Visiting Scholar	University of Pittsburgh, Pittsburgh, PA, USA
2009. Mar – 2014.Nov	Assistant Clinical Professor	Seoul National University Hospital, Seoul, South Korea
2005 Apr – 2008 Apr	Clinical Director	Gangwon-Do Rehabilitation Hospital, Chuncheon, South Korea

Academic Society

2011-present	Member	Organization of Human Brain Mapping
2011-present	Member	Society for Neuroscience

Publications

In 2022

1. Lee HY, Oh BM. Nutrition Management in Patients With Traumatic Brain Injury: A Narrative Review. Brain Neurorehabil. 2022 Mar 28;15(1):e4. doi:10.12786/bn.2022.15.e4. PMID: 36743843; PMCID: PMC9833460.

2. Hwang W, Choi JK, Bang MS, Park WY, Oh BM. Gene Expression Profile Changes in the Stimulated Rat Brain Cortex After Repetitive Transcranial Magnetic Stimulation. Brain Neurorehabil. 2022 Sep 30;15(3):e27. doi:10.12786/bn.2022.15.e27. PMID: 36742089; PMCID: PMC9833481.

3. Lee Y, Oh BM, Park SH, Han TR. Low-Frequency Repetitive Transcranial Magnetic Stimulation in the Early Subacute Phase of Stroke Enhances Angiogenic Mechanisms in Rats. Ann Rehabil Med. 2022 Oct;46(5):228-236. doi: 10.5535/arm.22040. Epub 2022 Oct 31. PMID: 36353835; PMCID: PMC9650368.

4. Kim MY, Park JY, Leigh JH, Kim YJ, Nam HS, Seo HG, Oh BM, Kim S, Bang MS. Exploring user perspectives on a robotic arm with brain-machine interface: A qualitative focus group study. Medicine (Baltimore). 2022 Sep 9;101(36):e30508. doi: 10.1097/MD.0000000000030508. PMID: 36086771.

5. Kim E, Seo HG, Seong MY, Kang MG, Kim H, Lee MY, Yoo RE, Hwang I, Choi SH, Oh BM. An exploratory study on functional connectivity after mild traumatic brain injury: Preserved global but altered local organization. Brain Behav. 2022 Sep;12(9):e2735. doi: 10.1002/brb3.2735. Epub 2022 Aug 22. PMID: 35993893; PMCID: PMC9480924.

SYM-A3-2

Proteomic discovery of prognostic protein biomarkers for persisting problems after cerebral concussion

Byung-Mo Oh, MD, PhD

Seoul National University Hospital

Individuals who experience mild traumatic brain injury (mTBI), commonly referred to as a concussion, often face a spectrum of neuropsychiatric and physical challenges that can persist well beyond the initial months following the incident. The complexity of symptoms that follow mTBI is influenced not only by the nature and severity of the initial injury but also by a variety of factors post-injury, including the individual's personal response to the trauma. This variability makes it challenging to predict long-term outcomes for those affected. Our study focused on identifying prognostic biomarkers in the blood that could predict outcomes six months after an injury within a cohort of 42 individuals who suffered from mTBI. We employed multiple-reaction monitoring-mass spectrometry techniques to quantify levels of 420 target proteins in blood samples taken from these individuals. Our findings revealed that 31 proteins measured within 72 hours post-injury, 43 proteins at one week, and 15 proteins at one month were significantly correlated with poor neuropsychological recovery. We meticulously examined the sequence of clinical assessments documenting depressive symptoms and cognitive functions and their impact on outcomes six months post-injury. This analysis helped in pinpointing candidate biomarker proteins that indirectly influenced the recovery trajectory through their association with neuropsychological symptoms. Leveraging these biomarkers, we developed prognostic models capable of predicting the six-month outcomes for patients with mTBI. The protein biomarkers identified, framed within the clinical progression of mTBI, show promising potential for enhancing clinical strategies aimed at managing and predicting long-term effects of concussion.

SYM-A3

Bum-Joon Park, Ph.D.

Position: CEO / Chair person in Department of Molecular Biology
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2. Pusan National University
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Education

1995.05 - 1999.02	Ph.D.	Korea University
1993.09 - 1995.08	M.S.	Korea University
1989.03 - 1993.02	B.S.	Korea University

Professional Experience

2023.09 - Present	Chair Person	Department of Molecular Biology, Pusan National University
2017.10 - Present	CEO	PRG S&Tech Inc.
2015.01 - 2017.02	Chair Person	Department of Molecular Biology, Pusan National University
2015.04 - Present	Professor	Department of Molecular Biology, Pusan National University

Publications

1. Kim, B.H., Chung, Y.H., Woo, T.K., Kang, S.M., Park, S.Y., Park, B.J., (2023) Progerin, an Aberrant Spliced Form of Lamin A, Is a Potential Therapeutic Target for HGPS. Cells,12(18)2299

2. Kang, S.M., Seo, S.W., Song, E.J., ... & Park, B. J., (2023) Progerinin, an Inhibitor of Progerin, Alleviates Cardiac Abnormalities in a Model Mouse of Hutchinson-Gilford Progeria Syndrome. Cells, 12(9):1232

3. Sim, J. W., Lee, A.R., Kim, D.S., ... & Kim, K.M. (2023) A Combination of Bio-Orthogonal Supramolecular Clicking and Proximity Chemical Tagging as a Supramolecular Tool for Discovery of Putative Proteins Associated with Laminopathic Disease. Small, 19(21):e2208088

4. Ahn, J. S., Lee, J.W., ... Park, B. J. & Ha, N. C., (2022) Structural basis for the interaction between unfarnesylated progerin and the Ig-like domain of lamin A/C in premature aging disorders. Biochemical and biophysical research communications, 637:210-217

5. Baek, Y. J., Woo, T. G., Ahn, J. S., ... Park, B. J. & Ha, N. C., (2022) Structural analysis of the overoxidized Cu/Zn-superoxide dismutase in ROS-induced ALS filament formation. Communications biology, 5(1):1085

6. Jeong, S.Y., Ahn, J.S., Jo, I.S., ... & Ha, N. C., (2022) Cyclin-Dependent Kinase 1 depolymerizes nuclear lamin filaments by disrupting the head-to-tail interaction of the lamin central rod domain. Journal of biological chemistry, 298(9):102256

7. Ahn, J. S., Jeong, S. Y., Kang, S. M., ... Park, B. J. & Ha, N. C., (2022) Crystal structure of progeria mutant S143F lamin A/C reveals increased hydrophobicity driving nuclear deformation. Communications biology, 5(1):267

SYM-A3-3

Inhibitor of TBR1-RKIP binding is new drug target for NF2 syndrome

Bum-Joon Park, Ph.D.

PRG S&Tech Inc

NF2 syndrome is rare genetic disorder, caused by deletion of NF2/merlin gene located in Ch 22. Patients are suffered by schwannoma in vestibular as well as auditory nerve system. In addition, schwannoma in dorsal root ganglion is frequently detected. However, until now, plausible treatment has not been suggested. In previous, we revealed the new pathological pathway of NF2 syndrome that loss of NF2 reduces RKIP expression by kinase activity of TbR1. In addition, small chemical inhibitor between TbR1 and RKIP can reduce the proliferation of NF2 deficient tumor cells and promote differentiation into matured schwann cell. In this study, we showed that our chemical (PRG-N-01) is very selective inhibitor of TbR1-RKIP and effectively suppressed the tumor formation in NF2 model mouse. Moreover, PRG-N-01 has druggable properties such as high B.A and low toxicity. Considering our result, selective binding inhibitor of TbR1-RKIP would be strong candidate for NF2 syndrome.

SYM-A4

New Technologies in Proteomics II

SYM-A4

New Technologies in Proteomics II

6.26 (Wed) 14:45 - 16:00

Chair: Je-Hyun Baek / Seegene Medical Foundation

SYM-A4-1 6.26 (Wed) 14:45 - 15:10

High resolution/accurate mass instrumentation for proteomics

Alexander Makarov
Thermo Fisher Scientific

SYM-A4-2 6.26 (Wed) 15:10 - 15:35

SomaScan Proteomics: From Biomarker Discovery to Clinical Diagnosis

Tala Khosroheidari
SomaLogic

SYM-A4-3 6.26 (Wed) 15:35 - 16:00

An implementation of anti-cancer drug miner using 3D protein structure prediction

Dongwan Hong
Catholic University of Korea

SYM-A4

ALEXANDER MAKAROV, PhD

Position: Director of Global Research
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Education

5/1989-3/1992	PhD in Physics and Mathematics (scientific advisor: Prof. A. A. Sysoev)	Dept. of Molecular Physics, Moscow Physics-Engineering Institute, Russia
9/1983-3/1989	MSc with Honors in Molecular Physics	Dept. of Molecular Physics, Moscow Physics-Engineering Institute, Russia

Professional Experience

6/2007-present	Director of Research, Life Sciences Mass Spectrometry	Thermo Fisher Scientific (Bremen) GmbH

Academic Society

04/2020-present	Fellow	Royal Society, UK
06/1997-present	Member	American Society for Mass Spectrometry

Publications

1. Neumann Adam P., Sage Eric, Boll Dmitri, Reinhardt-Szyba Maria, Fon Warren, Grinfeld Dmitry, Masselon Christophe, Hentz Sébastien, Sader John E., Makarov Alexander, Roukes Michael L. "A Hybrid Orbitrap-Nanoelectromechanical Systems Approach to Analysis of Individual, Intact Proteins in Real Time". Angew. Chem. Int. Ed. 2024, e202317064.

2. Deslignière, E., Yin, V.C., Ebberink, E.H.T.M. et al. "Ultralong transients enhance sensitivity and resolution in Orbitrap-based single-ion mass spectrometry". Nat. Methods (2024). https://doi.org/10.1038/s41592-024-02207-8

3. Serrano L.R., Peters-Clarke T. M., ... Makarov A.A, Zabrouskov V., Coon J.J. "The one hour human proteome". Mol. Cell. Proteomics, 2024, 100760.

4. Guzman, U.H., Martinez-Val, A., Ye, Z. ...Makarov A., Zabrouskov V., Olsen J.V. "Ultra-fast label-free quantification and comprehensive proteome coverage with narrow-window data-independent acquisition". Nat Biotechnol, 2024. https://doi.org/10.1038/s41587-023-02099-7

5.Wörner T. P., Thurman H.A., Makarov A. A., Shvartsburg A. A. "Expanding Differential Ion Mobility Separations into the MegaDalton Range", Anal. Chem. 96(14):5392-5398. olegDOI: 10.1021/acs.analchem.3c05012.

6. Stewart H, Grinfeld D, Petzoldt J, Hagedorn B, Skoblin M, Makarov A, Hock C. "Crowd control of ions in the Astral analyzer". J Mass Spectrom. 2024; 59(4): e5006.

7. Stewart H., Grinfeld D., Giannakopulos A., ... Makarov A.A., Hock C. "Proof of principle for enhanced resolution multi-pass methods for the astral analyzer". Int. J. Mass Spectrom., 2024, 498, 117203.

8. Steigerwald S., Sinha A., Fort K., Zeng W.F., Niu L., Wichmann C., Kreutzmann A., Mourad D., Aizikov K., Grinfeld D., Makarov A., Mann M., Meier F. " Full Mass Range ΦSDM Orbitrap Mass Spectrometry for DIA Proteome Analysis", Molecular & Cellular Proteomics 2024, doi: https://doi.org/10.1016/j.mcpro.2024.100713.

9. Grinfeld D., Stewart H., Balschun W., Skoblin M., Hock C., Makarov A.A. "Multi-reflection Astral mass spectrometer with isochronous drift in elongated ion mirrors". Nuclear Instrum. Methods in Phys. Research A 2024, 1060, 169017.

10. Ray S., Arévalo R. Jr, Southard A.,... Makarov A.A." Characterization of Regolith And Trace Economic Resources (CRATER): An Orbitrap-based laser desorption mass spectrometry instrument for in situ exploration of the Moon." Rapid Commun Mass Spectrom. 2024; 38(2): e9657.

SYM-A4-1

High resolution/accurate mass instrumentation for proteomics

Alexander Makarov

Thermo Fisher Scientific, Bremen, Germany

Principles of operation and performance envelopes are presented for three major types of high resolution accurate mass analysis such as Fourier transform ion cyclotron resonance (FT-ICR), Orbitrap™ and time-of-flight (TOF) techniques. Also, coupling with additional modalities such as electron-based dissociation (ExD), IRMPD, UVPD, ion mobility separation and their combinations is shown to expand the range of proteomic analysis.

Fascinating leaps of evolution and cross-pollination between different branches of mass spectrometry technology are demonstrated. As the latest example of such evolution, the asymmetric track lossless (Astral™) analyser is combining together Orbitrap and TOF features to dramatically improve sensitivity and throughput of proteomic analysis. Performance and operation of this newest analyser are described in detail.

An overview of main trends in evolution of proteomic mass spectrometry instrumentation demonstrates ample reserves in further expansion of analytical capabilities, mainly via combining advanced analysers with improved ion scheduling and utilization.

The talk concludes with the belief that the latest rapid progress in all aspects of proteomic instrumentation and analysis will enable mass spectrometry to remain competitive against alternative technologies and to rise to the challenge of unprecedented throughput of very deep analyses of very complex samples.

SYM-A4

Tala Khosroheidari, Ph.D.

Position: Senior Director
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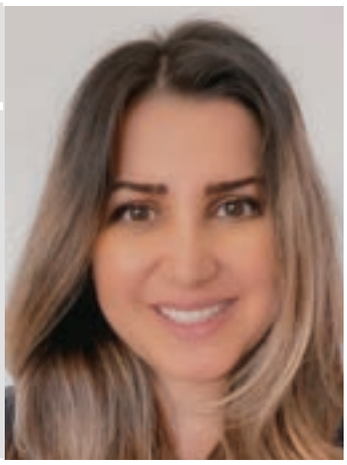
Office: 602-300-9572
E-mail: tkhosroheidari@somalogic.com



Education

Project Management(PMP) Degree	University of California, San Diego, CA, USA
Ph.D. Research Fellow	International Centre for Genetic Engineering & biotechnology (ICGEB), Trieste, Italy
M.S.	John Hopkins University, Baltimore, MD, USA
B.S.	Department of Microbiology, Azad University, Tehran, Iran

Professional Experience

2022 - Present	Senior Director	Global Scientific Engagement, SomaLogic
2021 - 2022	Director	Global Marketing Communication, Olink Proteomics
2020 - 2021	Director	Field Application Scientist, Olink Proteomics
2016 - 2020	Development Scientist	Illumina
2013 - 2016	Core Lab Director	IGM Genomics Center, UCSD
2010 - 2013	Research Scientist	Translational Genomics Research Institute (TGen)
2009 - 2010	Research Assistant	University of Arizona College of Medicine
2007 - 2008	Research Assistant	Molecular Genetics Lab, Special Medical Centre

SYM-A4-2

SomaScan Proteomics: From Biomarker Discovery to Clinical Diagnosis

Tala Khosroheidari

SomaLogic Inc.

The SomaScan® Assay is the only proteomic technology capable of high multiplex (measuring over half of the human proteome- 11,000 proteins), high throughput (rapidly), with high sensitivity (high-and low-abundance proteins). This state-of-art technology is enabled by SOMAmer® (Slow Off-rate Modified Aptamer) reagents that provide a highly specific and reproducible protein quantification tool which has been used from biomarker discovery to clinical and diagnostic methods.

The five major features of the SomaLogic technology , high specificity (powered by extensive reagent characterization and validations), high sensitivity through wide dynamic range (from fM to µM), high reproducibility (inter plate CV of 5%), low sample volume for a variety of sample types, and robust data normalization (no data bridging needed for core sample type) are the key reasons that the SomaScan technology has been used in major large cohort studies, a few examples of which will be discussed in this presentation.

The variety of SomaLogic product offerings, from the SomaScan 11k Assay for Discovery, Pre-Analytical Variation (PAV) tests (to assess sample handling impact), to SomaSignal Tests (SST) which provide multiple clinical assessments (LDT and RUO) create a unique tool for discovering previously unidentified biomarkers for drug discovery, pre-clinical and clinical drug development, and clinical diagnostics, across a wide range of important diseases and conditions.

SYM-A4

Dongwan Hong, Ph.D.

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Education

2022 - 2007	Ph.D.	Dept. of Computer Engineering, Hallym University
1992 - 1996	B.S.	Dept. of Computer Science, Hallym University

Professional Experience

2020 - Present	Professor	Catholic University of Korea, College of Medicine
2011 - 2022	Chief Researcher	National Cancer Center of Korea
2008 - 2011	Research Professor	Seoul National University, Medical Research Institute
2003 - 2007	Assistant Professor	Dept. of Multimedia, Sonngok University
2001 - 2003	Full time lecturer	Dept. of Computer Engineering, Hallym University

Publications

1. Park et. al., Clonal dynamics in early human embryogenesis inferred from somatic mutations, 597,393-397, Nature, 2021.

2. Kim et. al., FIREVAT: finding reliable variants without artifacts in human cancer samples using etiologically relevant, Genome Medicine, 11(1):81, 2019.

3. Park et. al., Tracing Oncogene Rearrangements in the Mutational History of Lung Adenocarcinoma, CELL, 177, 1842-1857, 2019

4. Yang et. al., RhoGAP domain-containing fusions and PPAPDC1A fusions are recurrent and prognostic in diffuse gastric cancer, NATURE COMMUNICATIONS, 9(1):4439~4439, 2018.

5. Lee el. al., Mutalisk: a web-based somatic MUTation AnaLyIS toolKit for genomic, transcriptional and epigenomic signatures, Nucleic Acids Research, 46(W1):W102~W108, 2018

SYM-A4-3

An implementation of anti-cancer drug miner using 3D protein structure prediction

Dongwan Hong

College of Medicine, Catholic University of Korea, Banpodae-ro 222, Seocho-gu, Seoul 06591, Republic of Korea

Recently, AI software can predict protein structures based on amino acid sequences. DeepMind (Alphafold2) and Meta (ESMFold) opened hundreds of millions of protein structures to world-wide clinical researchers. These tools are possible to generate protein structures in real-time and less cost than traditional protein study methods. Finally, they can lead to the advent of the protein rush generation.

To evaluate accurately and quickly the prediction of structures of mutations embedding in protein sequences, we developed a Novel anti-cancer therapeutic targEts miner supported by a Wise GathEring system using Ai aNd multi-omicS data (NEWGEANS;http://newgeans.org) that clinical researchers can use easily on web. The protein 3D structural comparison model of NEWGEANS uses geometric and spatial parameters to determine the stability of the protein structure. This model works on the notion that an equilateral triangle formed by atoms (probably at the ideal van der Waals distance) is the most stable structure, so it is assigned the value 1 in the interval [0,1]. A straight line representing an unstable structure was assigned a value of 0. This model can compare protein structures by quantifying their stability or conformity to these ideal geometrical parameters.

1. Protein Fold Prediction: This model can help predict how a protein folds based on the geometric properties of its AAs.
2. Protein Structure Comparison: This model can measure the similarity or difference between two protein structures.
It can be used to identify structural homologs or group proteins into families based on structural similarities.
3. Protein Stability Assessment: This model can be useful for evaluating the stability of a protein structure.
Theoretically, proteins with scores closer to 1 are more stable, and proteins with scores closer to 0 are less stable.
4. Drug repurposing: NEWGEANS provides the druggable candidates from pan-cancer targeted therapy.

While we were analyzing multi-omics data of castrate-resistant prostate cancer (CRPC) patients, we detected the BRAF—ACSL3 genefusion in tyrosine kinase domain of BRAF gene (~3% of all patients).
In addition, we found out that the protein structure between BRAF fusion and BRAF V600E mutation has similar shapes and validated drug repositioning using in-vitro experiments that constructed PC3 cell-lines containing lenti-virus vectors of BRAF fusion, BRAF V600E mutation and WT, respectively.

Finally, the validations showed that the number of cells (BRAF fusion and BRAF V600E variant) were decreased under anti-cancer inhibitor (Vemurafenib).
We are available to suggest clinical trials of CRPC patients with BRAF fusion using a targeted therapy (BRAF V600E) as an off-target drug.
The execution time of NEWGEANS (GPU based web server platform) depends on the length of the input sequence. NEWGEANS can suggest anti-cancer candidates in protein-level and present a precision medicine model which is available to implement close to real time.

Keywords: NEWGEANS, Drug Repositioning, Protein 3D Structure, Cancer, and Artificial Intelligence

SYM-A5

AI driven drug development

SYM-A5

AI driven drug development

6.26 (Wed) 16:15 - 17:30

Chair: Seungjin Na / Korea Basic Science Institute (KBSI)

SYM-A5-1 6.26 (Wed) 16:15 - 16:40

AI-Enhanced Proteomics: From Study Design to Data Interpretation

Sangtae Kim
NGeneBioAI, Inc

SYM-A5-2 6.26 (Wed) 16:40 - 17:05

AI-based acceleration of drug discovery

Woo Youn Kim
Korea Advanced Institute of Science and Technology (KAIST)

SYM-A5-3 6.26 (Wed) 17:05 - 17:30

AI induced indication expansion based on transcriptome

Yirang Kim
Oncocross

SYM-A5

Sangtae Kim, Ph.D.

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Education

2006-2012	Ph.D.	University of California San Diego, CA, USA
2000-2002	M.S.	Seoul National University, Seoul, Korea
1996-2000	B.S.	Seoul National University, Seoul, Korea

Professional Experience

2024-	Chief Executive Officer	NGeneBioAI, CA, USA
2021-2024	Chief Technology Officer	Bertis Bioscience, CA, USA
2020-2021	Principal Bioinformatics Scientist	Seer, Inc. CA, USA
2015-2020	Staff Bioinformatics Scientist	Illumina, Inc. CA, USA
2012-2015	Senior Research Scientist	Pacific Northwest National Laboratory, WA, USA
2005-2006	Researcher	Hanyang University, Seoul, Korea
2002-2005	Full-time Lecturer	Korea Military Academy, Seoul, Korea

Publications

1. “Strelka2: Fast and accurate variant calling for clinical sequencing applications”, S Kim, K Scheffler, AL Halpern, MA Bekritsky, E Noh, M Källberg, X Chen, Y Kim, D Beyter, P Krusche, CT Saunders. Nature Methods, 15:591-594 (2018). PMID: 30013048

2. “Informed-Proteomics: Open-Source Software Package for Top-down Proteomics” J Park, PD Piehowski, C Wilkins, M Zhou, J Mendoza, GM Fujimoto, BC Gibbons, JB Shaw, Y Shen, AK Shukla, RJ Moore, T Liu,VA Petyuk, N Tolic, L Pasa-Tolic, RD Smith, SH Payne, S Kim. Nature Methods, 14:909-914 (2017). PMID: 28783154

3. “MS-GF+ makes progress towards a universal database search tool for proteomics” S Kim and P Pevzner, Nature Communications, 5, 5277, (2014). PMID: 25358478

4. “Proteogenomic characterization of human colon and rectal cancer” B Zhang, J Wang, X Wang, J Zhu, Q Liu, Z Shi, MC Chambers, LJ Zimmerman, KF Shaddox, S Kim, SR Davies, S Wang, P Wang, CR Kinsinger, RC Rivers, H Rodriguez, RR Townsend, MJ Ellis, SA Carr, DL Tabb, RJ Coffey, RJ Slebos, DC Liebler, and the NCI CPTAC. Nature, 13, 382-387, (2014). PMID: 25043054

5. “The Generating Function of CID, ETD and CID/ETD Pairs of Tandem Mass Spectra: Applications to Database Search” S Kim, N Mischerikow, N Bandeira, JD Navarro, L Wich, S Mohammed, A JR Heck, and P Pevzner. Molecular & Cellular Proteomics, 9, 2840-2852, (2010). PMCID: PMC3101864

6. “Spectral Probabilities and Generating Functions of Tandem Mass Spectra: A Strike against DecoyDatabases” S Kim, N Gupta, and P Pevzner. Journal of Proteome Research, 7, 3354-3363 (2008). PMCID: PMC2689316 Please refer to http://goo.gl/1PtuNq for the full publication list.

SYM-A5-1

AI-Enhanced Proteomics: From Study Design to Data Interpretation

Sangtae Kim

NgeneBioAI, CA, USA

In translational proteomics, the integration of Artificial Intelligence (AI) with mass spectrometry (MS) presents a new era in drug discovery, diagnostics, and precision medicine. We present our journey from conventional MS-based proteomics to cutting-edge AI-enhanced proteomics, highlighting the breakthroughs through AI in study design, peptide identification/quantification, statistical analysis, and data interpretation. Leveraging AI technologies such as large language models and deep learning, our platform enhances the efficiency in proteomics laboratories and bridges the gap between large proteomic data and actionable insights in precision medicine.

SYM-A5

Woo Youn Kim, Ph.D.

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Education

2004.03 - 2009.02	Ph.D.	POSTECH
199703 - 2004.02	B.S.	POSTECH

Professional Experience

2011.01 - Present	Assist./Assoc./Full Professor	Department of Chemistry, KAIST
2020.05 - Present	CEO	HITS Inc.
2024.01 - 2024.03	Vice Director	Convergence AI Institute for Drug Discovery, Korea Pharmaceutical and Bio-Pharma Manufacturers
2022.03 - 2024.01	Director	Association

Publications

1. Wonho Zhung, Hyeongwoo Kim, and Woo Youn Kim* 3D Molecular generative framework for interaction-guided drug design. Nat. Comm. 15, 2688 (2024).

2. Hyeonsu Kim, Jeheon Woo, Seonghwan Kim, Seokhyun Moon, Jun Hyeong Kim, and Woo Youn Kim* GeoTMI: Predicting Quantum Chemical Property with Easy-to-Obtain Geometry via Positional Denoising. Advances in Neural Information Processing Systems 36 (2024).

3. Hyeonsu Kim,† Kyunghoon Lee,† Jun Hyeong KIm and Woo Youn Kim* Deep learning-based chemical similarity for accelerated OLED materials discovery. †equal contribution. J. Chem. Inf. Model (2024).

4. Seonghwan Kim,† Jeheon Woo,† and Woo Youn Kim* Diffusion-based Generative AI for Exploring Transition States from 2D Molecular Graphs. †equal contribution. Nat. Comm. 15, 341 (2024)

5. Seokhyun Moon,† Wonho Zhung,† and Woo Youn Kim* Toward Generalizable Structure-Based Deep Learning Models for Protein-Ligand Interaction Prediction: Challenges and Strategies.†equal contribution. Wiley Interdisciplinary Reviews: Computational Molecular Science 14, e1705 (2024).

SYM-A5-2

AI-based acceleration of drug discovery

Woo Youn Kim

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Since the AlphaGo moment in 2016, AI has attracted attention in various fields, including drug discovery. Unlike the existing physics-based CADD (Computer-aided Drug Design), data-driven modeling using deep learning is enabling more accurate and faster prediction methods than CADD. In particular, molecular design is being revolutionized by the emergence of generative AI. Early molecular design AIs were impractical due to the lack of synthesizability of the generated molecules. However, recently, studies have shown that computational synthetic methods can be incorporated in the generation process to overcome this problem. In addition, advanced deep learning models enabled fast and yet reliable prediction of protein-ligand interactions. In this talk, I will introduce Hyper Lab, a cloud-based web platform developed based on this research. Hyper Lab provides various functions such as AI-based prediction of protein-ligand interaction, high-throughput virtual screening (1 million compounds within 24 hours), molecular design, ADME/T prediction, etc. Hyper Lab provides a simple UI/UX that is useful especially for experimentalists. Hyper Lab address: https://hyperlab.ai/

SYM-A5

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Education

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2022.07-present	Chairman	Council for AI Drug Discovery & Development
2015.06-present	Founder & CEO	ONCOCROSS
2014.05-2015.02	Fellow (Medical Oncology specialist)	Department of Oncology, Seoul Asan Medical Center
2014.05-2015.02	Resident (Internal medicine specialist)	Department of Internal Medicine, Seoul Asan Medical Center

Academic Society

2021.09-present	Adjunct Professor	nstitute of Regulatory Innovation through Science, Graduate School of Kyunghee University

Publications

1. Min Hak Lee, Bada Lee, Se Eun Park, Ga Eul Yang, Seungwoo Cheon, Dae Hoon Lee, Sukyeong Kang, Ye Ji Sun, Yongjin Kim, Dong-sub Jung, Wonwoo Kim, Jihoon Kang, Yi Rang Kim*, Jin Woo Choi*. Transcriptome-based Deep Learning Analysis Identifies Drug Candidate Targeting Protein Synthesis and Autophagy for Muscle Wasting Disorder. Experimental & Molecular Medicine. 2024. https://doi.org/10.1038/s12276-024-01189-z.

2.Sun Kyung Kim, Peter C. Goughnour, Eui Jin Lee, Myeong Hyun Kim, Hee Jin Chae, Gwang Yeul Yun, Yi Rang Kim* and Jin Woo Choi*. Identification of drug combinations on the basis of machine learning to maximize anti-aging effects. PLOS one. 2021; 16(1): e0246106

3.Jun Ki Kim, Mi Ran Byun, Chi Hoon Maeng, Yi Rang Kim* and Jin Woo Choi*. Selective Targeting of Cancer Stem Cells (CSCs) Based on Photodynamic Therapy (PDT) Penetration Depth Inhibits Colon Polyp Formation in Mice. Cancers. 2020; 14:12(1)

4.Yi Rang Kim, Jung Ki Yoo, Chang Wook Jeong and Jin Woo Choi. Selective killing of circulating tumor cells prevents metastasis and extends survival. Journal of hematology and oncology.

5.Yi Rang Kim, Jun Ki Kim and Jin Woo Choi. Fluorescent cell-selective ablation using an adaptive photodynamic method. Chemical Communications. 2017; Nov 3. doi: 10.1039/c7cc07550b

6.Yi Rang Kim, Seonghoon Kim, Jin Woo Choi, Sung Yong Choi, Sang-Hee Lee, Homin Kim, Sei Kwang Hahn, Gou Young Koh, Seok Hyun Yun. Bioluminescence-Activated Deep-Tissue Photodynamic Therapy of Cancer. Theranostics. 2015; 5(8):805-817. doi:10.7150/thno.1152

SYM-A5-3

AI induced indication expansion based on transcriptome

Jaehak Lee[1], Jihoon Kang[1], Yirang Kim[1,2]

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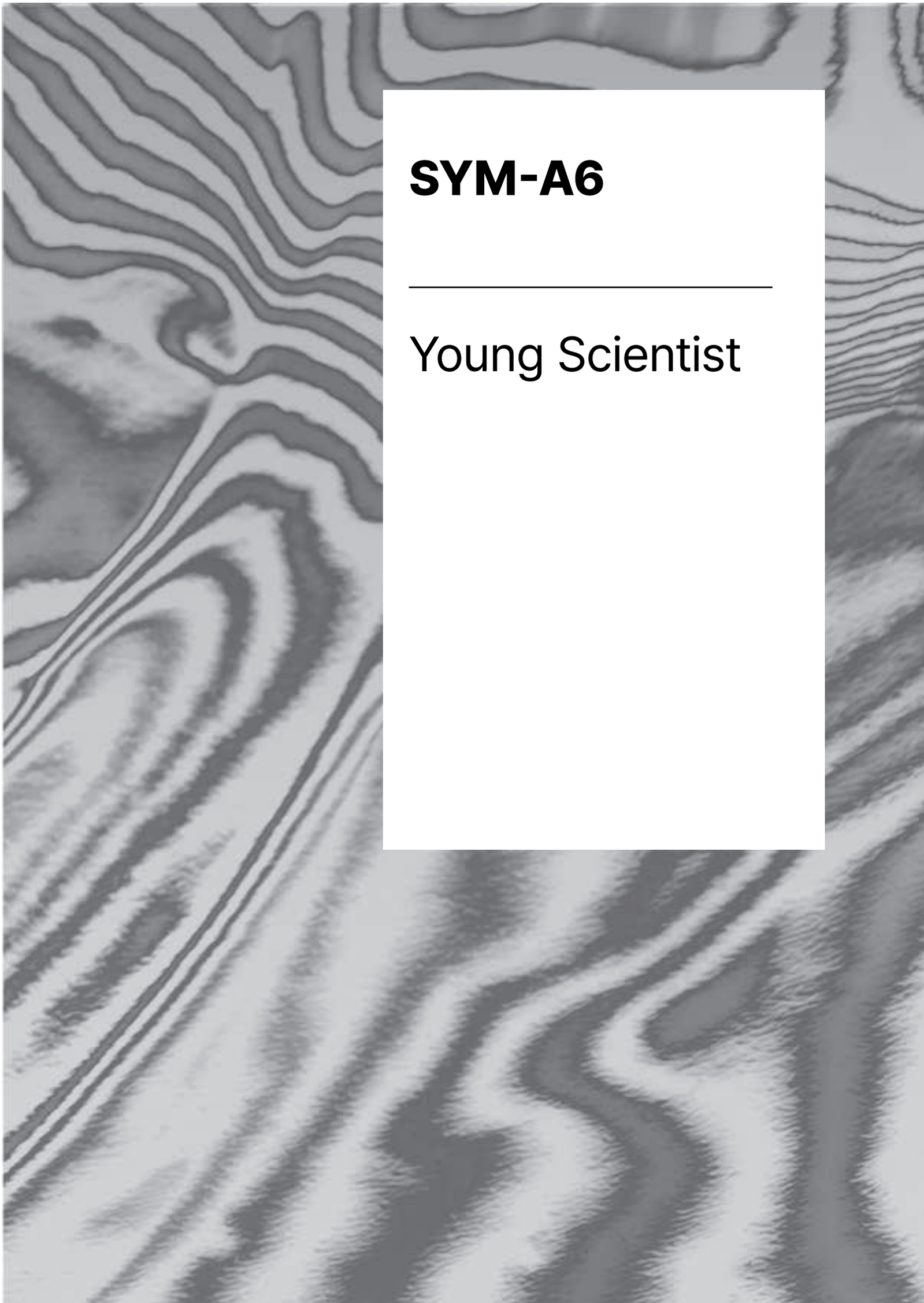
Indication expansion areas are basically included in drug repositioning as a large category, but unlike drug repositioning which generally finds additional indications for drugs already on the market and expired material patents, the indication expansion differs significantly in strategy and business as new indications are discovered using drugs undergoing clinical trials in which material patents are valid. Here, I introduce RAPTOR AI, AI drug development platform that predicts the relationship between disease and drugs by comparing and analyzing the characteristics of changes in gene expression patterns based on transcriptome information, and show that the results derived from RAPTOR AI are shortening the R&D period and reducing the risk of development failure in the process of developing new drugs.



SYM-A6

Young Scientist

SYM-A6

Young Scientist

6.27 (Thu) 09:00-10:10

Chair:
Kyunggon Kim / Asan Medical Center/Unversity of Ulsan
Jonghwa Jin / KBIOhealth
Kyung-Hee Kim / National Cancer Center (NCC)

SYM-A6-1 6.27 (Thu) 09:00 - 09:10

Multi-proteomic analyses of 5xFAD mice reveal new molecular signatures of early-stage Alzheimer's disease

Seulah Lee
Korea Brain Research Institute (KBRI)

SYM-A6-2 6.27 (Thu) 09:10 - 09:20

In vivo mitochondrial matrix proteome profiling reveals RTN4IP1/OPA10 as an antioxidant NAD(P)H oxidoreductase

Isaac Park
Seoul National University

SYM-A6-3 6.27 (Thu) 09:20 - 09:30

In-Depth Glycomic and Proteomic Characterization of Cell-Based Therapeutics

In-Seok Yeo
Chungnam National University

SYM-A6-4 6.27 (Thu) 09:30 - 09:40

Pan-cancer proteogenomic landscape of whole-genome doubling reveals putative therapeutic targets in various cancer types

Eunhyong Chang
Korea University

SYM-A6-5 6.27 (Thu) 09:40 - 09:50

Phosphorylation site prediction model using structural context

Yujin Choo
Hanyang University

SYM-A6-6 6.27 (Thu) 09:50 - 10:00

Protein damage drives the cellular senescence by compromising proteostasis

WooJun Kang
Daegu Gyeongbuk Institute of Science and Technology (DGIST)

SYM-A6-7 6.27 (Thu) 10:00 - 10:10

Proteomic biomarker profiling for discovering muscle, bone, and fat cross talk from elite athletes

Hyeon-Jeong Lee
Korea Institute of Science and Technology (KIST)

SYM-A6

Seulah Lee, Ph.D.

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Professional Experience

2022.02-	Postdoctoral researcher	Korea Brain Research Institute

Academic Society

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2022.05-	Member	The Korean Human Proteome Origanization
2017.03-	Member	Society for Neuroscience
2018.09-2021.12	Student Member	The Korean Society for Brain and Neural Sciences
2018.04-2021.12	Student Member	The Pharmaceutical Society of Korea

Publications

1. Lee S, Jang K-I, Lee H, Jo YS, Kwon D, Park G, Bae S, Kwon YW, Jang J-H, Oh Y-S, Lee C, Yoon, JH. Multi-proteomic analyses of 5xFAD mice reveal new molecular signatures for early-stage Alzheimer's disease. Aging Cell. 2024 Feb; e14137.

2. Yoon JH, Lee D, Lee C, Cho E, Lee S, Cazenave-Gassiot A, Kim K, Chae S, Dennis EA, Suh P-G. Paradigm shift required for translational research on the brain. Experimental & Molecular Medicine. 2024 May; 56(5):1043-1054.

3. Kim D, Lee S, Noh SG, Lee J, Chung HY. FoxO6-mediated ApoC3 upregulation promotes hepatic steatosis and hyperlipidemia in aged rats fed a high-fat diet. Aging (Albany NY). 2024 Mar; 16(5):4095-4115.

4. Kim J, Lee S, Hong DG, Yang S, Tran CS, Kwak J, Kim M-J, Rajarathinam T, Chung KW, Jung Y-S, Ishigami A, Chang S-C, Lee H, Yun H, Lee J. Amelioration of astrocyte-mediated neuroinflammation by El-16004 confers neuroprotection in an MPTP-induced Parkinson's disease model. Neuromolecular Medicine. 2024 Jan; 26(1):1.

5. Yang S, Lee S, Lee Y, Cho J-H, Kim SH, Ha E-S, Jung Y-S, Chung HY, Kim M-S, Kim HS, Chang, S-C, Min K-J, Lee J. Cationic nanoplastic causes mitochondrial dysfunction in neural progenitor cells and impairs hippocampal neurogenesis. Free Radical Biology and Medicine. 2023 Nov; 208:194-210.

6. Yoon JH, Seo Y, Jo YS, Lee S, Cho E, Cazenave-Gassiot A, Shin Y-S, Moon MH, An HJ, Wenk MR, Suh P-G. Brain lipidomics: From functional landscape to clinical significance. Science Advances. 2022 Sep;8(37): eadc9317.

7. Hong DG, Lee S, Kim J, Yang S, Lee M, Ahn J, Lee H, Chang S-C, Ha N-C, Lee J. Anti-inflammatory and neuroprotective effects of morin in an MPTP-induced Parkinson's disease model. International Journal of Molecular Sciences. 2022 Sep; 23(18):10578.

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SYM-A6-1

Multi-proteomic analyses of 5xFAD mice reveal new molecular signatures of early-stage Alzheimer's disease

Kuk-In Jang[2], Hagyeong Lee[1], Yeon Suk Jo, Dayoung Kwon, Geuna Park, Sungwon Bae, Yang Woo Kwon, Jin-Hyeok Jang, Yong-Seok Oh[3], Chany Lee[2], and Jong Hyuk Yoon[1*]

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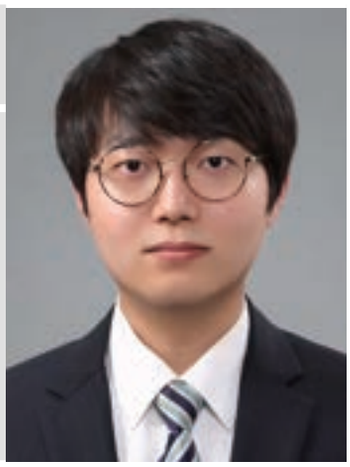
An early diagnosis of Alzheimer's disease (AD) is crucial as treatment efficacy is limited to the early stages. However, the current diagnostic methods are limited to mid or later stages of disease owing to the limitations of clinical examinations. Therefore, this study aimed to identify molecular signatures including blood plasma extracellular vesicle (EV) biomarker proteins associated with AD to aid early-stage diagnosis. The hippocampus, cortex, and blood plasma EVs of 3- and 6-month-old 5xFAD mice were analyzed using quantitative proteomics. Subsequent bioinformatics and biochemical analyses were performed to compare the molecular signatures between wild type and 5xFAD mice. There was a unique signature of significantly altered proteins in the hippocampal and cortical proteomes of 3- and 6-month-old mice. The plasma EV proteomes exhibited distinct informatic features compared with the other proteomes. Twelve potential biomarkers for the detection of early-stage AD were identified and validated using plasma EVs from stage-divided patients. Finally, ITGA2B, CKM, FLNC, TGM2, and MAN2B1 were selected as distinguishing biomarkers for healthy individuals and early-stage AD patients using machine learning modeling with approximately 79% accuracy. Our study identified novel early-stage molecular signatures associated with the progression of AD, thereby providing novel insights into its pathogenesis.

SYM-A6

Isaac Park, Ph.D.



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Professional Experience

2018.03 – present	Postdoctoral researcher	Seoul National University, Seoul, South Korea

Publications

1. **Park I***, Kim KE*, Kim J*, Kim AK, Bae S, Jung M, Choi J, Mishra PK, Kim TM, Kwak C, Kang MG, Yoo CM, Mun JY, Liu KH, Lee KS, Kim JS, Suh JM, and Rhee HW. "Mitochondrial matrix RTN4IP1/OPA10 is an oxidoreductase for coenzyme Q synthesis." Nat. Chem. Biol. 20, pages221–233 (2024) (*equally contributed) - Featured in News & Views, "Reducing mitochondrial mysteries", Nat. Chem. Biol. (2023)

2. Park A*, Kim KE*, **Park I**, Lee SH, Park KY, Jung M, Li X, Sleiman MB, Lee SJ, Kim DS, Kim J, Lim DS, Woo EJ, Lee EW, Han BS, Oh KJ, Lee SC, Auwerx J, Mun JY, Rhee HW, Kim WK, Bae KH, Suh JM. "Mitochondrial matrix protein Letmd1 maintains thermogenic capacity of brown adipose tissue in male mice." Nat. Commun. 14, 3746 (2023)

3. Mishra PK†, **Park I†**, Sharma N, Yoo CM, Lee HY, Rhee HW* "Enzymatic recording of local hydrogen peroxide generation using genetically encodable enzyme." Anal. Chem. 94, 14869-14877 (2022) (†equally contributed)

4. Sohn JH, Ji Y, Cho CY, Nahmgoong H, Lim S, Jeon YG, Han SM, Han JS, **Park I**, Rhee HW, Kim S, Kim JB* "Spatial Regulation of Reactive Oxygen Species via G6PD in Brown Adipocytes Supports Thermogenic Function. " Diabetes. 70, 2756-2770 (2021)

5. Kim KE*, **Park I***, Kim J, Kang MG, Choi WG, Shin H, Kim JS, Rhee HW, and Suh JM. "Dynamic tracking and identification of tissue-specific secretory proteins in the circulation of live mice." Nat. Commun. 12, 5204 (2021) - Featured in Research Highlights, "Revealing the secretome", Nat. Methods 18, 1273 (2021) (* equally contributed)

SYM-A6-2

In vivo mitochondrial matrix proteome profiling reveals RTN4IP1/OPA10 as an antioxidant NAD(P)H oxidoreductase

Isaac Park[1#], Kwang-eun Kim[2#], Jeesoo Kim[3#], Ae-Kyeong Kim[4], Minkyo Jung[5], Ji Young Mun[5]*, Kyu-Sun Lee[4*], Jong-Seo Kim[3*], Jae Myoung Suh[2*], Hyun-Woo Rhee[1*]

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Targeting proximity labeling enzymes to specific cellular locations is a viable strategy for profiling subcellular proteomes. Here, we generated transgenic mice (MAX-Tg) expressing a mitochondrial matrix-targeted ascorbate peroxidase (MTS-APEX2) to analyze tissue-specific matrix proteomes. Desthiobiotin-phenol labeling of muscle tissues from MAX-Tg mice allowed for the efficient profiling of tissue-specific matrix proteome. Comparative analysis of matrix proteomes from MAX-Tg muscle tissues revealed differential enrichment of mitochondrial proteins related to energy production. We identified that Reticulon 4 interacting protein 1 (RTN4IP1), also known as Optic Atrophy-10 (OPA10), is highly enriched in the mitochondrial matrix of muscle tissues and is an NADPH oxidoreductase. Interactome analysis and in vitro enzymatic assays revealed an essential role for RTN4IP1 in coenzyme Q (CoQ) biosynthesis by regulating the O-methylation activity of COQ3. Rtn4ip1 knockout C2C12 myoblasts had markedly decreased CoQ9 levels and impaired cellular respiration, which was rescued by exogenous CoQ treatment. Muscle-specific knockdown of the drosophila Rnt4ip1 ortholog resulted in impaired muscle function which was reversed by dietary supplementation with soluble CoQ. Collectively, RTN4IP1 is a mitochondrial antioxidant NAD(P)H oxidoreductase supporting mitochondrial respiration activity in muscle tissue.

SYM-A6

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Professional Experience

2024.05 – present	Research Professor	Chungnam National University
2020.09 – 2024.04	Postdoctoral Researcher	Korea Research Institute of Bioscience and Biotechnology
2018.03 – 2020.08	Postdoctoral Researcher	Korea Advanced Institute of Science and Technology

Academic Society

2024.09 – present	Junior Review Editorial Board Member	The Korean Society for Microbiology and Biotechnology

Publications

1. **IS Yeo**, WY Shim, JH Kim, Construction of genetically engineered Candida tropicalis for conversion of l-arabinose to l-ribulose, J Biotechnol, 2018 May, **274**: 9-14. (co-first author)

2. **IS Yeo**, YJ Joon, N Seo, HJ An, JH Kim, Biopurification of oligosaccharides by immobilized Kluyveromyces lactis, Appl Sci, 2019 Jul, **9**(14): 2845. (co-first author)

3.**IS Yeo**, BK Cho, JH Kim, Conversion of l-arabinose to l-ribose by genetically engineered Candida tropicalis, Bioprocess Biosyst Eng, 2021 Jun, **44**: 1147-1154.

4. G. Mwiti,**IS Yeo**, KH Jeong, HS Choi, JH Kim, Activation of galactose utilization by the addition of glucose for the fermentation of agar hydrolysate using Lactobacillus brevis ATCC 14869, Biotechn Lett, 2022 Jul, **44**(7): 823-830. (co-first author)

5. **IS Yeo**, KS Go, WY Jeon, MJ Jang, HJ Lee, SH Seo, YS Kim, HA Park, BW Min, KM Park, YH Yang, KY Choi, HW Lee, SG Jeon, JO Ahn, Integrating chemical and biological technologies in upcycling plastic waste to medium-chain α,ω-diacid, J Clean, 2024 Apr, **451**: 141890. (co-first author)

SYM-A6-3

In-Depth Glycomic and Proteomic Characterization of Cell-Based Therapeutics

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Cell-based therapeutics offer promising alternatives for treating diseases previously deemed incurable such as cancer and autoimmune diseases. However, these therapeutics can lead to side effects like carcinogenicity and immunogenicity, necessitating comprehensive characterization. Specifically, glycosylation of cell surface proteins significantly influences cellular interactions crucial for recognizing target cells in cell therapeutics. Despite their significance, membrane glycans and glycoproteins in these therapeutics are not well understood. This study unravels the glycomic landscape and proteomic profiles as novel approaches to characterizing cell therapeutics. We thoroughly analyzed the glycan compositions and structures on cell membranes across different types of cell therapeutics. Our findings show distinct glycosylation patterns: fibroblasts predominantly exhibited paucimannosylation, a simpler glycosylation type; natural killer (NK) cells were marked by bisecting glycans and neutral, highly branched glycans; induced pluripotent stem cells (iPSCs) displayed highly fucosylated and high mannose-type glycans. Interestingly, cardiomyocytes, derived from iPSCs, showed significant glycosylation alterations, with the presence of bisecting and acidic, highly branched glycans, highlighting further glycosylation modifications during cell differentiation. It was observed that changing the culture conditions with TGF-β or interleukins to enhance the cellular activity of fibroblasts and NK cells did not significantly affect the glycosylation patterns. Hierarchical analysis and principal component analysis (PCA) revealed cell-specific glycosylation mapping with distinct differences between cell lines. The proteomic analysis of cell membrane proteins has led to identify proteins with crucial functional roles and their interactions within each cell type. For instance, glycoproteins implicated in cell developmental processes, including ALT1, EPHA1, EPH4, and GPM6B, were uniquely identified in induced pluripotent stem cells (iPSCs), while glycoproteins associated with cardiac development, such as SLIT2, LTBP1, TGFB2, WNT11, and FZD1, were specifically detected in cardiomyocytes. Although the specific relationship between glycan expression patterns and cellular glycoproteins requires further investigation, these initial findings provide a foundation for future research. In conclusion, the integration of glycomics and proteomics approaches will enhance our understanding of cellular mechanisms and support the definition of specific molecular markers, ultimately improving the quality characterization of cellular therapeutics.

SYM-A6

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Publications

1. Chang E and An JY. Whole-genome doubling is a double-edged sword: the heterogeneous role of whole-genome doubling in various cancer types. BMB Rep. 2024 Mar; 57(3): 125-134.

2. Chang E, Hwang HS, Song KJ, Kim K, Kim MS, Jang SJ, Kim KP, You S, An JY. Pan-cancer proteogenomic landscape of whole-genome doubling reveals putative therapeutic targets in various cancer types. Clin Transl Med. Under revision.

3. Song KJ, Choi S, Kim K, Hwang HS, Chang E, Park JS, Shim SB, Choi S, Heo YJ, An WJ, Yang DY, Cho KC, Ji W, Choi CM, Lee JC, Kim H, Yoo J, Ahn HS, Lee GH, Hwa C, Kim S, Kim K, Kim MS, Paek E, Na S, Jang SJ, An JY, Kim KP. Proteogenomic Analysis of a Korean Cohort Reveals Lung Cancer Subtypes Predictive of Metastasis, Chromosome Instability, and Tumor Microenvironment. Nat Comm. Under revision.

SYM-A6-4

Pan-cancer proteogenomic landscape of whole-genome doubling reveals putative therapeutic targets in various cancer types

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Whole-genome doubling (WGD) is prevalent in cancer, driving tumor development and chromosomal instability. Recent studies have reported driver mutations in mitotic cell cycle genes and cell cycle upregulation as major molecular underpinnings of WGD tumors. Despite such efforts, questions remain about underlying genomic signatures and regulatory networks underlying gene transcription and kinase-phosphorylation. In this study, we performed a pan-cancer proteogenomic analysis to decipher a comprehensive molecular landscape underlying WGD tumors. For this, we compared 10 cancer types by integrating genomic, transcriptomic, proteomic, and phosphoproteomic datasets. Our study delineated distinct copy-number signatures characterizing WGD tumors into three major groups: highly unstable genome, focal instability, and tetraploidy. Furthermore, the analysis reveals heterogeneous mechanisms underlying WGD across cancer types, with specific structural variation patterns identified. Contrary to previous studies, the upregulation of the cell cycle and downregulation of the immune response were found to be specific to certain WGD tumor types. Transcription factors (TFs) and kinases exhibited cancer-type-specific activities, emphasizing the need for tailored therapeutic approaches. The study introduces an integrative approach to identify potential TF targets for drug development, highlighting BPTF as a promising candidate for head and neck squamous cell carcinoma. Additionally, drug repurposing strategies were proposed, suggesting potential drugs for treating WGD-associated cancers. These findings offer insights into the heterogeneity of WGD and provide implications for precision medicine approaches in cancer treatment.

SYM-A6

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Publications

Jae-Won Lee, Jong-Hyun Won, Yujin Choo, Seonggwang Jeon, Yubin Yeon, Jin-Seon Oh, Minsoo Kim, SeonHwa Kim, InSuk Joung, Cheongjae Jang, Sung Jong Lee, Tae Hyun Kim, Kyong Hwan Jin, Giltae Song, Eun Sol Kim, Jejoong Yoo, Eunok Paek, Yung-Kyun Noh, Keehyoung Joo. Enhancing protein structure prediction through optimized loss functions, improved template features, and re-optimized energy function. Bioinformatics. 2023 Dec; 39(12): 712-723.

Seungjin Na, Yujin Choo, Tae Hyun Yoon and Eunok Paek. CyGate provides a robust solution for automatic gating of single cell cytometry data. Analytical Chemistry. 2023 Nov; 95(45): 16918-16926.

SYM-A6-5

Phosphorylation site prediction model using structural context

Yujin Choo[1], Seungjin Na[2], and Eunok Paek[1,3,4]

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[3]Department of Computer Science, Hanyang University, Seoul, South Korea,
[4]Institute of Artificial Intelligence Research, Hanyang University, Seoul, South Korea

Post-translational modifications are covalent proceesing events that occur after protein synthesis and change the properties of a protein. In particular, phosphorylation is essential for cellular function and signaling and therefore, their identification is crucial for understanding the protein mechanisms. While various machine learning and deep learning models have been proposed to predict phosphorylation sites, the advent of AlphaFold2, with its high-accuracy protein structure predictions, presents new opportunities. We have developed a prediction model that leverages AlphaFold2's structural prediction, enhancing sequence embeddings with structural information through a Transformer-based cross-attention mechanism.

Our phosphorylation site prediction model was benchmarked against MusiteDeep, a sequence-based predictor, using an independent test set with an equal number of positive and negative phosphosite instances (5,074 each) from proteins not included in training/validation sets. MusiteDeep achieved an area under the ROC of 0.9118, whereas our model demonstrated an improved result of 0.9417. Additionally, our model showed enhanced precision (0.8321 over MusiteDeep's 0.8042) and improved recall (0.9253 over Musitedeep's 0.9034), at the same time. We also explored kinase-specific prediction through transfer learning to assess how effectively structural information is integrated into the embeddings. The results from our transfer learning approach surpassed those from fine-tuning and DeepPhos model, a sequence-based prediction tool, across all kinase-specific datasets.

SYM-A6

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Education

2017.03-2021.02	Bachelor's Degree	Daegu-Gyeongbuk Institute of Science and Technology
2021.03-present	Integrated Ph. D	Daegu-Gyeongbuk Institute of Science and Technology

Publications

Lim JJ, Noh S, Kang W, Hyun B, Song X, Na SJ, Yun HM, Lee BH, Hyun S. (2024). Pharmacological inhibition of USP14 delays proteostasis-associated aging in a proteasome-dependent but FOXO-independent manner. Autophagy, *provisionally accepted*

SYM-A6-6

Protein damage drives the cellular senescence by compromising proteostasis

Woojun Kang[1], Nguyen Ngoc Chau Thy[1], Jin Ju Lim[2], Sujin Noh[2], Young-Sam Lee[1], Seogang Hyun[2], Chihyun Park[3], Min-Sik Kim[1], Byung-Hoon Lee[1]

[1]Department of New Biology, Daegu-Gyeongbuk Institute of Science and Technology, Daegu 42988, Korea, [2]Department of Life Science, Chung-ang University, Seoul 06974, Korea, [3]Department of Computer Science and Engineering, Kangwon National University, Chuncheon 24341, Korea

Cellular senescence is a permanent growth arrest, defined by naturally occurring cell division cessation or triggered by various aging-associated stress. During the aging process, it is known that the proteome integrity, maintained by protein quality control system, is progressively compromised. But there is no conclusive evidence to prove that proteostasis decline by protein damage can be a driver of cellular senescence. Here we propose a new cellular aging model, protein damage-induced cellular senescence (PDIS). We showed that protein damage inducers, including amino acid analogs (AAAs), can induce the cellular aging phenotypes in both non-immortalized and immortalized fibroblast cell lines that were characterized by cell growth arrest, enlarged cell size and senescence-associated autofluorescence or β-galactosidase staining. Cells exposed to AAAs showed increased ubiquitin conjugate levels and decreased autophagic flux, reflecting the cellular protein damage and high burden to the protein quality control system. Transcriptome analysis of IMR-90 fibroblast cells chronically exposed to AAAs indicated that PDIS displays highly distinct gene expression profiles from other known senescence models. In PDIS transcriptome, differentially expressed genes (DEGs) are rarely found in protein quality control pathways, suggesting that PDIS is likely driven by global proteome disintegrity and proteostasis failure. Quantitative mass spectrometry analysis of PDIS cells showed enriched senescence-associated pathways like cell cycle regulations, lysosomal proteins, and ER stress responses, supporting that PDIS is a senescence phenotype. Importantly, protein damage-induced cellular aging process can be partially recovered by the treatment with proteasome activity-enhancing compounds. Moreover, AAA feeding dramatically decreased the lifespan and autophagic activity of flies, and this was also rescued by proteasome activity-enhancing compounds. Our research reveals a direct functional link between protein damage and cellular senescence, which may provide a fundamental basis for understanding cellular aging based on proteostasis.

SYM-A6

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Education

2020.09-2024.02	Doctor	Seoul national university
2016.03-2018.02	Master	Gyeongsang national university
2011.03-2015.08	Bachelor	Seoul national university

Professional Experience

2024.03-2024.06	Post-doc	Korea institute of science and technology; Doping control center
2019.02-2020.08	Intern	Korea institute of science and technology; Doping control center

Publications

1. Lee, H. J., Jin, J., Seo, Y., Kang, I., Son, J., Yi, E. C., & Min, H. (2023). Untargeted Metabolomics Analysis Reveals Toxicity Based on the Sex and Sexual Maturity of Single Low-Dose DEHP Exposure. Toxics, 11(9), 794.

2. Lee, H. J., Jeon, M., Seo, Y., Kang, I., Jeong, W., Son, J., ... & Min, H. (2023). Application of Skyline software for detecting prohibited substances in doping control analysis. PloS one, 18(12), e0295065.

3. Lee, H. J., Kim, B. M., Lee, S. H., Sohn, J. T., Choi, J. W., Cho, C. W., ... & Kim, H. J. (2020). Ginseng-induced changes to blood vessel dilation and the metabolome of rats. Nutrients, 12(8), 2238.

4. Seo, Y., Park, J., Lee, H. J., Kim, M., Kang, I., Son, J., ... & Min, H. (2023). Development and validation of a method for analyzing the sialylated glycopeptides of recombinant erythropoietin in urine using LC–HRMS. Scientific reports, 13(1), 3860.

5. Lee, K. M., Han, S. M., Lee, H. J., Kang, M., Jeong, T. Y., Son, J., ... & Lee, J. (2023). Influence of mobile phase composition on the analytical sensitivity of LC–ESI–MS/MS for the concurrent analysis of bisphenols, parabens, chlorophenols, benzophenones, and alkylphenols. Environmental Research, 221, 115305.

6. Lee, S., Lee, K. M., Han, S. M., Lee, H. J., Sung, C., Min, H., ... & Lee, J. (2022). Comprehensive LC-MS/MS method combined with tandem hybrid hydrolysis for multiple exposure assessment of multiclass environmental pollutants. Environmental Research, 211, 113053.

7. Kang, I., Seo, Y., Lee, K., Lee, H. J., Son, J., Lee, H. J., ... & Min, H. (2024). Development of an Ephedrine In-House Matrix Reference Material and Its Application to Doping Analysis. ACS omega, 9(11), 12689-12697.

8. Kim, B. M., Lee, H. J., Song, Y. H., & Kim, H. J. (2021). Effect of salt stress on the growth, mineral contents, and metabolite profiles of spinach. Journal of the Science of Food and Agriculture, 101(9), 3787-3794.

9 .Kim, D. W., Kim, B. M., Lee, H. J., Jang, G. J., Song, S. H., Lee, J. I., ... & Kim, H. J. (2017). Effects of different salt treatments on the fermentation metabolites and bacterial profiles of kimchi. Journal of food science, 82(5), 1124-1131.

10. Kang, N., Oh, H. J., Hong, J. H., Moon, H. E., Kim, Y., Lee, H. J., ... & Jin, J. (2024). Correction: Glial cell proteome using targeted quantitative methods for potential multi-diagnostic biomarkers. Clinical Proteomics, 21.

11. Kim, Y. J., Kim, H. M., Kim, H. M., Lee, H. R., Jeong, B. R., Lee, H. J., ... & Hwang, S. J. (2021). Growth and phytochemicals of ice plant (Mesembryanthemum crystallinum L.) as affected by various combined ratios of red and blue LEDs in a closed-type plant production system. Journal of applied research on medicinal and aromatic plants, 20, 100267.

11. Kim, Y. J., Kim, H. M., Kim, H. M., Jeong, B. R., Lee, H. J., Kim, H. J., & Hwang, S. J. (2018). Ice plant growth and phytochemical concentrations are affected by light quality and intensity of monochromatic light-emitting diodes. Horticulture, Environment, and Biotechnology, 59, 529-536.

SYM-A6-7

Proteomic biomarker profiling for discovering muscle, bone, and fat cross talk from elite athletes

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The health benefits of physical activity are widely acknowledged and impact various organ systems as promoting overall resilience and longevity. Following the research of discovering signaling molecules that are released in response to exercise from various organs such as skeletal muscle, heart, neurons, and adipose tissue exerting their effects through endocrine, paracrine, or autocrine pathways, numerous functional molecules caused by physical activity have been identified. However, controversial issues persist inconsistencies between responses to acute and chronic exercise, and differences observed between human and animal exercise models. Therefore, to understand the precise molecular mechanisms responsible for these benefits, and provide robust ground for future advancements in exercise biomarker research, well-structured biomarker profiling analysis with controlled sampling methods from elite athletes is essential. In this study, we identified various proteomic biomarkers from elite athletes and the suggested proteins showed promising relationships with enhancing cardiovascular, metabolic immune, and neurological health, suggesting potential applications in treating cardiovascular disease, type 2 diabetes, obesity, and promoting healthy aging. In addition, this study emphasizes the significance of using a meticulous sampling strategy to yield precise findings on functional molecules triggered by exercise.

SYM-A7

Degenerative Disease

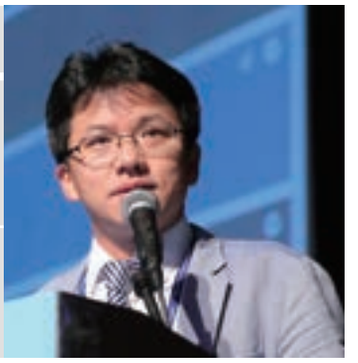
SYM-A7

Degenerative Disease

6.27 (Thu) 14:45 - 16:00

Chair: Junho Park / CHA University

SYM-A7-1 6.27 (Thu) 14:45 - 15:10



PROTEOMICS UNLIMITED DESIRE in Prostate cancer

Hong Koo Ha
Pusan National University Hospital

SYM-A7-2 6.27 (Thu) 15:10 - 15:35

Application of Integrative Proteomics for Understanding Neurodegenerative Diseases

Jong Hyuk Yoon
Korea Brain Research Institute (KBRI)

SYM-A7-3 6.27 (Thu) 15:35 - 16:00

Multi modal proteome platform for biomarker and new drug target discovery

Kyunggon Kim
Asan Medical Center/Unversity of Ulsan

SYM-A7

Hong Koo Ha, Ph.D.

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Education

2005.03 - 2010.02	Ph.D.	Pusan National University
2001.09 - 2003.08	M.S.	Pusan National University
1994.03 - 2000.02	M.D.	Pusan National University

Professional Experience

2018 - Present	Head	Department of Urology, Pusan National University
2020 - Present	Director	Precision Medicine Center, Biomedical Research Institute, Pusan National University Hospital
2016 - 2020	Director	Robotic Surgery Center, Pusan National University Hospital
2011 - Present	Head	Uro-oncologic Division, Department of Urology, Pusan National University

Academic Society

2005 - Present	Member	The Korean Urological Association
2005 - Present	Member	The Korean Prostate Society

Publications

1. Woo HK, Park J, Kim KH, Ku JY, Ha HK, Cho YK. Alix-normalized exosomal programmed death-ligand 1 analysis in urine enables precision monitoring of urothelial cancer. Cancer Sci 2024 Mar 13. doi: 10.1111/cas.16106

2. Jeong CW, Han JH, Byun SS, Song C, Hong SH, Chung J, Seo SI, Ha HK, Hwang EC, Seo IY, Cheaib JG, Pierorazio PM, Han M, Kwak C. Rate of benign histology after resection of suspected renal cell carcinoma: multicenter comparison between Korea and the United StatesBMC Cancer 2024 Feb 15;24(1):216. doi: 10.1186/s12885-024-11941-3.

3. Kim KH, Lee HW, Ha HK, Seo HK. Perioperative systemic therapy in muscle invasive bladder cancer: Current standard method, biomarkers and emerging strategies Investig Clin Urol. 2023 May;64(3):202-218. doi: 10.4111/icu.20230006.

4. Hong SH, Chung HS, Seo IY, Kwon TG, Jeong H, Chung JI, Jeon SH, Park JY, Ha HK, Chung BH, Song W, Kim YJ, Kim SH, Lee JS, Lee J, Chung J. Patients' self-management of adverse events and patient-reported outcomes in advanced renal cell carcinoma treated with targeted therapies: A prospective, longitudinal, observational study J Patient Rep Outcomes. 2022 Dec 16;6(1):125. doi: 10.1186/s41687-022-00532-0.

SYM-A7-1

PROTEOMICS UNLIMITED DESIRE in Prostate cancer

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Prostate cancer (PCa) is the fifth leading cause of death worldwide in men and the second most frequent cancer diagnosis in men in 112 countries. According to GLOBOCAN 2020 estimates, 1,414,259 men worldwide were newly diagnosed with PCa in 2020. PCa may be asymptomatic during its early stages and often has an indolent course, which may require only active surveillance. Men are screened for PCa by measuring the serum concentration of prostate-specific antigen (PSA). Men with high PSA concentrations, usually >4 ng/ mL, undergo prostate biopsy to confirm the diagnosis of PCa. High PSA, however, is not a specific marker of PCa, indicating a need for new biomarkers diagnostic of PCa. Analysis of protein samples may enable identification of the pathological signal and subtype of PCa and administration of drugs appropriate to each patient. Many molecular-level mechanisms for multiomics, especially proteomics, analysis of specimens have been developed. Although prostate tissue specimens can be collected by prostate biopsy, the limitation of biopsy samples is that they are very small. Instead of biopsy, tissue can be obtained with transurethral resection of the prostate (TUR-P). Samples obtained from TUR-P are usually much larger and we can get the tissues in patients with castration resistant prostate cancer (CRPC). Because of electric current during TUR-P, this current may cause protein denaturation at the surface of the tissue. To our knowledge, however, no studies to date have describes about changes in proteins after TUR-P and sample preparation for this analysis with prostate tissues.

SYM-A7

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Education

2008.09 - 2012.08	Ph.D.	Department of Life Sciences, Pohang University of Science and Technology (POSTECH)
2005.03 - 2007.02	M.S.	Department of Life Sciences, Gwangju Institute of Science and Technology (GIST)
1998.03 - 2005.02	B.S.	Department of Genetic Engineering (Major in Genetic Engineering) Kyungpook National University

Professional Experience

2020.03 - Present	Principal Researcher	Korea Brain Research Institute
2019.12 - Present	Group Leader	Neurodegenerative Diseases Research Group, Korea Brain Research Institute
2016.08 - 2020.02	Senior Researcher	Korea Brain Research Institute
2014.12 - 2016.06	Senior Researcher	MOGAM Institute for Biomedical Research

Academic Society

2020 - Present	Editor-in Chief	Editorial committee, The Korean Human Proteome Organization(KHIPO)
2022 - 2023	Editor-in Chief	Local Organizing Committee, The Human Proteome Organization (HUPO) World Congress 2023

Publications

1. Yeo, Y-G., Park, J., Kim, Y., Rah, J-C., Shin, C-H., Oh, S-J., Jang, J-H., Lee, Y., Yoon, J.H., Oh, Y- S. (2024) "Retinoic Acid Modulation of Granule Cell Activity and Spatial Discrimination in the Adult Hippocampus" Frontiers in Cellular Neuroscience accepted

2. Yoon, J.H.*,&, Lee, D.*, Lee, C.*, Cho, E.*, Lee, S., Cazenave-Gassiot A., Kim, K., Chae, S., Dennis EA., Suh, P-G., (2024) "Paradigm shift required for translational research on the brain." Experimental & Molecular Medicine in press (1st & corresponding author)

3. Lee, S., Jang, K-I., Lee, H., Jo, Y.S., Kwon, D., Park, G., Bae, S., Kwon, Y.W., Jang, J-H., Oh, Y-S., Lee, C., Yoon, J.H. (2024) "Multi-proteomic analyses of 5xFAD mice reveal new molecular signatures for early-stage Alzheimer's disease." Aging Cell Mar 4:e14137 (corresponding author)

4. Lee, H., Cho, S., Kim, M-J., Park, Y.J., Cho, E., Jo, Y.S., Kim, Y-S., Woo, S-H., Lee, Y-S., Suh, B-C., Yoon, J.H., Go, Y., Lee, I-K., Seo, J. (2023) "ApoE4-dependent lysosomal cholesterol accumulation impairs mitochondrial homeostasis and oxidative phosphorylation in human astrocytes." Cell Reports Oct 31;42(10):113183

SYM-A7-2

Application of Integrative Proteomics for Understanding Neurodegenerative Diseases

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The application of a proteomics approach provides diverse insights to solve biological questions. This method can make it possible to understand diseases that have been relatively insufficient. Diagnostics of Alzheimer's disease (AD) are still difficult by clinically available methods such as clinical exams and amyloid plaque imaging. The situation originated from insufficient biological understanding, which cannot provide notable molecular mechanisms to explain the progression of AD. To find new molecular signatures that can explain the molecular pathology of AD, I applied integrative proteomics technology as a platform technology to profile multi-proteomes of age-dependent AD model mice. According to subsequent multi-dimensional experiments, including a machine-learning approach, I found new molecular signatures and diagnostic biomarkers for the early stage of AD. Meanwhile, I also found new drug target candidates for cancers that enable new treatment methods for drug resistance using the platform technology. I will introduce those results and also briefly introduce the brain lipidomics project.

SYM-A7

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Education

2010	Ph.D.	Seoul National University, Korea
2006	M.S.	Seoul National University, Korea
2000	B.S.	Yonsei University, Korea

Professional Experience

2023 - Present	Associated Professor	University of Ulsan
2015 - Present	Associated Professor	Asan Medical Center
2015	Post doctoral Researcher	Northwestern University, IL, USA
2013	Senior Researcher	Institute of Medical Research, SNU

Academic Society

2021 - Present	Director of Planning	Korean Human Proteome Organization(K-HUPO)
2022 - 2023	Secretary General	2023 HUPO Busan World Congress

Publications

1. Generating Detailed Spectral Libraries for Canine Proteomes Obtained from Serum and Urine, Scientific Data, 2023 (Corresponding, IF:8.5)

2. Magnetic transferrin nanoparticles (MTNs) assay as a novel isolation approach for exosomal biomarkers in neurological diseases, Biomaterial Research, 2023 (Corresponding, IF:11.3)

3. Advanced 3D dynamic culture system with transforming growth factor-β3 enhances production of potent extracellular vesicles with modified protein cargoes via upregulation of TGF-β signaling, Journal of Advanced Research, 2023 (Corresponding, IF:12.88)

4. Identification of a novel therapeutic target underlying atypical manifestation of Gaucher disease, Clinical and translational medicine (Corresponding, IF:10.6)

5. Discovery of urine biomarkers for lupus nephritis via quantitative and comparative proteome analysis, Clinical and translational medicine (Corresponding, IF:10.6)

SYM-A7-3

Multi modal proteome platform for biomarker and new drug target discovery

Jiyoung Yu[1], Kyunggon Kim[1, 2, 3]

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[2]Department of Digital Medicine, Brain Korea 21 plus, University of Ulsan, Collage of Medicine, South Korea
[3]Department of Convergence Medicine, Asan Medical Center, South Korea

Combintion of liquid chromatography technology and state-of-art mass spectrometry has driven the omics-based translation resarch. In era of quantitative proteome, data independent acquisition (DIA) have been applied on quantitative proteomics not only for biomarker discovery but also for drug target discovery. Compare to DDA approach, there are many advantages on DIA manner. In a DIA method, precursor ions can be isolated into defined isolation windows of m/z and fragmented at the same time. All fragmented ions in each window area can be analyzed by a high-resolution mass spectrometer such as Time of Flight MS or Orbitrap MS. DIA proteomics analysis is characterized by a broad protein coverage, high reproducibility, and accuracy, and its combination with advances in other techniques such as sample preparation and computational data analysis could lead to further improvements in biomarker study. In this lecture, principle of DIA will be introduced and characteristics of DIA will be discussed. And some pilot translational study using DIA/DDA platform using clinical sample will be introduced as an example of biomarker discovery.

SYM-B1

Disease Models

SYM-B1

Disease Models

6.25 (Tue) 14:00 - 15:15

Chair: Byeonggyu Kim / Institute for Basic Science (IBS)

SYM-B1-1 6.25 (Tue) 14:00 - 14:25

Acquired epithelial WNT secretion drives niche independence of developing gastric cancer

Bon-Kyoung Koo
Institute for Basic Science (IBS)

SYM-B1-2 6.25 (Tue) 14:25 - 14:50

Establishment, characterization and applications of patient-derived organoids and biobanking

Ja-Lok Ku
Seoul National University

SYM-B1-3 6.25 (Tue) 14:50 - 15:15

Emergent Multi-Cellular Engineered Microphysiological Systems

Seok Chung
Korea University

SYM-B1

Bon-Kyoung Koo, PhD

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Education

2002 - 2006	Ph.D.	Div. of Molecular Life Science, POSTECH
2000 - 2002	M.S.	Div. of Molecular Life Science., POSTECH
1996 - 2000	B.S.	Dept. of Life Science, POSTECH

Professional Experience

2022 - Present	Editorial Board Member	Experimental and Molecular Medicine (EMM)
2019 - Presen	Academic Editor (Editorial Board Member)	PLOS Biology
2021 - 2021	Scientific Consultan	Hubrecht Organoid Technology (HUB)
2020 - 2021	Adj. Professor	Gwangju Institute of Science and Technology (GIST), South Korea

Publications

1. . Lee JH, Kim S, Han S, Min J, Caldwell B, Bamford AD, Rocha ASB, Park J, Lee S, Wu SS, Lee H, Fink J, Pilat-Carotta S, Kim J, Josserand M, Szep-Bakonyi R, An Y, Ju YS, Philpott A, Simons BD, Stange DE, Choi E, Koo BK, Kim JK. p57Kip2 imposes the reserve stem cell state of gastric chief cells. Cell Stem Cell. 2022 May 5;29(5):826-839.e9. doi: 10.1016/j.stem.2022.04.001.

2. Kim J, Koo BK, Clevers H. Organoid Studies in COVID-19 Research. Int J Stem Cells. 2022 Feb 28;15(1):3-13. doi: 10.15283/ijsc21251.

3. Belenguer G, Mastrogiovanni G, Pacini C, Hall Z, Dowbaj AM, Arnes-Benito R, Sljukic A, Prior N, Kakava S, Bradshaw CR, Davies S, Vacca M, Saeb-Parsy K, Koo BK, Huch M. RNF43/ZNRF.3 loss predisposes to hepatocellular-carcinoma by impairing liver regeneration and altering the liver lipid metabolic ground-state. Nat Commun. 2022 Jan 17;13(1):334. doi: 10.1038/s41467-021-7923-z.

4. Lu C, Lin X, Yamashita J, Xi R, Zhou M, Zhang YV, Wang H, Margolskee RF, Koo BK, Clevers H, Matsumoto I, Jiang P. RNF43/ZNRF3 negatively regulates taste tissue homeostasis and positively regulates dorsal lingual epithelial tissue homeostasis. Stem Cell Reports. 2022 Feb 8;17(2):369-383. doi: 10.1016/j.stemcr.2021.12.002. Epub 2022 Jan 6.

5. Kim SC, Park JW, Seo HY, Kim M, Park JH, Kim GH, Lee JO, Shin YK, Bae JM, Koo BK, Jeong SY, Ku JL. Multifocal Organoid Capturing of Colon Cancer Reveals Pervasive Intratumoral Heterogenous Drug Responses. Adv Sci (Weinh). 2022 Feb;9(5):e2103360. doi: 10.1002/advs.202103360. Epub 2021 Dec 17.

6. **Koo BK**. Methods in organoids: a model that goes beyond our imagination. ***Exp Mol Med***. 2021 Oct;53(10):1449-1450. doi: 10.1038/s12276-021-00685-w. Epub 2021 Oct 18.

SYM-B1-1

Acquired epithelial WNT secretion drives niche independence of developing gastric cancer

Bon-Kyoung Koo

Center for Genome Engineering, Institute for Basic Science, Daejeon, Korea

Recent studies have shed light on the signaling pathways required for gastric tissue maintenance and how aberrations in these key pathways lead to gastric cancer development. Although it has been shown that the WNT pathway is important for gastric epithelial homeostasis, the identity and source of the responsible canonical WNT ligands remain unknown. Furthermore, it is unclear how gastric cancer acquires WNT niche independence -an important early step in tumorigenesis. Using human and mouse gastric organoids and in vivo mouse models, we found that mesenchymal WNT2B and WNT7B maintain gastric epithelium in homeostasis. Next, mouse genetic studies and single-cell multi-omics analyses revealed that activation of MAPK signaling induces secretion of WNT7B in the epithelium itself. We further confirmed that in human gastric cancer, MAPK pathway activation through HER2 overexpression or copy number gains of WNT2 confers WNT independence.Importantly, the epithelium-intrinsic WNT expression could be therapeutically inhibited. Taken together, our results reveal that normal gastric epithelial turnover relies on WNT ligands secreted by niche mesenchymal cells, while transformation involves acquisition of a WNT secretory phenotype in the epithelium - representing a potential target for therapeutic interventions.

SYM-B1

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Education

1998	Ph.D.	Seoul National University (Veterinary pathology)
1994	M.S.	Seoul National University (Veterinary pathology)
1992	B.S & D.V.M.	Seoul National University

Professional Experience

2021 - Present	PI of Central Bank of Cell Culture Cluster	NRF of Korea
2001 - Present	Professor	Seoul National University College of Medicine
2008 - Present	Executive Vice Director	Cancer Research Institute, Seoul National University College of Medicine
2002 - 2020	PI of Korean Cell Line Bank	NRF of Korea

Publications

1. Kim SC, Seo HY, Lee JO, Maeng JE, Shin YK, Lee SH, Jang JY, **Ku JL**. Establishment, characterization, and biobanking of 36 pancreatic cancer organoids: prediction of metastasis in resectable pancreatic cancer. Cell Oncol (Dordr). 2024 Apr 15. doi: 10.1007/s13402-024-00939-5. Online ahead of print.

2. Kim SC, Cho YE, Shin YK, Yu HJ, Chowdhury T, Kim S, Yi KS, Choi CH, Cha SH, Park CK, **Ku JL**. Patient-derived glioblastoma cell lines with conserved genome profiles of the original tissue. Sci Data. 2023 Jul 12;10(1):448

3. Jeong N, Kim SC, Park JW, Park SG, Nam KH, Lee JO, Shin YK, Bae JM, Jeong SY, Kim MJ, **Ku JL**. Multifocal organoids reveal clonal associations between synchronous intestinal tumors with pervasive heterogeneous drug responses. NPJ Genom Med. 2022 Jul 19;7(1):42

4. Lee JH, Kim H, Lee SH, **Ku JL**, Chun JW, Seo HY, Kim SC, Paik WH, Ryu JK, Lee SK, Lowy AM, Kim YT. Establishment of Patient-Derived Pancreatic Cancer Organoids from Endoscopic Ultrasound-Guided Fine-Needle Aspiration Biopsies. Gut Liver. 2022 Jul 15;16(4):625-636 (corresponding author)

5. Song MH, Park JW, Kim MJ, Shin YK, Kim SC, Jeong SY, **Ku JL**. Colon cancer organoids using monoclonal organoids established in four different lesions of one cancer patient reveal tumor heterogeneity and different real-time responsiveness to anti-cancer drugs. Biomed Pharmacother. 2022 Jun 9;152:113260.

6. Seo HY, Kim SC, Roh WL, Shin YK, Kim S, Kim DW, Kim TM, **Ku JL**. Culture and multiomic analysis of lung cancer patient-derived pleural effusions revealed distinct druggable molecular types. Sci Rep. 2022 Apr 15;12(1):6345.

7. Kim SC, Park JW, Seo HY, Kim M, Park JH, Kim GH, Lee JO, Shin YK, Bae JM, Koo BK, Jeong SY, **Ku JL**. Multifocal Organoid Capturing of Colon Cancer Reveals Pervasive Intratumoral Heterogenous Drug Responses. Adv Sci (Weinh). 2022 Feb;9(5):e2103360.

SYM-B1-2

Establishment, characterization and application of patient-derived organoids and biobanking

Ja-Lok Ku

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An organoid is a miniaturized and simplified version of an organ produced in vitro in three dimensions that shows realistic micro-anatomy. Organoids as well as cell lines are important because they provide a consistent renewable source of cell material for study. Organoids like as cell lines can be also established from original tumor tissues, metastatic tumor tissues, PDX, ascites, pleural effusions or circulating tumor cells of cancer patients. Cancer cells that are grown in organoid culture system retain cell-cell and cell-matrix interactions that more closely resemble those of the original tumor compared with cells grown in two dimensions on plastic. Utilizing organoid culture system, high-throughput drug screening (HTS) from patient-derived tumor samples offers a unique opportunity to identify effective cancer drugs for individual patients. Over 2,600 human normal and cancer organoids derived from colorectal, pancreatic, breast, gastric, ovarian, prostate, lung, cervical cancers, hepatocellular and renal cell carcinomas have been established since 2016 in our laboratory. The characteristics of these human cancer organoids have been analyzed (DNA fingerprinting analysis, mycoplasma contamination test, and NGS (WES and RNA seq.) for detections of mutations and expressions of genes). We have been also conducting high throughput anticancer drug screening assay on these cancer organoids. Organoids can be maintained through passage and preserve genetic stability by bio-banking. The organoid biobank will be made publicly available and thus can serve as a resource for others. Some of human organoids established in our laboratory are currently available through the Korean Cell Line Bank or Korean Organoid Biobank(https://cellbank.snu.ac.kr, https://organoid.snu.ac.kr, www.organoid.kr)

SYM-B1

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Education

1992.3 - 1996.2	B.S.	Dept Mechanical Design & Production Eng. Seoul National University
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Professional Experience

2005.6 - 2009.2	Postdoc Associate	Massachusetts Institute of Technology
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2022.9 -	Professor	Dept. of Future Science & Technology Business
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Academic Society

2023.1 -	Member	The National Academy of Engineering of Korea

Publications

1. Ahn J, Ohk K, Won J, Choi D-H, Jung YH, Yang JH, Jun Y, Kim J-A*, Chung S*, Lee S-H. Modeling of three-dimensional innervated epidermal like-layer in a microfluidic chip-based coculture system. Nat Commun. 2023 Apr; 14(1): 1488.

2. Kim H, Sa JK, Kim J, Cho HJ, Oh HJ, Choi D-H, Kang S-H, Jeong DE, Nam D-H, Lee H, Lee HW*, Chung S*. Recapitulated Crosstalk between Cerebral Metastatic Lung Cancer Cells and Brain Perivascular Tumor Microenvironment in a Microfluidic Co-Culture Chip. Advanced Science. 2022 Aug; 9(22): 2201785.

3.Lee YA, Cho S, Choi S, Kwon O-C, Yoon SM, Kim SJ, Park K-C, Chung S*, Moon M-W*. Slippery, Water-Infused Membrane with Grooved Nanotrichomes for Lubricating-Induced Oil Repellency. Advanced Science. 2022 May; 9(13): 2103950.

4.Jun Y, Lee JS, Choi S, Yang JH, Sander M, Chung S*, Lee SH. In vivo–mimicking microfluidic perfusion culture of pancreatic islet spheroids. Science Advances. 2019; 5 (11): eaax4520.

SYM-B1-3

Emergent Multi-Cellular Engineered Microphysiological Systems

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A simple microfluidic platform has been created for 3D and heterotypic cell culture, which involves the use of hydrogel within microfluidic channels. The innovative platform utilizes distinct biochemical and biophysical stimuli to be administered to several cell types that are interacting with each other, hence replicating various characteristics of tissues. There are tools available that allow for accurate control of microflows and chemical gradients, as well as high-resolution real-time imaging for observing the spatio-temporal activity of individual cells. These tools also enable the study of interactions and communications between cells, as well as interactions between cells and their surrounding matrix. The assay is applicable for studying the intricate and diverse characteristics of tissues during disease states, such as the advancement of cancer. This includes examining aspects like survival, proliferation, and collective migration within precisely regulated cancer microenvironments. Additionally, the assay can be used to investigate cancer growth and spread, interactions between cancer cells and immune cells, as well as localized morphogenesis. Applications also encompass the investigation of hitherto undiscovered aspects of treatment resistance due to microenvironmental factors, offering novel perspectives on how microenvironmental factors emerge as cancer patient-specific attributes.

SYM-B2

Proteogenomics in translation

SYM-B2

Proteogenomics in translation

6.25 (Tue) 15:30 - 16:45

Chair: Sangkyu Lee / Sungkyunkwan University

SYM-B2-1 6.25 (Tue) 15:30 - 15:55

Proteogenomic approaches in non-small-cell lung cancer for precision medicine

Kwang Pyo Kim
Kyunghee University

SYM-B2-2 6.25 (Tue) 15:55 - 16:20

Integrated proteogenomic characterization of glioblastoma evolution

Kyung-Hee Kim
National Cancer Center (NCC)

SYM-B2-3 6.25 (Tue) 16:20 - 16:45

Holotomography and artificial intelligence: label-free 3D imaging, classification, and inference of live cells, tissues, and organoids

YongKeun Park
Korea Advanced Institute of Science and Technology (KAIST)

SYM-B2

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Education

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1990.03-1992.02	M.S	Seoul National University
1997.09-2002.02	Ph.D	Univ. of Illinois at Chicago

Professional Experience

2004.03-2013.08	Professor	Konkuk University
2013.08-	Professor	Kyung Hee University

Publications

1. Le HT, Nguyen DPL, Jung GT, Kim E, Yang SH, Lee SM, Lee EA, Jung W, Kim TW, Kim KP., Enrichment and MALDI-TOF MS Analysis of Phosphoinositides in Brain Tissue. J Am Soc Mass Spectrom. 2024 Jun 5;35(6):1069-1075.

2. Shin J, Park J, Jeong J, Lam JH, Qiu X, Wu D, Kim K, Lee JY, Robinson CV, Hyun J, Katritch V, Kim KP, Cho Y.. Constitutive activation mechanism of a class C GPCR. Nat Struct Mol Biol. 2024 Apr;31(4):678-687.

3. Lim JM, Anwar MA, Han HS, Koo SH, Kim KP., CREB-Regulated Transcriptional Coactivator 2 Proteome Landscape is Modulated by SREBF1. Mol Cell Proteomics. 2023 Oct;22(10):100637.

SYM-B2-1

Proteogenomic approaches in non-small-cell lung cancer for precision medicine

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1732 Deokyoung-daero, Yongin, Korea

Non-small cell lung cancer (NSCLC) can be histologically divided into lung adenocarcinoma (LUAD) and lung squamous cell carcinoma (LSCC), though some tumors display ambiguous characteristics. Other pathophysiological and microenvironmental factors often play a significant role. In our study, we performed integrative multiomics analyses on a Korean NSCLC cohort alongside previous studies. This revealed five molecular subtypes, including a novel NSCLC subtype characterized by upregulated PI3K-Akt pathway activity, associated with high metastasis rates and poor survival outcomes across NSCLC histologies. We developed a method to pinpoint driver genomic alterations, underscoring the crucial role of multiomics in tumor classification, diagnostic accuracy, and prognosis assessment. We will also explore the benefits and scientific significance of multi-omics integration in cancer research.

SYM-B2

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Education

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2004 - 2007	M.S. Molecular Medicine	Seoul National University, Seoul, Korea
2008 - 2013	Ph.D. Tumor Biology	Seoul National University, Seoul, Korea

Professional Experience

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2023 - Present	Associate Professor	Cancer Biomedical Science, Graduate School of Cancer Science and Policy, National Cancer Center, Korea

Publications

2024 Integrated proteogenomic characterization of glioblastoma evolution: CANCER CELL. 42(3):358~377.e8 (50.3)

2024 Fam20C Kinase as A Key Regulator of Bevacizumab Resistance in Mesenchymal Glioblastoma: ADVANCED THERAPEUTICS. 7(2):2300309~ (4.6)

2023 Oncogenic KRAS mutation confers chemoresistance by upregulating SIRT1 in non-small cell lung cancer: EXPERIMENTAL AND MOLECULAR MEDICINE. 55(10):2220~2237 (12.8)

2023 Nivolumab after Induction Chemotherapy in Previously Treated Non-Small-Cell Lung Cancer Patients with Low PD-L1 Expression: CANCERS. 15(18):4460~ (5.2)

2023 Protection of c-Fos from autophagic degradation by PRMT1-mediated methylation fosters gastric tumorigenesis: INTERNATIONAL JOURNAL OF BIOLOGICAL SCIENCES. 19(12):3640~3660 (9.2)

2023 Refining classification of cholangiocarcinoma subtypes via proteogenomic integration reveals new therapeutic prospects: GASTROENTEROLOGY. 164(7):1293-1309 (29.4)

2022 The EEF1AKMT3/MAP2K7/TP53 axis suppresses tumor invasiveness and metastasis in gastric cancer: CANCER LETTERS. 544:215803 (9.756)

2022 Different Metabolomic and Proteomic Profiles of Cerebrospinal Fluid in Ventricular and Lumbar Compartments in Relation to Leptomeningeal Metastases: METABOLITES. 12(1):80 (5.581)

2021 Experimental Assessment of Leptomeningeal Metastasis Diagnosis in Medulloblastoma Using Cerebrospinal Fluid Metabolomic Profiles: METABOLITES. 11(12):851 (4.932)

SYM-B2-2

Integrated proteogenomic characterization of glioblastoma evolution

Kyung-Hee Kim, Simona Migliozzi, Harim Koo, Jun-Hee Hong, Seung Min Park, Sooheon Kim, Hyung Joon Kwon, Seokjun Ha, Luciano Garofano, Young Taek Oh, Fulvio D'Angelo, Chan Il Kim, Seongsoo Kim, Ji Yoon Lee, Jiwon Kim, Jisoo Hong, Eun-Hae Jang, Bertrand Mathon, Anna-Luisa Di Stefano, Franck Bielle, Alice Laurenge, Alexey I. Nesvizhskii, Eun-Mi Hur, Jinlong Yin, Bingyang Shi, Youngwook Kim,1 Kyung-Sub Moon, Jeong Taik Kwon, Shin Heon Lee, Seung Hoon Lee, Ho Shin Gwak, Anna Lasorella, Heon Yoo,1 Marc Sanson, Jason K. Sa, Chul-Kee Park, Do-Hyun Nam, Antonio Iavarone, and Jong Bae Park

National Cancer Center

The evolutionary trajectory of glioblastoma (GBM) is a multifaceted biological process that extends beyond genetic alterations alone. Here, we perform an integrative proteogenomic analysis of 123 longitudinal glioblastoma pairs and identify a highly proliferative cellular state at diagnosis and replacement by activation of neuronal transition and synaptogenic pathways in recurrent tumors. Proteomic and phosphoproteomic analyses reveal that the molecular transition to neuronal state at recurrence is marked by post-translational activation of the wingless-related integration site (WNT)/ planar cell polarity (PCP) signaling pathway and BRAF protein kinase. Consistently, multi-omic analysis of patient-derived xenograft (PDX) models mirror similar patterns of evolutionary trajectory. Inhibition of B-raf proto-oncogene (BRAF) kinase impairs both neuronal transition and migration capability of recurrent tumor cells, phenotypic hallmarks of post-therapy progression. Combinatorial treatment of temozolomide (TMZ) with BRAF inhibitor, vemurafenib, significantly extends the survival of PDX models. This study provides comprehensive insights into the biological mechanisms of glioblastoma evolution and treatment resistance, highlighting promising therapeutic strategies for clinical intervention.

SYM-B2

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Education

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Professional Experience

2010.06-current	Professor	KAIST

Publications

1. Y. Park, C. Depeursinge and G. Popescu, Nature Photonics 12 (10), 578-589 (2018)

2. Y. Baek and Y. Park, Nature Photonics 15 (5), 354-360 (2021)

3. S. Shin and Y. Park, Nature Materials 21, 317-324 (2022)

4. Y. Jo et al., Nature Cell Biology 23, 1329-1337 (2022)

5. J. Park et al., Nature Methods, 20, pages1645–1660 (2023)

6. G. Kim et al., Nature Methods Review Primers, accepted for publication

SYM-B2-3

Holotomography and artificial intelligence: label-free 3D imaging, classification, and inference of live cells, tissues, and organoids

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Holotomography (HT) is a powerful label-free imaging technique that enables high-resolution, three-dimensional quantitative phase imaging (QPI) of live cells and organoids through the use of refractive index (RI) distributions as intrinsic imaging contras. Similar to X-ray computed tomography, HT acquires multiple two-dimensional holograms of a sample at various illumination angles, from which a 3D RI distribution of the sample is reconstructed by inversely solving the wave equation.

By combining label-free and quantitative 3D imaging capabilities of HT with machine learning approaches, there is potential to provide synergistic capabilities in bioimaging and clinical diagnosis. In this presentation, we will discuss the potential benefits and challenges of combining QPI and artificial intelligence (AI) for various aspects of imaging and analysis, including segmentation, classification, and imaging inference. We will also highlight recent advances in this field and provide insights on future research directions. Overall, the combination of QPI and AI holds great promise for advancing biomedical imaging and diagnostics.

SYM-B3

PTMs in diseases

SYM-B3

PTMs in diseases

6.26 (Wed) 10:30 - 11:45

Chair: Young Hye Kim / Korea Basic Science Institute (KBSI)

SYM-B3-1 6.26 (Wed) 10:30 - 10:55

Distinguishing N-Terminal Methylation from Near-isobaric Modifications by Statistical Analysis of Mass Error Distributions of Fragment Ions

Cheolju Lee
Korea Institute of Science and Technology (KIST)

SYM-B3-2 6.26 (Wed) 10:55 - 11:20

Lysine acetylation and its regulatory enzymes in Cyanobacteria

Feng Ge
Chinese Academy of Sciences

SYM-B3-3 6.26 (Wed) 11:20 - 11:45

Protein language: post-translational modifications (PTMs) talking to each other in cancer

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SYM-B3

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Education

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Professional Experience

2022.09 - Present	Tenured Fellow	Korea Institute of Science and Technology (KIST)
2016.02 - 2021.02	Adjunct Professor	KHU-KIST Department of Converging Science and Technology, Kyung Hee University
2014.04 - 2017.03	Director	Center for Theragnosis, Biomedical Research Institute, KIST
2005.03 - Present	Associate Professor & Professor	KIST school, University of Science and Technology (UST)
2002.12 - Present	Senior/Principal Researcher	Korea Institute of Science and Technology (KIST)
2001.12 - 2002.11	Senior Researcher	KRIBB
2000.01 - 2001.11	Postdoctoral research fellow	Department of Biochemistry, Molecular Biology and Cell Biology, Northwestern University, Illinois, USA
1997.09 - 1999.11	Postdoctoral research fellow	Korea Research Institute of Bioscience and Biotechnology (KRIBB)

Publications

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SYM-B3-1

Distinguishing N-Terminal Methylation from Near-isobaric Modifications by Statistical Analysis of Mass Error Distributions of Fragment Ions

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α-N-terminal methylation is an understudied post-translational modification with presumed functions involving protein-protein and/or protein-DNA interaction. The covalent addition of mono-, di-, trimethyl groups to free α-amino group has proven to be difficult to profile globally due to trace endogenous amount and interference from near-isobaric modifications such as Nt-acetylation, even after N-terminome enrichment. We assume that in each MS2 spectrum b-fragments will have a different mass error distribution compared to y fragments if the spectrum is falsely assigned to near-isobaric Nt-modification, and exploit this statistically to correct the Nt-modification, a procedure we name as mass error test (MET). We confirmed that MET worked well by manual inspection on chemically methylated BSA peptides. MET was further confirmed by comparing physiochemical properties between Nt-methylation and Nt-acetylation in complex samples. We apply MET to potentially Nt-methylated spectra from repurposed dataset and assign correct Nt-modification without further validation experiment. This indicates that MET is a useful tool for detection Nt-methylated proteins in complex proteomes.

SYM-B3

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Education

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Professional Experience

2010.08 - Present	Professor	Institute of Hydrobiology, Chinese Academy of Sciences, China
2009.07 - 2010.08	Visiting Scholar	Nagasaki University, Nagasaki, Japan
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1997.09 - 2000.07	Assistant Professor	University of Science and Technology of China, Hefei, China

Academic Society

2012.09 - Present	Board Member	China Human Proteome Organization (CNHUPO)
2010.08 - 2015.08	Board Member	The Chinese Society of Mass spectrometry
2010.09 - Present	Associated Editor	Current Proteomics

Publications

2024

1. Li Q, Lin J, Ma H, Yuan L, Liu X, Xiong J, Miao W, Yang M, Ge F*. Identification and Functional Analysis of Lysine 2-Hydroxyisobutyrylation in Cyanobacteria. J Proteome Res. 2024 Apr 2. doi: 10.1021/acs.jproteome.3c00843.

2. Liu X, Cai F, Zhang Y, Luo X, Yuan L, Ma H, Yang M, Ge F*. Interactome Analysis of ClpX Reveals Its Regulatory Role in Metabolism and Photosynthesis in Cyanobacteria. J Proteome Res. 2024 Apr 5;23(4):1174-1187.

2023

1. Cao G, Lin X, Ling M, Lin J, Zhang Q, Jia K, Chen B, Wei W, Wang M, Jia S, Yang M, Ge F*. cKMT1 is a New Lysine Methyltransferase That Methylates the Ferredoxin-NADP(+) Oxidoreductase and Regulates Energy Transfer in Cyanobacteria. Mol Cell Proteomics. 2023 Feb 28;22(4):100521.

2. Wang Y, Yang M, Ge F, Jiang B, Hu R, Zhou X, Yang Y, Liu M. Lysine Succinylation of VBS Contributes to Sclerotia Development and Aflatoxin Biosynthesis in Aspergillus flavus. Mol Cell Proteomics. 2023 Feb;22(2):100490.

SYM-B3-2

Lysine acetylation and its regulatory enzymes in Cyanobacteria

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Lysine acetylation is a conserved regulatory posttranslational protein modification that is performed by lysine acetyltransferases (KATs). By catalyzing the transfer of acetyl groups to substrate proteins, KATs play critical regulatory roles in all domains of life; however, no KATs have yet been identified in cyanobacteria. Here, we tested all predicted KATs in the cyanobacterium Synechococcus sp. PCC 7002 (Syn7002) and demonstrated that A1596, which we named cyanobacterial Gcn5-related N-acetyltransferase (cGNAT2), can catalyze lysine acetylation in vivo and in vitro. Eight amino acid residues were identified as the key residues in the putative active site of cGNAT2, as indicated by structural simulation and site-directed mutagenesis. The loss of cGNAT2 altered both growth and photosynthetic electron transport in Syn7002. In addition, quantitative analysis of the lysine acetylome identified 548 endogenous substrates of cGNAT2 in Syn7002. We further demonstrated that cGNAT2 can acetylate NAD(P)H dehydrogenase J (NdhJ) in vivo and in vitro, with the inability to acetylate K89 residues, thus decreasing NdhJ activity and affecting both growth and electron transport in Syn7002. In summary, this study identified a KAT in cyanobacteria and revealed that cGNAT2 regulates growth and photosynthesis in Syn7002 through an acetylation-mediated mechanism.

Key words: Lysine acetylation, lysine acetyltransferases (KATs), Cyanobacteria, mass spectrometry, photosynthesis

SYM-B3

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Professional Experience

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2020.03 - 2024.02	The Chief Professor	Biochemistry Department, Chungnam National University College of Medicine
2015.09 - 2020.08	Assistant Professor	Chungnam National University College of Medicine
2012.07 - 2015.08	Postdoctoral Associate	Sanford Burnham Prebys Medical Discovery Institute

Publications

1. Kang, J. A., Kim, Y. J., Jang, K. Y., Moon, H. W., Lee, H., Lee. S., Song, H. K., Cho, S. W., Yoo, Y. S., Han, H. G., Kim, M-J., Chung, M. J., Choi, C. Y., Lee, C., Chung, C., Hur, G. M., Kim, Y-S., and #Jeon, Y. J. (2024) SIRT1 ISGylation accelerates tumor progression by unleashing SIRT1 from the inactive state to promote its deacetylase activity. Exp. Mol. Med. 56, 656-673 [IF: 12.8]

2. Kang, J. A., Kim, Y. J., and #Jeon, Y. J. (2022) The Diverse Repertoire of ISG15: More Intricate Than Initially Thought. Exp. Mol. Med. 54, 1779-1792 [IF: 12.8]

3. *Jeon, Y. J., Khelifa, S., Ratnikov, B., Scott, D. A., Feng, Y., Parisi, F., Ruller, C., Lau, E., Kim, H., Brill, L. M., Jiang, T., Rimm, D., Cardiff, R., Mills, G., Smith, J., Osterman, A. L., Kluger, Y., and Ronai, Z. A. (2015) Regulation of glutamine carrier proteins by RNF5 determines breast cancer response to ER stress-inducing chemotherapies. Cancer Cell 27, 354-369 [IF: 50.3] (Highlighted in Previews: Moses, M. A and Neckers, L. (2015) The GLU that holds cancer together: Targeting glutamine transporters in breast cancer. Cancer Cell 27, 317-319)

4. Park, J. H., Lee, S. W., Yang, S. W., Yoo, H. M., Park, J. M., Seong, M. W., Ka, S. H., Oh, K. H., #Jeon, Y. J., and Chung, C. H. (2014) Modification of DBC1 by SUMO2/3 is crucial for p53- mediated apoptosis in response to DNA damage. Nature Commun. 5:5483, 1-12 [IF: 16.6]

5. Yoo, H. M., Kang, S. H., Kim, J. Y., Lee, J. E., Seong, M. W., Lee, S. W., Ka, S. H., Sou, Y., Komasu M., Tanaka K., Lee, S. T., Noh, D. Y., Baek, S. H., #Jeon, Y. J., and Chung, C. H. (2014) Modification of ASC1 by UFM1 is crucial for ERα transactivation and breast cancer development. Mol. \ Cell 56, 261-274 [IF: 16.0]

SYM-B3-3

Protein language: post-translational modifications (PTMs) talking to each other in cancer

Young Joo Jeon

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Eukaryotic proteomes are tremendously sophisticated by protein processing and diversity of post-translational modifications (PTMs). PTMs can occur very rapidly in cells and are highly dynamic to accommodate constantly changing signals in the cells. In addition to single regulatory PTMs, there are also PTMs that function in orchestrated manners. Regulation of proteins via PTMs by ubiquitin or ubiquitin-like proteins such as ISG15, SUMO, NEDD8, and UFM1 underlies a wide variety of cellular activities, involving protein stability, intracellular trafficking, cell cycle control, stress responses, signal transduction, and immune modulation. Moreover, deregulation of these PTM systems gives rise to numerous human diseases, including cancers, neurodegenerative diseases, and immune diseases. Recent suggestion that targeting of these PTMs can be efficacious in the treatment of human cancers drives attempts to modulate the activities of the components involved in the PTM pathways. Especially, understanding the mechanisms underlying tumor cell responsiveness to therapy might be expected to allow stratification of patients for personalized treatment. Here, I will present the intriguing roles of PTMs not only in the pathogenesis of cancer but also in the response to therapies for cancer, which could contribute to therapeutic intervention in cancer.

Keywords: Ubiquitin, ISG15, Post-translational modification (PTM), Cancer, Therapeutic efficacy

SYM-B4

Glycoproteomics and Glycomics

SYM-B4

Glycoproteomics and Glycomics

6.26 (Wed) 14:45 - 16:00

Chair: Heeyoun Hwang / Korea Basic Science Institute (KBSI)

SYM-B4-1 6.26 (Wed) 14:45 - 15:10

Glycoprotoemic and Glycomic analysis of haptoglobin: possible implication for the differential diagnosis of cancer

Miyako Nakano
Hiroshima University

SYM-B4-2 6.26 (Wed) 15:10 - 15:35

Glycoproteomic Insights into Neuropsychiatric Disorders

Hyun Joo An
Chungnam National University

SYM-B4-3 6.26 (Wed) 15:35-16:00

Magnetic-bead-based sample preparation for glycoproteomics and clinical sample application

Kazuki Nakajima
Gifu University

SYM-B4

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Education

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Professional Experience

2012 - Present	Associate Professor	Graduate School of Integrated Sciences for Life, Hiroshima University
2010 - 2012	Assistant Professor	Graduate School of Advanced Sciences of Matter, Hiroshima University
2008 - 2010	Research Fellow	Faculty of Sciences, Macquarie University (Sydney, Australia)
2004 - 2008	The 21st COE Project Researcher	Graduate School of Medicine, Osaka University (Osaka, Japan)

Publications

1. Exogenous l-fucose attenuates neuroinflammation induced by lipopolysaccharide. Xu X, Fukuda T, Takai J, Morii S, Sun Y, Liu J, Ohno S, Isaji T, Yamaguchi Y, Nakano M, Moriguchi T, Gu J. J Biol Chem. 2024 Jan;300(1):105513.

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SYM-B4-1

Glycoprotoemic and Glycomic analysis of haptoglobin: possible implication for the differential diagnosis of cancer

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Most serum proteins are glycosylated. Especially, fucosylation is an important event because it results in the formation of blood-type antigens and cancer-associated carbohydrate antigens. Previously, we reported that fucosylated N-glycans on haptoglobin (Hpt) in the sera of patients with pancreatic cancer were increased. Hpt protein consists of two α chains (α 1 or/and α2) and two β chains linked by a disulfide bond. Therefore, there are genetically three major Hpt phenotypes (Hpt α1- α1, Hpt α2- α1, Hpt α2- α2). The β chain is identical for all phenotypes, and has four N-glycan-binding sites (Asn184, Asn207, Asn211, Asn241). For structural determination of the N-glycans, Hpt was purified from sera of patients with various types of gastroenterological cancer (pancreatic, biliary, esophageal, stomach, colon), a non-gastroenterological cancer (prostate) and normal controls using anti-Hpt antibody. The site-specific analysis of N-glycans (= glycoproteomic analysis) and the linkage analysis of fucosylation (= glycomic analysis) were performed by LC(ODS)-ESI MS and LC(Graphitized Carbon)-ESI MS, respectively. The glycoproteomic analysis showed monofucosylated N-glycans were significantly increased at all glycosylation sites in all cancer samples. Moreover, difucosylated N-glycans were detected at Asn 184, Asn207 and Asn241 only in cancer samples. Remarkable differences in N-glycan structure among cancer types were not observed. The glycomic analysis showed Lewis-type fucosylated N-glycan was increased in gastroenterological cancer samples, but core-type fucosylated N-glycan was increased in prostate cancer samples. In metastatic prostate cancer, Lewis-type fucosylated N-glycan was also increased. In biliary tract cancer samples, only Lewis-type fucosylated N-glycan was increased in gallbladder cancer samples, but core-type fucosylated N-glycan was also increased in bile duct cancer samples. We found that the difference in the fucosylation type of Hpt can be used to distinguish between metastatic or non-metastatic in prostate cancer, and between bile duct cancer or gallbladder cancer in biliary tract cancer. Furthermore, we revealed that the Lewis-type fucose on Hpt N-glycan was not LewisA-type fucose recognized by the CA19-9 antibody, which is currently used as a tumor marker for gastroenterological cancers, but it was LewisX-type fucose. These results indicate that Hpt can be used as a tumor marker even in humans who do not genetically carry the gene of fucosyltransferase 3, which produces LewisA-type fucose. Next, we investigated whether Hpt can be used as a tumor marker in any Hpt phenotype. We are currently developing a method that allows Hpt N-glycans to be measured simply and quickly in hospitals.

SYM-B4

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Biography

Dr. Hyun Joo An is a professor at Chungnam National University (CNU) in the Graduate School of Analytical and Science and Technology. She is also director of the Asia-Pacific Glycomics Reference Site (AGRS), which develops and validates new analytical platforms for glycomic and glycoproteomic analysis in collaboration with government agencies and regional industry. She received her PhD from the University of California at Davis (United States) in 2003 and worked as an associate specialist and postdoctoral researcher at UC Davis. Dr. An returned to Korea and has been at CNU since 2011. Dr. An was also the co-founder of Glycometrix, Inc, an ovarian cancer diagnostic company based on the first glycomics patent for cancer. She is the editorial advisory board of Mass Spectrometry Reviews, Scientific Reports, Bioanalysis, and Journal of Analytical Science and Technology.

Dr. An's research focuses on bioanalytical mass spectrometry, with applications to glycomics, glycolipidomics, and glycoproteomics. She is developing mass spectrometry-based tools for biopharmaceutical characterization, cancer biomarker discovery, xenoplantation, and brain glycome. She has authored and co-authored more than 170 peer-reviewed publications on these subjects and holds 35 related patents.

SYM-B4-2

Glycoproteomic Insights into Neuropsychiatric Disorders

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Neuropsychiatric disorders significantly impact mental health and brain functionality, presenting substantial challenges to both individuals and society. Despite the relatively small glycan content in the brain, our most complex organ, subtle changes in glycosylation patterns can significantly influence the development of disorders such as depression and schizophrenia. While the link between glycosylation and these disorders is increasingly recognized, research in this area lags behind other diseases. This study explores glycosylation alterations in brain proteins through glycoproteomic analysis, using Wild-type (WT), plcβ1 knockout (a model for schizophrenia), and CVS-stressed (a model for depression) mice. We examined both micro-heterogeneity and macro-heterogeneity in glycosylation patterns of proteins such as the sodium/potassium-transporting ATPase subunit beta-2 (Atp1β2) and Thy-1 membrane glycoprotein (Thy1). Our findings show a decrease in high-mannose type glycopeptides in the Plcβ1 KO model, contrasted with an increase in core-fucosylated glycopeptides in the CVS-stressed model. Notably, we observed alterations in the high-mannose type glycan at specific glycosites on the Atp1β2 protein in the Plcβ1 KO model and changes in the glycan types at crucial glycosites in the CVS stressed model, highlighting the intricate nature of glycosylation. These variations can occur even with consistent protein expression, driven by genetic and environmental differences. Our research emphasizes the critical role of glycosylation patterns in understanding neurological disorders and identifying key proteins linked to brain diseases, potentially paving the way for innovative diagnostic and therapeutic strategies for neuropsychiatric disorders.

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[Keywords]

Neuropsychiatric disorders, Protein Glycosylation, Mass Spectrometry

SYM-B4

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Professional Experience

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2019.04 - 2012.12	Senior Assistant Professor	Center for Joint Research Facilities Support, Research Promotion and Support Headquarters, Fujita Health University
2016.04 - 2019.03	Senior Assistant Professor	Division of Clinical Research Promotion and Support Center for Research Promotion, Fujita Health University
2013.04 - 2016.04	Research Scientist	Lab for Molecular Membrane Neuroscience, Brain Science Institute, RIKEN

Publications

1. Iwamoto S, Kobayashi T, Hanamatsu H, Yokota I, Teranishi Y, Iwamoto A, Kitagawa M, Ashida S, Sakurai A, Matsuo S, Myokan Y, Sugimoto A, Ushioda R, Nagata K, Gotoh N, **Nakajima K**, Nishikaze T, Furukawa JI, Itano N. Tolerable glycometabolic stress boosts cancer cell resilience through altered N-glycosylation and Notch signaling activation, *Cell Death Dis*, 15(1):53, 2024.

2. Farshadyeganeh P, Nazim M, Zhang R, Ohkawara B, **Nakajima K**, Rahman MA, Nasrin F, Ito M, Takeda JI, Ohe K, Miyasaka Y, Ohno T, Masuda A, Ohno K. Splicing regulation of GFPT1 muscle-specific isoform and its roles in glucose metabolisms and neuromuscular junction, *iScience*, 26(10): 107746, 2023.

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Racial heterogeneity of IgA1 hinge-region O-glycoforms in patients with IgA nephropathy. *iScience.* 25(11):105223, 2022.

SYM-B4-3

Magnetic-bead-based sample preparation for glycoproteomics and clinical sample application

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Glycoproteomics has enormous potential for identifying personalized biomarkers for disease diagnosis. A rapid and streamlined workflow is essential for standardized processing in large-scale cohort analyses. To this end, we optimized a magnetic-bead-based sample preparation method and developed a fully automated sample preparation system. Human plasma, from which abundant proteins were depleted using an anti-immobilized column, was digested with trypsin/Lys-C on magnetic beads using the SP3 method. The remaining digests were directly added to the loading solution to remove non-glycopeptides; the glycopeptides were efficiently enriched through hydrophilic interaction chromatography under neutral conditions. Using LC/MS/MS, 2024 N-glycoforms from 141 glycoproteins were identified by Byonic. The results were described by the Progenesis software as a two-dimensional map showing the point with m/z and the retention time of each glycopeptide. The reproducibility of the method was evaluated as median coefficients of variation in intra-day and inter-day assays. Subsequently, the method was applied for disease diagnosis of patients with cancer. Several glycopeptides derived from a1-acid glycoproteins and a1-anti-chymotrypsin were significantly altered during disease progression and were clearly monitored by glycopeptide mapping.

In order to apply the method to large cohort analyses and under conditions with low sample input amounts, we explored the use of surfactants via LC-MS/MS that do not interfere with peptide analysis. Dodecyl-maltoside-assisted sample preparation effectively reduced protein and peptide loss in samples, and a significant improvement was observed in the recovery of digested glycopeptides from cerebrospinal fluid samples. Thus, the as-prepared automated platform enabled facile glycoproteomics analyses using multiple samples for biomarker discovery.

SYM-B5

Immunotherapeutics

SYM-B5

Immunotherapeutics

6.26 (Wed) 16:15 - 17:30

Chair: Min-Sik Kim / Daegu Gyeongbuk Institute of Science and Technology (DGIST)

SYM-B5-1 6.26 (Wed) 16:15 - 16:40

Harnessing knowledge of the tumor cell surface for immunotherapeutic design

Wei Wu
Agency for Science, Technology and Research(A*STAR)

SYM-B5-2 6.26 (Wed) 16:40 - 17:05

Logic gate-based combinatorial target discovery for CAR switches using AI and large-scale single-cell transcriptome DB

Joonha Kwon
National Cancer Center (NCC)

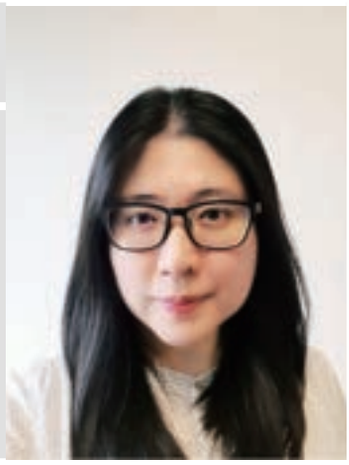
SYM-B5-3 6.26 (Wed) 17:05 - 17:30

T cell immunity to Epstein-Barr virus: From novel insight to therapeutic application

Il-Kyu Choi
Daegu Gyeongbuk Institute of Science and Technology (DGIST)

SYM-B5

Wei Wu, Ph.D.



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Professional Experience

2021.12 - Present	Tenured Associate Professor	Dept. Pharmaceutical Sciences, Fac. Science, Utrecht University, The Netherlands
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2024 - Present	Executive committee	HUPO Biology/Disease-driven Human Proteome Project (B/D-HPP)
2021 - Present	Council	World Human Proteome Organisation (HUPO)
2018 - Present	Executive Committee	Human Immuno-Peptidome Project (HIPP)

Publications

2024 PNAS. 2024 Mar 19;121(12):e2309902121.
2024 Cell. 2024 Feb 1;187(3):712-732.e38. [JCR Top 10%]
2024 Cell Stem Cell. 2024 Feb 1;31(2):227-243.e12. [JCR Top 10%]
2024 Cancer Cell. 2024 Feb 12;42(2):283-300.e8. [JCR Top 10%]
2024 Mol Cell Proteomics. 2024 Jan;23(1):100692. * corresponding author [JCR Top 10%]
2023 J. Extracell Ves. 2024 Jan;13(1):e12396. [JCR Top 10%]
2023 Mol Cell Proteomics. 2023 Dec 9:100692. * corresponding author [JCR Top 10%]
2023 Cancer Cell. 2023 Oct 9;41(10):1817-1828.e9. [JCR Top 10%]
2023 Commun Biol. 2023 Aug 1;6(1):800. * corresponding author [JCR Top 10%]
2023 Cells. 2023 Mar 30;12(7):1055. * corresponding author
2023 Mol Cell Proteomics. 2023 Jan;22(1):100455. [JCR Top 10%]
2022 PNAS. 2022 Nov 16;119(46):e2212057119. * corresponding author
2022 Cell Stem Cell. 2022 Sep 1;29(9):1333-1345.e6. [JCR Top 10%]
2022 J. Extracell Ves. 2022 Jul;11(8):e12245. * corresponding author [JCR Top 10%]

SYM-B5-1

Harnessing knowledge of the tumor cell surface for immunotherapeutic design.

Wei Wu[1,2]

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Our immune system does an amazing job of daily surveillance on every cell in the body. While extremely efficient, immune cells cannot look beyond the plasma membrane. To design good immunotherapy, we mimic the vision of immune cells, to identify druggable irregularities in the tumor cell surface. This aligns well with antibody therapy since these also do not require penetration of the therapeutic moiety through biological membranes. In this talk, I share our recent work on (1) identifying and targeting cancer antigens presented by cancer cells, and (2) engineering nanobody bi-specifics that target gain-of-function CXCR4 receptor dimerization and signaling.

SYM-B5

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Publications

1. Junho Kang, Jun Hyeong Lee, Hongui Cha, Jinhyeon An, Kwon J, Mert Yakup Baykan, So Yeon Kim, Dohyeon An, Se-Hoon Lee, Jung Kyoon Choi, Jong-Eun Park. Systematic dissection of tumor-normal ecosystems at single-cell resolution across a thousand tumors of 30 cancer types. Nat Commun. 2024. (Accepted)

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SYM-B5-2

Logic gate-based combinatorial target discovery for CAR switches using AI and large-scale single-cell transcriptome DB

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Identification of optimal target antigens that distinguish cancer cells from normal surrounding tissue cells remains a key challenge in chimeric antigen receptor (CAR) cell therapy for tumors with intratumoral heterogeneity. In this study, we dissected tissue complexity to the level of individual cells through the construction of a single-cell expression atlas that integrates ~1.4 million tumor, tumor-infiltrating normal and reference normal cells from 412 tumors and 12 normal organs. We used a two-step screening method using random forest and convolutional neural networks to select gene pairs that contribute most to discrimination between individual malignant and normal cells. Tumor coverage and specificity are evaluated for the AND, OR and NOT logic gates based on the combinatorial expression pattern of the pairing genes across individual single cells. Single-cell transcriptome-coupled epitope profiling validates the AND, OR and NOT switch targets identified in ovarian cancer and colorectal cancer.

SYM-B5

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Professional Experience

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2020.01 - 2021.11	Instructor	Department of Medicine, Harvard Medical School Department of Medical Oncology, Dana-Farber Cancer Institute, Boston, MA, USA
2013.11 - 2019.12	Postdoctoral Fellow	Department of Medicine, Harvard Medical School Department of Medical Oncology, Dana-Farber Cancer Institute, Boston, MA, USA
2012.03 - 2013.10	Postdoctoral Fellow	Department of Bioengineering, Hanyang University

Publications

1. Jeong S*, Jang N*, Kim M, Choi IK. CD4+ cytotoxic T cells: an emerging effector arm of anti-tumor immunity. BMB Rep. 2023; 56(2):140-144. *Co-first authors.

2. Zhang B§, Choi IK§, Panaampon J, Wang Z. Does Delayed EBV Infection contribute to Rising Childhood Cancers? Trends Immunol. 2022; 43(12):956-958. §Co-corresponding authors.

3. Zhang B, Choi IK. Facts and hopes in the relationship of EBV with cancer immunity andimmunotherapy. Clin Cancer Res. 2022; 28(20):4363-4369.

4. Choi IK*, Wang Z*, Ke Q, Hong M, Paul DW, Fernandes SM, Hu Z, Stevens J, Guleria I, Kim HJ, Cantor H, Wucherpfennig KW, Brown JR, Ritz J, Zhang B. Mechanism of EBV inducing anti-tumour immunity and its therapeutic use. Nature. 2021; 590:157-162. *Co-first authors.

5. Choi IK, Wang Z, Ke Q, Hong M, Qian Y, Zhao X, Liu Y, Kim HJ, Ritz J, Cantor H, Rajewsky K, Wucherpfennig KW, Zhang B. Signaling by the Epstein-Barr virus LMP1 protein induces potent cytotoxic CD4+ and CD8+ T cell responses. Proc Natl Acad Sci U S A. 2018; 115(4):E686-E695.

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SYM-B5-3

T cell immunity to Epstein-Barr virus: From novel insight to therapeutic application

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Tumor-associated antigens (TAAs) comprise a large collection of non-mutated cellular antigens recognized by T cells in human and murine cancers. Their potential as immunotherapy targets has been explored for over two decades, yet the genesis of TAA-specific T cells remains elusive. While tumor cells may be a major source of TAAs for T cell priming, several recent studies suggest that infection with some viruses, including Epstein-Barr virus (EBV), can elicit cytotoxic T cell responses against some abnormally expressed cellular antigens that function as TAAs. However, the cellular and molecular basis of such responses remain undefined. Here, we show that expression of the EBV signaling protein LMP1 in B cells provokes T cell responses to multiple TAAs. LMP1 signaling leads to overexpression of many cellular antigens previously shown to be TAAs, their presentation on MHC-I and -II (mainly through the endogenous pathway), and the upregulation of costimulatory ligands CD70 and OX40 ligand, thereby inducing potent cytotoxic CD4+ and CD8+ T cell responses. These findings delineate a novel mechanism of infection-induced anti-tumor immunity. Furthermore, by ectopically expressing LMP1 in patient tumor B cells and thereby empowering them to prime T cells, we develop a general approach for rapid production of autologous cytotoxic CD4+ T cells against a broad array of endogenous tumor antigens, such as TAAs and neoantigens, for treating B cell malignancies. This work stresses the need to revisit classical concepts concerning viral and tumor immunity, which will be critical to fully understand the impact of common infections on human health and improve the rational design of immune approaches for cancers.

SYM-B6

New Role of HPP: Protein Function Annotation

SYM-B6

New Role of HPP: Protein Function Annotation

6.27 (Thu) 09:00 - 10:15

Chair: Heeyoun Hwang / Korea Basic Science Institute (KBSI)

SYM-B6-1 6.27 (Thu) 09:00 - 09:25

AlphaFun: Structural-Alignment-Based Proteome Annotation Reveals why the Functionally Unknown Proteins (uPE1) Are So Understudied

Gong Zhang
Jinan University

SYM-B6-2 6.27 (Thu) 09:25 - 09:50

ARID3C, a Chromosome 9 protein, Acts as a Regulator of Monocyte-to-Macrophage Differentiation Interacting with NPM1

Je-Yoel Cho
Seoul National University

SYM-B6-3 6.27 (Thu) 09:50 - 10:15

Functional exploration of new cancer biomarker from functionally unannotated proteome (uPE1) of pancreatobiliary tract cancer

Yun-Hee Kim
National Cancer Center (NCC)

SYM-B6

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2009 - 2011	Postdoc	Universität Potsdam, Germany

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2015 - Present	Member	ACS(American Chemistry Society)
2017 - Present	Committee Member	China Molecular System Biology Association
2022 - 2023	Member-At-Large	C-HPP(Human Proteome Project)
2023 - Present	Specialist	College of Physical Education, Jinan University
2024 - Present	Co-Chair	C-HPP(Human Proteome Project)

SYM-B6-1

AlphaFun: Structural-Alignment –Based Proteome Annotation Reveals why the Functionally Unknown Proteins(uPE1) Are So Understudied

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With the rapid expansion of sequencing of genomes, the functional annotation of proteins becomes a bottleneck in understanding proteomes. The Chromosome-centric Human Proteome Project (C-HPP) aims to identify all proteins encoded by the human genome and find functional annotations for them. However, until now there are still 1137 identified human proteins without functional annotation, called uPE1 proteins. Sequence alignment was insufficient to predict their functions, and the crystal structures of most proteins were unavailable. In this study, we demonstrated a new functional annotation strategy, AlphaFun, based on structural alignment using deep-learning-predicted protein structures. Using this strategy, we functionally annotated 99% of the human proteome, including the uPE1 proteins and missing proteins, which have not been identified yet. The accuracy of the functional annotations was validated using the known-function proteins. The uPE1 proteins shared similar functions to the known-function PE1 proteins and tend to express only in very limited tissues. They are evolutionally young genes and thus should conduct functions only in specific tissues and conditions, limiting their occurrence in commonly studied biological models. Such functional annotations provide hints for functional investigations on the uPE1 proteins. This proteome-wide-scale functional annotation strategy is also applicable to any other species.

SYM-B6

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1989 - 1991	M.S.	Veterinary Physiology, Seoul National University, S. Korea

Professional Experience

2015 - Present	Professor	Department of Biochemistry, College of Veterinary Medicine, Seoul National University
2011 - 2015	Associate Professor	Department of Biochemistry, College of Veterinary Medicine, Seoul National University
2003 - 2011	Lecturer, Assistant and Associate Professor	Department of Biochemistry, School of Dentistry, Kyungpook National University
2001 - 2003	Postdoctoral Research Fellow	BIDMC Genomics Center, Harvard Medical School, Boston MA

Academic Society

2023	Congress Chair	HUPO 2024 Busan
2022 - 2024	Council Member	Human Proteome Organization(HUPO)
2021 - 2028	Director	Comparative Disease

Publications

1.Son KH, Aldonza MBD, Nam AR, Lee KH, Lee JW, Shin KJ, Kang K, Cho JY. Integrative mapping of the dog epigenome: Reference annotation for comparative intertissue and cross-species studies. Sci Adv. 2023 Jul 7;9(27):eade3399. doi: 10.1126/sciadv.ade3399. (IF 14.98)

2. Kim HS, Lee KH, Son KH, Shin TJ & Cho JY. Extracellular Vesicle-Mediated Transfer of miRNA-1 from Primary Tumors Represses the Growth of Distant Metastases. Exp Mol Med. 2024 Apr 56(4); 10.1038/s12276-024-01181-7 (IF 12.8)

3. Oh JH, Kim CY, Jeong DS, Kim YC, Kim MH, Cho JY. The homeoprotein HOXB2 limits triple-negative breast carcinogenesis via extracellular matrix remodeling. Int J Biol Sci. 2024 Jan 20;20(3):1045-1063. (IF 9.2)

4. Oh JH, Cho JY. Comparative oncology: overcoming human cancer through companion animal studies. Exp Mol Med. 2023 Apr;55(4):725-734. (IF 12.8).

SYM-B6-2

ARID3C, a Chromosome 9 protein, Acts as a Regulator of Monocyte-to-Macrophage Differentiation Interacting with NPM1

Hui-Su Kim[1,2], Yong-In Kim[1,2], and Je-Yoel Cho[1,2]

[1]Department of Biochemistry, College of Veterinary Medicine, Research Institute for Veterinary Science, and BK21 FOUR Future Veterinary Medicine Leading Education and Research Center, Seoul National University, Seoul 08826, Republic of Korea.[2]Comparative Medicine Disease Research Center (CDRC), Science Research Center (SRC), Seoul National University, Seoul 08826, Republic of Korea.

ARID3C is a protein located on human chromosome 9 and expressed at low levels in various organs, yet its biological function has not been elucidated. In this study, we investigated both the cellular localization and function of ARID3C. Employing a combination of LC-MS/MS and deep learning techniques, we identified NPM1 as a binding partner for ARID3C's nuclear shuttling. ARID3C was found to be predominantly localized in the nucleus, where it functioned as a transcription factor for genes STAT3, STAT1, and JUNB, thereby facilitating monocyte-to-macrophage differentiation. The precise binding sites between ARID3C and NPM1 were predicted by AlphaFold2. Mutating this binding site prevented ARID3C from interacting with NPM1, resulting in its retention in the cytoplasm instead of translocation to the nucleus. Consequently, ARID3C lost its ability to bind to the promoters of target genes, leading to a loss of monocyte-to-macrophage differentiation. Collectively, our findings indicate that ARID3C forms a complex with NPM1 to translocate to the nucleus, acting as a transcription factor that promotes the expression of the genes involved in monocyte-to-macrophage differentiation.

SYM-B6

Yun-Hee Kim, Ph.D.

Position: Chief Scientist
Department: Division of Convergence Technology
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Education

2002 - 2006	Ph.D.	Dep. Life Science, POSTECH, Korea
1994 - 1996	M.S.	Dep. Biochemistry, Yonsei University, Korea
1989 – 1994	B.S.	Dep. Biology, Kyunghee University, Korea

Professional Experience

2007.04 - present	Chief Scientist	Division of Convergence Technology, Research Institute of National Cancer Center
2012.03- present	Professor	Graduate School of Cancer Science and Policy (GCSP), National Cancer Center

Publications

1. Lee YS, Im, JE, Yang Y, Lee HJ, Lee MR, Woo SM, Park SJ, Kong SY, Kim JY, Hwang H*, Kim YH*. New Function Annotation of PROSER2 in Pancreatic Ductal Adenocarcinoma. J Proteome Res. 2024; 23(3): 905–915

2. Lee MR, Woo SM, Kim MK, Han SS, Park SJ, Lee WJ, Lee DE, Choi SI, Choi W, Yoon KA, Chun JW, Kim YH*, Kong SY*. Application of plasma circulating KRAS mutations as a predictive biomarker for targeted treatment of pancreatic cancer. Cancer Science 2024; 115: 1283–1295. Choi SI, Lee YS, Lee YM, Kim HJ, Kim WJ, Jung S, Im, JE, Lee MR, Kim JK, Jeon AR, Woo SM, Oh GT, Heo K*, Kim YH*, In-Hoo Kim. Complexation of drug and hapten-conjugated aptamer with universal hapten antibody for pancreatic cancer treatment. J Control Release 2023; 360: 940-952.
3. Cho SY*, Hwang H*, Kim YH*, Yoo BC, Han N, Kong SY, Baek MJ, Kim KH, Lee MR, Park JK, Han SS, Lee WJ, Park C, Park JB, Kim JY*, Park SJ*, Woo SM*. Refining classification of cholangiocarcinoma subtypes via proteogenomic integration reveals new therapeutic prospects. Gastroenterology 2023; 164(7): 1293

4. Choi W*, Kim YH*, Woo SM, Yu Y, Lee MR, Lee WJ, Chun JW, Sim SH, Chae H, Shim H, Lee KS, Kong SY. Establishment of Patient-Derived Organoids Using Ascitic or Pleural Fluid from Cancer Patients. Cancer Res Treat 2023; 55(4): 1077-1086

5. Mwesige B, Lee MR, Lee YS, Han N, Im, JE, Kim JK, Choi SI, Hong EK, Jeon AR, Park SJ, Woo SM, Kim YH*. Establishment of patient-derived preclinical models for invasive papillary cholangiocarcinoma. Anticancer Res. 2022; 42(1): 599

6. Yang Y, Hwang H, Im, JE, Bhoo SH, Yoo JS, Kim YH*, Kim JY *. Flashlight into Function Unannotated C11orf52 Using Affinity Purification Mass Spectrometry. Journal of Proteome Res. 2021; 20(12): 5340

SYM-B6-3

Functional exploration of new cancer biomarker from functionally unannotated proteome (uPE1) of pancreatobiliary tract cancer

Yun-Hee Kim

Division of Convergence Technology, Research Institute of National Cancer Center Korea

Pancreatobiliary tract cancer is a representative refractory tumor with a high incidence rate, but the absence of diagnostic markers, lack of therapeutic targets, high recurrence rate, distant metastasis, and other unmet needs have resulted in the lack of appropriate treatments and low long-term survival rates. This signifies the low efficacy of the currently identified biomarkers, indicating the necessity to explore new perspectives beyond conventional marker discovery. uPE1 (uncharacterized protein 1), defined as a protein analyzable although its function has not been elucidated, has been overlooked due to limitations in analytical techniques for low abundant, membrane-localized, very small-sized proteins, limitations in detectability only under specific conditions, and limitations in analysis based on existing protein databases. However, comprehensive functional studies associated with cancer are believed to reveal significant value as new candidates for biomarker and therapeutic targets. In this study, we elucidated the new role of the PROSER2 (proline and serine-rich 2) molecule in tumor progression, derived from uPE1 proteome present in pancreatic cancer and intrahepatic cholangiocarcinoma (iCCA). For pancreatic cancer, candidate groups were selected from 8784 pancreatic cancer-related uPE1 entries in the neXtProt database. For iCCA, target candidates were selected based on an algorithm from uPE1 proteome derived from proteomic analysis of tumors versus normal samples from 100 patients. Subsequently, functional analyses were conducted on candidates to assess cancer cell growth, migration, invasion, and signaling interactions with binding molecules, based on their overexpression and knockdown. PROSER2, identified through selection algorithms for both cancer types, unveiled a novel function of antagonizing tumor progression upon its overexpression in tumors mediated by STK-AMPK pathway. Moreover, in iCCA patients, the negative correlation between PROSER2 expression levels and survival rates, based on clinical data, further solidified these findings. In conclusion, comprehensive functional investigations into uPE1 proteins expressed across various cancer types can surmount the dearth of functional correlation data and the absence of database links and interaction studies, thereby broadening the scope of discovering novel cancer biomarkers.

SYM-B7

Chemical Proteomics and drug development

SYM-B7

Chemical Proteomics and drug development

6.27 (Thu) 14:45 - 16:00

Chair: Heung Sik Hahm / UPPTHERA

SYM-B7-1 6.27 (Thu) 14:45 - 15:10

Spray modifications and Spatial biology

Hyun-Woo Rhee
Seoul National University

SYM-B7-2 6.27 (Thu) 15:10 - 15:35

Proteomic Approach to Site-Specific Covalent Ligand Screening for Developing PROTACs Targeting MDM2

Jin Young Kim
Korea Basic Science Institute (KBSI)

SYM-B7-3 6.27 (Thu) 15:35 - 16:00

Targeting the proteasome-associated deubiquitinase for actively regulating proteostasis

Byung-Hoon Lee
Daegu Gyeongbuk Institute of Science and Technology (DGIST)

SYM-B7

Hyun-Woo Rhee, Ph.D.

Position : Associate Professor
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Education

2000.03-2004.02	B.S.	Biological Science & Chemistry (Double Major), Seoul National University, Korea
2004.03-2009.08	Ph.D.	Organic Chemistry, Seoul National University, Korea

Professional Experience

2018.03-current	Associate Professor	Department of Chemistry, Seoul National University, Korea
2013.01-2018.02	Assistant/ Associate	Department of Chemistry, Ulsan National Institute of Science and Technology (UNIST), Korea
2010.07-2012.12	Postdoc	MIT Chemistry, USA

Academic Society

2017-current	Organization committee	Korean Society for Mitochondrial Research and Medicine (KSMRM)
2020-current	Organization committee	Korean Human Proteome Organization (KHUPO)
2021-current	Editorial Advisory Board	Molecules and Cells (KSMCB)

Publications

1. **Lee YB, Rhee HW*** Spray-Type Modifications: An Emerging Paradigm in Post-translational Modifications, *Trends Biochem*. Sci. **2024**, 3, 208-223

2. **Park I†, Kim KE†, Kim J†**, AK Kim, Bae S, Jung M, Choi J, **Mishra PK**, TM Kim, **Kwak C, Kang MG, Yoo CM**, Mun JY, Liu KH, Lee KS*, Kim JS*, Suh JM*, **Rhee HW*** Mitochondrial matrix RTN4IP1/OPA10 is an oxidoreductase for coenzyme Q synthesis , Nat. Chem. Biol. **2024**, 20, 221–233 (†equally contributed, Highlighted in *Nature Chemical Biology*)

3. **Mishra PK*, Sharma N**, Kim H, Lee C, **Rhee HW*** GEN-Click: Genetically Encodable Click Reactions for Spatially Restricted Metabolite Labeling, *ACS Cent. Sci*. **2023**, 9, 1650–1657

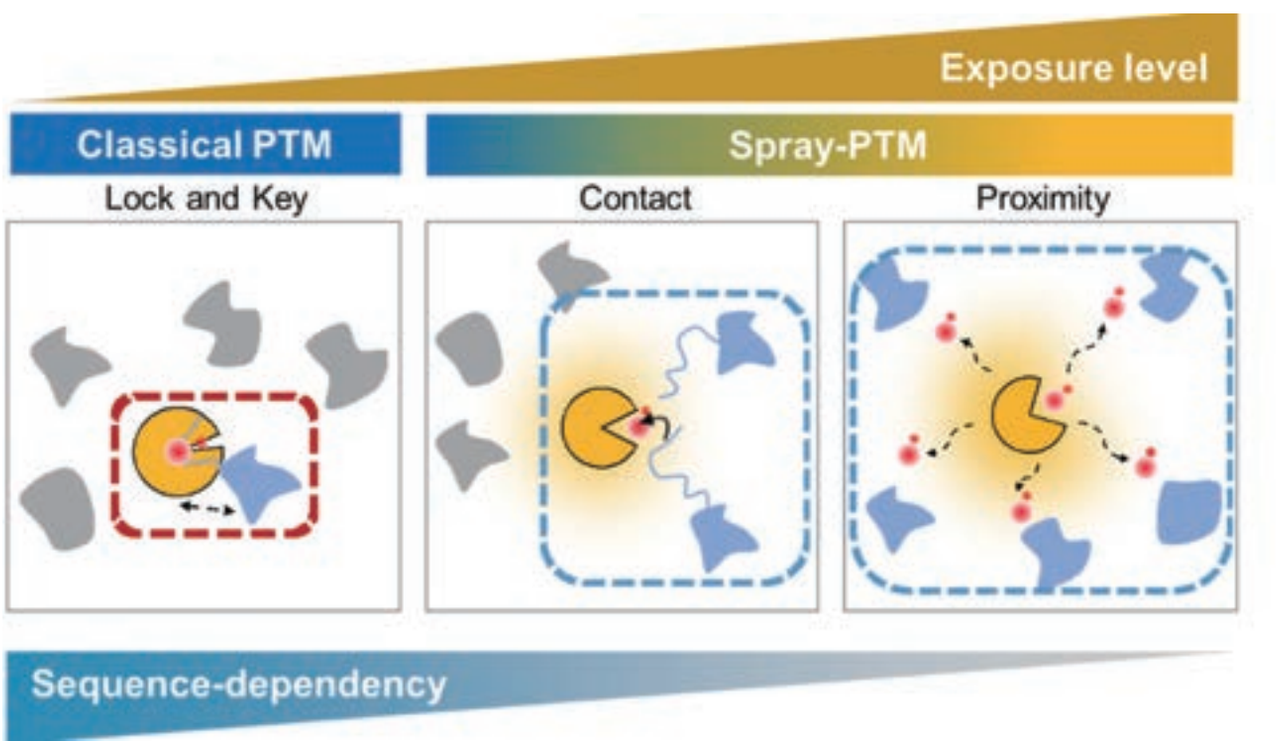
SYM-B7-1

Spray modifications and Spatial biology

Hyun-Woo Rhee

Department of Chemistry, Seoul National University, Seoul 08826, Korea;

Proximity labeling can be defined as an enzymatic "in-cell" chemical reaction that catalyzes the proximity-dependent modification of biomolecules in live cells. As this labeling reaction is proximity-dependent due to the short lifetime of reactive species, it can be used to map spatial proteomes, transcriptomes, and cellular networks. In our lab, we have developed a super-resolution proximity labeling technique (SR-PL) and we used it for architecture mapping of metabolic components of mitochondria in live mammalian cells and in mammalian tissues[1]. Recently, we recognized parallels between spray-type modifications (e.g., Acetyl Spray, ADPR Spray, SUMO Spray, etc) and proximity labeling techniques, as both involve chemical interactions between electrophilic groups and nucleophilic moieties in close proximity[2]. In this talk, I will explore how spray-type modifications can impact spatial biological components, offering a promising avenue for unraveling the complexities of spatial biology.



Reference:

1. Park I, Kim KE, Kim J, et al. Mitochondrial matrix RTN4IP1/OPA10 is an oxidoreductase for coenzyme Q synthesis. Nat. Chem. Biol. **2024,** 20, 221-233.

2. Lee YB, Rhee HW. Spray-type modifications: an emerging paradigm in post-translational modifications. Trends Biochem. Sci. **2024**, 49, 208-223.

SYM-B7

Jin Young Kim, Ph.D.

Position: Principal Researcher
Affiliation:
1.Bioconvergence Analysis Research Center, Korea Basic Science Institute (KBSI)
2.Critical Diseases Diagnostics Convergence Research Center, Korea Research Institute of Bioscience and Biotechnology (KRIBB)
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Education

1997 - 2002	Ph.D.	Department of Chemistry, Yonsei University
1991 - 1993	M.S.	Department of Chemistry, Yonsei University
1987-1991	B.S,	Department of Chemistry Education, Kongju National University

Professional Experience

1993 - Present	Principal Researcher	Korea Basic Science Institute (KBSI)
2007 - 2009	Postdoctoral Research Associate	Professor Yates's Cell Biology Laboratory at The Scripps Research Institute (TSRI)
2015 - 2020	Head	Research Center for Bioconvergence Analysis, Ochang, Korea Basic Science Institute (KBSI)

Academic Society

2016 - Present	Korea Human Proteome Organization
2018 - 2019	The Korean Chemistry Society

Publications

1. Discovery of proteolysis-targeting chimera targeting undruggable proteins using a covalent ligand screening approach. Lee H, Lee JY, Jang H, Cho HY, Kang M, Bae SH, Kim S, Kim E, Jang J, Kim JY*, Jeon YH. Eur J Med Chem. 2024 Jan 5;263:115929. doi: 10.1016/j.ejmech.2023.115929. Epub 2023 Nov 2.PMID: 37956552

2. Dysregulation of the Wnt/β-catenin signaling pathway via Rnf146 upregulation in a VPA-induced mouse model of autism spectrum disorder. Park G, Jang WE, Kim S, Gonzales EL, Ji J, Choi S, Kim Y, Park JH, Mohammad HB, Bang G, Kang M, Kim S, Jeon SJ, Kim JY, Kim KP, Shin CY, An JY, Kim MS, Lee YS. Exp Mol Med. 2023 Aug;55(8):1783-1794. doi: 10.1038/s12276-023-01065-2. Epub 2023 Aug 1.PMID: 37524878

3. Adnp-mutant mice with cognitive inflexibility, CaMKIIα hyperactivity, and synaptic plasticity deficits. Cho H, Yoo T, Moon H, Kang H, Yang Y, Kang M, Yang E, Lee D, Hwang D, Kim H, Kim D, Kim JY, Kim E. Mol Psychiatry. 2023 Aug;28(8):3548-3562. doi: 10.1038/s41380-023-02129-5. Epub 2023 Jun 26.PMID: 37365244

SYM-B7-2

Proteomic Approach to Site-Specific Covalent Ligand Screening for Developing PROTACs Targeting MDM2

Hyeonjun Lee [2], Ju Yeon Lee [1], Minhee Kang [2], Suin Kim[2], Jaebong Jang[2,3], Young Ho Jeon[2], **Jin Young Kim [1]**

[1] Research Center for Digital Omics, Korea Basic Science Institute, Cheongju, 28119, Republic of Korea
[2] College of Pharmacy, Korea University, Sejong, Sejong, Republic of Korea
[3] College of Pharmacy, Seoul National University, Seoul, Republic of Korea

We conducted a site-specific, fragment-based covalent ligand screening using LC-MS/MS to identify compounds binding to the target sites of the protein of interest (POI). Hits from this screening were explored in PROTAC development, a method leveraging targeted protein degradation (TPD) for therapeutics. MDM2, chosen as a model due to its involvement in protein-protein interactions (PPIs) and known degradability, was used for validation. Western blot analysis confirmed the degradation induced by newly synthesized PROTACs containing reversible analogs from the screening. Employing LC-MS/MS, fragment compounds interacting with the target protein were correctly identified. Cysteine introduction enabled covalent bond formation with electrophilic fragments. Compounds with higher binding affinity were identified and ranked based on relative intensity ratios. Strong binders were selected, and their non-covalent binding affinity to native MDM2 was evaluated via NMR experiments. Through this approach, promising covalent ligands were identified, showcasing the potential of our methodology in drug discovery.

SYM-B7

Byung-Hoon Lee, Ph.D.

Position: Associate Professor
Department: Department of New Biology
Affiliation: DGIST
E-mail: byung-hoon_lee@dgist.ac.kr

Education

2004	Ph.D.	Department of Pharmacology, UT Southwestern Medical Center
1998	M.S.	Department of Microbiology, Seoul National University
1996	B.S.	Department of Microbiology, Seoul National University

Professional Experience

2016 - Present	Assistant&Associate Professor	Department of New Biology, DGIST
2007 - 2016	Postdoctoral Fellow	Department of Cell Biology, Harvard Medical School, USA
2006 - 2007	Postdoctoral Fellow	The Picower Institute, MIT, USA

Publications

1. Chung S, Kang MS, Alimbetov DS, Moon GI, Yunn NO, Kim Y, Kim BG, Wie M, Lee EA, Ra JS, Oh JM, Lee DH, Lee K, Kim J, Han SH, Kim KT, Chung WK, Nam KH, Park J, Lee BH, Kim S, Zhao W, Ryu SH, Lee YS, Myung K, and Cho Y (2022) Regulation of BRCA1 stability through the tandem UBX domains of isoleucyl-tRNA synthetase 1. Nat. Commun. Nov 8;13(1):6732.

2. Hung KY, Klumpe S, Eisele M, Elsasser S, Tian G, Sun S, Moroco J, Cheng T, Joshi T, Seibel T, van Dalen D, Feng XH, Lu Y, Ovaa H, Engen J, Lee BH#, Rudack T#, Sakata E#, and Finley D# (2022) Allosteric control of Ubp6 and the proteasome via a bidirectional switch. Nat. Commun. Feb 11;13(1):838. (#Co-corresponding authors)

3. Tran NN and Lee BH (2022) Functional implication of ubiquitinating and deubiquitinating mechanisms in TDP-43 proteinopathies. Front. Cell Dev. Biol. Sep 9;10:931968.

4. Muniyappan S and Lee BH (2019) In vitro analysis of proteasome-associated USP14 activity for substrate degradation and deubiquitylation. Methods Enzymol. Feb 1;619:249-268.

5. Lee BH#, Lu Y, Prado MA, Shi Y, Sun S, Elsasser S, Gygi SP, King RW#, and Finley D#. (2016) USP14 deubiquitinates proteasome-bound substrates that are ubiquitinated at multiple sites. Nature, Apr 21;532(7599):398-401. (#Co-corresponding authors)

6. Lee BH*, Lee MJ*, Park S, Oh DC, Elsasser S, Chen PC, Gartner C, Dimova N, Hanna J, Gygi SP, Wilson SM, King RW, and Finley D. (2010) Enhancement of proteasome activity by a small-molecule inhibitor of USP14. Nature, Sep 9;467(7312):179-84. (* Co-first authors)

SYM-B7-1

Targeting the proteasome-associated deubiquitinase for actively regulating proteostasis

Byung-Hoon Lee

Department of New Biology, DGIST

The ubiquitin-proteasome system (UPS) plays an essential role in maintaining proteostasis and regulates almost every aspect of cellular processes in eukaryotes. Among the UPS, the 26S proteasome, which is the most complex protease in nature, serves as a master player for the proteolysis pathway due to the selective recognition of ubiquitin tags. Notably, deubiquitinases (DUBs) exclusively reverse the ubiquitination process, thus being capable of regulating protein turnover. DUBs are prominent because they not only recycle ubiquitins but also impose a critical checkpoint during the UPS pathway. We previously discovered that USP14/Ubp6, a major DUB on the proteasome, acts as a critical inhibitory component on the proteolytic pathway and also developed small-molecule inhibitors selectively targeting USP14 as proteasome activators. Our mechanistic studies suggest that USP14/Ubp6-mediated reactions exert dynamic influence over proteasome in both catalytic activity-dependent and -independent manner. USP14/Ubp6 and the proteasome are also mutually linked through an allosteric bidirectional switch for fine-tuning the degradation and proteolytic outcome. In this talk, I also show some proof-of-concept of targeting the DUB to regulate TDP-43 proteopathy. Given that the UPS is among the most important drug targets, the biology of DUBs should be further elucidated for its potential application to human diseases.

EDUCATION SESSION 1

Introduction to proteomics

EDUCATION SESSION 1

Introduction to proteomics

6.25 (Tue) 10:15-11:30

Chair: Ji Eun Lee / Korea Institute of Science and Technology (KIST)

ES1-1 6.25 (Tue) 10:15-10:35

Introduction to Proteomics - Basics and Biological Insights

Jae-Young Kim
Chungnam National University

ES1-2 6.25 (Tue) 10:35-10:55

Introducing Protein Extraction and Preparation in Urine and Blood Samples for Doping Analysis

Hophil Min
Korea Institute of Science and Technology (KIST)

ES1-3 6.25 (Tue) 10:55-11:12

Protein characterization using Cyclic Ion Mobility QTOF and introduction to DESI XS MS imaging technology

Hyunwoo Kim
Waters Korea

ES1-4 6.25 (Tue) 11:12-11:30

4D-Proteomics technology of MS-based Proteomics: Principle & Application

Kwangseon Lee
Bruker Korea

EDUCATION SESSION 1

Jae-Young Kim, Ph.D.

Position: Associate Professor
Department: Graduate School of Analytical Science and Technology (GRAST)
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Education

2004.08-2009.05	Ph.D.	North Carolina State University
2001.03-2003.02	M.S.	Catholic University, College of Medicine
1994.03-2001.02	B.S.	Seoul National University, College of Agriculture and Life Sciences

Professional Experience

2022.03-Present	Associate Professor	Chungnam National University
2016.10-2022.02	Assistant Professor	Chungnam National University
2010.08-2016.09	Postdoc	H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL USA
2009.02-2010.07	Postdoc	Sanford-Burnham Medical Research Institute, La Jolla, CA USA

Academic Society

2017.03-Present	Member	KHUPO
2016.10-Present	Member	KSMCB

Selected Publications

1. Choi KM, Kim B, Lee SM, Han J, Bae HS, Han SB, Lee D, Ham IH, Hur H, Kim E, Kim JY. (2024) Characterization of gastric cancer-stimulated signaling pathways and function of CTGF in cancer-associated fibroblasts. Cell Commun Signal 2;22(1):8.

2. Park SG, Ji MJ, Ham IH, Shin YH, Lee SM, Lee CH, Kim E, Hur H, Park HM, Kim JY. (2022) Secretome analysis reveals reduced expression of COL4A2 in hypoxic cancer-associated fibroblasts with a tumor promoting function in gastric cancer. J Cancer Res Clin Oncol (https://doi.org/10.1007/s00432-022-04361-y).

3. Kim E*, Hwang EJ, Lee J, Kim DY, Kim JY*, Kim DW*. (2022) Patient-specific molecular response dynamics can predict the possibility of relapse during the second treatment-free remission attempt in chronic myelogenous leukemia. Neoplasia 32:100817 (* : co-corresponding authors).

4. Lee SJ, Choi KM, Bang G, Park SG, Kim EB, Choi JW, Chung YH, Kim J, Lee SG, Kim E*, Kim JY*. (2021) Identification of nucleolin as a novel AEG-1-interacting protein in breast cancer via interactome profiling. Cancers 13, 2842 (* : co-corresponding authors).

5. Choi KM, Cho E, Bang G, Lee SJ, Kim B, Kim JH, Park SG, Han EH, Chung YH, Kim JY, Kim E*, Kim JY*. (2020) Activity-based protein profiling reveals potential dasatinib targets in gastric cancer. Int J Mol Sci 21(21):9276 (* : co-corresponding authors).

ES1-1

Introduction to Proteomics - Basics and Biological Insights

Jae-Young Kim[1]

Graduate School of Analytical Science and Technology (GRAST)
Chungnam National University, Daejeon, Korea

Proteomics is a crucial field in the interface of biology and technology, offering deep insights into the molecular mechanisms of life. This talk aims to elucidate both foundational and applied aspects of proteomics. The first segment of the presentation will cover essential principles of proteomics, including its definition, the different types of proteomics analyses, the general workflow, and the principles of peptide sequencing using mass spectrometry. The second part will focus on the practical applications of proteomics in biological and clinical research. This includes detailed examples of how proteomics has been utilized to address unmet medical needs, such as understanding the mechanisms behind cancer drug resistance and the discovery of novel predictive biomarkers for COVID-19. This session is designed to provide attendees with a comprehensive overview of proteomics, from basic concepts to significant biomedical applications.

EDUCATION SESSION 1

Hophil Min, Ph.D.

Position: Associated Professor
Department: Divison of Bio-Medical, KIST school
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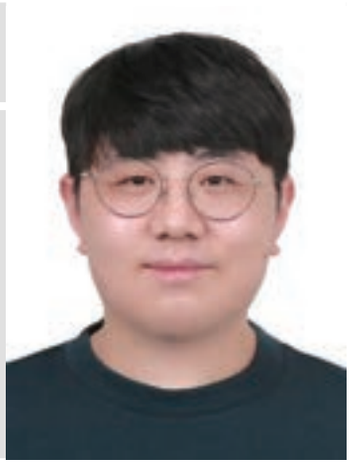
E-mail: mhophil@kist.re.kr



Education

2024. 01 - Present	Associated Professor	Division of Bio-Medical, KIST school, UST
2018. 03 - Present	Senior Researcher	Doping control center, KIST
2015.11 - 2018.02	Researcher	Doping control center, KIST
2008.03 - 2015.08	Ph D	Departments of Biomedical Sciences, College of Medicine, Seoul National University, Korea (Ph.D Advisor: Youngsoo Kim)
2004.03 - 2008.02	B.S	Departments of Biological Sciences, Gachon Medical School

Professional Experience

2022.02 – 2022.02	Doping international expert	2022 China Beijing Olympic & Paralympic Games, Beijing, China
2010.08 - 2011.08	Visiting Researcher with Ph.D course	Fred Hutchinson Cancer Research Center, WA, USA
2016.09 – 2016.09	Doping international expert	2016 Brazil Rio Olympic & Paralympic Games, Rio de Janeiro, Brazil

Publications

1. Development of an Ephedrine In-House Matrix Reference Material and Its Application to Doping Analysis, *ACS Omega*, (2024.03), **Corresponding Author***

2. Simultaneous quantification of TB-500 and its metabolites in in-vitro experiments and rats by UHPLC-Q Exactive orbitrap MS/MS and their screening by wound healing activities in-vitro, *Journal of Chromatography B*, (2024.02), **Co-Author**

3. Application of Skyline software for detecting prohibited substances in doping control analysis, *PLoS ONE*, (2023.12) **Corresponding Author***

4. Detection and quantification of the metabolite Ac-Tβ1-14 in in vitro experiments and urine of rats treated with Ac-Tβ4: A potential biomarker of Ac-Tβ4 for doping tests, *Drug Testing and Analysis*, (2023.11) Co-Author

5. Glial cell proteome using targeted quantitative methods for potential multi-diagnostic biomarkers, *Clinical Proteomics*, (2023.10) Co-Author

6. Monitoring and exposure assessment of ricinine in castor plant-based foods and dietary supplements, *Journal of Food Composition and Analysis*, (2023.09), Co-Author

ES1-2

Introducing Protein Extraction and Preparation in Urine and Blood Samples for Doping Analysis

Hophil Min

Doping Control Center, Korea Institute of Science and Technology
Division of Bio-Medical Science and Technology, KIST school, University of Science and Technology

Doping analysis has become a critical issue in modern society, addressing the fairness of athletes in sports and their medical well-being. Specifically, with the increasing prominence of protein pharmaceuticals among prohibited substances in doping, protein extraction and preparation in urine or blood samples play a pivotal role in determining the quality and reliability of analysis. This presentation aims to introduce the importance of protein sample preparation and various techniques employed in doping analysis. We will explore the current primary techniques for efficient protein extraction, considering the types of amino acids and matrices involved. Furthermore, it will discuss methods such as antibody-based enrichment for low-concentration proteins, enzymatic digestion for quantitative analysis, and the utilization of top-down approaches for high-resolution protein analysis. Overall, this presentation seeks to comprehensively introduce the significance of protein sample preparation in doping analysis and highlight the current major techniques, contributing to advancements in research and applications in this field.

EDUCATION SESSION 1

Hyunwoo Kim

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E-mail: xenon_kim@waters.com
Homepage: www.waters.com

Education

2015 ~Current	Ph.D	ABD in Chemistry in Pukyung National Univrsity, Korea
2003~2005	MS	Chemistry in Pukyung National Univrsity, Korea
1996~2003	BS	Chemistry in Pukyung National Univrsity, Korea

Professional Experience

2012~2019	Sales account Manager	GM Science
2019~2023	A&R Team Sales Manager	WATERSKOREA
2023~Current	GIA Tema Sales Manager	WATERSKOREA

ES1-3

Protein characterization using Cyclic Ion Mobility QTOF and introduction to DESI XS MS imaging technology

Hyunwoo Kim

WatersKorea (Government & Industry & Academia Research Team)

In most proteomics analyses, bottom-up analysis is used to perform qualitative and quantitative analysis. Recently, as research requiring protein analysis in its native state has increased, interest in separation using SEC and analysis methods that can confirm this through MS has increased. The Cyclic Ion Mobility Q-TOF system will provide a new direction for research in which it is impossible to identify isoforms showing structural differences in proteins if they are not separated from LC in the native state. We would also like to introduce DESI XS technology for MS imaging, which is of great interest recently

EDUCATION SESSION 1

Kwangseon Lee

Position: Application Chemist
Department:-
Affiliation: Bruker
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Education

2012.03~2015.08	Bachelor	Ajou university
2015.09~2018.08	Master	Ajou university

Professional Experience

2021.09 ~	Application Chemist	Bruker Korea

ES1-4

4D-Proteomics technology of MS-based Proteomics : Principle & Application secondary metabolites by LC-MS/MS system

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Over the past two decades, significant technological advancements and the development of new methodologies have transformed proteomics into a highly potent tool for protein scientists, biologists, and clinical researchers. The incorporation of ion mobility has not only pushed the boundaries in terms of speed, sensitivity, selectivity, and robustness but has also facilitated the exploration of previously inaccessible parts of the proteome. Through 4D-Proteomics, researchers can consistently measure the Collisional Cross Section (CCS) values for all detected ions, enhancing the system's selectivity and providing more reliable relative quantitation information, even from complex samples and short gradient analyses.

Accurate relative protein quantitation is fundamental in quantitative proteomics, crucial for understanding biological assemblies and conducting biomarker discovery experiments. While Data Independent Acquisition (DIA) remains the most widely used strategy for addressing the missing value problem, its implementation requires the construction of spectral libraries, which can be challenging, particularly for rare organisms. Additionally, traditional DIA methods may not be suitable for short gradient analysis due to their slow speed. In such scenarios, 4D-Proteomics-LFQ offers a solution with its combination of speed, flexibility, and reliability. Moreover, the reproducible determination of Collisional Cross Sections enables the 4D-Match Between Runs (MBR) approach, maximizing the quantification of proteins in Label-Free Quantification experiments while ensuring confidence in high-throughput sample analysis. The 4D-MBR approach is supported by the latest analytical tools.

4D-Proteomics is adept at addressing various analytical challenges, ranging from tissue and biofluid analysis to single-cell studies. Protein expression is influenced by an individual's genetic background, as well as factors such as time, localization, and physiological responses to external stimuli. Furthermore, the intricate interplay of alternative splicing, point mutations, post-translational modifications, and endogenous proteolysis can result in a single protein being expressed in multiple proteoforms, each with distinct biological activities. Addressing this complexity necessitates the comprehensive capabilities of 4D-Proteomics.

EDUCATION SESSION 2

Targeted Proteomics

EDUCATION SESSION 2

Targeted Proteomics

6.25 (Tue) 10:15-11:30

Chair: Dohyun Han / Seoul National University Hospital

ES2-1 6.25 (Tue) 10:15-10:35

Targeted proteomics 101

Junho Park
CHA University

ES2-2 6.25 (Tue) 10:35-10:55

Instruction on Multiple Reaction Monitoring-Mass Spectrometry and Its Applications in Clinical Proteomics

Dongyoon Shin
CHA Future Medicine Research Institut

ES2-3 6.25 (Tue) 10:55-11:15

Targeted proteomics: Alternative approaches

Dohyun Han
Seoul National University Hospital

ES2-4 6.25 (Tue) 11:15-11:30

Introduction to Targeted proteomics workflow that has difference with Non-Targeted proteomics workflow

Joon Seok Lee
Agilent Technologies Korea

EDUCATION SESSION 2

Junho Park, Ph.D.

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Education

2014.03-2019.08	Ph.D.	Seoul National University
2010.03-2014.02	B.S.	Sogang University

Professional Experience

2022.04-present	Assistant Professor	CHA University
2021.08-2022.04	Postdoctoral researcher	Pacific Northwest National Laboratory
2021.02-2021.08	Associate research scientist	Columbia University Medical Center
2020.04-2020.12	Postdoctoral researcher	Seoul National University

Academic Society

2023.01-present	Member of Scientific Committee	KHUPO

Publications

1. J Park, F Yu, J Fulcher, S Williams, K Engbrecht, R Moore, G Clair, V Petyuk, A Nesvizhskii, and Y Zhu; Evaluating linear ion trap for MS3-based multiplexed single-cell proteomics. Analytical Chemistry, 2023

2. D Kim*, J Park*, D Han*, J Yang, A Kim, J Woo, Y Kim, I Mook-Jung; Molecular and functional signatures in a novel Alzheimer's disease mouse model assessed by quantitative proteomics. Molecular Neurodegeneration, 2018

3. J Park*, H Oh*, D Han, I Park, J Wang, H Ryu, Y Kim; Parallel Reaction Monitoring-Mass Spectrometry (PRM-MS)-Based Targeted Proteomic Surrogates for Intrinsic Subtypes in Breast Cancer: Comparative Analysis with Immunohistochemical Phenotypes. Journal of Proteome Research, 2019

ES2-1

Targeted proteomics 101

Junho Park[1,2]

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Targeted proteomics refers to a method of measuring tens to thousands of proteins of interest (more precisely, peptides of interest) using various instruments and methods, including liquid chromatography coupled to mass spectrometry (LC-MS). Due to the capability to quantify low abundant proteins in biological samples with high precision and reproducibility, targeted proteomics is gaining attention as an increasingly important analytical method in modern molecular biology and translational medicine. In the first lecture of this education session, I will introduce the LC-MS-based methods that are frequently used in targeted proteomic analysis and the principles of the corresponding methods

EDUCATION SESSION 2

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Education

2017.03 - 2022.08	MS and Ph.D	Seoul National University Medical Research Center
2013.03 - 2017.02	B.E	Yonsei University

Professional Experience

2021.09 ~	Senior Research Scientist	Proteomics Research Team/Advanced Omics Research Center/CHA Future Medicine Research Institute
2021.09 ~	Postdoctoral Researcher	Institute of Medical and Biological Engineering, Seoul National University Medical Research Center

Publications

1. **Dongyoon Shin***, Jihyeon Lee*, Yeongshin Kim, Junho Park, Daun Shin, Yoojin Song, Eun-Jeong Joo, Sungwon Roh, Kyu Young Lee, Sanghoon Oh, Yong Min Ahn, Sang Jin Rhee, Youngsoo Kim. Evaluation of nondepleted plasma multiprotein-based model for discriminating psychiatric disorders using multiple reaction monitoring-mass spectrometry: Proof of concept study. *Journal of Proteome Research. 2023. IF=5.37*

2. Junho Park*, Seung Hak Lee*, **Dongyoon Shin***, Yeongshin Kim, Youngsik Kim, Min Yong Seong, Jin Ju Lee, Han Gil Seo, Won-Sang Cho, Young Sun Ro, Youngsoo Kim, Byung-Mo Oh. Multiplexed quantitative proteomics reveals proteomic alterations in two rodent traumatic brain injury models. *Journal of Proteome Research. 2023. IF=5.37*

3. Sang Jin Rhee, **Dongyoon Shin**, Daun Shin, Yoojin Song, Eun-Jeong Joo, Hee Yeon Jung, Sungwon Roh, Sang-Hyuk Lee, Hyeyoung Kim, Minji Bang, Kyu Young Lee, Jihyeon Lee, Jaenyeon Kim, Yeongshin Kim, Youngsoo Kim, and Yong Min Ahn. Network analysis of plasma proteomes in affective disorders. *Translational Psychiatry. 2023*. https://doi.org/10.1038/s41398-023-02485-4. *IF=7.99*

4. Sang Jin Rhee*, **Dongyoon Shin***, Daun Shin, Yoojin Song, Eun-Jeong Joo, Hee Yeon Jung, Sungwon Roh, Sang-Hyuk Lee, Hyeyoung Kim, Minji Bang, Kyu Young Lee, Se Hyun Kim, Minah Kim, Jihyeon Lee, Jaenyeon Kim, Yeongshin Kim, Jun Soo Kwon, Kyooseob Ha, Youngsoo Kim, and Yong Min Ahn. Latent class analysis of psychotic-affective disorders with data-driven plasma proteomics. Translational Psychiatry. 2023. 10.1038/s41398-023-02321-9. *IF=7.99*

5. **Dongyoon Shin***, Sang Jin Rhee*, Daun Shin, Eun-Jeong Joo, Hee Yeon Jung, Sungwon Roh, Sang-Hyuk Lee, Hyeyoung Kim, Minji Bang, Kyu Young Lee, Se Hyun Kim, Jihyeon Lee, Yoseop Kim, Injoon Yeo, Yeongshin Kim, Jaenyeon Kim, Jun Soo Kwon, Kyooseob Ha, Yong Min Ahn, and Youngsoo Kim. Integrating proteomic and clinical data to discriminate major psychiatric disorders: Applications for major depressive disorder, bipolar disorder, and schizophrenia. *Clin Transl Med. 2022*. 10.1002/ctm2.929. *IF=11.49*

ES2-2

Instruction on Multiple Reaction Monitoring-Mass Spectrometry and Its Applications in Clinical Proteomics

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Recent advances in mass spectrometry (MS)-based proteomics have improved the development of high-throughput techniques for quantifying proteins. Espatially in clinical proteomics, MS-based proteomics is suitable for discovering and quantifying multiple proteins that are associated with diseases and disorders.

One of the analytical technologies contributing to clinical proteomics is targeted MS, which is characterized by high sensitivity and selectivity in the quantitation of specific proteins of interest during the analysis of multiple proteins, minimizing interfering signals of them. Representative targeted MS technology—multiple reaction monitoring (MRM)—is based on its ability to quantify the hundreds of protein biomarkers with high reproducibility, and is specialized for verifying and validating candidate biomarkers as well as screening target proteins of interest. Furthermore, the feasibility of MRM-based assays was already demonstrated, representing the potential for reproducible assays in large-scale clinical proteomics research.

In this educational session, The step-by-step processes of MRM-MS-based clinical proteomics research will be introduced. Additionally, the application of MRM-MS in clinical proteomics will be addressed through several previous studies.

EDUCATION SESSION 2

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Education

2023.09 - 2011.02	Doctor (Ph.D)	Genetic Engineering, Seoul National University
1999.03 - 2003.02	Bachelor	Department of biological sciences, Sungkyunkwan University

Professional Experience

2021.09 - Present	Associate Professor	Department of Transdisciplinary Medicine, SNUH
2015.12 - Present	Director	Proteomic core facility, Transdisciplinary Research and Collaboration, Biomedical research institute, SNUH
2015.12 - 2021.08	Research Professor	Proteomic core facility, Transdisciplinary Research and Collaboration, Biomedical research institute, SNUH
2014.03 - 2015.11	Research Progessor	Biomedical research institute, SNUH

Publications

1. Kong SH, Bae JM, Kim JH, Kim SW, Han D, Shin CS. Protein Signatures of Parathyroid Adenoma according to Tumor Volume and Functionality. Endocrinol Metab (Seoul). 2024 Mar 21. Epub head of print. PMID: 38509667. [공동교신저자]

2. Kang C, Yun D, Yoon H, Hong M, Hwang J, Shin HM, Park S, Cheon S, Han D, Moon KC, Kim HY, Choi EY, Lee EY, Kim MH, Jeong CW, Kwak C, Kim DK, Oh KH, Joo KW, Lee DS, Kim YS, Han SS. Glutamyl-prolyl-tRNA synthetase (EPRS1) drives tubulointerstitial nephritis-induced fibrosis by enhancing T cell proliferation and activity. Kidney Int. 2024 Feb 5:S0085 2538(24)00067-X. PMID: 38320721. [공동저자]

3. Kim YH, Yoon SJ, Kim M, Kim HH, Song YS, Jung JW, Han D, Cho SW, Kwon SW, Park YJ. Integrative Multi-omics Analysis Reveals Different Metabolic Phenotypes Based on Molecular Characteristics in Thyroid Cancer. Clin Cancer Res. 2024 Feb 16;30(4):883-894. PMID: 38088902.[공동저자]

4. Lim Y, Kim HY, Han D, Choi BK. Proteome and immune responses of extracellular vesicles derived from macrophages infected with the periodontal pathogen Tannerella forsythia. J Extracell Vesicles. 2023 Dec;12(12):e12381.PMID: 38014595. [공동교신저자] (Top 10% in Cell Biology)

5. Byun I, Seo H, Kim J, Jeong D, Han D, Lee MJ. Purification and characterization of different proteasome species from mammalian cells. STAR Protoc. 2023 Nov 23;4(4):102748. PMID: 37999974. [공동교신저자]

ES 2-3

Targeted proteomics: Alternative approaches

Dohyun Han[1,2,3]

[1]Department of Transdisciplinary Medicine, Seoul National University Hospital
[2]Department of Medicine, Seoul National University College of Medicine
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In this lecture, we will cover the latest alternative technologies and applications of targeted proteomics. Targeted proteomics is a technique used to validate biomarker candidates or study the function of interesting proteins, and has recently seen significant advances with the development of new technologies such as data independent acquisition (DIA) and proximity extension assay (PEA).
Through this lecture, we will provide detailed explanations of the principles and applications of these new technologies, and help you understand them through clinical and translational research examples. We will also discuss how these technologies can be applied to disease diagnosis, drug target discover, and novel drug development.

EDUCATION SESSION 2

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Education

	Ph.D	Kyungpook National University, Daegu, Korea
	M.S.	Kyungpook National University, Daegu, Korea
	B.S	Kyungpook National University, Daegu, Korea

Professional Experience

2018.12 - Present	Product Specialist Manager	Agilent Technologies Korea
2015.07 - 2018.11	Product Specialist Manager	LCMS Products in Agilent Technologies Korea
2013.01 - 2015.06	Application Engineer for Pre & Post sales	Thermo Scientific Korea
2011.10 - 2012.12	Pharmaceutical Team leader	Solution Center of Waters Korea
2005.10 - 2011.09	Application Engineer for Pre & Post sales	Waters Korea
2003.08 - 2005.05	Researcher	Yonsei Proteome Research Center

ES2-4

Introduction to Targeted Proteomics workflow that has difference with Non-targeted proteomics workflow

Joon-Seok Lee[1], Yanan Yang[2], Linfeng Wu[2]

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In Proteomics research area, the general researching workflow is Non-targeted proteomics using High-resolution Mass Spectrometers (HR-MS). Identifying protein bio-markers in biological samples can be implemented by this Non-targeted proteomics workflow which researchers are usually using screening methods with HR-MS, so the number of identified proteins is a critical point because there are low abundant but have very important role in biological pathways. In addition, the high-throughput analysis for Non-targeted proteomics workflow using HR-MS is one of the focusing area that the researcher are considering. However, Targeted proteomics workflow is also another important method because the researchers should validate the bio-markers to clarify if they are still conducting important role in biological pathways with reproducible results in their samples. After identifying the bio-markers, it is a critical to validate them using Triple Quad Mass Spectrometers. Here is how to setup Targeted proteomics workflow more easily and efficiently using software options to quantify the bio-markers.

EDUCATION SESSION 3

Proteomics meets AI

EDUCATION SESSION 3

Proteomics meets AI

6.26 (Wed) 09:00 - 10:15

Chair: Jae-Young Kim / Chungnam National University

ES3-1 6.26 (Wed) 09:00 - 09:20

Interpretation of Mass Spectrometry-Based Proteomics Data for Biological Research

Sunghyun Huh
Bertis Inc.

ES3-2 6.26 (Wed) 09:20 - 09:40

Leveraging AI for Knowledge-based Omics Studies

Sangsoo Lim
Dongguk University

ES3-3 6.26 (Wed) 09:40 - 10:00

Deep Learning Methods for Cancer Drug Response Prediction

Minsik Oh
Myongji University

ES3-4 6.26 (Wed) 10:00 - 10:15

Immuno-Oncology Biomarkers: Toward Personalized Immunotherapy

Kwang Hoe Kim
Cellkey Inc.

EDUCATION SESSION 3

Sunghyun Huh, Ph.D.

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Education

2021.02	Ph.D.	Systems Biology, DGIST
2016.02	B.S.	Physics, Sogang University

Professional Experience

Since 2021.10	At Bertis	Proteomics/Multi-Omics & Team Management
Before 2021.10	Pre-Bertis	Progeomics/Transcriptomics/Epigenomics /Metabolomics

Publications

1. Kim H#, Huh S#, Park J#, Ahn K, Noh Y, Lee S, Kim S, Han Y, Jung H, Yun W, Cho Y, Kwon W, Jang J*, and Kang U* (2024). Development of a fit-for-purpose multi-marker panel for early diagnosis of pancreatic ductal adenocarcinoma. Molecular & Cellular Proteomics. In review.

2. Vu, H. M., Huh, S., Lee, J. H., Lee, S. H.*, & Kim, M.-S.* (2024). Parallel accumulation-serial fragmentation method for in-depth proteomic analysis of bronchoalveolar lavage fluid collected from patients with nonsmall cell lung cancer. Proteomics. Clinical Applications, 18(2), e2300053. https://doi.org/10.1002/prca.202300053

3. Yoon, K.-H., Chu, H., Kim, H., Huh, S., Kim, E.-K., Kang, U.-B., & Shin, H.-C.* (2024). Comparative profiling by data-independent acquisition mass spectrometry reveals featured plasma proteins in breast cancer: a pilot study. Annals of Surgical Treatment and Research, 106(4), 195–202. https://doi.org/10.4174/astr.2024.106.4.195

4. Kang, C.#, Huh, S.#, Nam, D., Kim, H., Hong, J., Hwang, D.*, & Lee, S.-W.* (2022). Novel Online Three-Dimensional Separation Expands the Detectable Functional Landscape of Cellular Phosphoproteome. Analytical Chemistry, 94(35), 12185–12195. https://doi.org/10.1021/acs.analchem.2c02641

5. Huh, S.#, Kang, C.#, Park, J. E., Nam, D., Kim, S. I., Seol, A., Choi, K., Hwang, D., Yu, M.-H., Chung, H. H., Lee, S.-W.*, & Kang, U.-B.* (2022). Novel Diagnostic Biomarkers for High-Grade Serous Ovarian Cancer Uncovered by Data-Independent Acquisition Mass Spectrometry. Journal of Proteome Research, 21(9), 2146–2159. https://doi.org/10.1021/acs.jproteome.2c00218

7. Jeong, Y. S., Huh, S., Kim, J. C., Park, J. Y., Lee, C., Kim, M.-S., Koo, J.*, & Bae, Y.-S.* (2022). 2-Undecanone derived from Pseudomonas aeruginosa modulates the neutrophil activity. BMB Reports, 55(8), 395–400. https://doi.org/10.5483/BMBRep.2022.55.8.009

ES3-1

Interpretation of Mass Spectrometry-Based Proteomics Data for Biological Research

Sunghyun Huh

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Mass spectrometry (MS)-based shotgun proteomics has become an indispensable approach to elucidating complex biological systems. Due to recent advancements in liquid chromatography (LC) and MS instruments, acquisition of proteomics data with high analytical depth and robust quantitative accuracy and precision is now more available than ever. However, the complexity of MS data, which stems from the tedious procedure of sample preparation and LC-MS experiment, as well as the biological intricacy of the proteome, hampers easy interpretation of the acquired mass spectra. Bioinformaticians in the proteomics field have traditionally focused on developing algorithms for confidently identifying peptide sequences from tandem mass spectra. As a result, search tools like SEQUEST, MS-GF+, Comet, MaxQuant, MSFragger, and SAGE have enabled proteomics researchers to gain reliable peptide or protein information from their complex tandem mass spectrum data, although significant progress is still being made in this avenue. Besides peptide identification, however, other post-processing challenges remain, such as false discovery rate control, protein inference, quantification, feature selection, normalization/batch correction, and data filtering. Still, the post-processing pipeline is yet to be standardized, which partly makes MS-based proteomics data less consistent and reproducible when compared to NGS-based data. Ultimately, meaningful interpretation of proteomics data is predicated upon relevant biological information the final processed data contains. Thus, the post-processing steps ought to be adjusted according to the expected biological patterns, whenever these information are available. Here, I will give a brief introduction to the analysis, handling, and interpretation of MS-based proteomics data. I will also mention a few examples where machine learning or artificial intelligence is utilized.

EDUCATION SESSION 3

Sangsoo Lim, Ph.D.

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Education

2014 - 2019	Ph.D.	Seoul National University
2011 - 2013	M.S.	Yonsei University
2006 - 2011	B.S.	Yonsei University

Professional Experience

2023 - Present	Assistant Professor	Dongguk University
2019 - 2023	Postdoc	Seoul National University

Publications

1. Dongmin Bang, Sangsoo Lim, Sangseon Lee, and Sun Kim "Biomedical knowledge graph learning for drug repurposing by extending guilt-by-association to multiple layers", Nature Communications 14(1), 2023 [IF: 17.694]

2. Sangsoo Lim, Youngkuk Kim, Jeonghyeon Gu, Sunho Lee, Wonseok Shin, and Sun Kim "Supervised chemical graph mining improves drug-induced liver injury prediction", iScience 26(1), 2023

3. Sangsoo Lim*, Sangseon Lee*, Yinhua Piao, MinGyu Choi, Dongmin Bang, Jeonghyeon Gu, Sun Kim "On modeling and utilizing chemical compound information with deep learning technologies: A task-oriented approach", Computational and Structural Biotechnology Journal 20, 2022

4. Gung Lee, Ye Young Kim, Hagoon Jang, Ji Seul Han, Hahn Nahmgoong, Yoon Jeong Park, Sang Mun Han, Changyun Cho, Sangsoo Lim, Jung-Ran Noh, Won Keun Oh, Chul-Ho Lee, Sun Kim, Jae Bum Kim "SREBP1c-PARP1 axis tunes anti-senescence activity of adipocytes and ameliorates metabolic imbalance in obesity", Cell Metabolism 34(5), 2022

5. Yoon Jeong Park, Sangseon Lee*, Sangsoo Lim*, Hahn Nahmgoong, Yul Ji, Jin Young Huh, Assim A. Alfadda, Sun Kim, and Jae Bum Kim "DNMT1 maintains metabolic fitness of adipocytes through acting as an epigenetic safeguard of mitochondrial dynamics", Proceedings of the National Academy of Sciences 118(11), 2021

ES3-2

Leveraging AI for Knowledge-based Omics Studies

Sangsoo Lim

Division of AI Software Convergence, Dongguk University, Seoul, Korea

The integration of AI into knowledge-based omics studies is revolutionizing our understanding of complex biological systems. This presentation explores the use of AI to enhance the analysis of large-scale biological data through knowledge graphs like HetioNet, and detailed mapping of biological pathways and protein-protein interactions. By leveraging machine learning and graph-based approaches, we can systematically interpret these intricate data structures, enabling more accurate predictions of disease association, and potential therapeutic targets. These AI-enhanced methods not only streamline data integration but also deepen our insights into the molecular underpinnings of health and disease, paving the way for breakthroughs in precision medicine.

EDUCATION SESSION 3

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Education

2015.09 - 2021.08	Ph.D	Seoul National University
2011.03 - 2015.08	B.S.	Seoul National University

Professional Experience

2022.03 - Present	Assistant Professor	Myongji University
2021.10 - Present	Postdoctoral Research fellow	SNU BK21 FOUR Intelligence Computing , Seoul National University
2021.09 - 2021.09	Postdoctoral Research fellow	SNU Bioinformatics Institute, Seoul National University

Publications

1. Moon, J. H., & Oh, M. (2023). TFNetPropX: A Web-Based Comprehensive Analysis Tool for Exploring Condition-Specific RNA-Seq Data Using Transcription Factor Network Propagation. Applied Sciences (SCIE, IF=2.7), 13(20), 11399. Jeong, D., Koo, B., Oh, M., Kim, T. B., & Kim, S. (2023). GOAT: Gene-level biomarker discovery from multi-Omics data using graph ATtention neural network for eosinophilic asthma subtype. Bioinformatics (SCIE, IF=5.8), 39(10),

2. Han, J. S., Jeon, Y. G., Oh, M., Lee, G., Nahmgoong, H., Han, S. M., ... & Kim, J. B. (2022). Adipocyte HIF2α functions as a thermostat via PKA Cα regulation in beige adipocytes. Nature Communications (SCIE, IF=16.6), 13(1), 3268.

3. Jeong D, Lim S, Lee S, Oh M, Cho C, Seong H, Jung W, Kim S. (2021). Construction of Condition-Specific Gene Regulatory Network using Kernel Canonical Correlation Analysis. Frontiers in Genetics (SCIE, IF=4.599).

4. Oh M (*), Park S (*), Kim S, Chae H. (2021). Machine learning-based analysis of multi-omics data on the cloud for investigating gene regulations. Briefings in bioinformatics (SCIE, IF=11.622).

5. Kang H, Ahn H, Jo K, Oh M, Kim S. (2021). mirTime: identifying condition-specific targets of MicroRNA in time-series transcript data using Gaussian process model and spherical vector clustering. Bioinformatics (SCIE, IF=6.937).

6. Oh M, Park S, Lee S, Lee D, Lim S, Jeong D, Jo K, Jung I, Kim S. (2020). DRIM: A web-based system for investigating drug response at the molecular level by condition-specific multi-omics data integration. Frontiers in Genetics (SCIE, IF=4.599).

7. Seo S, Oh M, Park Y, Kim S. (2018). DeepFam: deep learning based alignment-free method for protein family modeling and prediction. Bioinformatics (SCIE, IF=6.937), 34(13), i254-i262.

ES3-3

Deep Learning Methods for Cancer Drug Response Prediction

Minsik Oh

School of Software Convergence, Myongji University

The variability in drug response among cancer patients remains a major challenge in cancer therapy. Multi-omics data is one of several factors predicting this variability. This session aims to present a comprehensive database for cancer drug response prediction research, along with basic concepts in machine learning and deep learning. It will also review recently proposed deep learning methods for cancer drug response prediction.

EDUCATION SESSION 3

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Education

2012.03 - 2019.02	Ph.D.	Chungnam National University
2010.03 - 2012.02	M.S.	Chungnam National University
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Professional Experience

2021.01 - Present	Head of Bio R&D Center	CellKey
2019.03 - 2020.12	Postdoctoral Researcher	Research Center for Bioconvergence Analysis, Korea Basic Science Institute
2012.03 - 2019.02	Ph.D. student and research assistant	Research Center for Bioconvergence Analysis, Korea Basic Science Institute

Publications

1. Kim, K. H., Lee, S. Y., Baek, J. H., Lee, S. Y., Kim, J. Y., & Yoo, J. S. (2021). Measuring fucosylated alpha-fetoprotein in hepatocellular carcinoma: A comparison of μTAS and parallel reaction monitoring. PROTEOMICS–Clinical Applications, 2000096.

2. Kim, K. H., Lee, S. Y., Kim, D. G., Lee, S. Y., Kim, J. Y., & Yoo, J. S. (2020). Absolute Quantification of N-Glycosylation of Alpha-Fetoprotein Using Parallel Reaction Monitoring with Stable Isotope-Labeled N-Glycopeptide as an Internal Standard. Analytical Chemistry, 92(18), 12588-12595.

3. Lee, S., Hwang, S., Seo, M., Shin, K. B., Kim, K. H., Park, G. W., & No, K. T. (2020). BMDMS-NP: A comprehensive ESI-MS/MS spectral library of natural compounds. Phytochemistry, 177, 112427.

4. Kim, K. H., Kim, J. Y., & Yoo, J. S. (2019). Mass spectrometry analysis of glycoprotein biomarkers in human blood of hepatocellular carcinoma. Expert review of proteomics, 16(7), 553-568.

5. Kim, K. H., Park, G. W., Jeong, J. E., Ji, E. S., An, H. J., Kim, J. Y., & Yoo, J. S. (2019). Parallel reaction monitoring with multiplex immunoprecipitation of N-glycoproteins in human serum for detection of hepatocellular carcinoma. Analytical and bioanalytical chemistry, 411(14), 3009-3019.

6. Ji, E. S., Lee, H. K., Park, G. W., Kim, K. H., Kim, J. Y., & Yoo, J. S. (2019). Isomer separation of sialylated O-and N-linked glycopeptides using reversed-phase LC–MS/MS at high temperature. Journal of Chromatography B, 1110, 101-107

ES3-4

Immuno-Oncology Biomarkers: Toward Personalized Immunotherapy

Kwang Hoe Kim

CellKey Inc, Seoul, Republic of Korea

Cancer immunotherapy has markedly transformed the treatment landscape for cancer patients, notably improving overall survival rates. Particularly, immune checkpoint blockade therapy has emerged as a significant advancement in the treatment of various cancer types in recent years. Combined with novel immune-oncology drugs, checkpoint blockade therapies have become the recent focus of numerous clinical trials in cancer, although response rates vary widely. Therefore, discovering biomarkers that predict the clinical efficacy of immune-oncology treatments can help in selecting tumor types and patient subgroups with a high likelihood of response. In this study, we present an integrated analysis using liquid chromatography-tandem mass spectrometry (LC-MS/MS) to examine protein expression, phosphorylation, and N-glycosylation in serum samples from cervical cancer patients undergoing immune-oncology therapy. We administered immuno-oncology treatment to cervical cancer patients twice and monitored changes in proteins, their phosphorylation, and N-glycosylation at each time point post-administration. Consequently, we identified proteins exhibiting differences in treatment response among cervical cancer patients. Protein biomarkers capable of predicting the response to immune-oncology drugs are expected to play a very important role in personalized immunotherapy in the future.

EDUCATION SESSION 4

Public MS Data Repository

EDUCATION SESSION 4

Public MS Data Repository

6.26 (Wed) 09:00 - 10:15

Chair: Heeyoun Hwang / Korea Basic Science Institute (KBSI)

ES4-1 6.26 (Wed) 09:00 - 09:20

Introduction of the Korea BioData Station (K-BDS)

Kiwon Jang
Korea Research Institute of Bioscience and Biotechnology (KRIBB)

ES4-2 6.26 (Wed) 09:20 - 09:40

KPOP: Korea ProteOme rePository

Seungjin Na
Korea Basic Science Institute (KBSI)

ES4-3 6.26 (Wed) 09:40 - 10:00

Development of a web-based tool for visual analysis of multi-omics information of cancer patients

Hyun-Jin Kim
National Cancer Center (NCC)

ES4-4 6.26 (Wed) 10:00 - 10:15

ChatSQ in KPOP: Unlocking the Future of No-Code Proteomics Data Analysis

Sangtae Kim
NGeneBioAI, Inc

EDUCATION SESSION 4

Kiwon Jang, Ph.D.

Position: Senior Researcher
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Korea Bioinformation Center (KOBIC)
Korea Research Institute of Bioscience & Biotechnology (KRIBB)
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Education

2015.09 - 2019.02	Ph.D.	Bio and Brain Engineering, KAIST
2013.09 - 2015.08	M.S.	Bio and Brain Engineering, KAIST
2006.03 - 2013.02	B.S.	Bioengineering, Hanyang University

Professional Experience

2023.03 - Present	Senior Researcher	KOBIC, KRIBB, Korea
2019.03 - 2020.02	Post-Doctoral researcher	OMICS lab, KAIST,

Publications

1. Shim, H. *, Jang, K. *, Bang, Y. H. *, Chu, H. B. K., Kang, J., Lee, J. Y., Cho, S., Lee, H. S., Jeon, J., Hwang, T., Joe, S., Lim, J., Choi, J. H., Joo, E. H., Park, K., Moon, J. H., Han, K. Y., Hong, Y., Lee, W. Y., Kim, H. C., ... Kim, Y. J. (2024). Comprehensive profiling of DNA methylation in Korean patients with colorectal cancer. BMB reports, 57(2), 110–115. (*Co-first author)

2. Lee, B., Hwang, S., Kim, P. G., Ko, G., Jang, K., Kim, S., Kim, J. H., Jeon, J., Kim, H., Jung, J., Yoon, B. H., Byeon, I., Jang, I., Song, W., Choi, J., & Kim, S. Y. (2023). Introduction of the Korea BioData Station (K-BDS) for sharing biological data. Genomics & informatics, 21(1), e12.

3. Jang, K.*, Park, M.J.*, Park, J.S., Hwangbo, H., Sung, M.K., Kim, S., Jung, J., Lee, J.W.,Ahn, S.-H., Chang, S., and Choi, J.K. (2020). Computational inference of cancer-specific vulnerabilities in clinical samples. Genome Biol. 21, 155.

4. Jung, J., Jang, K., Ju, J.M., Lee, E., Lee, J.W., Kim, H.J., Kim, J., Lee, S.B., Ko, B.S., Son, B.H., et al. (2018). Novel cancer gene variants and gene fusions of triple-negative breast cancers (TNBCs) reveal their molecular diversity conserved in the patient-derived xenograft (PDX) model. Cancer Lett. 428, 127–138.

5. Jang, K.*, Kim, K*., Cho, A., Lee, I., and Choi, J.K. (2017). Network perturbation by recurrent regulatory variants in cancer. PLoS Comput. Biol. 13. (*Co-first author)

6. Yang, W., Bang, H., Jang, K., Sung, M.K., and Choi, J.K. (2016). Predicting the recurrence of noncoding regulatory mutations in cancer. BMC Bioinformatics 17.

7. Kim, K.*, Jang, K.*, Yang, W.*, Choi, E.-Y., Park, S.-M., Bae, M., Kim, Y.-J., and Choi, J.K. (2016). Chromatin structure–based prediction of recurrent noncoding mutations in cancer. Nat. Genet. (*Co-first author)

ES4-1

Introduction of the Korea BioData Station (K-BDS)

Kiwon Jang[1]

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A wave of new technologies has created opportunities for the cost-effective generation of high-throughput profiles of biological systems, foreshadowing a "data-driven science" era. The large variety of data available from biological research is also a rich resource that can be used for innovative endeavors. However, we are facing considerable challenges in big data deposition, integration, and translation due to the complexity of biological data and its production at unprecedented exponential rates. To address these problems, in 2020, the Korean government officially announced a national strategy to collect and manage the biological data produced through national R&D fund allocations and provide the collected data to researchers. To this end, the Korea Bioinformation Center (KOBIC) developed a new biological data repository, the Korea BioData Station (K-BDS), for sharing data from individual researchers and research programs to create a data-driven biological study environment. The K-BDS is dedicated to providing free open access to a suite of featured data resources in support of worldwide activities in both academia and industry.

EDUCATION SESSION 4

Seungjin Na, Ph.D.

Position: Senior Researcher
Department: Digital Omics Research Center
Affiliation: Korea Basic Science Institute
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Education

2007.03-2012.02	Ph.D.	Mechanical and Information Engineering, University of Seoul, Seoul, Korea
2004.03- 2006.02	M.S.	Mechanical and Information Engineering, University of Seoul, Seoul, Korea
1997.03 - 2004.02	B.S.	Mechanical Engineering, University of Seoul, Seoul, Korea

Professional Experience

2023.12-present	Senior Researcher	Digital Omics Research Center, Korea Basic Science Institute, Cheongju, Korea
2018.04~2023.12	Research Professor	Department of Computer Science, Hanyang University, Seoul, Korea
2012.03~2018.02	Postdoctoral Scholar	Department of Computer Science and Engineering, University of California, San Diego, La Jolla, US

Publications

1. Na S, Choo Y, Yoon TH, Paek E. CyGate provides a robust solution for automatic gating of single cell cytometry data. Ana Chem. 2023 Nov; 95(46): 16918-16926.

2. Son J, Na S*, Paek E*. DbyDeep: Exploration of MS detectable peptides via deep learning. Anal Chem. 2023 Aug; 95(30): 11193-11200.

3. Na S, Choi H, Paek E. Deephos: Predicted spectral database search for TMT-labeled phosphopeptides and its false discovery rate estimation. 2022 May; Bioinformatics. 38(11): 2980-2987.

4. Li H, Na S, Hwang KB, Paek E. TIDD: tool-independent and data-dependent machine learning for peptide identification. BMC Bioinformatics. 2022 Mar; 23(1): 109.

5. Song I, Na S, Paek E, Lee KJ. Cataract-associated new mutants S175G/H181Q of βB2-Crystallin and P24S/S31G of γD-Crystallin are involved in protein aggregation by structural changes. Int J Mol Sci. 2020 Sep; 21(18): 6504.

6. Na S, Paek E. Computational methods in mass spectrometry-based structural proteomics for studying protein structure, dynamics, and interactions. Comput Struct Biotechnol J. 2020 Jun; 18: 1391-1402.

7. Choi S, Ju S, Lee J, Na S, Paek E. Proteogenomic approach to UTR peptides identification. J Proteome Res. 2020 Jan; 19(1): 212-220.

8. Shin J, Kwon Y, Lee S, Na S, Hong EY, Ju S, Jung HG, Kaushal P, Shin S, Back JH, et al. Common repository of FBS proteins (cRFP) to be added to a search database for mass spectrometric analysis of cell secretome. J Proteome Res. 2019 Oct; 18(10): 3800-3806.

9. Na S, Kim J, Paek E. MODplus: robust and unrestrictive identification of post-translational modifications using mass spectrometry. Anal Chem. 2019 Sep; 91(17): 11324-11333.

10. Na S, Lee JJ, Joo JWJ, Lee KJ, Paek E. deMix: Decoding deuterated distributions from heterogeneous protein states via HDX-MS. Sci Rep. 2019 Feb; 9(1): 3176.

ES4-2

KPOP: Korea ProteOme rePository

Seungjin Na

Digital Omics Research Center., Korea Basic Science Institute., 162Yeongudanji-ro, Ochang-eup, Cheongwon-gu, Cheongju 28119, Republic of Korea

With the surge in mass spectrometry (MS)-based proteomics, there is a growing abundance of data from proteomics projects worldwide. Since 2012, the ProteomeXchange (PX) consortium has played a key role in standardizing the submission and dissemination of public MS proteomics data. To promote the global sharing and reuse of proteomic resources, we introduce KPOP repository (https://kbds.re.kr/KPOP), a public platform facilitating open access to a wealth of proteomic resources, encompassing various types of MS data, analysis results, and metadata. KPOP has implemented user-friendly interfaces, accelerated file transfers, and flexible file management, significantly enhancing the usability and value of proteomics data for scientific research.

The primary goal of KPOP is to curate meticulously maintained data sets, supporting prevalent "big data" approaches in proteomics, including machine learning and computational modeling. These approaches enable researchers to decipher complex data patterns and associations from proteomics data, driving innovation in the field. In addition to sample information, KPOP retains metadata related to fractionation, digestion, quantification, modifications, experiment type, and the MS instrument employed. KPOP is a member of K-BDS (Korea BigData Station), which serves as a comprehensive repository for various biological research data, promoting integrated "multi-omics" analyses. This integration is particularly beneficial when datasets, such as whole exome and RNA sequencing data, are simultaneously available, originating from the same project. Researchers can combine proteomics data with other omics data to gain deeper insights into biological processes and disease mechanisms.

EDUCATION SESSION 4

Hyun-Jin Kim, Ph.D.

Position: Principal Researcher, Cancer Big Data Center Team Leader, Data Link & Operation Team Adjunct Associate Professor
Department: Department of Cancer Control and Population Health, NCC
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Education

2013.02	Ph.D.	Seoul National University
2009.02	MPH in Epidemiology	Seoul National University
2007.02	M.S.	Kangwon National University
2005.02	B.A.	Kangwon National University

Professional Experience

2021.04 - Present	Team Leader	Data Link & Operation Team, National Cancer center
2023.09 - Present	Adjunct Associate Professor	Department of Cancer Control and Population Health, NCC GCSP
2022.03 - Present	Principal Research Engineer	Cancer Big Data Center, National Cancer Control Institute, National Cancer Center

Publications

1. Effects of the abdominal fat distribution on the relationship between exposure to air pollutants and thyroid hormones among Korean adult males (2023) Hyun Jin Kim , Byungmi Kim, Seyoung Kim, Hyuktae Kwon, Jae Moon Yun, Belong Cho, Jin Ho Park. Eur J Med Res. 28(1):423.

2. A genome wide by PM 10 exposure interaction study for blood pressure in Korean adults (2023) Hyun Jin Kim , Ho Young Son, Philiip Park, Jae Moon Yun, Hyuktae Kwon, Belong Cho, Jong Il Kim, Jin Ho Park . Sci Rep. 13(1):13060.

3. Effects of vitamin D on associations between air pollution and mental health outcomes in Korean adults: Results from the Korea National Health and Nutrition Examination Survey ((2023) Hyun Jin Kim , Hyo Seon Kim, Seyoung Kim, Juyeon Hwang, Hyejin Lee, Bohyun Park, Byungmi Ki m. J Affect Disord. 320:390 396.

4. A whole genome reference panel of 14,393 individuals for East Asian populations accelerates discovery of rare functional variants (Jaeyong Choi, Sungjae Kim, Juhyun Kim, Ho Young Son, Seong Keun Yoo, Chang Uk Kim, Young Jun Park, Sungji Moon, Bukyoung Cha, Min Chul Jeon1, Kyunghyuk Park, Jae Moon Yun, Belong Cho, Namcheol Kim, Changhoon Kim, Nak Jung Kwon, Young Joo Park, Fumihiko Matsuda, Yukihide Momozawa, Michiaki Kubo; Biobank Japan Project; Hyun Jin Kim , Jin Ho Park, Jeong Sun Seo, Jong Il Kim, Sun Wha Im . Sci Adv. 9(32):eadg6319.

5. Annual exposure to PM10 is related to cerebral small vessel disease in general adult population (Han Yeong Jeong, Hyun Jin Kim , Ki Woong Nam, Su Min Jeong, Hyuktae Kwon, Jin Ho Park,Hyung Min Kwon . Sci Rep 12(1):19693.

6. Association between long term air pollution exposure and insulin resistance independent of abdominal adiposity in Korean adults (Seo Eun Hwang, Hyuktae Kwon, Jae Moon Yun,Kyungha Min, Hyun Jin Kim , Jin Ho Park . Sci Rep 12(1):19147.

ES4-3

Development of a web-based tool for visual analysis of multi-omics information of cancer patients

Hyun-Jin Kim

Principal Researcher , Cancer Big Data Center Team Leader, Data Link & Operation Team Adjunct Associate Professor, Department of Cancer Control and Population Health, NCC GCSP, National Cancer Center, Goyang si, Gyeonggi do, South Korea

Multi-omics analysis in cancer research is an important approach to integrate high-dimensional datasets to better understand the molecular biology of cancer. In addition, integrating individual clinical information with omics profile may provide significant opportunities for precision oncology. An open-access web portal called Korea-Cancer Omics REsearch (K-CORE) was developed to provide visualization and download of analysis results through multidimensional linkage of omics data and clinical information. This web portal allows users to upload their data to the portal for integrated analysis of various clinical and omics profiles. Users can implement a variety of integrated visualization analysis within this portal (e. g. Circos Plot, Oncoprint, Lollipop Plot, Heatmap, Kaplan-Meier, Cox-regression, Correlation Plot, CNV Plot, and Boxplot). Patient-specific drug information can be also checked through the report function. In addition to integrated analysis, we provide a single analysis for each dimension of data and plan to continue to expand. K-CORE (https://cancerdata.re.kr/k-core) may be used as a meaningful web analysis tool in precision oncology by enabling integrated analysis of high-dimensional information including clinical and omics data in cancer patients. In addition, we introduce various omics data on cancer patients released by the National Cancer Data Center and introduce K-CORE Analytics, which enables raw data processing as well as more detailed analysis.

EDUCATION SESSION 4

Sangtae Kim, Ph.D.

Position: CEO
Department:
Affiliation: NGeneBioAI
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E-mail: sangtae.kim@ngenebio.ai
Homepage: http://www.ngenebio.ai

Education

2006.09-2012.05	Ph.D.	University of California, San Diego
2000.03-2002.02	M.S.	Seoul National University
1996.03-2000.02	B.S.	Seoul National University

Professional Experience

2024.04-current	Chief Executive Officer	NGeneBioAI
2021.10-2024.03	Chief Technology Officer	Bertis Bioscience
2020.06-2021.10	Principal Bioinformatics Scientist	Seer
2015.06-2020.05	Staff Bioinformatic Scientist	Illumina
2012.07-2015.05	Senior Research Scientist	Pacific Northwest National Laboratory

Publications

1. S Kim, K Scheffler, AL Halpern, MA Bekritsky, E Noh, M Källberg, X Chen, Y Kim, D Beyter, P Krusche, CT Saunders. Strelka2: Fast and accurate variant calling for clinical sequencing applications. *Nature Methods*, 15:591-594 (2018).

2. J Park, PD Piehowski, C Wilkins, M Zhou, J Mendoza, GM Fujimoto, BC Gibbons, JB Shaw, Y Shen, AK Shukla, RJ Moore, T Liu, VA Petyuk, N Tolic, L Pasa-Tolic, RD Smith, SH Payne, S Kim. Informed-Proteomics: Open-Source Software Package for Top-down Proteomics. *Nature Methods*. 14:909-914 (2017).

3. S Kim and P Pevzner. MS-GF+ makes progress towards a universal database search tool for proteomics. *Nature Communications*, 5, 5277, (2014). PMID: 25358478

4. B Zhang, J Wang, X Wang, J Zhu, Q Liu, Z Shi, MC Chambers, LJ Zimmerman, KF Shaddox, S Kim, SR Davies, S Wang, P Wang, CR Kinsinger, RC Rivers, H Rodriguez, RR Townsend, MJ Ellis, SA Carr, DL Tabb, RJ Coffey, RJ Slebos, DC Liebler, and the NCI CPTAC. Proteogenomic characterization of human colon and rectal cancer. *Nature*, 13, 382-387, (2014). PMID: 25043054

5. S Kim, N Mischerikow, N Bandeira, JD Navarro, L Wich, S Mohammed, A JR Heck, and P Pevzner. The Generating Function of CID, ETD and CID/ETD Pairs of Tandem Mass Spectra: Applications to Database Search. *Molecular & Cellular Proteomics*, 9, 2840-2852, (2010).

6. **S Kim**, N Gupta, and P Pevzner. Spectral Probabilities and Generating Functions of Tandem Mass Spectra: A Strike against Decoy Databases. *Journal of Proteome Research*, 7, 3354-3363 (2008).

Please refer to http://goo.gl/1PtuNq for the full publication list.

ES4-4

ChatSQ in KPOP: Unlocking the Future of No-Code Proteomics Data Analysis

Sangtae Kim

NGeneBioAI, Inc

KPOP facilitates big data science in proteomics by providing open access to curated mass spectrometry datasets. Achieving KPOP's full potential hinges on enabling researchers to efficiently access its data to test hypotheses, free from the burden of data downloads and the complexities of programming. We present ChatSQ, a pioneering platform that innovates big data analysis. By integrating Large Language Models (LLMs) with Python environments, ChatSQ offers a no-code data science experience through intuitive natural language commands. ChatSQ's unique capabilities, including its specialization in spectrum data analysis and systems biology, democratize data analysis for a broader scientific community and significantly streamline the data interpretation process. By facilitating direct interaction with KPOP, ChatSQ enhances the accessibility, sharing, and reusability of proteomic data analyses, eliminating the hurdle of large data downloads. We delve into the practical applications of ChatSQ within KPOP and highlight its role in advancing open science and accelerating discoveries in proteomics research.

SATELLITE SESSION

SATELLITE SESSION 1

2024년도 다중오믹스기반 정밀의료기술개발 사업단 성과 보고회

6.26 (Wed) 09:00-12:00

주최 : 한구연구재단 / 다중오믹스 기반 정밀의료기술개발사업단

09:00~09:05	**개회사**	**김광표** 경희대학교
09:05~09:20	**다중오믹스 기반 정밀의료기술 개발 사업 소개**	**남진우** 한국연구재단
09:20~09:30	**단체 사진 촬영**	
09:30~09:50	**P-DIAMOND (폐암 정밀오믹스) 연구단 총괄 성과보고**	**김광표** 경희대학교
09:50~10:10	**다중오믹스 기반 천식 정밀의료 COREA/PRISM 연구 총괄 성과보고**	**김태범** 서울아산병원
10:10~10:30	**CKD 엑소좀 정밀오믹스 연구단 성과 보고**	**류성호** 순천향대학교
10:30~10:40	**Coffee Break**	
10:40~11:00	**P-DIAMOND (폐암 정밀오믹스) 연구단 대표 연구 성과** - 난치성 폐암 다중오믹스 연구 - 난치성 유방암 다중오믹스 연구	**나승진** KBSI **김경곤** 울산의대
11:00~11:20	**다중오믹스 분석을 통한 천식 예후 예측 바이오마커 개발**	**김경곤** 서울아산병원
11:20~11:40	**CKD 엑소좀 정밀오믹스 연구단 대표 연구 성과**	**김광표/김태범/류성호**
11:40~12:00	**발전 토론**	**김광표/김태범/류성호**
12:00	**폐회식 / 식사 이동**	**김광표** 경희대학교

SATELLITE SESSION 2

Chair: Myeong-Hee Yu / Bertis Inc.
Jong Bae Park / National Cancer Center (NCC)

6.26 (Wed) 14:00 - 17:00

ST-2-1 6.26 (Wed) 14:05–14:20

National Cancer Data Center

Kui Son Choi
National Cancer Center (NCC)

ST-2-2 6.26 (Wed) 14:20–14:40

Cancer Proteogenomics in KNCC

Jong Bae Park
National Cancer Center (NCC)

ST-2-3 6.26 (Wed) 14:40-14:55

Proteogenomic analysis reveal prognostic subclass in early-onset breast cancer patients

Sun-Young Kong
National Cancer Center (NCC)

ST-2-4 6.26 (Wed) 14:55-15:15

Comprehensive genomic characterization of Korean advanced pan-cancer patients facilitates personalized treatment

Jason K. Sa
Korea University

ST-2-5 6.26 (Wed) 15:20–15:35

Introduction and Utilization of Open Data in the National Cancer Data Center

Hyun-Joo Kong
National Cancer Center (NCC)

ST-2-6 6.26 (Wed) 15:35-15:50

Comprehensive Proteogenomic Characterization of Renal Cell Carcinoma

Harim Koo
National Cancer Center (NCC)

ST-2-7 6.26 (Wed) 15:50-16:05

Integrated proteogenomic analysis characterizes clinically relevant molecular subtypes associated with medulloblastoma progression

Seong-Min Park
National Cancer Center (NCC)

ST-2-8 6.26 (Wed) 16:05-16:20

Development of a web-based tool for visual analysis of multi-omics information of cancer patients

Hyun-Jin Kim
National Cancer Center (NCC)

ST-2-9 6.26 (Wed) 16:20–16:35

Multi-omics data analysis method using K-CORE Analytics

JaeWoo Ahn
National Cancer Center (NCC)

SATELLITE SESSION-2

Kui Son, CHOI, Ph.D.

Position: Professor
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Affiliation: National Cancer Center
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Homepage:

Education

1991.03-1995.02	B.S.	Dongduk Women's University
1995.03-1997.02	M.P.H.	Yonsei University Graduate School
1997.03-2000.02	Ph.D.	Yonsei University Graduate School

Professional Experience

2002.01-2013.12	Scientist	National Cancer Center
2008.01-2008.12	Visiting Professor	Feinberg School of Medicine, Northwestern Univ.
2014.01-current	Professor	Graduate School of Cancer Science and Policy, National Cancer Center
2018.01-current	Director	Cancer Data Center, National Cancer Center

Academic Society

2017..02-current	Editorial board member	The Korean Academy of Health Policy and Management
2017.03-current	Board member	The Korean Cancer Association
2016.06-current	Member	The Korean Society of Medical Informatics

Publications

1. Bui CN, Hong S, Suh M, Jun JK, Jung KW, Lim MC, Choi KS. Effect of Pap smear screening on cervical cancer stage at diagnosis: results from the Korean National Cancer Screening Program. J Gynecol Oncol. 2021 Sep;32(5):e81.

2. Choi E, Jun JK, Suh M, Jung KW, Park B, Lee K, Jung SY, Lee ES, Choi KS. Effectiveness of the Korean National Cancer Screening Program in reducing breast cancer mortality. NPJ Breast Cancer. 2021 Jun 28;7(1):83.
Hwangbo Y, Kang D, Kang M, Kim S, Lee EK, Kim YA, Chang YJ, Choi KS, Jung SY, Woo SM, Ahn JS, Sim SH, Hong YS, Pastor-Barriuso R, Guallar E, Lee ES, Kong SY, Cho J. Incidence of Diabetes After Cancer Development: A Korean National Cohort Study. JAMA Oncol. 2018 Aug 1;4(8):1099-1105.

3.Jun JK, Choi KS, Lee HY, Suh M, Park B, Song SH, Jung KW, Lee CW, Choi IJ, Park EC, Lee D. Effectiveness of the Korean National Cancer Screening Program in Reducing Gastric Cancer Mortality. Gastroenterology. 2017 May;152(6):1319-1328.e7.

4. Yoo JE, Shin DW, Han K, Kim D, Jeong SM, Koo HY, Yu SJ, Park J, Choi KS. Association of the Frequency and Quantity of Alcohol Consumption With Gastrointestinal Cancer. JAMA Netw Open. 2021 Aug 2;4(8):e2120382

ST-2-1

National Cancer Data Center

Kui Son Choi

National Cancer Center, Korea

Cancer big data is essential to understand better the underlying mechanisms for cancer development, diagnosis, treatment, and outcome. The National Cancer Center (NCC) Korea recognized the value of big data as a core resource for next-generation cancer research and developed a Clinical Research Data Warehouse (CRDW) consisting of clinical data, genomic data (e.g., NGS sequencing), and medical image data (e.g., CT, MRI, mammography, pathology). The CRDW contains approximately 440,000 patients and regularly accumulates data for all types of cancer. These datasets have been refined and into cancer registry consisting of clinically meaningful features.

In 2021, an amendment to the Cancer Control Act was implemented to ensure the collection and use of cancer data at the national level. Under the law, the NCC has been designated as the National Cancer Data Center (NCDC) and will play a role in collecting, linking, and utilizing data held by public institutions. In 2022, the Ministry of Health and Welfare launched the "Korea-Clinical Data Utilization Network for Research Excellence (K-CURE)" to build a network for cancer research by building a linked database consisting of clinical data from hospitals and public data from public institutions. The K-CURE project plans to establish and operate “Cancer Clinical Libraries” for ten 10 cancer types and “Public Data Libraries,” linked databases from the Korea Central Cancer Registry, National Health Insurance Service (NHIS), Health Insurance Review & Assessment Service (HIRA), and Statistics Korea. This project will establish 1.65 million cancer patients’ clinical data and 4.50 million cancer patients’ public data by 2025, and clinical and public data integration will be promoted.

The NCDC will drive scientific discovery by connecting data sets with analytics tools, allowing users to share, integrate, analyze, and visualize cancer research. Specifically, multi-omics data produced by the Cancer Proteogenomics Research Group was collected in the NCDC database. The Cancer Proteogenomic Research Group has produced a comprehensive multi-omics dataset containing WGS, WES, transcriptome, and proteome from 1,500 paired normal and tumor samples across 12 tumor sites. Following the project’s conclusion, the multi-omics data with clinical data have been deposited with the NCDC. Additionally, the NCDC has developed a platform to support multi-omics data analysis. This platform facilitates integrated analysis and visualization between clinical and omics data. It provides a variety of analytical tools, covering quality control and analysis of WGS/WES data as well as analysis of transcriptome and proteome data.

This presentation will introduce the challenges and measures that the National Cancer Center will take to promote the construction of multi-omics and tumor image data in the future.

SATELLITE SESSION-2

Jong Bae Park, phD

Position: Professor
Department: Dept. Biomedical Science
Affiliation: National Cancer Center Graduate School
Office: 031-920-2450
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Education

1994	B.S.	Department of biochemistry, College of Natural Science, Gyeongsang National University, Chinju , Korea
1998	M.S.	Department of Life Science, Pohang University of Science and Technology, Pohang, Korea
2001	Ph.D.	Division of Molecular and Life Sciences, Pohang University of Science and Technology, Pohang, Korea

Professional Experience

2002-2006	Post-doctoral fellow	Division of Neuroscience, Harvard medical school
2001. 10. – 2004. 12	Principle investigator	Specific Organs cancer Branch, National Cancer Center
2006-2013	Associate professor/ chair	System Cancer Science, Graduate School of Cancer Science and Policy
2014-2017	Professor/Dean	Graduate School of Cancer Science and Policy

Publications

1. Integrated proteogenomic characterization of glioblastoma evolution: Cancer Cell (2024) 1:S1535-6108(23)00443-9.

2. Cross-talk between PARN and EGFR-STAT3 Signaling Facilitates Self-Renewal and Proliferation of Glioblastoma Stem Cells.: ***Cancer Research*** (2023) 15;83(22):3693-3709.

3. IGFBP5 is an ROR1 ligand promoting glioblastoma invasion via ROR1/HER2-CREB signaling axis: ***NATURE COMMUNICATIONS***. (2023) 22;14(1):1578

4. Modulation of Nogo receptor 1 expression orchestrates myelin-associated infiltration of glioblastoma: ***BRAIN*** (2021) 3:144(2):636-654

5. Transcriptional regulatory networks of tumor-associated macrophages that drive malignancy in mesenchymal glioblastoma: ***GENOME BIOLOGY***(2020). 21(1):216~

6. ARS2/MAGL signaling in glioblastoma stem cells promotes self-renewal and M2-like polarization of tumor-associated macrophages: ***NATURE COMMUNICATIONS***(2020). 11(1):2978~

Partial List of Published Work from Year 1994 (out of ~100peer-reviewed manuscripts, citations, ~4,500)

ST-2-2

Cancer Proteogenomics in KNCC

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Over the past decades, our understanding of cancer-related molecular mechanisms and cancer diagnosis has advanced exponentially, thanks to cancer genomics. However, our knowledge based on genomic and transcriptomic data remains incomplete. Many clinical trials based on this information are still struggling due to the lack of comprehensive insights that can fully explain cancer phenotypes. To address the current gaps in our molecular understanding of cancer biology, we leveraged recent advancements in mass spectrometry-based protein sequencing and the identification of protein modifications to predict more precise mechanisms of cancer progression. By analyzing 12 cancer types and 1,600 tumor samples using proteogenomics, we have tackled the challenges posed by glioblastoma's high recurrence rate—95% within five years—and the limited treatment options for recurrent cases. Our study included 123 longitudinal pairs of glioblastoma patient samples, covering whole exome, transcriptome, global proteome, and phosphoproteome analyses. This approach has illuminated the dynamic regulation of cancer signaling during recurrence. Our findings highlight the fluid nature of gene expression-based subtypes and the diversification of oncogenic signaling pathways. This comprehensive insight into tumor-stromal interactions has led to the identification of novel therapeutic targets for recurrent glioblastoma.

SATELLITE SESSION-2

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Education

1991-1997	MD	Ewha Womens University College of Medicine, Seoul, Korea
1998-2001	MS	Ewha Womens University Graduate School of Medicine, Korea
2002-2005	PhD	Sungkyunkwan University Graduate School of Medicine, Korea

Professional Experience

1997.03-2002.02	Internship &Resident	Samsung Medical Center
2002.03-2005.02	Clinical Fellowship	Samsung Medical Center & NCC
2005.03-present	Faculty, Department of Laboratory Medicine	National Cancer Center
2005.03-present	Associate Scientist	Hematologic Malignancies Branch, National Cancer Center
2009.02-2012.01	Senior Scientist	Hematologic Malignancies Branch, National Cancer Center
2009.09-2011.08	Research Fellow	Dana-Farber Cancer Institute
2013.03-2017.02	Chief	Translational Epidemiology Branch, National Cancer Center
2014.03-Present	Associate Professor & Professor	Department of System Cancer Science, Graduate School of Cancer Science & Policy
2017.03-2017.11	Chief	Translational Research Branch, National cancer center
2017.03-2019.01	Chief	Flow Cytometry Unit
2018.01-2021.02	Chief	Department of Laboratory Medicine, National cancer center
2021.09- Present	Chief Scientist	Cancer Diagnostics Branch, National cancer center
2021.09- Present	Chief Scientist	Targeted Therapy Branch, National cancer center

Academic Society

2015-present	Board member	Korean Society for Genetic Diagnostics
2016-present	Board member	Korean Cancer Association
2018-present	Member of Academic committee	Korean Society of Medical Oncology
2020-present	Councilor	Korean Society for Laboratory Medicine
2021-present	PM (part-time)	National Research Foundation of Korea

Publications

1. A 10-Gene Signature to Predict the Prognosis of Early-Stage Triple-Negative Breast Cancer: CANCER RESEARCH AND TREATMENT. (4.6)(2024)

2. PRMT1 promotes pancreatic cancer development and resistance to chemotherapy: CELL REPORTS MEDICINE. 5(3):101461~ (14.3)(2024)

3. Application of plasma circulating KRAS mutations as a predictive biomarker for targeted treatment of pancreatic cancer: CANCER SCIENCE. (5.7)(2024)

4. New Function Annotation of PROSER2 in Pancreatic Ductal Adenocarcinoma: JOURNAL OF PROTEOME RESEARCH. 23(3):905~915 (4.4)(2024)

5. Prospective analysis of pre and postoperative laboratory parameters associated with thrombosis in patients with ovarian cancer: JOURNAL OF THROMBOSIS AND THROMBOLYSIS. 57(3):492~496 (4)(2024)

6. Issues, challenges, and future perspectives of genetic counseling in Republic of Korea: Perspectives of laboratory physicians based on a 2022 survey: JOURNAL OF GENETIC COUNSELING. (1.9)(2024)

7. Clinical Practice Guideline for Blood-Based Circulating Tumor DNA Assays: ANNALS OF LABORATORY MEDICINE. 44(3):195~209 (4.9)(2024)

ST-2-3

Proteogenomic analysis reveal prognostic subclass in early-onset breast cancer patients

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Early-onset breast cancer is characterized by aggressive clinical behavior and a high prevalence in East Asian populations, yet a comprehensive molecular characterization remains elusive. This study conducted a proteogenomic analysis on 126 untreated primary tumor samples from Korean patients with young breast cancer (YBC) aged ≤40 years. Through the integration of genomic, transcriptomic, and proteomic data, we delineated five distinct functional subgroups that accurately encapsulated the clinical features and biological behaviors of YBC patients. Our integrated methodology elucidated the proteogenomic status of HER2, enhancing its clinical relevance and prognostic significance. Additionally, we introduced a proteome-based homologous recombination deficiency (HRD) analysis that addresses the limitations of traditional genomic HRD assays, thereby facilitating the identification of new patient cohorts for targeted HR-deficiency treatments. Our study also revealed that protein–RNA correlations are prognostically significant for predicting late recurrence in hormone receptor-positive breast cancer. Within each molecular subtype of breast cancer, we identified functionally significant protein clusters whose differential expression was closely associated with clinical progression. Furthermore, we developed a recurrence predictive index capable of forecasting late recurrence specifically in luminal subtypes, thereby providing critical insights for optimizing treatment durations in YBC.

These findings enhance the stratification and clinical management of YBC patients, contributing to the optimization of adjuvant therapy and improving clinical outcomes through more tailored treatment strategies.

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Education

2005.09-2009.06	B.S.	University of California Santa Barbara
2011.08-2013.06	M.S.	Sungkyunkwan University (SAIHST)
2013.08-2017.02	Ph.D.	Sungkyunkwan University (SAIHST)

Professional Experience

2017.01-2019.08	Senior Scientist	Samsung Medical Center
2019.09-2023.08	Assistant Professor	Korea University College of Medicine
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Publications

1. Kim KH, Migliozzi S, Koo H, Hong JH, Park SM, Kim S, Kwon HJ, Ha S, Garofano L, Oh YT, D'Angelo F, Kim CI, Kim S, Lee JY, Kim J, Hong J, Jang EH, Mathon B, Di Stefano AL, Bielle F, Laurenge A, Nesvizhskii AI, Hur EM, Yin J, Shi B, Kim Y, Moon KS, Kwon JT, Lee SH, Lee SH, Gwak HS, Lassorella A, Yoo H, Sanson M*, Sa JK*, Park CK*, Nam DH*, Iavarone A*, Park JB* (2024) Integrated proteogenomic characterization of glioblastoma evolution, Cancer Cell, 42(3):358-377

2. Kim JW, Lee HJ, Lee JY, Park SR, Kim YJ, Hwang IG, Kyun Bae W, Byun JH, Kim JS, Kang EJ, Lee J, Shin SJ, Chang WJ, Kim EO, Sa JK*, Park KH* (2024) Phase II study of nivolumab in patients with genetic alterations in DNA damage repair and response who progressed after standard treatment for metastatic solid cancer (KM-06), Journal for Immunotherapy of Cancer, 12(3):e008638

3. Park KH, Choi JY, Lim AR, Kim JW, Choi YJ, Lee S, Sung JS, Chung HJ, Jang B, Yoon D, Kim S, Sa JK*, Kim YH* (2022) Genomic landscape and clinical utility of Korean advanced pan-cancer patients from prospective clinical sequencing: K-MASTER program, Cancer Discovery, 12(4):938-948

4. Kim H*, Sa JK*, Kim J, Cho HJ, Oh HJ, Choi DH, Kang SH, Jeong DE, Nam DH, Lee H, Lee HW, Chung S (2022) Recapitulated crosstalk between cerebral metastatic lung cancer cells and brain perivascular tumor microenvironment in a microfluidic co-culture chip, Advanced Science, 9(22):e2201785

5. Hong JY*, Cho HJ*, Sa JK*, Liu X*, Ha SY*, Lee T, Kim H, Kang W, Sinn DH, Gwak GY, Choi MS, Lee JH, Koh KC, Paik SW, Park HC, Kang TW, Rhim H, Lee SJ, Cristescu R, Lee J, Paik YH, Lim HY (2022) Hepatocellular carcinoma patients with high circulating cytotoxic T cells and intra-tumoral immune signature benefit from pembrolizumab: results from a single-arm phase 2 trial, Genome Medicine, 14(1):1

6. Kim ST*, Sa JK*, Oh SY*, Kim K, Hong JY, Kang WK, Kim KM, Lee J (2021) Comprehensive molecular characterization of gastric cancer patients from phase II second-line ramucirumab plus paclitaxel therapy trial, Genome Medicine, 13(1):11

7. Hong JH*, Kang S*, Sa JK*, Park G*, Oh YT, Kim TH, Yin J, Kim SS, D'Angelo F, Koo H, You Y, Park S, Kwon HJ, Kim CI, Ryu H, Lin W, Park EJ, Kim YJ, Park MJ, Kim H, Kim MS, Chung S, Park CK, Park SH, Kang YH, Kim JH, Saya H, Nakano I, Gwak HS, Yoo H, Lee J, Hur EM, Shi B, Nam DH, Iavarone A, Lee SH, Park JB (2021) Modulation of Nogo receptor 1 expression orchestrates myelin-associated infiltration of glioblastoma, Brain, 144(2):636-654

ST-2-4

Comprehensive genomic characterization of Korean advanced pan-cancer patients facilitates personalized treatment

Kyong Hwa Park[1,2], Jung Yoon Choi[1,2], Ah-Reum Lim[1,2], Ju Won Kim[1,2], Yoon Ji Choi[1,2], Sooheyon Lee[1,2], Jae Sook Sung[1,2], Hee-Joon Chung[1,2], Byunghyun Jang[3,4], Dayoung Yoon[3,4], Sukwon Kim[3,4], Jason K. Sa[3,4], Yeul Hong Kim[1,2]

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The fundamental principle of precision oncology is centralized on the identification of therapeutically exploitable targets that provide individual patients an opportunity to make informed decisions on a personalized level. To facilitate and adopt such concepts within clinical practice, several large-scale genomic studies have been initiated to identify and explore essential molecular aberrations and their functional impacts across various tumor types. However, as the vast majority of the patients enrolled in these studies have originated from European Ancestry, several limitations prevent the implementation of such profound insights for treating East Asian cancer patients. To address such challenges, we have collected and explored the complex genome of 4,028 Korean advanced pan-cancer patients. Considerable levels of genomic diversity existed at both pan-cancer and individual tumor levels between patients from different ethnic origins; for example, mutations in key chromatin remodeling genes, including IDH1 were only observed in cholangiocarcinoma patients of European origin, while Korean cancer patients were marked by recurrent ablations in KRAS and TP53. Furthermore, Korean patients were characterized by mutations in mismatch repair (MMR) encoding molecules, which subsequently led to increased MMRd mutational signature activities. Lastly, we provided a clinical proof-of-concept where patients who carried a PIK3CA-activating mutation with liver metastasis demonstrated a remarkable response to PI3K-mediated therapy. Our results collectively highlighted the significance of employing an ethnic-based personalized approach in cancer therapy.

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Education

1990.03. - 1994.02.	B.S. in Statistics	Inje University, Kimhae, Korea 2005
2000.03. - 2005.02.	M.S. in Data Science	Inje University, Kimhae, Korea 2005

Professional Experience

1994.03. - 2000.02.	Assistant	Department of Statistics, Inje University
2001.09. - 2004.12.	Data Manager & Statistician	Busan Cancer Registry
2005.01. - current	Data Manager & Statistician	Korea Central Cancer Registry, National Cancer Center
2020.07. - current	Team manager	National Cancer Data Center, National Cancer Center

Publications

1. Eun Hye Park, Kyu-Won Jung, Nam Ju Park, Mee Joo Kang, E Hwa Yun, Hye-Jin Kim, Jeong-Eun Kim, Hyun-Joo Kong, Jeong-Soo Im, Hong Gwan Seo; The Community of Population-Based Regional Cancer Registries, Cancer statistics in Korea: Incidence, Mortality, Survival, and Prevalence in 2021: CANCER RESEARCH AND TREATMENT. 2024, 56(2):357~371 (4.6)

2. Kyu-Won Jung, Mee Joo Kang, Eun Hye Park, E Hwa Yun, Hye-Jin Kim, Hyun-Joo Kong, Jeong-Soo Im4, Hong Gwan Seo, Prediction of Cancer Incidence and Mortality in Korea, 2024: CANCER RESEARCH AND TREATMENT. 2024, 56(2):372~379 (4.6)

ST-2-5

Introduction and Utilization of Open Data in the National Cancer Data Center

Hyun-Joo Kong

National Cancer Center(NCC)

Introduction and Utilization of Open Data in the National Cancer Data Center

SATELLITE SESSION-2

Harim Koo, Ph.D

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Education

2016 ~ 2021	Ph.D.	Sungkyunkwan University
2012 ~ 2016	B.S.	Chonnam National University

Professional Experience

2022 ~ Present	Assistant Professor	National Cancer Center
2021 ~ 2022	Senior Scientist	AIMED BIO
2019 ~ 2021	Researcher	National Cancer Center

Publications

1. Kim KH, Migliozzi S, Koo H, Hong JH, Park SM, Kim S, Kwon HJ, Ha S, Garofano L, Oh YT, D'Angelo F, Kim CI, Kim S, Lee JY, Kim J, Hong J, Jang EH, Mathon B, Di Stefano AL, Bielle F, Laurenge A, Nesvizhskii AI, Hur EM, Yin J, Shi B, Kim Y, Moon KS, Kwon JT, Lee SH, Lee SH, Gwak HS, Lasorella A, Yoo H, Sanson M, Sa JK, Park CK, Nam DH, Iavarone A, Park JB. Integrated proteogenomic characterization of glioblastoma evolution. Cancer Cell. 2024 Jan 1:S1535-6108(23)00443-9.

2. Nam Y, Koo H, Yang Y, Shin S, Zhu Z, Kim D, Cho HJ, Mu Q, Choi SW, Sa JK, Seo YJ, Kim Y, Lee K, Oh JW, Kwon YJ, Park WY, Kong DS, Seol HJ, Lee JI, Park CK, Lee HW, Yoon Y, Wang J. Pharmacogenomic profiling reveals molecular features of chemotherapy resistance in IDH wild-type primary glioblastoma. Genome Med. 2023 Mar 13;15(1):16

3. Lee K, Koo H, Kim Y, Kim D, Son E, Yang H, Lim Y, Hur M, Lee HW, Choi SW, Nam DH (2020) Cancers. Therapeutic Efficacy of GC1118, a Novel Anti-EGFR Antibody, against Glioblastoma with High EGFR Amplification in Patient-Derived Xenografts. 2020 Oct 31;12(11):3210

4. Koo H, Choi SW, Cho HJ, Lee IH, Kong DS, Seol HJ, Lee JI, Choi JW, Sa JK, Nam DH (2020) Cancer Medicine. Ethnic delineation of primary glioblastoma genome. 2020 Oct;9(19):7352-7359

5. Choi SW, Cho HH, Koo H, Cho KR, Nenning KH, Langs G, Furtner J, Baumann B, Woehrer A, Cho HJ, Sa JK, Kong DS, Seol HJ, Lee JI, Nam DH, Park H (2020) Cancers. Multi-Habitat Radiomics Unravels Distinct Phenotypic Subtypes of Glioblastoma with Clinical and Genomic Significance. 2020 Jun 27;12(7):1707

ST-2-6

Comprehensive Proteogenomic Characterization of Renal Cell Carcinoma

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Although histologically defined subtypes exist, renal cell carcinoma (RCC) is a heterogenous disease, resulting in various treatment outcomes and prognosis. Multiomics strategies encompassing genome and expression profiling of multiple tumor types have elucidated novel molecular subtypes and abnormally activated signaling pathways, as well as potential therapeutic targets. Here, we conduct comprehensive profiling of RCC with histopathologic, proteomic, phosphoproteomic, genomic, and transcriptomic analyses on tumor and paired adjacent normal tissues from 113 patients. RCC tumors are distinctly separated from corresponding normal tissues through multi-omics clustering, a distinction further supported by pathway analysis. In addition, various hallmarks of cancer were differentially observed at the individual patient level, highlighting the intertumoral heterogeneity of RCC.

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Education

2007-2015	M.S. & Ph.D.	Department of Functional Genomics University of Science and Technology (UST), Daejeon, Korea
1994-2002	B.S.	Department of Biological Sciences Korea Advanced Institute of Science and Technology (KAIST), Daejeon, Korea

Professional Experience

2021-present	Assistant Professor of R&D Business Foundation	Department of Cancer Biomedical Science Graduate School of Cancer Science and Policy, National Cancer Center (NCC), Goyang, Korea
2019-2021	Researcher	Cancer Proteogenomic Analysis Consortium Research Institute, National Cancer Center (NCC), Goyang, Korea
2017-2019	Postdoctoral Fellow	Personalized Genomic Medicine Research Center Korea Research Institute of Bioscience and Biotechnology (KRIBB), Daejeon, Korea
2013-2016	Postdoctoral Fellow	Specific Organs Cancer Branch Research Institute, National Cancer Center (NCC), Goyang, Korea
2007-2013	Research Student	Medical Genomics Center Korea Research Institute of Bioscience and Biotechnology (KRIBB), Daejeon, Korea
2004-2006	Technical Employee	Korean Bioinformation Center (KOBIC) Korea Research Institute of Bioscience and Biotechnology (KRIBB), Daejeon, Korea

Publications

1. . Lin W., Niu R., Park SM*., Zou Y., Kim SS., Xia X., Xing S., Yang Q., Sun X., Yuan Z., et al. (2023). IGFBP5 is an ROR1 ligand promoting glioblastoma invasion via ROR1/HER2-CREB signaling axis. Nat Commun 14, 1578. *co-first

2. Park SM, Seo EH, Bae DH, Kim SS, Kim J, Lin W, Kim KY, Park JB, Kim YS, Yin JL, Kim SY, Phosphoserine Phosphatase Promotes Lung Cancer Progression through the Dephosphorylation of IRS-1 and a Noncanonical L-Serine-Independent Pathway, Mol Cells. 42(8):604-616. 2019

3. Park SM, Choi EY, Bae DH, Sohn HA, Kim SY, Kim YJ, The LncRNA EPEL Promotes Lung Cancer Cell Proliferation Through E2F Target Activation, Cellular Physiology and Biochemistry. 45(3):1270-1283, 2018

4. Park SM, Choi EY, Bae MG, Choi JK, Kim YJ, A long-range interactive DNA methylation marker panel for the promoters of HOXA9 and HOXA10 predicts survival in breast cancer patients. Clinical Epigenetics. 24;9:73, 2017

5. Kim KE, Jang KW, Yang WJ, Choi EY, Park SM, Bae MG, Kim YJ, Choi JK, Chromatin structure-based prediction of recurrent noncoding mutations in cancer. Nature Genetics. 48(11):1321-1326, 2016

6. Park SM, Choi EY, Bae MG, Kim SS, Park JB, Yoo H, Choi JK, Kim YJ, Lee SH, Kim IH. Histone variant H3F3A promotes lung cancer cell migration through intronic regulation. Nature Communications 7:12914, 2016

ST-2-7

Integrated proteogenomic analysis characterizes clinically relevant molecular subtypes associated with medulloblastoma progression

Seong-min Park, Kyung-Hee Kim, Jong Hyuk Yoon, Fulvio D'Angelo, Seung Ah Choi, Chan Il Kim, Seungmin Park, Hyondeog Kim, Harim Koo, Sung Soo Kim, Ae Kyung Park, Eun Jung Koh, Seong-Ik Kim, Yu-Mi Shim, Kwang-Hoon Lee, Ji Hoon Phi, Yeon Suk Jo, Do Hyun Nam, Seokjun Ha, Sanha Park, Jason K. Sa, Youngwook Kim, Antonio Iavarone, Sung-Hye Park, Seung-Ki Kim, Jong Bae Park

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Despite previous reports on the hallmarks of medulloblastoma, their impact on treatment has been limited. In this study, we conducted an integrated analysis incorporating five layers of omics data, including mass-spectrometry-based proteome analyses. Our findings unveil new medulloblastoma subtypes associated with the lineage of neuronal differentiation and distinct therapeutic vulnerabilities. We identified the subdivision of the SHH subtype into SHHa, as marked by activation of cell cycle, and SHHb manifesting a neuronal differentiation. We subdivided the enigmatic Group 4 into divergent G4a, G4b, and G4g subtypes, each exhibiting unique features discernible only through integrated multiomics analyses. These analyses include lineage dependency inferred from the transcriptome and kinase–substrate activity inferred from the phosphoproteome resulting in a kinase-centered functional modularity highlighting a kinase-centered functional modularity. The subtype-specific features demonstrated strong associations with clinical variables such as tumor recurrence, providing insights for rational therapeutic stratification. Our study provides validation of the subtype-specific biomarkers and therapeutic targets, thus allowing for more accurate diagnosis and therapeutic stratification of medulloblastoma patients

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Education

2001.03-2005.02	BA (Statistics)	College of Natural Sciences, Kangwon National University
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2007.03-2009.02	MPH (Epidemiology)	Graduate School of Public Health, Seoul National University
2009.03-2013.02	PhD (Genetics)	Seoul National University College of Medicine, Seoul National University

Professional Experience

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2023.09-current	Adjunct Associate Professor	Department of Cancer Control and Population Health, NCC-GCSP
2022.03-current	Principal Research Engineer	Cancer Big Data Center, National Cancer Control Institute, National Cancer Center
2019.02-2022.02	Senior Research Engineer	Cancer Big Data Center, National Cancer Control Institute, National Cancer Center
2018.04-2019.01	Assistant Research Engineer	Cancer Big Data Center, National Cancer Control Institute, National Cancer Center
2015.12-2018.03	Research Assistant Professor	Institute of Health and Environment & Graduate School of Public Health, Seoul National University
2014.09-2015.11	Senior Research Engineer	Institute of Health and Environment & Graduate School of Public Health, Seoul National University
2013.05-2014.08	Assistant Research Engineer (Postdoctoral researcher)	Genomic Medicine Institute, Medical Research Institute, Seoul National University College of Medicine

Academic Society

2020.01-current	Experimental and Molecular Medicine (EMM) journal management committee member	Korean Society for Biochemistry and Molecular Biology (KSBMB)
2018.01-2020.12	Ilcheon committee member	Korean Society for Biochemistry and Molecular Biology (KSBMB)

Publications (Only First- or Corresponding-Author Publications)

1. Effects of the abdominal fat distribution on the relationship between exposure to air pollutants and thyroid hormones among Korean adult males (2023) Hyun-Jin Kim, Byungmi Kim, Seyoung Kim, Hyuktae Kwon, Jae Moon Yun, Belong Cho, Jin-Ho Park. Eur J Med Res. 28(1):423.

2. A genome-wide by PM10 exposure interaction study for blood pressure in Korean adults (2023) Hyun-Jin Kim, Ho-Young Son, Philiip Park, Jae Moon Yun, Hyuktae Kwon, Belong Cho, Jong-Il Kim, Jin-Ho Park. Sci Rep. 13(1):13060.

3. Effects of vitamin D on associations between air pollution and mental health outcomes in Korean adults: Results from the Korea National Health and Nutrition Examination Survey (KNHANES) (2023) Hyun-Jin Kim, Hyo-Seon Kim, Seyoung Kim, Juyeon Hwang, Hyejin Lee, Bohyun Park, Byungmi Kim. J Affect Disord. 320:390-396.

ST-2-8

Development of a web-based tool for visual analysis of multi-omics information of cancer patients

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Multi-omics analysis in cancer research is an important approach to integrate high-dimensional datasets to better understand the molecular biology of cancer. In addition, integrating individual clinical information with omics profile may provide significant opportunities for precision oncology. An open-access web portal called Korea-Cancer Omics REsearch (K-CORE) was developed to provide visualization and download of analysis results through multidimensional linkage of omics data and clinical information. This web portal allows users to upload their data to the portal for integrated analysis of various clinical and omics profiles. Users can implement a variety of integrated visualization analysis within this portal (e. g. Circos Plot, Oncoprint, Lollipop Plot, Heatmap, Kaplan-Meier, Cox-regression, Correlation Plot, CNV Plot, and Boxplot). Patient-specific drug information can be also checked through the report function. In addition to integrated analysis, we provide a single analysis for each dimension of data and plan to continue to expand. K-CORE (https://cancerdata.re.kr/k-core) may be used as a meaningful web analysis tool in precision oncology by enabling integrated analysis of high-dimensional information including clinical and omics data in cancer patients.

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Professional Experience

2024.03-	Researcher	National Cancer Data Center
2022.08-2024.03	Lead scientist	AIMEDBIO – AI Precision Medicine Team

ST-2-9

Multi-omics data analysis method using K-CORE Analytics

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Global bio-data groups, including TCGA (The Cancer Genome Atlas), have been building multi-omics data (genome, transcriptome, and proteome). Additionally, a public analysis portal was developed along with the construction of multi-omics data. However, little progress has been made in developing analytical portals that provide advanced analysis of multi-omics. Accordingly, the National Cancer Data Center (NCDC) developed a portal to analyze Korean multi-omics data. K-CORE Analytics, developed by NCDC, provides various analysis tools for multi-omics data. K-CORE Analytics can only be used in the air-gapped environment of the National Cancer Data Center and it suggested as a good option for analyzing Korean multi-omics data provided by NCDC.

SATELLITE SESSION-3

세포배양식품 개발 기술 워크샵

SATELLITE SESSION-3

세포배양식품 개발 기술 워크샵

6.26 (Wed) 14:00 - 17:00

ST3-1 6.26 (Wed) 14:00-14:30

Revolutionizing The Food Industries with Cell-Based Ingredients

Bong Jong Seo
SIMPLE Planet Inc.

ST3-2 6.26 (Wed) 14:30-15:00

Development of Cultured Meat Prototypes Based on Cell Culture from Aquatic Organisms

Dae-Hee Lee
Gangneung-Wonju National University

ST3-3 6.26 (Wed) 15:00-15:30

Property Assessment of Reverse-Engineered Meat Substitutable Materials by Multi-Dimensional Spatial Re-Arrangement

Jin-Kyu Rhee
Ewha Womans University

ST3-4 6.26 (Wed) 16:00-16:30

Culture of Adipose-derived Stem Cells for Edible Bovine Adipose Tissue

Hyun Sook Hong
Kyung Hee University

ST3-5 6.26 (Wed) 16:30-17:00

The Sustainable Photosynthesis Producing of Squalene Through Metabolically-engineered Cyanobacteria

Sun Young Choi
Korea Polytechnics

SATELLITE SESSION-3

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Education

2014.03-2021.01	Ph.D.	Konkuk university
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Professional Experience

2024.04-	Senior researcher	SIMPLE Planet Inc.
2022.01-2024.04	Senior researcher	iPSbio Inc.
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Publications (first-authored)

1. Seo, B. J., Na, S. B., Choi, J., Ahn, B., Habib, O., Park, C., ... & Do, J. T. (2023). Metabolic and cell cycle shift induced by the deletion of Dnm1l attenuates the dissolution of pluripotency in mouse embryonic stem cells. Cellular and Molecular Life Sciences, 80(10), 302.

2. Seo, B. J., Hong, T. K., Yoon, S. H., Song, J. H., Uhm, S. J., Song, H., ... & Do, J. T. (2023). Embryonic Stem Cells Lacking DNA Methyltransferases Differentiate into Neural Stem Cells that Are Defective in Self-Renewal. International Journal of Stem Cells, 16(1), 44.

3. Ryu, M. J., Seo, B. J., Choi, Y. J., Han, M. J., Choi, Y., Chung, M. K., & Do, J. T. (2020). Mitochondrial and metabolic dynamics of endometrial stromal cells during the endometrial cycle. Stem Cells and Development, 29(21), 1407-1415.

4. Seo, B. J., Choi, J., La, H., Habib, O., Choi, Y., Hong, K., & Do, J. T. (2020). Role of mitochondrial fission-related genes in mitochondrial morphology and energy metabolism in mouse embryonic stem cells. Redox Biology, 36, 101599.

5. Choi, J., Seo, B. J., La, H., Yoon, S. H., Hong, Y. J., Lee, J. H., ... & Do, J. T. (2020). Comparative analysis of the mitochondrial morphology, energy metabolism, and gene expression signatures in three types of blastocyst-derived stem cells. Redox biology, 30, 101437.

6. Lee, J. E., Seo, B. J., Han, M. J., Hong, Y. J., Hong, K., Song, H., ... & Do, J. T. (2020). Changes in the expression of mitochondrial morphology-related genes during the differentiation of murine embryonic stem cells. Stem Cells International, 2020(1), 9369268.

7. Seo, B. J., Jang, H. S., Song, H., Park, C., Hong, K., Lee, J. W., & Do, J. T. (2019). Generation of mouse parthenogenetic epiblast stem cells and their imprinting patterns. International Journal of Molecular Sciences, 20(21), 5428.

8. Seo, B. J., Yoon, S. H., & Do, J. T. (2018). Mitochondrial dynamics in stem cells and differentiation. International journal of molecular sciences, 19(12), 3893.

9. Seo, B. J., Hong, Y. J., & Do, J. T. (2017). Cellular reprogramming using protein and cell-penetrating peptides. International journal of molecular sciences, 18(3), 552.

ST-3-1

Revolutionizing The Food Industries with Cell-Based Ingredients

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The current livestock industry's meat production system is environmentally unsustainable and inefficient. While plant-based meats have gained popularity as alternative protein sources in recent decades, they often fall short in replicating the taste and nutritional profile of real meat. To address this, cell-based meat has emerged as a promising solution for producing sustainable, animal-free protein. We are focusing specifically on the developing cell-based food ingredients, including high-protein concentrates and fats rich in unsaturated fatty acids. These ingredients aim to enhance the taste and nutrition of a variety of food products. Unlike other cell-based approaches that focus on meat analogs, our focus is on producing versatile ingredients for broader applications. The core technology involves a suspension cell culture platform utilizing edible, food-grade culture media suitable for mass production using bioreactors. We have successfully established 13 distinct cell lines from 5 species (bovine, porcine, chicken, duck, and flatfish) and developed edible culture medium compliant with the Korea Food Additives Standard Code. Cell-based food ingredients produced with this medium are stable, safe, and affordable. Large-scale cultivations of these cell lines are performed through suspension culture techniques in bioreactors. Rigorous analyses have confirmed that the intrinsic properties of cells remain unchanged during the conversion from adherent to suspension culture, validating the reliability of this production method. The versatility of these cell-based ingredients from our platform technology allows for targeting various food types such as health functional food, soft food (for kids and old people), and pet food. This approach not only addresses the limitations of conventional alternatives but also contributes to a more sustainable and secure food system, mitigating the environmental destruction of traditional meat production.

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Education

1994.03-2000.02	Bachelor's	Korea University
2000.03-2002.02	Master's	Korea University
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Professional Experience

2005.03-2006.07	Post-Doc	KyungHee University
2006.08-2010.03	Post-Doc	University of Pittsburgh
2006.08-2010.03	Researcher	University of Virginia
2010.02-2014.01	Research Professor	University of Pittsburgh
2014.02-2015.01	Research Professor	Korea University
2015.09-Present	Professor	Gangneung-Wonju National University

Publications

1. Lee, D. H., Jun, W. J., Shin, D. H., Cho, H. Y., and Hong, B. S. Effect of Culture Conditions on Production of 5-Aminolevulinic Acid by Recombinant Escherichia coli. Bioscience, Biotechnology, and Biochemistry. 69(3): 470-476. (2005)

2. Lee, D. H., Jun, W. J., Yoon, J. W., Cho, H. Y., and Hong, B. S. Process Strategies to Enhance the Production of 5-Aminolevulinic Acid with Recombinant E. coli. J. Microbiol. Biotechnol. 14(6): 1310-1317. (2004)

3. Jun, W. J., Kim, S. H., Lee, D. H., Jung, J. W., Shim, S. I., Lee, K. W., Cho, H. Y., and Hong, B. S. In Vitro and In Vivo Effects of Gelidium amansii on Intestinal Immune System. Food Science and Biotechnology. 14(1): 147-151. (2005)

4. Lee, D. H., Jun, W. J., Kim, K. M., Shin, D. H., Cho, H. Y., and Hong, B. S. Inhibition of 5-aminolevulenic acid dehydratase in recombinant Escherichia coli using D-glucose. Enzyme and Microbial Technology 32: 27-34. (2003)

5. Lee, D. H, Ha, N., Bu, Y.M., Choi, H.I., Park, Y.G., Kim, Y.B., Kim, M.Y., and Kim, H. Neuroprotective effect of Buddleja officinalis extract on transient middle cerebral artery occlusion in rats. Biol. Pharm. Bull. 29(8): 1608-1612. (2006)

6. Bu, Y. M., LLee, D. H, Kim, M.Y., Oh, S., Hwang, M., Chung, J., Jin, Z., and Kim, H. Neuroprotective effect of Neubo153 on Transient Focal Cerebral Ischemia in Rats. The Korea Journal of Herbology, 21(2): 151-158. (2006)

7. Bu, Y., Rho, S., Kim, J., Kim, M.Y., Lee, D. H., Kim, S.Y., Choi, H., and Kim, H. Neuroprotective effect of tyrosol on transient focal cerebral ischemia in rats. Neuroscience letter. 414(3):218-21.) (2007)

8. Chung, H., Lee, D. H., Kim, E., Seo, S., Ju, S., Lee, D., Kim, H., and Park, S. Ghrelin Inhibits Apoptosis in Hypothalamic Neuronal Cells during Oxygen-Glucose Deprivation. Endocrinology 148(1):148–159. (2007)

9. Kim, Y. H., Lee, D. H., Jeong, J. H., Zong Sheng Guo, and Lee, Y. J. Quercetin augments TRAIL-induced apoptotic death: involvement of the ERK signal transduction pathway. Biochemical Pharmacology, 75(10):1946-1958. (2008) – IF 5.091

10. Lee, D. H., Kim, Clifford., Zhang, Lin., and Lee, Y. J. Role of p53, PUMA, and Bax in wogonin-induced apoptosis in human cancer cells. Biochemical Pharmacology, 75(10):2020-2033. (2008) – IF 5.091

ST3-2

Development of Cultured Meat Prototypes Based on Cell Culture from Aquatic Organisms

Kim Hyun Hee [1], Kwak Min Jae [2], Kyung Gyu Hyeok [2], Kim Geun Ho [2], Hong Sang Yeol [2], Kim Ji Yun [2], Dae-Hee Lee [1*]

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Cell-cultivated meat and seafood is getting closer to a reality for consumers around the world. Nevertheless, regulators are still largely lagging behind on regulating production and labelling of these products. Our findings will allow us to take a major step toward reducing production costs and environmental impacts, leading to an expansion of the cultured meat market.

The present study relates to a support for cell culture using alginate and cellulose extracted through culture medium of Lactobacillus. Our team will study (1) development of cell-based cultured aquatic meat and raw materials: Cell-based food material processing technology derived from high-value species that ensures consumption safety. (2) Optimization of stem cell culture and differentiation technology using algae- and plant-derived scaffolds: exploration of scaffold materials for development of hybrid aquatic cultured meat combining edible scaffolds and cells derived from high-value species, coating and fat differentiation conditions, and DB construction for each culture method. (3) Establishment of approval data for food approval of hybrid aquaculture-cultured meat prototype.

Finally, our studies will allow us to take a major step toward reducing production costs and environmental impacts, leading to an expansion of the cultured meat market.

SATELLITE SESSION-3

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Education

2000.03-2006.02	Doctor of Philosophy	Yonsei University
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2019.08.-2021.02	Director	Ewha Business Incubator
2019.08.-2021.02	Department Chair	Joint Major of Entrepreneurship
2012.12.-2015.03	Senior Researcher (Director eq.)	Korea Basic Science Institute
2007.04.-2012.12	Research Associate	The Scripps Research Institute

Academic Society

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Publications

1. Highly Porous and Rigid, Full-thickness Human Skin Model from the Slime-webbed Fiber Scaffold. Biotechnology and Bioprocess Engineering, 2023, v.28 no.2, 246-254

2. Improving the Three-Dimensional Printability of Potato Starch Loaded onto Food Ink. Journal of Microbiology and Biotechnology, 2024, v.34 no.4, 1-10

3. Printing Optimization of 3D Structure with Lard-like Texture Using a Beeswax-Based Oleogels. Journal of microbiology and biotechnology, 2022, v.32 no.12, 1573-1582

4. Cobalt ferrite microspheres as a biocompatible anode for higher power generation in microbial fuel cells. Journal of Power Sources, 2021, v.483, 229170

5. Fiber manufacturing apparatus. US Patent 11,091,853

6. Printer apparatus. US Patent 10,953,658

ST3-3

Property Assessment of Reverse-Engineered Meat Substitutable Materials by Multi-Dimensional Spatial Re-Arrangement

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In recent times, there has been a significant surge in global demand for meat alternatives due to their social, environmental, and economic impacts on human life. Consequently, numerous researchers and developers are directing their efforts toward mimicking the texture, flavor, and appearance of meat-based foods derived from livestock farming, dairy, and fisheries. These products are anticipated to offer healthier, more sustainable, and eco-friendly options. Initially, this transition involves the substitution of meat products with those made from plant/microbial proteins or innovative methods such as cellular cultivation. However, regardless of their source, consumers continue to select meat-like foods based on their resemblance in texture, flavor, and appearance to conventional meat. The market is witnessing a burgeoning array of alternative raw materials tailored to seamlessly replace animal-derived meat products, indicating the rapid growth of new offerings. Furthermore, understanding the edible behavior of meat involves exploring the spatial arrangements and interactions of its components. Analyzing the composition and morphology of structural elements and their interactions can reveal how these elements contribute to the material's function and macroscopic behavior during chewing and digestion, facilitating the development of edible materials through reverse engineering.

To meet the criteria for meat substitutes, current processing technologies should be adapted or developed anew. This adaptation is fundamental for the development and supply of products closely mimicking meat. In this study, our approaches to imitate meat alternatives involve modifying the characteristics and functions of food ingredients to achieve a texture and mouthfeel akin to real meat will be reviewed. Furthermore, some results how edible raw materials are fabricated to cultivate cells for meat production and geometrically structure these materials by novel multidimensional spatial re-arrangement technology will be demonstrated. Additionally, the potential future developments and prospects in this field will be discussed.

SATELLITE SESSION-3

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Education

2009.09-2012.08	Ph D	Kyung Hee University

Professional Experience

2013.09-2019.08	Assistant prof.	College of medicine, Kyung Hee University/Kyung Hee Institute of Regenerative Medicine (KIRM), Kyung Hee University Hospital
2012.09-2013.08	Post Doc.	Kyung Hee Institute of Regenerative Medicine, Kyung Hee University
2007.04-2009.3	Team manager	Drug development. Biosolutions. Co. Ltd
2003.04-2007.03	Researcher	Korea Institute of radiological and medical science (KIRAMS),

Publications

1. Jeong Seop Park, Do Young Kim, Hyun Sook Hong, FGF2/HGF priming facilitates adipose-derived stem cell-mediated bone formation in osteoporotic defects, Heliyon (2024)

2. Doyoung Kim†, Jiyuan Piao†, Jeong Seop Park, Dahyun Lee, Dae Yeon Hwang, Hyun Sook Hong* Substance P-mediated vascular protection ameliorates bone loss. Oxidative medicine and cellular longevity (2023)

3. Jeong Seop Park, Doyoung Kim, Hyun Sook Hong*. Priming with a combination of FGF2 and HGF restores the impaired osteogenic \ differentiation of adipose-derived Stem cells. Cells (2022)

4. Dahyeon Lee, Jeong Seop Park, Doyoung Kim, Hyun Sook Hong*. Substance P hinders Bile Acid-induced hepatocellular injury by modulating oxidative stress and inflammation. Antioxidants (2022)

5. Jiyuan Piao, Jeong Seop Park, Dae Yeon Hwang, Hyun Sook Hong*, Youngsook Son* Substance P blocks β-aminopropionitrile-induced aortic injury through modulation of M2 monocyte-skewed monocytopoiesis. Translational research (2020)

6. Sang Min Baek†, Kiyoung Kim†, Suna Kim, Youngsook Son, Hyun Sook Hong*, Seung-Young Yu*. SP prevents T2DM complications by immunomodulation. Scientific reports (2020)

ST3-4

Culture of adipose-derived stem cells for ‘edible bovine adipose tissue

Seyoung Hong[1], Do Young Kim[2], Hyun Sook Hong[2], and Ki Hyun Yoo[1]

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Cultivated meat, developed through cell culture technology, is emerging as a promising solution that closely mimics both the flavor and nutrient profiles of conventional meat. One key component that contributes to the flavor of meat is its fat content. In this study, bovine adipose-derived stem cells (bADSCs) from bovine fat were isolated and cultured for the production of alternative fat. To characterize bADSCs, the expression of mesenchymal stem cell (MSC) markers (CD29, CD73, and CD105) and colony forming efficiency were assessed. Subsequently, bADSCs were differentiated into adipocytes to produce cultivated fat in 2D or 3D culture. The cultivated fat was analyzed by gas chromatography to verify the similarity of the fatty acids of animal-derived fat. Resultantly, bADSCs have characteristics of MSC and could differentiate into adipocyte. The ratio of unsaturated fatty acids and saturated fatty acids in cultivated fat and adipose tissue was similar. Adipogenic differentiation of ADSCs using textured vegetable protein (TVP) as a scaffold could form the lipid droplets within the TVP. In conclusion, this study demonstrated the establishment of a culture system for the fat production from bADSCs in vitro. The fat produced through bADSCs holds the potential to be used in the composition of hybrid-cultivated meat.

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Education

1998.3~2002.2	BS	Korea University
2002.3~2005.2	MS	Korea University
2014.9~2017.8	Ph.D	Korea University

Professional Experience

2021.9~2023.8	Assistant professor	Gyeonggi University of science and technology
2024.9~ 2024.1	Research professor	Korea university
2024.2~ present	Assistant professor	Bio Campus of KOREA Polytechnic

Academic Society

2021.9 ~ present	Expert Committee member	Korean society of chemical Engineers
2021.9 ~ present	Expert Committee member	Korean society of Biotechnology and Bioengineering

Publications

1. CRISPRi-dCas12a: A dCas12a–mediated CRISPR interference for repression of multiple genes and metabolic engineering in cyanobacteria. ACS Synth. Biol. Choi, S.Y., Woo, H.M. Under review

2. Scalable cultivation of engineered cyanobacteria for squalene production from flue gas in a closed photobioreactor under seasonal outdoor conditions. Bioresource tech. Choi, S.Y., Sim, S.J., KO, S.C., Son., J.G., Lee, J.S., Lee, H.J,. Chang,W.S., Woo,H.M . Under review

3. Identification of small droplets of photosynthetic squalene in engineered Synechococcus elongatus PCC 7942 using TEM and selective fluorescent Nile red analysis. LETTERS IN APPLIED MICROBIOLOGY.66,523-529. (IF=1.575). Choi, S.Y., Sim, S.J., Choi. J.-I., Woo, H.M. (2018.06)

4. Bio-solar cell factories for photosynthetic isoprenoids production. Planta. 249:181-193 (IF=3.249). Ko, S.C., Lee, H.J., Choi, S.Y., Choi. J.-I., Woo, H.M. (2019.01).

5. Improvement of Squalene Production from CO2 in Synechococcus elongatus PCC 7942 by Metabolic Engineering and Scalable Production in a Photobioreactor. ACS Synth. Biol.6(7) p. 1289-1295 (IF=6.076). Choi, S.Y., Wang, J.Y., Kwak, H.S., Lee, S.M., Um, Y., Kim, Y., Sim, S.J., Choi. J.-I., Woo, H.M. (2017.07)

6. Photosynthetic conversion of CO2 to farnesyl diphosphate-derived phytochemicals (amorpha-4,11-diene and squalene) by engineered cyanobacteria. Biotechnol. Biofuels. 9:202 (IF=6.44). Choi, S.Y., Lee, H.J., Choi, J., Kim, J., Sim, S.J., Um, Y., Kim, Y., Lee, T.S., Keasling, J., Woo, H.M., (2016.09)

7. Transcriptome landscape of Synechococcus elongatus PCC 7942 for nitrogen starvation responses using RNA-seq. Sci. Rep. 6:30584 (IF=5.578) Choi, S.Y., Park, B., Choi, I.G., Sim, S.J., Lee, S.M., Um, Y., Woo, H.M., (2016.08)

8. Extreme furfural tolerance of a soil bacterium Enterobacter cloacae GGT036. J. Biotechnol. 193:11-13 (IF=2.884). Choi, S.Y., Gong, G., Park, H.-S., Um, Y., Sim, S.J., Woo, H.M., (2015.01)

ST3-5

The sustainable photosynthesis production of squalene through metabolically-engineered Cyanobacteria

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Metabolic engineering of cyanobacteria has enabled photosynthetic conversion of CO2 to value added chemicals as bio-solar cell factories. The using cyanobacterial for direct production of squalene is advantage, since they can sustainably grow carbon dioxide from air and sunlight without energy sources based on glucose. However, the production levels of squalene among several isoprenoids in engineered cyanobacteria were quite low, compared to other microbial hosts. Here, we engineered S. elongatus PCC 7942 with modular metabolic pathways consisting of the methylerythritol phosphate pathway enzymes and the squalene synthase for production of squalene. Sequentially, to increase production of squalene from CO2 by application of the push-and-pull strategy with fusion protein, application of the CRISPR dCas12a system to regulate gene repression. More, we engineered recombinant S. elongatus PCC 7942 mutant (SeSC37S_MEP(const)) to product squalene with non-inducer system which have low economic cost affect. Furthermore, we apply Indoor& outdoor large scale up cultivation by using sunlight and flue gas (contain 5% CO2) as energy source, design to make cultivation system, light and temperature were monitored in short-term (August and October) with growth of mass and squalene production level. The confirmation of quantification and accumulation of squalene was performed by GC-MS (gas chromatography-mass spectrometry). The optimized modular OverMEP strain with either expression of SQS demonstrated the highest production levels of squalene, resulting in significantly increased levels (7.4-fold). Also, The CRISPR dCas12a system to regulate gene repression will promote to expand the genome-wide metabolic engineering of the construct of biosolar cell factories to produce value added chemicals. Moreover, the best squalene producer was cultivated in a scalable photobioreactor (6 L ~100L) with light optimization, which produced 7.08 ± 0.5 mg/L/OD730 squalene. In conclusion, strain improvement through metabolic engineering tool and development of the photo-bioprocessing conditions will promote establishment of an engineered bio-solar cell factory for industrial-scale CO2 conversion.

Keywords: Metabolic engineering, Cyanobacteria, Synthetic biology, squalene, Bio processing

COPRORATATE WORKSHOP-1

Thermo Fisher
SCIENTIFIC

COPRORATATE WORKSHOP-1

Thermo Fisher SCIENTIFIC

6.25 (Tue) 11:40 - 12:40

CW-1-1 6.25 (Tue) 11:40-12:00

Frontiers of high resolution accurate mass analysis

Alexander Makarov
Thermo Fisher Scientific

CW-1-2 6.25 (Tue) 12:00-12:20

New Product Introduction: Hybrid Quadrupole - Dual Pressure Cell Linear Ion Trap Mass Spectrometry

Hyunho Kim
Thermo Fisher Scientific

CW-1-3 6.25 (Tue) 12:20-12:40

Streamline the biomarkers transformation from discovery to validation at unprecedented scale

Yue Xuan
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COPRORATATE WORKSHOP-1

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Education

5/1989-3/1992	PhD in Physics and Mathematics (scientific advisor: Prof. A. A. Sysoev)	Dept. of Molecular Physics, Moscow Physics-Engineering Institute, Russia
9/1983-3/1989	MSc with Honors in Molecular Physics	Dept. of Molecular Physics, Moscow Physics-Engineering Institute, Russia

Professional Experience

6/2007-present	Director of Research, Life Sciences Mass Spectrometry	Thermo Fisher Scientific (Bremen) GmbH

Academic Society

04/2020-present	Fellow	Royal Society, UK
06/1997-present	Member	American Society for Mass Spectrometry

Publications

1. Neumann Adam P., Sage Eric, Boll Dmitri, Reinhardt-Szyba Maria, Fon Warren, Grinfeld Dmitry, Masselon Christophe, Hentz Sébastien, Sader John E., Makarov Alexander, Roukes Michael L. "A Hybrid Orbitrap-Nanoelectromechanical Systems Approach to Analysis of Individual, Intact Proteins in Real Time". Angew. Chem. Int. Ed. 2024, e202317064.

2. Deslignière, E., Yin, V.C., Ebberink, E.H.T.M. et al. "Ultralong transients enhance sensitivity and resolution in Orbitrap-based single-ion mass spectrometry". Nat. Methods (2024). https://doi.org/10.1038/s41592-024-02207-8

3. Serrano L.R., Peters-Clarke T. M., ... Makarov A.A, Zabrouskov V., Coon J.J. "The one hour human proteome". Mol. Cell. Proteomics, 2024, 100760.

4. Guzman, U.H., Martinez-Val, A., Ye, Z. ...Makarov A., Zabrouskov V., Olsen J.V. "Ultra-fast label-free quantification and comprehensive proteome coverage with narrow-window data-independent acquisition". Nat Biotechnol, 2024. https://doi.org/10.1038/s41587-023-02099-7

5.Wörner T. P., Thurman H.A., Makarov A. A., Shvartsburg A. A. "Expanding Differential Ion Mobility Separations into the MegaDalton Range", Anal. Chem. 96(14):5392-5398. olegDOI: 10.1021/acs.analchem.3c05012.

6. Stewart H, Grinfeld D, Petzoldt J, Hagedorn B, Skoblin M, Makarov A, Hock C. "Crowd control of ions in the Astral analyzer". J Mass Spectrom. 2024; 59(4): e5006.

7. Stewart H., Grinfeld D., Giannakopulos A., ... Makarov A.A., Hock C. "Proof of principle for enhanced resolution multi-pass methods for the astral analyzer". Int. J. Mass Spectrom., 2024, 498, 117203.

8. Steigerwald S., Sinha A., Fort K., Zeng W.F., Niu L., Wichmann C., Kreutzmann A., Mourad D., Aizikov K., Grinfeld D., Makarov A., Mann M., Meier F. " Full Mass Range ΦSDM Orbitrap Mass Spectrometry for DIA Proteome Analysis", Molecular & Cellular Proteomics 2024, doi: https://doi.org/10.1016/j.mcpro.2024.100713.

9. Grinfeld D., Stewart H., Balschun W., Skoblin M., Hock C., Makarov A.A. "Multi-reflection Astral mass spectrometer with isochronous drift in elongated ion mirrors". Nuclear Instrum. Methods in Phys. Research A 2024, 1060, 169017.

10. Ray S., Arévalo R. Jr, Southard A.,... Makarov A.A." Characterization of Regolith And Trace Economic Resources (CRATER): An Orbitrap-based laser desorption mass spectrometry instrument for in situ exploration of the Moon." Rapid Commun Mass Spectrom. 2024; 38(2): e9657.

CW1-1

Frontiers of high resolution accurate mass analysis

Alexander Makarov

Thermo Fisher Scientific, Bremen, Germany

Since its commercial debut nearly two decades ago, the utility of the Orbitrap analyzer has been continuously extended by additional capabilities such as quantitative analysis, new fragmentation methods, diverse vacuum and ambient ion sources, imaging, ion mobility and unprecedented extension of mass range. These enhancements are exemplified across major families of Orbitrap-based instruments and types of analysis, from small molecules to intact proteins and even viruses.

The most recent development, the asymmetric track lossless (Astral™) analyzer merges Orbitrap and TOF features in a new type of instrument to dramatically improve sensitivity and throughput of analysis of complex mixtures in proteomics and metabolomics.

These latest advancements promise to keep mass spectrometry competitive against alternative technologies and allow it to rise to the challenge of unprecedented throughput of very deep analyses of very complex samples.

COPRORATATE WORKSHOP-1

Hyunho Kim

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CW1-2

New Product Introduction: Hybrid Quadrupole - Dual Pressure Cell Linear Ion Trap Mass Spectrometry

Hyunho Kim

Thermo Fisher Scientific, Seoul, Korea, Republic of

Accelerate biomarker verification with confidence by quantifying more analytes with increased sensitivity, specificity, and throughput using the Thermo Scientific Next Generation mass spectrometer. By synergistically combining the robust quantitative performance of triple-quadrupole technology with the sensitive, hyper-fast full-scan MSn acquisition of dual-pressure linear ion trap technology, The next generation mass spectrometer extends its unprecedented analytical capabilities to a wider range of compounds. Next generation mass spectrometry gives you the ability to verify your findings in ways that bridge the gap between discovery and the clinic for the very first time.

COPRORATATE WORKSHOP-1

Yue Xuan, PhD, MBA

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Education

2001 – 2004	Master of Science (MS) Chemistry	Free University Berlin
2004 – 2007	Dr.rer.nat Chemistry	TU Dortmund University
2019 – 2021	Executive Master of Business Administration (MBA)	ESMT Berlin

Professional Experience

2007.04 – 2017.06	Product Speialist FT-MS	Thermo Fisher Scientific
2017.09 - present	Sr. Global Product Marketing Manager, Precision Medicine	Thermo Fisher Scientific

Publications

1. Xuan, Y. et al. Standardization and harmonization of distributed multi-center proteotype analysis supporting precision medicine studies. Nat. Commun. 11, 5248 (2020).

2. Martínez-Val, A., Fort, K., Koenig, C. et al. Hybrid-DIA: intelligent data acquisition integrates targeted and discovery proteomics to analyze phospho-signaling in single spheroids. Nat Commun 14, 3599 (2023).

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4.Goetze, S., van Drogen, A., Albinus, J.B. et al. Simultaneous targeted and discovery-driven clinical proteotyping using hybrid-PRM/DIA. Clin Proteom 21, 26 (2024).

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CW1-3

Streamline the biomarkers transformation from discovery to validation at unprecedented scale

Yue Xuan

Thermo Fisher Scientific, Bremen, Germany

The streamlined transformation of biomarkers from discovery to validation at an unprecedented scale is essential for advancing research and improving clinical applications. By optimizing and simplifying the process, researchers can efficiently validate biomarkers, ensuring their reliability and effectiveness. This streamlined approach enables the translation of biomarkers into clinical practice on a larger scale, facilitating their widespread use and impact in healthcare.

Powered by the synergy of a high-resolution quadrupole mass filter, the Thermo Scientific™ Orbitrap™ mass analyzer and the novel Thermo Scientific™ Astral™ mass analyzer, this revolutionary new instrument achieves unsurpassed performance and experimental flexibility. The combination of the three mass analyzers enables the rapid acquisition of exceptional quality high resolution accurate mass (HRAM) spectra with high sensitivity and dynamic range. The new performance characteristics of the Thermo Scientific™ Orbitrap™ Astral™ mass spectrometer make it ideally suited for accurate and precise quantitation at an unprecedented depth of coverage and throughput for samples from single cells to body fluids to bulk tissues for discovery studies.

To streamline the biomarkers transformation from discovery to the downstream, a next generation mass spectrometer is designed to estbalish a new paradigm to drive biomarker verification by ten times the sensitivity for five times more compounds at scale compared to existing technologies. By synergistically combining the robust quantitative performance of triple quadrupole technology with the sensitive, rapid full scan MSn acquisition of dual-pressure linear ion trap technology, the next generation mass spectrometer extends the unprecedented analytical capabilities to a wider range of compounds. Single-ion detection capabilities expand robust targeted quantitation for single cell or low protein load studies minimizing the potential for missing data. Novel software tools streamline highly multiplexed targeted quantitative method creation, implementation, and data acquisition, bypassing lengthy and costly replicate injections associated with existing technology. The new experimental capabilities of the next generation mass spectrometer make it ideally suited for transitioning putative biomarker candidates from discovery to validation for translational proteomics, metabolomics, and lipidomics research.

COPRORATATE WORKSHOP-2

SCIEX

COPRORATATE WORKSHOP-2

6.26 (Wed) 12:30 - 13:00

CW-2 6.26 (Wed)

Next Generation SCIEX HRMS – Zeno TOF System for BioPharm and Omics

Doyoung Choi
Sciex Korea

COPRORATATE WORKSHOP-2

Doyoung Choi, Ph.D

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Education

2002. 3 ~ 2009. 2	Bachelor	Department of Molecular Biotechnology, Konkuk University
2009. 3 ~ 2011	Master	Department of Molecular Biotechnology, Konkuk University
2011. 3 ~ 2014. 9	Ph.D	Department of Chemistry, Kyung Hee University Lab. Of Functional Systems Biochemistry

Professional Experience

2014. 3 ~ 2015. 6	Research Scientist	National Cancer Center
2015. 7 ~ 2020. 5	Researcher	CJ Healthcare

Publications

1. Extracellular vesicles shed from gefitinib-resistant non-small cell lung cancer regulate the tumor microenvironment, Proteomics. 2014 Aug, 14(16), 1845-1856

2. Identification and characterization of proteins isolated from microvesicles derived from human lung cancer pleural effusions, Proteomics. 2013 Jul;13(14):2125-34. doi: 10.1002/pmic.201200323.

3.Comprehensive Characterization of N-Glycosylation in Darbepoetin Alfa, Bulletin of the Korea Chemical Society. 2019 Aug, 40(10), 976-982

CW2-1

Next Generation SCIEX HRMS – Zeno TOF System for BioPharm and Omics

Doyoung Choi

Sciex Korea

In biopharmaceutical research and development, the ID of the charge variant has been a major hurdle. We introduce the Intabio ZenoTOF system, which can quickly separate and identify charge variants of proteins by overcoming the limitations of separation methods using mobile phases with low ionization efficiency. Additionally, improvements have been made to proteomics applications using SCIEX Zeno TOF. We introduce the ZT scan DIA method, which can excellent quantitative performance in samples with a larger number of Protein IDs and lower concentration than the existing method.

COPRORATATE WORKSHOP-3

Agilent

COPRORATATE WORKSHOP-3

6.26 (Wed) 12:30 - 13:00

CW-3 6.26 (Wed)

Intelligent Instrumentation for Targeted Proteomics, Advanced Protein Characterization, and High Throughut Quality Control

Daniel J. Cuthbertson
Agilent Technologies

COPRORATATE WORKSHOP-3

Daniel J. Cuthbertson, Ph.D.

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Education

2005.08-2011.12	Doctor of Philosophy Molecular Plant Sciences	Washington State University

Professional Experience

Present-2022.09	Director, Global Life Science Research Marke	Agilent Technologies
2022.09-2019.06	Senior Omics Application Scientist	Agilent Technologies
2012.06-2019.06	Omics Application Scientist	Agilent Technologies

CW-3

Intelligent Instrumentation for Targeted Proteomics, Advanced Protein Characterization, and High Throughut Quality Control

Daniel J. Cuthbertson[1], Lingfeng Wu[1], Christoph Borchers[2], Kyle Luttgeharm[1], Joeseph Meeuwsen[1]

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Today's proteomics lab is increasingly challenged by evering increasing demands for not only high throughput and productivity but also for providing deeper biological insights as well. Here we will discuss intelligent instrumentation designed to provide predictive analytics for instrument performance as well as advanced workflows ensuring the highest dataquality for routine applications in targeted proteomics for not only basic research but large cohort studies in translational omics. Additionally, in protein characterization studies alternative fragmentation mechanisms such as ExD promise to deliver not only deeper insights to peptide and protein sequence but for top-down approaches more insight into tertiary/quaternary and native structures. Finally, we will discuss new automated approaches for protein sample QC allowing labs to increase throughput and focus on acquiring the highest quality data with their mass spec instrumentation.

COPRORATATE WORKSHOP-4

Somalogic

COPRORATATE WORKSHOP-4

6.26 (Wed) 13:00 - 13:30

CW-4	**6.26 (Wed)**	
High Throughput Proteomics (Somascan Assay)		
Jong-So Kim Somalogic		

COPRORATATE WORKSHOP-4

Jong-So Kim, Ph.D

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Education

1999.03-2000.08	PhD	POSTECH

Professional Experience

2001.03-2008.01	Research Fellow	NIH, US
2008.02-2010.01	연구조교수	POSTECH
2010.05-2014.12	연구위원(이사)	마크로젠
2015.01-2020.06	이사	테라젠바이오
2020.07-2021.06	이사	셀레믹스
2021.08-2022.12	상무	젠큐릭스
2023.01-현재	한국총괄대표	Somalogic

CW-4

High Throughput Proteomics (Somascan Assay)

Jong-So Kim

Somalogic, Boulder, CO, US

SomaLogic은 2000년 Dr. Larry Gold에 의해서 설립되었다. 미국 콜로라도 볼더에 위치한 단백질 바이오마커 발견 및 임상 진단 회사로 2021년 9월에 나스닥에 상장되었다. 회사 설립 후 20여년동안 modified aptamer (SOMAmer)를 이용한 high-throughput proteomics platform을 개발하였다. 현재 혈장 55ul에서 11,000개의 단백질을 동시에 측정할 수 있다. 이는 SOMAmer의 정교한 specificity, high reproducibility, high sensitivity, 10 Log dynamic range로 가능하게 했다. 현재 전 세계에서 Somalogic platform을 이용한 연구가 활발히 진행되고 있고 550,000개 이상의 샘플들을 수행했고, 1,000개 이상의 논문 발표, 1,000개 이상의 특허가 있다. 또한 세계에서 가장 큰 clinical proteomic database를 보유하고 있다. 이를 이용하여 할 수 있는 분야는 biomarkers and drug targets discovery, 각종 질병 및 투약 후 모니터링, 임상시 환자 선택, 부작용 조기발견, action mechanism 결정, risk prediction, 환자 계층화 등이 있다.
현재 제공되고 있는 서비스는 아래와 같다.

1. Somascan Assay: 혈장 55ul에서 11,000개 이상의 단백질을 측정할 수 있는 플랫폼
   a. 11,000개 이상의 단백질 측정
   b. 정교한 specificity
   c. Reproducible with median 5% CV
   d. 10-Log dynamic range

2. Somascan Panels: 7개의 fixed panels 과 custom panels
   a. Cardiovascular Disease (953 analytes)
   b. Inflammation and Immune Response (938 analytes)
   c. Oncology (863 analytes)
   d. Metabolic Diseases (890 analytes)
   e. Neuroscience (1316 analytes)
   f. Cytokines (168 analytes)
   g. Respiratory (627 analytes)
   h. Custom (1~100, 101~1500)

3. SomaSignal tests: proteomics data 를 clinical data 전환
   Cardiovascular related, Liver fat, Diabetes, Heart related, NASH related, Dementia risk, Kidney prognosis 등 21 종의 clinically validated tests

COPRORATATE WORKSHOP-5

BRUKER

COPRORATATE WORKSHOP-5

6.27 (Thu) 12:30 - 13:30

CW-5 6.27 (Thu)

4D-Proteomics technology of MS-based Proteomics : Principle & Application secondary metabolites by LC-MS/MS system

Kwangseon Lee
Bruker Korea

COPRORATATE WORKSHOP-5

Kwangseon Lee

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Education

2012.03~2015.08	Bachelor	Ajou university
2015.09~2018.08	Master	Ajou university

Professional Experience

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CW-5

4D-Proteomics technology of MS-based Proteomics : Principle & Application secondary metabolites by LC-MS/MS system

Kwangseon Lee[1], Shinkwon Kang[1]

[1]Bruker Korea, Seongnam 13493, Korea

Over the past two decades, significant technological advancements and the development of new methodologies have transformed proteomics into a highly potent tool for protein scientists, biologists, and clinical researchers. The incorporation of ion mobility has not only pushed the boundaries in terms of speed, sensitivity, selectivity, and robustness but has also facilitated the exploration of previously inaccessible parts of the proteome. Through 4D-Proteomics, researchers can consistently measure the Collisional Cross Section (CCS) values for all detected ions, enhancing the system's selectivity and providing more reliable relative quantitation information, even from complex samples and short gradient analyses.

Accurate relative protein quantitation is fundamental in quantitative proteomics, crucial for understanding biological assemblies and conducting biomarker discovery experiments. While Data Independent Acquisition (DIA) remains the most widely used strategy for addressing the missing value problem, its implementation requires the construction of spectral libraries, which can be challenging, particularly for rare organisms. Additionally, traditional DIA methods may not be suitable for short gradient analysis due to their slow speed. In such scenarios, 4D-Proteomics-LFQ offers a solution with its combination of speed, flexibility, and reliability. Moreover, the reproducible determination of Collisional Cross Sections enables the 4D-Match Between Runs (MBR) approach, maximizing the quantification of proteins in Label-Free Quantification experiments while ensuring confidence in high-throughput sample analysis. The 4D-MBR approach is supported by the latest analytical tools.

4D-Proteomics is adept at addressing various analytical challenges, ranging from tissue and biofluid analysis to single-cell studies. Protein expression is influenced by an individual's genetic background, as well as factors such as time, localization, and physiological responses to external stimuli. Furthermore, the intricate interplay of alternative splicing, point mutations, post-translational modifications, and endogenous proteolysis can result in a single protein being expressed in multiple proteoforms, each with distinct biological activities. Addressing this complexity necessitates the comprehensive capabilities of 4D-Proteomics.

POSTER SESSION

POSTER SESSION

A. Molecular interactions With Proteins

A-001 AI-Predicted Structural Insights into Mutant Huntingtin Interactions and Huntington's Disease

Eunseo Kim[1,2,4], Hong-Beom Park[1,2,4], Hoseok Seo[1,2,5], Sinae Lee[1,2,6], Jayun Choi[1,2,6],Hyeon Chang Lee[1,2,3],Gyuri Park[1,2,3] and Dohyun Han[1,2]

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Huntingtin (HTT) is a pivotal protein essential for embryonic development and involved in various cellular processes, including vesicular transport, endocytosis, autophagy, and transcription regulation. Huntington's disease (HD) results from a pathological expansion of a polyglutamine repeat at the amino terminus of the HTT gene, which alters its normal functions and interactions. Due to the scarcity of structural data on HTT and its interacting complexes, this study leverages AI-driven structural predictions using public HTT IP-MS data and Alphafold3. The innovative use of in silico structure prediction models offers significant advantages by allowing for the rapid generation and analysis of protein structures and interactions that are otherwise difficult to observe experimentally. We have discovered HTT-interacting protein complex structure models that suggest potential new direct causes of HTT dysfunction and propose mechanisms by which these complexes could serve as genetic disease modifiers. Future work will experimentally validate these functions using in vitro pulldown assay and site-directed mutagenesis. This study not only advances our understanding of HTT's role in cellular function but also opens new avenues for therapeutic strategies in Huntington's disease.

A-002 Analysis of Protein Expression Patterns Based on LC-MS/MS in Individual COVID-19 Patients Stratified by Immune Specificity

Yerim Lee[1], Wonseok Lee[1], Pyoeng Gyun Choe[2], Chang Kyung Kang[2], Wan Beom Park[2], Dong-Hyun Kim[3], Hyunsoo Kim[1,4,5,6]

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[6]SCICS, Sciences for Panomics

Introduction
A comprehensive understanding of the immunopathology and clinical biomarkers related to Coronavirus Disease 2019 (COVID-19) remains a complex challenge. Pre-existing comorbidities not only increase mortality rates but also exacerbate immune responses to Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection, potentially leading to more severe symptoms and causing prolonged COVID-19 and post-COVID-19 complications. In this study, we aim to identify protein expression patterns using LC-MS/MS by stratifying patients based on their immunological disorders versus those with normal immune function, further categorized by symptom severity into mild and severe groups. Through this analysis, we seek to uncover protein expression patterns that may contribute to immune-specific responses and disease progression, elucidating potential differences.

Methods
Proteins were extracted from plasma samples obtained from the blood of individual patients. These blood plasma samples were stratified into groups based on normal immune function and immune suppression, maintaining a gender ratio of 2:1. Within each group, severity was equally divided into mild and severe cases, resulting in a ratio of 3:3. Subsequently, the depleted plasma was concentrated and subjected to digestion. Proteome profiling was conducted, followed by analysis using Maxquant-Perseus. Patients were divided into subgroups based on severity, within the categories of immune disorders and normal immune function, and protein expression patterns were examined using LC-MS/MS.

Results
To elucidate protein alterations associated with coronavirus infection at a systemic level, LC-MS/MS proteomic profiling was performed on depleted plasma samples from 12 individual COVID-19 patients. The analysis revealed significant differences in protein expression patterns corresponding to immune specificity in COVID-19 patients. Utilizing this data, our objective is to delineate directions for identifying crucial changes in cellular signaling responses correlated with disease severity and immune specificity.

Conclusion
Our study has revealed substantial variances in protein expression profiles based on immune specificity among COVID-19 patients. These discoveries offer crucial insights into the interplay among disease severity, immune reactions, and protein modifications. Further inquiries are imperative to enhance our comprehension of how these distinctions might impact the initiation and advancement of the disease, particularly concerning the diagnosis, prognosis, and the formulation of therapeutic approaches for COVID-19.

A. Molecular interactions With Proteins

A-003 Analysis of the Proteome Variation Induced by a Mutation in the Hepatitis B Virus

Sangwoon Lee[1], Yongho Park[1], Woojin Kim[1], Bum-Joon Kim[2], Su Jong Yu[3], Eun Ju Cho[3], Hyunsoo Kim[1,4,5,6]

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[3]Department of Internal Medicine and Liver Research Institute, College of Medicine, Seoul National University
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[5]Protein AI Design Institute, Chungnam National University
[6]SCICS, Sciences for Panomics

Interduction:
Hepatitis B virus (HBV) is associated with inflammation, cirrhosis, and hepatocellular carcinoma (HCC), posing a global medical challenge. HBV consists of four major proteins: surface antigens, core proteins, polymerase, and HBx. The limited proofreading ability of HBV's reverse transcriptase results in mutation rate ten times higher than that of other DNA viruses. This heightened mutation rate is significant because single amino acid variants in HBV have been found to be associated with patient prognosis. We identified differences in protein expression related to mutations within the genotype of HBV proteins in blood samples from Korean patients. Our proteomic study suggests these mutations can elucidate the clinical phenotypes of patients.

Methods:
After identifying mutations through PCR results from HBV patients at Seoul National University Hospital, we grouped the patients based on their mutation trypes. We employed LC-MS/MS proteomic analysis to identify target proteins exhibiting differential expression related to phenotype in a cohort of 65 patients. The analysis results were normalized using the Internal Standard Method with a 6×5 reference mix, and the fold changes (FC) was evaluated for all identified proteins. Statistical analyses were performed to assess the significance of differences between the groups.

Results:
To discover differentially expressed proteins (DEPs) by HBV genotypes, we performed targeted proteomics analysis on serum samples without depletion of highly abundant proteins. In total, 2433 peptides from 1890 proteins were detected, of which 78 peptides from 78 proteins were identified as significant DEPs following an independent two-sample t-test with a p-value of ≤ 0.05 and a fold change greater than 1.5. We investigated the relationship between DEPs and clinical phenotypes based on genotypes. Notably, Protein A, B, and C were found to explain specific clinical phenotypes commonly observed with HBV surface antigen mutations in Koreans.

Conclusion:
We observed differential protein expression among patients with different HBV genotypes. Our research suggests the presence of potential biomarkers that could guide treatment strategy selection for HBV. Further investigations could explore the functional implications of these biomarkers, and their verification in broader patient populations would be instrumental in advancing personalized treatment strategies for HBV management.

A-004 Cereblon role in the ferroptosis progress in the Psoriasis disease.

Thien Nguyen Huu[1], Eun Seol Jung[1], Hyoung Kyu Kim[1], Jin Han[1*]

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Psoriasis is a chronic inflammatory skin disease with complicated symptoms and has many effects on patient life quality. The pathogenesis of psoriasis relates to immune cells and the increase of proinflammatory cytokines, especially in the IL-23/Th17 axis. Recently, there are many studies found the role of ferroptosis in the pathogenesis of many diseases related to the immune system as well as psoriasis. Cereblon (CRBN) is a protein with multiple functions related to immunomodulatory drugs, cell metabolism, and cell death. Previous studies found that CRBN relates to apoptosis, TLR4, p38 MAPK pathway, and activation of the T cells. So, in this study, we discover the roles of CRBN in the process of ferroptosis in the Psoriasis model.
Material and methods: The psoriasis model on WT and CRBN KO mice was induced with 5% Imiquimod cream and the ferroptosis model on WT and CRBN knockdown keratinocyte cells by erastin. We investigate cell viability, and ferroptosis makers in these models. Skin parameters were measured, and skin lesions were by hematoxylin and eosin staining. Western blot was used for protein levels evaluation and mRNA levels were measured by RT-PCR.
Results and discussion: CRBN knockdown keratinocytes are more sensitive to erastin treatment than WT keratinocytes. The cell viability decreases and ferroptosis makers (GPX4, ACSL4, HNE) change more in the CRBN knock-down keratinocyte group. In the vivo model study, the data suggested that CRBN KO mice have higher ferroptosis progress than WT mice.
Conclusion: The study shows that CRBN has a role in the anti-ferroptosis process in the keratinocytes in the Psoriasis model. This thing suggests a new target to improve Psoriasis and ferroptosis-related diseases.
Keywords: CRBN, ferroptosis, psoriasis, cell death program.

A. Molecular interactions With Proteins

A-005 Cereblon-mediated ubiquitination regulates L-type calcium channel function in the heart

Nammi Park[1], Jubert Marquez[1], Jessa Flores[1], and Jin Han[1*]

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Cereblon (CRBN) is a substrate receptor of the E3 ubiquitin ligase complex, which has been reported to target ion channel proteins. Modulation of the L-type voltage-dependent Ca2+ channel α1c subunit (Cav1.2α) is a critical player in heart failure associated with reduced ejection fraction (HFrEF), but the underlying cellular mechanisms are unclear. Here, we explored the role of CRBN in HFrEF by investigating the direct regulatory role of CRBN in Cav1.2α activity, and how it can serve as a target to address myocardial dysfunction. Cardiac tissues from HFrEF patients exhibit increased levels of CRBN, suggesting its involvement in heart failure (HF). In vivo and ex vivo animal model studies demonstrate that whole body CRBN-knockout (CRBN-/-) and cardiac-specific knockout mice (Crbnfl/fl/Myh6Cre+,) enhanced cardiac contractility with increased L-type calcium channel current (ICaL), modulated by the direct interaction of CRBN with Cav1.2α subunit. Mechanistically, we discovered that the Lon domain of CRBN directly interacts with the N-terminal of Cav1.2α. Increasing CRBN levels enhanced ubiquitination and proteasomal degradation of Cav1.2α and decreased L-type Ca2+ channel currents. By contrast, genetic or pharmacological depletion of CRBN via TD-165, a novel CRBN-targeting degrader, increased the surface expression of Cav1.2α and enhanced L-type Ca2+ channel currents. We have also discovered that CRBN-/- mice exhibited resistance to doxorubicin-induced HF. findings indicate that CRBN selectively degrades Cav1.2α, which in turn facilitates cardiac dysfunction, suggesting that reducing CRBN levels could serve as a new target of cardioprotective therapeutic strategy for HF

A-006 Elucidating Interactome Dynamics in a ADORA2A Interactome Through Targeted LC-MS Analysis

Wonseok Lee[1], Hee Jeong Kong[2], Young-Ok Kim[2], Hyunsoo Kim[1,3,4,5]

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[5]SCICS, Sciences for Panomics

Introduction
PDRN (Polydeoxyribonucleotide) is a tissue regeneration substance that resembles human DNA and present in human cells, mullets, salmons, and flatfish. It stimulates physiological regeneration and metabolic activity. The regenerative and metabolic effects of PDRN are attributed to the activation of Adenosine A2A receptors (ADORA2A), which increases the production of angiogenesis factors and growth factors. Activation of ADORA2A also leads to an increase in the expression of ADORA2A-interacting proteins with similar functions. Therefore, our research aimed to investigate the differential expression of ADORA2A and interactome proteins in the presence of PDRN.

Methods
To investigate the changes and dynamics of proteins in the presence of PDRN from different species, we established experimental and control groups, analyzing the expression levels of the ADORA2A-interacting protein using HUVEC cells incubated with salmon sperm, flatfish sperm, flatfish testis for 6 hours. Information regarding the targeted interactome was obtained from approximately ten interactome databases, and we integrated targets on 513 proteins and 6503 peptides. To ensure reliable analysis, proteins were enzymatically digested, and peptide-level analysis was conducted using selected reaction monitoring-mass spectrometry (SRM-MS).

Result
Through SRM-MS analysis, we identified 491 proteins, 3852 peptides within the ADORA2A-interacting protein. Furthermore, through additional statistical analysis with P-values of 0.05 or less and fold changes greater than 2, we identified differentially expressed proteins and peptides between each group. We found 374 proteins and 1193 peptides demonstrating both upregulation and downregulation in expression. Next, to elucidate the functions associated with the differentially expressed ADORA2A-interacting protein, we conducted gene ontology (GO) analysis and physical network analysis and discovered a novel network of proteins related to neuronal differentiation among the ADORA2A-interacting protein. Based on network analysis, we found indirect interactions with MAPK1 and MP2K1, which are known to influence neuronal cell differentiation and suggests the formation of a network involving MAPK signaling transduction. Finally, using AlphaFold multimer, we were able to predict interaction sites among ADORA2A-interacting proteins in the network associated with neuronal cell differentiation. Specifically, we predicted 5 interaction sites between ADORA2A and NTRK1(which interacts with ADORA2A) forming the edge.

Conclusion
Our study enabled the quantitative assessment of how activation of ADORA2A via PDRN influences the ADORA2A-interacting protein at the mass level, revealing a novel network associated with neuronal differentiation. Thus, we provided indicators for further research using ADORA2A present in a robust network and highlighted the potential of PDRN to impact neuronal differentiation.

A. Molecular interactions With Proteins

A-007 Identification of Plasma Biomarkers for CADASIL Diagnosis and Monitoring: Insights from Inflammation Pathway Analysis

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Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy (CADASIL) presents a formidable challenge in clinical management due to its wide array of neurological symptoms and genetic complexity. While genetic testing for NOTCH3 mutations serves as the primary diagnostic method, there exists a pressing need for supplementary blood-based biomarkers, especially in cases where genetic testing is impractical or inconclusive. This study aims to identify such biomarkers through plasma protein analysis, aiming to enhance CADASIL diagnosis and treatment approaches. Plasma samples were meticulously collected from CADASIL patients, stroke patients, and healthy controls, ensuring demographic parity among the groups. Employing the proximity extension assay (PEA), we meticulously examined 92 inflammation-related proteins, seeking potential biomarkers that could effectively differentiate CADASIL from stroke. Our comprehensive analysis unveiled notable differential expression of two inflammation-related proteins in CADASIL patients compared to stroke patients, suggesting their candidacy as novel biomarkers for CADASIL diagnosis. These findings not only deepen our understanding of CADASIL pathophysiology but also hold promise for the development of targeted therapeutic interventions. The identification of plasma biomarkers for CADASIL diagnosis and monitoring represents a significant stride forward in the field, furnishing clinicians and researchers with invaluable diagnostic tools. Further validation studies are imperative to ascertain the clinical utility of these biomarkers and explore their potential in tailoring personalized treatment regimens for CADASIL patients.

A-008 Identification of proteins in extracellular vesicles derived from Lactobacillus crispatus

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Extracellular vesicles (EVs) play a crucial role as mediators that regulate various functions through interactions with the host. Recent research suggests that EVs derived from probiotics, along with their constituent proteins, demonstrate superior effects in disease management compared to the probiotic strains themselves. These enhanced effects arise not only from their pivotal role in modulating immune responses but also from their inherent antimicrobial properties, enabling the specific targeting of pathogenic molecules or cells. Despite the well-known health-promoting effects of lactic acid bacteria, knowledge about their EVs is limited. Accordingly, we conducted research aimed at isolating EVs from major strains of lactic acid bacteria proven effective in treating various diseases. We isolated EVs from Enterococcus faecium, Weissella confusa, Bacillus subtilis, Bacillus sonorensis, Lactobacillus crispatus, Lactobacillus plantarum, Pediococcus pentosaceus, and Pediococcus acidilactici. Compared to MRS, a higher yield of EVs was observed when cultured in food-grade medium (FGM). Detailed isolation and characterization of EVs in this strain have been attempted, especially because of the large amount of EVs obtained from L. crispatus. Isolation of EVs from L. crispatus was achieved through ultracentrifugation (UC) and size exclusion chromatography (SEC). Following nanoparticle tracking analysis (NTA) to confirm their size and particle concentration. Higher yields were observed with UC than with SEC. Therefore, EVs isolated through UC were performed proteomic analysis. A total of 64 proteins were identified in EVs derived from L. crispatus strains, notably enriched in S-layer and splX proteins. Based on the proteome data, predictions were made regarding the biological pathway and protein-protein interactions of proteins in EVs derived from L. crispatus. The results of this study can assist in selecting an optimized method for isolating EVs from lactic acid bacteria, thereby facilitating their isolation. Additionally, the functional roles and interactions of secreted proteins were predicted, but further research is needed to accurately identify them.

Keywords : Probiotics, Lactobacillus crispatus, Proteomics, Extracellular vesicles

A-009 In vivo mitochondrial matrix proteome profiling reveals RTN4IP1/ OPA10 as an antioxidant NAD(P)H oxidoreductase

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Targeting proximity labeling enzymes to specific cellular locations is a viable strategy for profiling subcellular proteomes. Here, we generated transgenic mice (MAX-Tg) expressing a mitochondrial matrix-targeted ascorbate peroxidase (MTS-APEX2) to analyze tissue-specific matrix proteomes. Desthiobiotin-phenol labeling of muscle tissues from MAX-Tg mice allowed for the efficient profiling of tissue-specific matrix proteome. Comparative analysis of matrix proteomes from MAX-Tg muscle tissues revealed differential enrichment of mitochondrial proteins related to energy production. We identified that Reticulon 4 interacting protein 1 (RTN4IP1), also known as Optic Atrophy-10 (OPA10), is highly enriched in the mitochondrial matrix of muscle tissues and is an NADPH oxidoreductase. Interactome analysis and in vitro enzymatic assays revealed an essential role for RTN4IP1 in coenzyme Q (CoQ) biosynthesis by regulating the O-methylation activity of COQ3. Rtn4ip1 knockout C2C12 myoblasts had markedly decreased CoQ9 levels and impaired cellular respiration, which was rescued by exogenous CoQ treatment. Muscle-specific knockdown of the drosophila Rnt4ip1 ortholog resulted in impaired muscle function which was reversed by dietary supplementation with soluble CoQ. Collectively, RTN4IP1 is a mitochondrial antioxidant NAD(P)H oxidoreductase supporting mitochondrial respiration activity in muscle tissue.

A. Molecular interactions With Proteins

A-010 Phenolic Drug-derived Metabolite Labeling by Engineered Peroxidase: Case of 4-hydroxytamoxifen (4-OHT)

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Engineered ascorbate peroxidase (APEX2) is a genetically encodable enzyme which can catalyze radical generation reactions in phenolic moiety and has proven its versatility in proteomics field by deployments in various subcellular locations in cultured cell lines or live animal models. In this work, the scope of APEX2 labeling reaction is expanded to drug-derived metabolites using post-APEX2-labeling metabolite extraction followed by LC-MS analysis. 4-hydroxytamoxifen (4-OHT), which is derivatized from approved breast cancer drug tamoxifen, can be labeled using desthiobiotin-phenol (DBP) using APEX2 expressed in subcellular organelles such as cytoplasm, nucleus, mitochondria, endoplasmic reticulum. Also, APEX2 labeling revealed 4-OHT is accumulated in intermembrane space of mitochondria, which might be accountable for its previously reported mitochondrial toxicity. These results suggest that APEX2 can contribute to the field of spatial metabolomics, as it can reveal subcellular distribution of a set of metabolites in live cells.

A-011 Regulation of ubiquitin-proteasome system via ER stress modulator, VCP/p97 induces autophagy

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The endoplasmic reticulum (ER) is involved in many important cellular functions including calcium storage, protein folding/processing, and lipid metabolism, etc. However, when unfolded or misfolded proteins accumulate, protein quality control such as the unfolded protein response (UPR), autophagy, and ER-associated degradation (ERAD) is triggered to resolve the ER stress. In particular, the VCP/p97 AAA-ATPase (valosin-containing protein, VCP) is required for the degradation of ERAD substrates. Due to the uncontrolled cell division in cancers, VCP/p97 tends to be overexpressed in many cancers, which has led to the discovery of VCP/p97 inhibitors. In this study, we found that VCP/p97 inhibitor has a cytostatic effect on the proliferation of human umbilical vein endothelial cells (HUVECs) through the induction of autophagy. In addition, using a proximity ligation assay, we confirmed that VCP/p97 inhibitor increased mitochondria-associated ER membranes (MAMs). Conversely, siRNA-mediated knockdown of VCP/p97 has less cytostatic effect on HUVECs proliferation, indicating off-target effects of VCP/p97 inhibitor. To discover potential binding targets of VCP/p97 inhibitor, we performed a label-free target protein identification method, cellular thermal shift assay (CETSA)-LC-MS/MS. Further studies will focus on identifying potential binding targets of VCP/p97 inhibitor and elucidating its novel mechanism of action.

Keywords: ERAD, MAM, Autophagy, CETSA-LC-MS/MS

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A-012 Revealing the Influence of ARRDC1 in Breast Cancer

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The Human Proteome Project (HPP), an extension of the Human Genome Project (HGP), aims to address various phenomena that cannot be resolved at the genomic level by expanding to the protein level, thereby facilitating a comprehensive understanding of human biology. The Chromosome-Centric Human Proteome Project (C-HPP) is a large-scale international project focused on studying the human proteome based on individual chromosomes. We are investigating the function of ARRDC1, a protein located on human chromosome 9, in the context of cancer. This protein is highly expressed in breast tissue, and our proliferation assay results have confirmed that knocking down ARRDC1 led to reduced proliferation and migration of breast cancer cells. Based on this, we hypothesize that ARRDC1 may influence the malignancy of breast cancer. Our aim is to study the function of this protein by analyzing its interactome to identify potential partners, confirm their interactions, and elucidate the mechanisms through which ARRDC1 operates.

A. Molecular interactions With Proteins

A-013 Super-resolution proximity labeling reveals antiviral protein network and its structural changes against SARS-CoV-2 viral proteins

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Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) replicates in human cells by interacting with host factors after infection. To understand the virus and host interactome, proximity labeling methods (biotin ligase or APEX) have been utilized. However, conventional proximity labeling workflow often provides rather ambiguous results likely due to the indirect identification of biotinylated proteins. Herein, we developed a super-resolution proximity labeling (SR-PL) method with “plug and playable” PL enzyme, TurboID-GFP binding protein (GBP) and we applied it for interactome mapping of GFP-tagged SARS-CoV-2 ORF3a and M proteins, which generated highly perturbed ER structures. Through SR-PL analysis of the biotinylated interactome of ORF3a and M, 224 and 272 peptides were robustly determined as ORF3a and M interactomes, respectively. Within the ORF3a interactome, RNF5 co-localized with ORF3a and generated ubiquitin modifications of ORF3a related to protein degradation. We also observed that SARS-CoV-2 infection rate was efficiently reduced by the overexpression of wild-type RNF5 in the host cells compared to cells overexpressing the nonfunctional mutant RNF5C42S. Overall, we introduced a new virus–host interactome mapping workflow using SR-PL and we could identify novel anti-viral ubiquitin ligase (RNF5) interfering with SARS-CoV-2 infection in human cells. This interactome data obtained using this SR-PL method was presented as a web-based platform (https://sarscov2.spatiomics.org) for readers to make it more accessible. This method contributes to revealing virus–host interactomes of other viruses in an efficient way in the future.

A-014 Target identification of the natural compound from ginseng by chemical proteomics

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Autophagy is a key process that removes unnecessary or damaged cellular components, thereby maintaining cellular health and functionality. This mechanism may play a critical role in reversing aging or reducing the rate of aging. Previous studies have shown that the natural compound ginseng has anti-cellular senescence activity in HDFs (human dermal fibroblasts). However, the underlying mechanisms and mode of action of the compound have remained elusive. We discovered that the compound attenuates cellular senescence by activating Ca2+-AMPK-mediated autophagy. To investigate the mode of action of the compound, a label-free method Cellular Thermal Shift Assay (CETSA) and LC-MS/MS were performed. As a result, a plasma membrane calcium ion channel ORAI1 was identified as the target protein of the compound. In addition, the binding between the compound and the identified target protein was validated by point mutations of the hotspot amino acid residues of the binding protein. Taken together, this study identifies a novel direct binding protein of the compound from ginseng and reveals the underlying mechanism by which ginseng attenuates cellular senescence through the induction of autophagy.

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A-015 The CRL3gigaxonin ubiquitin ligase–USP15 pathway governs the destruction of neurofilament proteins

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Giant axonal neuropathy (GAN) is caused by mutations in the GAN gene encoding for gigaxonin (GIG), which functions as an adaptor of the CUL3-RBX1-GIG ($CRL3^{GIG}$) E3 ubiquitin ligase complex. The pathological hallmark of GAN is characterized by the accumulation of densely packed neurofilaments (NFs) in the axons. However, there are fundamental knowledge gaps in our understanding of the molecular mechanisms by which the ubiquitin–proteasome system controls the homeostasis of NF proteins. Recently, the deubiquitylating enzyme USP15 was reported to play a crucial role in regulating ubiquitylation and proteasomal degradation of $CRL4^{CRBN}$ substrate proteins. Here, we report that the $CRL3^{GIG}$–USP15 pathway governs the destruction of NF proteins NEFL and INA. We identified a specific degron called $NEFL^{L12}$ degron for $CRL3^{GIG}$. Notably, mutations in the C-terminal Kelch domain of GIG, represented by L309R, R545C, and C570Y, disrupted the binding of GIG to NEFL and INA, leading to the accumulation of these NF proteins. This accounts for the loss-of-function mutations in GAN patients. In addition to regulating NFs, $CRL3^{GIG}$ also controls actin filaments by directly targeting actin-filament-binding regulatory proteins TPM1, TPM2, TAGLN, and CNN2 for proteasomal degradation. Thus, our findings broadly impact the field by providing fundamental mechanistic insights into regulating extremely long-lived NF proteins NEFL and INA by the $CRL3^{GIG}$–USP15 pathway and offering previously unexplored therapeutic opportunities to treat GAN patients and other neurodegenerative diseases by explicitly targeting downstream substrates of $CRL3^{GIG}$

A-016 Unveiling the Role of Branched-Chain Amino Acids in Bone Diseases Using Targeted LC-MS/MS Analysis

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Introduction
Chronic liver disease is increasingly recognized as a risk factor for osteoporosis development. In patients with chronic liver disease, serum concentrations of branched-chain amino acids (BCAAs) are observed to decrease. While BCAAs are suspected to be closely related to osteoporosis, the mechanisms underlying this relationship remain unclear. Mesenchymal stem cells differentiate into osteoblasts through the activation of TCF transcription factors within the Wnt/β-catenin signaling pathway. This study aims to elucidate the novel role of BCAAs by investigating how BCAA deficiency regulates the Wnt/β-catenin pathway using LC-MS/MS analysis. We hypothesize that BCAA deficiency impacts the Wnt/β-catenin signaling pathway, as well as other pathways such as the GCN2 and mTOR, potentially contributing to bone metabolic diseases like osteoporosis.

Methods
Mouse bone marrow-derived stromal cells (ST2 cells) were cultured in the presence of Wnt3a protein, with individual deprivation of Valine, Leucine, and Isoleucine. After growing the cells under these conditions, they were harvested for proteomics analysis. LC-MS/MS analysis was performed on the collected cells. Results were normalized using the Internal Standard Method with a 6×5 reference mix. This approach allowed for the quantification of differences in protein expression between groups. Statistical methods were employed to verify the reliability of the samples.

Results
LC-MS/MS analysis was conducted on 30 proteins and 216 peptides located within the Wnt/β-catenin, GCN2, and mTOR signaling pathways under BCAA deficiency conditions. We identified 11 proteins and 14 peptides that demonstrated significant changes in expression levels between conditions, with a p-value below 0.05 and either a fold change greater than 1.5 or less than 0.66. Among these, Protein A exhibited consistent differential expression under deficiency conditions for each BCAA and is involved in the amino acid metabolic pathway.

Conclusion
This study highlights the impact of BCAA deficiency on key pathways, including Wnt/β-catenin, GCN2, and mTOR, crucial for bone metabolism. Our findings demonstrate that changes in protein and peptide expression due to BCAA deficiency could significantly disrupt bone remodeling processes. These results suggest a potential therapeutic role for BCAA supplementation in managing bone metabolic diseases like osteoporosis, especially in those with chronic liver disease. Further research is needed to explore the clinical benefits of BCAA supplementation on bone health.

A-017 Varing proteomic responses of human dermal fibroblasts induced by an elastin-gradient 3D hydrogel environment

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Human dermal fibroblasts (HDFs) play an important role in coordinating physiological tissue repair. These fibroblasts also control the extracellular matrix (ECM) of connective tissue, contributing to maintaining tissue homeostasis in response to positive and negative feedbacks. Among the ECM components of skin, collagen mainly determines the mechanical properties of the tissues, while elastin regulates the mechanical properties of the tissues and is involved in aging and pathological processes. In particular, elastin content is known to be of great importance in controlling the physiological and pathological conditions of the skin. However, the relationship between excess elastin content and pathological responses of the skin has not been reported. In this study, we investigated the influence of the surrounding microenvironment, specifically the ratio of collagen and elastin as the cell culture conditions on HDF. Proteomic analysis was performed using nanoLC-ESI-MS/MS on HDFs cultured in four different matrices with different compositions of collagen and elastin [100% collagen/0% elastin (100C), 80% collagen/20% elastin (4C1E), 50% collagen/50% elastin (1C1E), and 20% collagen/80% elastin (1C4E)]. Label-free quantitative analysis showed that changes in protein expression were most pronounced at 0 h in HDFs cultured in the 4C1E condition. The proteins upregulated under the 4C1E condition were associated with activation of calcium ion channels in early culture and with collagen fibrils and ECM organization after 72 h. In conclusion, we identified a mechanism by which changes in the skin environment induce calcium ion channel activity in fibroblasts to form collagen fibrils and to stimulate ECM organization, which in turn causes fibrosis. Our findings can be used to support the development therapeutic reagents of skin diseases.

A. Molecular interactions With Proteins

A-018 Serum Proteomic Profiling Reveals Differential Protein Expression Linked to Survival Outcomes in Pancreatic Cancer Post-Surgery

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Pancreatic cancer remains one of the most lethal malignancies, with a dismal 5-year survival rate. Despite advancements in surgical techniques and adjuvant therapies, the prognosis for pancreatic cancer patients continues to be poor, primarily due to late diagnosis and high recurrence rates. This study aims to identify potential biomarkers that could predict survival outcomes in pancreatic cancer patients post-surgery. Specifically, we performed a comparative proteomic analysis on serum samples from two cohorts of pancreatic cancer patients: those who succumbed within one year post-surgery (bad group) and those who survived beyond one year (good group). The objective is to discover biomarkers in blood proteins at the time of diagnosis that can predict treatment outcomes.

In this study, serum samples from both groups underwent depletion of high-abundance proteins using High-Performance Liquid Chromatography (HPLC). Subsequent protein extraction was carried out using a lysis buffer containing SDS, followed by peptide generation through the S-Trap method. Peptides were purified using Solid Phase Extraction (SPE), and analyzed via Liquid Chromatography-Mass Spectrometry (LC-MS) on a Q Exactive HF-X Hybrid Quadrupole-Orbitrap Mass Spectrometer. Data processing and protein identification were conducted using Proteome Discoverer (PD 2.4), with statistical analysis performed using Perseus software. Additionally, gene ontology analysis was conducted to further interpret the data.

Results indicated several proteins with significant differential expression between the good and bad groups. Specifically, proteins associated with immune response, cell adhesion, and metabolic processes exhibited notable variations. These findings suggest that certain serum proteins could serve as potential biomarkers for predicting post-surgical survival in pancreatic cancer patients. The identification of these proteins paves the way for further research into their roles in tumor progression and patient prognosis, potentially leading to improved therapeutic strategies and patient management.

Keywords: Pancreatic cancer, Proteomic Analysis, Biomarkers, Mass spectrometry

A-019 Homoisoflavonoid Derivatives Inhibit Osteoclast Differentiation via Specific Receptor-Mediated Signaling Pathway

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Introduction
Several flavonoids have been known to exert anti-osteoporosis activity. However, the structure-activity relationship and the mechanism of anti-osteoporosis activity of flavonoids remain unknown.
Material and Methods
In this study, a series of novel homoisoflavonoid (HIF) derivatives were prepared based on previously published procedures, and their inhibitory effects on osteoclastogenesis using TRAP activity in vitro assay were evaluated. This was followed by a preliminary structure-activity relationship analysis. The chosen lead compound was then subjected to further in vitro assays namely immunofluorescence staining, bone resorption assay, qPCR, and western blot. The compound was also tested in vivo through an ovariectomized osteoporotic mouse model. Virtual screening by protein-protein interaction (PPI) network analysis and molecular docking was then performed to elucidate candidate osteoporosis-related targets of the HIF derivatives.
Results
Of the 25 HIF derivatives synthesized, the selected lead compound with the highest inhibitory activity against osteoclastogenesis had an IC50 value of 2.387 μM based on TRAP staining assay without interfering with osteogenesis. The compound was also able to block the formation of RANKL-induced F-actin belts and the resorption activity of mature osteoclasts. Moreover, gene and protein expression of osteoclast-specific markers such as nfatc1, c-fos, and cathepsin k were reduced upon lead compound treatment. Meanwhile, micro-CT scan results of OVX mice femur depicted bone loss (measured by bone volume, trabecular bone mineral density, etc.) was prevented upon small molecule administration. Docking results supported by biological mechanism of action investigation analysis of the lead compound suggested that it likely directly binds to the fibroblast growth factor receptor 1 (FGFR1). Consequently, the activation of ERK1/2 and IκBα/NF-κB signaling pathways was decreased, which in turn blocked osteoclastogenesis in vitro and osteoclastic bone loss in vivo.
Conclusions
Our study shows that HIF derivatives can serve as novel putative candidates for treating osteoporosis via inhibition of potential target, FGFR1. Further confirmation through proteomic studies of the direct interaction between the lead compound and FGFR1 is needed.

A. Molecular interactions With Proteins

A-020 Clonal architecture, 3D tumor growth, transcriptional states, proteomic states and in-vitro drug response in glioblastoma

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Glioblastoma (GBM) is one of the deadliest types of cancer with median overall survival of little more than a year. It is the prototypic example of a molecularly diverse tumor associated with multiple subclones and high transcriptional plasticity. We here set out to map the clonal architecture and link it with growth patterns, transcriptional states and drug response in-vitro. Seventy-eight multiregional samples from 24 GBM patients (F/M ratio = 0.60, median age= 65.5ys) were profiled using deep whole-exome sequencing with a nominal coverage of >300x. Clonal complexity was assessed by the Euclidean distance based on somatic mutations between regions. Molecular distance was integrated with 3D neuronavigation-based physical distances and patient survival. Fresh tumor slices of 8 patients were cultured in minimal essential media and treated with 4.2Gy plus 200µM temozolomide for 48h. Spatial Transcriptomics wasperformed on matched tumor slices with /without treatment. Integrative characterization revealed two evolutionary trajectories termed expansive and stochastic diversification based on the correlation between physical and molecular distance (RE=0.6, RS=-0.2). High molecular distance was associated with reduced PFS (R=-0.5538, p=0.026). Tumors with expansive evolution demonstrated volume-based growth that directly correlated with increased molecular diversification, whilestochastic models showed irregular and discordant patterns. Patients with stochastic evolution were characterized by unfavorable prognosis (p=0.35) and tumors appeared more frequently in the frontal lobe. In-vitro drug response varied considerably between patients based on cell proliferation (minus 0.5-13.8%), apoptosis (30.1-44.4%), and viability (minus 7.8-34.1%). Under treatment an increase of mesenchymal states with peculiar redistribution of transcriptional, proteomic patterns and increased clonal complexity was observed. In sum, we report on an ongoing study in glioblastoma that seeks to link the clonal architecture with tumor growth, transcriptional patterns and in-vitro drug response. Our study will provide new insights into the clinical relevance of the clonal composition of this deadly cancer.

A-021 Proteomic molecular difference between bladder and upper tract urothelial carcinomas and its impacts in treatment response

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Bladder Urothelial Carcinoma (BLCA) and Upper Tract Urothelial Cancer (UTUC) have been speculated to derive from similar cellular origins. However, recent studies have highlighted both molecular properties and therapeutic response were significantly different between the two entities. Therefore, we aim to further dissect and identify molecular diversity as well as clinical utility between two diseases in East Asian urothelial cancer patients. 175 BLCA and 56 UTUC patients were enrolled from the K-master consortium and subjected to NGS panels to detect major genomic aberrations. Interestingly, ERBB2 and ERCC2 mutations were significantly enriched in BLCA, while a mutation in BRIP1 was prominent in UTUC. Pathway analysis further discovered that the RTK pathway is highly activated in BLCA while RAS was predominant in UTUC. BLCA was distinguished by increased proliferation kinetics, whereas UTUC was distinguished by enhanced invasiveness and migratory capabilities. Furthermore, pharmacogenomic analysis revealed that TP53 mutations were significantly enriched in non-responders, while mutations in FGFR3 and KRAS were highly observed in responders. Immune checkpoint blockades demonstrated that BLCA patients exhibited relatively favorable response compared to UTUC patients and MTOR mutations were highly selective in the responder group. Our results collectively suggest the significance of molecular profiling in guiding personalized treatment approach in urothelial carcinoma patients.

A-022 The role of Vinblastine as a Promisisng Drug for Osteoporosis Treatment

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Osteoporosis is a bone metabolic disorder caused by dysregulation of bone metabolism or homeostasis, which increases the risk of bone fractures and poses a major burden on human health worldwide. Vinblastine, an alkaloid derived from Catharanthus roseus, is known for its anticancer properties, primarily through disrupting microtubule formation and inhibiting cell division in previous reports. This study explores vinblastine's effects on osteoclastogenesis and bone resorption. Osteoclasts are crucial cells responsible for bone resorption, when activated, they proliferate rapidly and degrade bone tissue. Our TRAP staining results suggested that at above 5 nM vinblastine completely inhibits osteoclastogenesis. This study also explores vinblastine's effects on osteoclastogenesis and bone resorption. F-actin belt formation assays were used to assess osteoclast function, while Western blot and qPCR analyzed the expression of osteoclast-associated proteins and genes. Our results indicate that vinblastine inhibits osteoclast differentiation and activity, suggesting its potential in managing bone disorders like osteoporosis. In our further study, we will be focus to identifying vinblastine-target protein through proteomic analysis.

A. Molecular interactions With Proteins

A-023 Identification and Evaluation of PMSA-D-11: A Potent Inhibitor of Osteoclastogenesis

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This study aimed to identify potent inhibitor of osteoclast formation, focusing on a series of synthesized PMSA derivatives. Our results showed that PMSA derivative 11 exhibited the most promising bioactivity, with an IC50 value of 322.9 nM, which was ~ 15-fold better than PMSA-3-Ac in suppressing osteoclastogenesis in vitro. Additionally, PMSA-D-11 blocked the formation of F-action belts and bone resorption in a concentration-dependent manner. Mechanistically, PMSA-D-11 decreased the expression of genes required for osteoclastogenesis by blocking NFATc1 translocation from the cytoplasm to nucleus. Furthermore, PMSA-D-11 demonstrated a therapeutic inhibitory effect on the differentiation of human iPSC-derived primary osteoclasts. In vivo investigation showed that PMSA-D-11 prevented excessive osteoclastogenesis-mediated bone loss in ovariectomized osteoporosis mimic mice. These findings highlighted the therapeutic potential of PMSA-D-11 as a lead compound for anti-osteoporosis by targeting NFATc1 translocation. Our findings suggested that the therapeutic potential of PMSA-D-11 as a hit compound for anti-osteoporosis treatment by targeting NFATc1 translocation. Future research will focus on identifying the target proteins of PMSA-D-11 through proteomic analysis, further elucidating its mechanism of action and enhancing its therapeutic efficacy.

A-024 Analysis of serum exosome proteome in pancreatic cancer patients identified distinct biomarkers based on the operation and recurrence.

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Early detection and prediction of recurrence are crucial for improving pancreatic cancer prognosis. This study aimed to identify protein biomarkers from patient serum for early diagnosis and recurrence prediction of pancreatic cancer. Exosomes were isolated from pre- and post-operative serum of pancreatic cancer patients. Proteins were extracted from the exosomes and analyzed using a mass spectrometer. Various statistical analyses were performed based on pre- and post-operative status and recurrence. We identified 91 proteins with significant differences between pre- and post-operative samples, and a model using only 2 of these proteins achieved an AUC of 0.999. From the pre-operative serum, 56 proteins with differential expression according to recurrence were identified, and a model using only 2 proteins again achieved an AUC of 1. In the post-operative setting, 21 proteins were differentially expressed according to recurrence, and a model using 8 proteins achieved an AUC of 0.99. Our study demonstrates the potential of serum protein biomarkers for early diagnosis and recurrence prediction of pancreatic cancer. Further validation is needed, but these biomarkers could contribute to improved clinical outcomes for pancreatic cancer patients.eywords: Pancreatic cancer, Recurrence prediction, Biomarkers, Exosomes, Mass spectrometry

A-025 Development of metaproteomics analysis methods for patient fecal samples.

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Inflammatory bowel disease (IBD), including Crohn's disease and ulcerative colitis, is a growing health concern. However, the precise cause of IBD and its relationship with the gut microbiome remain poorly understood. This study aimed to establish a metaproteomics analysis platform using patient fecal samples to investigate IBD. Microbiomes were isolated from 1g of patient stool by centrifugation. Two lysis methods were used: a conventional lysis solution (5% SDS in 50mM TEAB) and a lysis solution supplemented with urea. The resulting lysates were analyzed using LC-MS/MS. Additionally, human proteome analysis was performed on the pellet fraction, which was expected to contain patient's intestinal epithelial cells. The conventional lysis method identified 4823 proteins, while the urea-supplemented lysis method identified 5086 proteins. Human proteome analysis identified 340 proteins. We successfully established a metaproteomics analysis platform using only 1g of patient stool and constructed a monitoring platform that simultaneously analyzes the metaproteome and human proteome. This dual-information approach could potentially be used to identify markers for monitoring patient treatment outcomes. This study demonstrates the feasibility of using a metaproteomics analysis platform to study IBD. Further research is needed to explore their potential applications in clinical settings.

Keywords: Inflammatory bowel disease (IBD), Metaproteomics, Fecal sample, Biomarker, Monitoring platform

A. Molecular interactions With Proteins

A-026 Umbelliferone Potentially Inhibits Osteoclast Differentiation by Disrupting RANKL-Activated NF-κB Signaling Pathway

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Osteoporosis is a skeletal disease caused by excessive osteoclastic activity, characterized by bone loss. Among 89 compounds from an in-house chemical library, umbelliferone was chosen as the lead chemical inhibiting RANKL-induced osteoclastogenesis. It is already known that umbelliferone shows anti-inflammatory effects by attenuating the nuclear translocation of NF-κB pathway and osteoclast-specific genes. However, direct evidence of umbelliferone on osteoclastogenesis molecular mechanisms remains unknown. We investigated the expression of key proteins and genes related to osteoclast differentiation through umbelliferone treatments during in vitro osteoclastogenesis. Our results indicate that it regulates the NF-κB signaling pathway, thereby inhibiting osteoclast differentiation. However, it is not clear whether this compound modulates NF-κB activity through signal transduction or expression regulation. We plan to identify specific proteins regulated by umbelliferone and study their characteristics through future proteomic analysis studies. Overall, these results suggest that if the target proteins of umbelliferone are identified, they could be potential candidates for osteoporosis therapeutic agents.

A-027 Single-cell analysis reveals pan-cancer immune cell characteristics associated with response to immune checkpoint blockade therapy

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Immune checkpoint blockade (ICB) therapy has shown clinical efficacy in several cancer types. However, its effectiveness is limited to specific cancer types, with variable responses or resistance observed in others due to the heterogeneity of each tumor. Consequently, single-cell analysis is currently being actively pursued to analyze the tumor microenvironment (TME) of patients undergoing ICB therapy, although it is often limited to a single cancer type. We processed an integrated analysis of single-cell RNA sequencing data from eight cohorts, involving 66 patients who received ICB therapy. We characterized the cell population of TME in ICB patients and observed cell proportions based on treatment response to ICB. Overall exhausted T cells were abundant in the responder. We also found significantly upregulated gene expression in Tex cells of non-responders, particularly suggesting a potential role of Tex cells in immunotherapy resistance. We further processed analyses of immune cell types beyond T cells, including B cells and myeloid cells, to explore factors associated with responsiveness to ICB therapy. Our results demonstrate new treatment options for patients who resistance to ICB therapy Also, provide insights into ICB therapy response in Pan-cancer levels.

A-028 Piezo1-Mediated Enhancement of Collagen Synthesis by Poly-L-Lactic Acid in Aging Models

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Aging is often associated with loss of skin elasticity and the development of wrinkles, which is primarily due to decreased collagen synthesis. In recent years, poly-L-lactic acid (PLLA) fillers have emerged as a promising intervention for skin rejuvenation due to their ability to stimulate collagen production. We investigate the role of Piezo1, a mechanosensitive ion channel, in mediating the effects of PLLA filler on collagen synthesis in H2O2-induced fibroblast aging model and aged animal skin. In cells, PLLA treatment increased intracellular Ca2+ levels, which was attenuated by the Piezo1 inhibitor GsMTx4. In addition, PLLA treatment in cells and animals increased phosphorylated ERK and AKT and contributed to fibroblast cell proliferation by upregulating cell cycle regulatory proteins. Treatment with PLLA not only increased phosphorylated mTOR/S6K1/4EBP1, but also promoted the expression of TGF-b and collagen. Our findings confirm the interplay between Piezo1 signaling and collagen synthesis and suggest the involvement of Piezo1 in PLLA-induced collagen synthesis.

A. Molecular interactions With Proteins

A-029 High-Intensity Focused Ultrasound Enhances Adipogenesis in Swine Face Various Fat

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High-Intensity Focused Ultrasound (HIFU) is a non-invasive therapeutic technique increasingly explored for aesthetic applications, including skin tightening and body contouring. This study investigates the impact of HIFU on the thickness of facial subcutaneous adipose tissue in swine, a model organism with anatomical and physiological similarities to humans, to determine its potential for facial fat augmentation.
The study evaluated HIFU's effects on the right side of the swine's face, using the left side as a control. The expression CD166, an ASC marker, was measured in different facial regions: zygomatic arch fat (ZAF), and lateral temporal fat (LTF).
HIFU treatment increased HSP70 expression and decreased NF-kB expression, especially in the ZAF. CD166 expression was highest in the ZAF compared to LTF. Additionally, HIFU notably increased the expressions of PPARγ and C/EBPα, which regulate adipogenesis, in the ZAF. Ultrasound measurements showed significant increases in both the thickness and volume of facial adipose tissue in the ZAF following HIFU treatment.
These changes were accompanied by alterations in cilia disassembly, cilia length, and the expression of adipogenesis markers. These results suggest that HIFU could be used to enhance facial volume by modulating adipogenesis.

A-030 The Effective Method to Capture Endogenous Direct Binding Between Metabolite and Protein

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Interactions between metabolites and proteins(MPIs) play a crucial role in regulating protein function and various cellular processes. Although metabolites comprise the largest portion of molecules in cells, understanding metabolite-protein interactions lags behind protein-protein interactions, necessitating active research in this area. Herein, we present a methodology for chemically investigating the interactions between proteins and metabolites through covalent bonding. In this method, we focused on metabolites with a chemically reactive aldehyde group and an enrichable phosphate group. We chose pyridoxal phosphate (PLP) as a representative metabolite. We employ NaBH4 to reduce the Schiff base form of lysine and PLP, making the interaction irreversible. This fixing of interactions in situ enables analysis through mass spectrometry. To further develop this method, alkaline phosphatase was used to remove the phosphate group, allowing the PLP modification site to be identified more accurately. Finally, we were able to capture endogenous interactions between metabolite and protein. Further, We expect that we will be able to apply our approach to cells and identify unknown interactome.

A-031 High-multiplex proximity labeling platform for spatiotemporal mapping of suborganellar proteomes

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We report a high-multiplex proximity labeling platform for accurate quantification of spatiotemporally altered proteomes in suborganelle space. Utilizing four versions of stable isotope-coded desthiobiotin-phenol (DBP-4plex) probes, our method enriches biotinylated peptides rather than proteins, enabling direct identification and quantification of labeled peptides via mass spectrometry (MS). This approach allows multiplexing capacity to extend up to 10-plex when combined with the SILAC technique, facilitating detailed mapping of mitochondrial sub-organellar proteomic architecture. Our DBP-4plex platform demonstrated robust chromatographic and quantitative features. Comparative analyses with label-free quantification (LFQ) confirmed superior performance. Additionally, DBP-SILAC-10plex profiling under mtDNA damage conditions identified over 300 protein groups. This new MS1-level quantification platform enables high-throughput, accurate analysis in proximity labeling studies, advancing our understanding of sub-organelle proteomics.

A. Molecular interactions With Proteins

A-032 Robust Profiling of RNA-Binding Regions Enabled by Formaldehyde Crosslinking coupled RNA Interactome Capture at peptide-Level

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RNA-protein interactions are crucial for regulating various biological processes. UV crosslinking (UVX) is commonly employed to study these interactions, but it suffers from limitations such as low crosslinking efficiency, restricted base coverage, and shallow penetration depth, which make it difficult to produce comprehensive RNA-binding region profiles. To address these challenges, we propose using formaldehyde crosslinking (FAX) coupled with RNA interactome capture (RIC) at the peptide-level, referred to as pepFAX-RIC, for efficient and robust profiling of RNA-binding regions. Based on the FAX-RIC method, samples are treated with formaldehyde to form covalent bonds between RNA and proteins, capturing their interactions. After trypsin digestion and RNA-specific enrichment, bound peptides are separated by applying heat, and their identification by LC-MS/MS analysis allows mapping of RNA-binding regions. By employing the pepFAX-RIC method, we identified 1015 proteins and approximately 3100 RNA-binding regions in the HeLa cell line, with 95% previously reported as RNA-binding proteins and enrichment in well-characterized domains such as RRM, KH, and DEAD. Notably, the pepFAX-RIC method revealed exclusive RNA-binding domains that were not detected by UVX-based methods. These findings can be integrated with other datasets to generate a more comprehensive and detailed RNA-binding map. This approach provides substantial insights into RNA-protein interactions and their dynamic binding regions.

A-033 Super-resolution cell surfaceome profiling by proximity labeling

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Cell surface proteins play a crucial role in maintaining cellular function and structure. Our research enhances the understanding of ectodomain protein topology through a peroxidase-mediated tyrosine labeling approach. Employing this technique, peroxidase can be attached to the cell surface, and DesthioBiotinPhenol (DBP) can label the exposed tyrosine residues of surface proteins. This method significantly improves labeling efficiency and accuracy, offering a more precise delineation of protein topology on the cell surface. In the cellular context, we use a fusion protein, Lectin-HRP, combining Lectin and HRP to target glycan on the cell surface, facilitating proteome studies. In mice, we developed a cre-dependent model to express HRP-TM, designed to expose HRP to the cell surface ectodomain, allowing for enzyme expression in specific cell groups. This enables the analysis of the proteome in targeted cell lines.

B. Artificial Intelligence for Proteomics and Biomarker Discovery

B-001 Biomarker Discovery in Humidifier Disinfectant Using Integration of Multiomics, Network-Based Analysis, and Artificial Intelligence

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Introduction:
First reported in South Korea in 2011, the humidifier disinfectant case was a national environmental health disaster affecting approximately 950,000 individuals and resulting in nearly 20,000 deaths. Its effects are still being felt today. Previous research has demonstrated that toxic chemicals in disinfectants, such as polyhexamethylene guanidine (PHMG), can cause fatal lung damage and lead to a condition known as humidifier disinfectant-related lung injury (HDLI). Subsequent studies have indicated an increased risk of developing respiratory diseases such as chronic obstructive pulmonary disease (COPD) and asthma, yet the specific link between these diseases and humidifier disinfectants remains elusive. Particularly, paediatric patients exhibit different mechanisms of lung injury compared to adults, and research on factors related to lung function in this demographic is scarce. Our study aims to identify factors associated with lung injury through network analysis using multiomics data from paediatric patients and to discover biomarkers for potential respiratory diseases using artificial intelligence.
Methods:
We analyzed multiomics data (transcriptome, proteome, metabolome, methylome) from patients categorized into five groups based on pulmonary function test (PFT) results. We employed network analysis techniques, such as non-negative matrix factorization (NMF) and multi-omics factor analysis (MOFA), and algorithms like random walk with tensors (RWRT) to identify significant factors. Additionally, machine learning analyses were used to pinpoint biomarkers associated with respiratory diseases based on patient data.
Results:
Comparative analysis of the first and last lulmonary function measurements highlighted key factors linked to impaired lung function in children and adolescents. Utilizing these factors, we constructed a protein-gene network, incorporating previously validated respiratory disease markers as seeds. Anaysis of this network with algorithms such as RWRT helped identify promising candidate markers. To validate these candidates, further machine learning-based analyses were conducted.
Conclusion:
Our research provides crucial insights into the pulmonary function abnormalities observed in paediatric patients exposed to humidifier disinfectant. By integrating advanced techniques such as multiomics, network analysis, and machine learning, we offer a novel approach to understanding the impact of humidifier disinfectants. Our findings could enhance further analysis of this issue, supplemented by traditional pulmonary function tests, potentially leading to new, group-specific medical interventions.

B-002 Deep Learning Approach for Biomarker and Tumor Stage Prediction Using Multi-Omics Data in Korean Lung Cancer Patients

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The integration of multi-omics data offers a promising avenue for enhancing the precision of biomarker identification and tumor stage prediction. However, accumulation of extensive datasets because of the decrease of the production cost and time for multi-omics data and the lack of standardized analytical methods poses significant challenges for effective data integration and analysis. In this study, we present a novel deep learning framework tailored to the Korean lung cancer population, leveraging genomics, transcriptomics, and proteomics data. Our approach utilizes a convolutional neural network (CNN) architecture, coupled with a multi-omics integration strategy, to analyze comprehensive datasets from 231 Korean lung cancer patients. Key biomarkers were identified through feature importance analysis, and their roles in tumor stage prediction were evaluated. Preliminary results indicate that our deep learning model achieves higher accuracy in predicting tumor stages and identifying potential biomarkers compared to traditional statistical methods. The integration of multi-omics data significantly enhances model performance, underscoring the importance of a holistic data approach in cancer prognosis. This study highlights the potential of deep learning in transforming lung cancer diagnostics and personalized treatment strategies. Future work will focus on expanding the dataset to include diverse populations and refining the model to incorporate clinical data for even greater predictive power.

B. Artificial Intelligence for Proteomics and Biomarker Discovery

B-003 Enhancing Exosome Research with AI: Development of a ChatGPT-Based Data Curator and Analysis Copilot

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Exosome research is pivotal for advancing our understanding of cellular communication and the mechanisms underlying various diseases. Despite its importance, the field faces significant obstacles due to the complexity and sheer volume of data involved. In response, our study introduces an advanced ChatGPT-based exosome data curator and copilot. Utilizing cutting-edge prompt engineering techniques, our tool automates the extraction and organization of data from scientific literature and provides insights in response to users' queries. The development of our system was guided by a thorough analysis of user requirements, leading to the identification and selection of essential data in our model processes. **This includes the extraction of protein-related information from exosomes, which is crucial for proteomics and biomarker discovery within the realm of exosome research.** By applying precisely engineered prompts, our exosome data curator successfully processed data from over 1,000 exosome-related publications, streamlining the extraction and organization of information, **including detailed protein analyses**, to meet the rigorous demands of exosome research. Utilizing these structured datasets, we developed a copilot adept at delivering precise and pertinent insights in response to exosome research inquiries. Significantly, the copilot offers comprehensive assistance across various aspects of exosome research, including the identification of exosome types and origins, optimization of isolation and separation methods, and analysis techniques. It also provides a detailed analysis of the proteins involved, further enhancing the understanding and study of exosomes. Through extensive testing, the copilot has demonstrated exceptional proficiency in parsing, extracting, and summarizing intricate datasets, establishing itself as an indispensable tool for exosome researchers. Our ChatGPT-based curator and copilot facilitates accelerated advancements in exosome research and has the potential to benefit various scientific fields. Our initiative, rooted in a deep understanding of user needs and a rigorous data selection process, contributes a vital resource for exploring complex disease mechanisms and advancing the development of diagnostic and therapeutic biomarkers in exosome research.

B-004 Multi-proteomic analyses of 5xFAD mice reveal new molecular signatures of early-stage Alzheimer's disease

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An early diagnosis of Alzheimer's disease (AD) is crucial as treatment efficacy is limited to the early stages. However, the current diagnostic methods are limited to mid or later stages of disease owing to the limitations of clinical examinations. Therefore, this study aimed to identify molecular signatures including blood plasma extracellular vesicle (EV) biomarker proteins associated with AD to aid early-stage diagnosis. The hippocampus, cortex, and blood plasma EVs of 3- and 6-month-old 5xFAD mice were analyzed using quantitative proteomics. Subsequent bioinformatics and biochemical analyses were performed to compare the molecular signatures between wild type and 5xFAD mice. There was a unique signature of significantly altered proteins in the hippocampal and cortical proteomes of 3- and 6-month-old mice. The plasma EV proteomes exhibited distinct informatic features compared with the other proteomes. Twelve potential biomarkers for the detection of early-stage AD were identified and validated using plasma EVs from stage-divided patients. Finally, ITGA2B, CKM, FLNC, TGM2, and MAN2B1 were selected as distinguishing biomarkers for healthy individuals and early-stage AD patients using machine learning modeling with approximately 79% accuracy. Our study identified novel early-stage molecular signatures associated with the progression of AD, thereby providing novel insights into its pathogenesis.

B-005 Novel Diagnostic Biomarkers for prostate cancer discovered using a mass spectrometry-based pipeline

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Prostate cancer (PCa) has become one of the leading male cancers in worldwide. Notably, the incidence and mortality rates of prostate cancer is rapidly rising in Asia including South Korea. The occurrence of PCa is influenced by a combination of various factors including lifestyle, environment, and genetics, among which aging is considered the most important risk factor. PCa can often be detected by testing the levels of Prostate-Specific Antigen (PSA) in blood. However, the levels of PSA is also rise in cases of benign prostatic hyperplasia and prostatitis, which means there are considerable limitations to diagnosing cancer solely through PSA tests. In this study, we used liquid chromatography data-independent acquisition tandem-mass spectrometry (LC-DIA-MS/MS) to analyze the human serum of 50 healthy controls (HCs), 42 individuals with benign conditions, and 90 patients with PCa, aiming to discover potential biomarkers for the diagnosis of PCa. In the total sample set, an average of 743 proteins per sample, total 1,344 proteins, were identified. In which, 24 was differentially expressed proteins (DEPs) in PCa patients compared to healthy individuals and those with benign conditions. In addition, bioinformatic analysis on public data of prostate cancer-associated biomarkers and prognosis before and after treatment, a list of 50 proteins was created. Takes together, a total of 74 serum proteins were selected as potential prostate cancer biomarker candidates. We applied a multiple reaction monitoring (MRM)-based targeted proteomic method to verify their usability as markers for PCa diagnosis. Based on peak intensity and retention time, we confirmed the detection on endogenous level of each peptide in serum.
keyword: prostate cancer, serum biomarker, proteomics, mass spectrometry, multiple reaction monitoring

B. Artificial Intelligence for Proteomics and Biomarker Discovery

B-006 Proteo-metabolomic study suggests a unique hazardous mechanism for formaldehyde-induced liver injury in rats via ferroptosis

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Known to be a toxicant, formaldehyde finds widespread application in a variety of industries, including the textile, agricultural, and biomedical sectors. Even though the hepatotoxic mechanism was the subject of numerous earlier investigations, its toxic mechanism is still unknown. Therefore, it is indispensable to study the biomarkers that have been affected by FA exposure for the therapeutic intervention of FA toxicity. Thus, this study hypothesized to explore the hepatotoxic mechanism of FA using an integrative analysis of the proteome and metabolome in rat models. It has been shown that it is composed of 84 significant differentially expressed proteins and 66 significant differentially expressed metabolites that contain both up- and down-regulated. Three clusters derived from xMWAS underwent reactome analysis, revealing ferroptosis as a pivotal pathway in FA-induced liver toxicity. STAT3/HO-1 emerged as major protein biomarkers driving liver toxicity, ultimately leading to ferroptosis through the accumulation of lipid peroxides via free iron ion efflux. Validation of ferroptosis was achieved through qPCR analysis, highlighting highly correlated genes such as complement genes and coagulation-related genes. In conclusion, this study shows a new complement and coagulation pathway-related hepatotoxic mechanism of FA. These results may represent a major advancement in the creation of treatment strategies to address FA toxicity.

B-007 Serum proteomic multi-marker model for discriminating obsessive compulsive disorder using multiple reaction monitoring-mass spectrometry

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Obsessive compulsive disorder (OCD) is a neuropsychiatric condition characterized by recurring unwanted thoughts and repetitive actions. Currently, the diagnosis of OCD relies on clinical interviews conducted by experts, which may not always yield objective results. Investigating potential protein biomarkers for OCD in blood, which contains numerous biomarkers reflecting changes in the body, may contribute to diagnosing OCD in a less subjective manner. In this study, potential serum protein biomarker candidates for OCD were analyzed using multiple reaction monitoring-mass spectrometry (MRM-MS), and a serum protein multi-marker model was developed to distinguish OCD patients from normal (NL) subjects.

A total of 205 serum samples were collected, comprising 109 from OCD patients and 96 from NL subjects. MRM-MS analysis was conducted on non-depleted serum samples to quantify 490 targets using stable isotope-labeled standard (SIS) peptides. Peak areas of transitions were calculated using Skyline. Machine learning-based algorithms were applied to the training set to develop a model combining multiple biomarker candidates for OCD. The discriminative performance of the model was assessed using the receiver operating characteristic curve (ROC).

Our lab-developed biomarker candidates were screened to assess their detectability in pooled serum samples from randomly selected 50 OCD patients and 50 NL subjects. Signals of targets were confirmed using stable isotope-labeled standard (SIS) peptides corresponding to each target. A total of 490 targets were selected as detectable biomarker candidates, showing intensities higher than 100 and co-eluting peaks with those of SIS peptides. A single scheduled MRM method comprising 490 peptide targets was constructed and applied to 205 individual samples for the quantification of biomarker candidates. The model for discriminating OCD from NL was developed by combining multiple candidate biomarkers using machine learning-based algorithms. The performance of the model was evaluated using the area under the curve (AUC) of ROC and measures of sensitivity, specificity, and accuracy. The model could distinguish OCD from NL with improved performance compared to single candidate biomarkers.

B. Artificial Intelligence for Proteomics and Biomarker Discovery

B-008 Targeted Mass Spectrometry-Based Validation of Race- and Gender-Specific Disease Diagnostic Protein Profiling in Laboratory-Developed Tests

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Introduction
The occurrence and progression of diseases are influenced by the physiological and genetic diversity among individuals. These differences, especially across races and gender, emphasize the importance of considering race and gender specific target proteins for disease diagnosis. In this study, we developed Laboratory Developed Tests (LDTs) that incorporate racial and gender differences in protein-targeted assays for disease diagnosis.

Methods
The effectiveness of the LDTs targeting specific proteins was validated using liquid chromatography-tandem mass spectrometry (LC-MS/MS). Blood samples were collected from diverse races including African American, Caucasian, and Hispanic individuals. Eighty-seven protein targets were selected from the list of LDTs, commonly utilized in clinical diagnostics targets, along with 93 representative peptides. The goal was to validate target proteins and assess the differences in protein expression among the various racial groups, considering gender differences.

Results
Blood samples from individuals of various races were analyzed to determine the expression levels of target proteins and identify significant differences among races and gender. Analysis of target protein expression levels in blood samples from individuals of diverse races revealed 28 proteins exhibiting significant differences based on race and gender. These differences were statistically significant, with P-values of 0.05 or less, and fold changes either greater than 1.5 or less than 0.66. To validity the SRM-MS (Selected Reaction Monitoring-Mass Spectrometry) assay data, correlation coefficient analyses were conducted between samples, considering race and gender. Additionally, LDA analysis was performed to evaluate trends among sample groups based on gender and race, confirming distinct characteristics shared within each group and significant differences from samples in other groups. Method validation confirmed the significance of the analysis for the target proteins. The robustness of the analysis and the determination of potential racial and gender variability in protein expression levels were evaluated through method validation including calibration curves, stability, specificity, precision and accuracy, dilution integrity, matrix effect, and reproducibility as outlined by the US FDA, EMA, KFDA, and CLSI guidelines for each target protein.

Conclusion
Our study contributes to the understanding of racial and gender differences in the expression of disease diagnostic target proteins. By identifying disparities in protein expression among races, our study aims to establish a personalized approach to disease diagnosis that considers individual racial characteristics. This research holds promise for improving the accuracy and efficacy of disease diagnosis process.

B-009 Phosphorylation site prediction model using structural context

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Post-translational modifications are covalent proceesing events that occur after protein synthesis and change the properties of a protein. In particular, phosphorylation is essential for cellular function and signaling and therefore, their identification is crucial for understanding the protein mechanisms. While various machine learning and deep learning models have been proposed to predict phosphorylation sites, the advent of AlphaFold2, with its high-accuracy protein structure predictions, presents new opportunities. We have developed a prediction model that leverages AlphaFold2's structural prediction, enhancing sequence embeddings with structural information through a Transformer-based cross-attention mechanism.
Our phosphorylation site prediction model was benchmarked against MusiteDeep, a sequence-based predictor, using an independent test set with an equal number of positive and negative phosphosite instances (5,074 each) from proteins not included in training/validation sets. MusiteDeep achieved an area under the ROC of 0.9118, whereas our model demonstrated an improved result of 0.9417. Additionally, our model showed enhanced precision (0.8321 over MusiteDeep's 0.8042) and improved recall (0.9253 over Musitedeep's 0.9034), at the same time. We also explored kinase-specific prediction through transfer learning to assess how effectively structural information is integrated into the embeddings. The results from our transfer learning approach surpassed those from fine-tuning and DeepPhos model, a sequence-based prediction tool, across all kinase-specific datasets.

B. Artificial Intelligence for Proteomics and Biomarker Discovery

B-010 Identification of Proteomic Biomarkers in Intrahepatic Cholangiocarcinoma

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Intrahepatic cholangiocarcinoma (iCC), a rare and challenging cancer that occurs in the bile ducts, is characterized by heterogeneous molecular profiles that complicate diagnosis and treatment. Recent advancements in proteogenomic integration have identified three iCC subtypes—metabolic, stem-like, and poorly immunogenic—each associated with distinct clinical outcomes. In this study, proteomic results from tumor and paired adjacent normal tissue samples were compared to identify subtype-specific proteomic biomarkers that could enhance diagnostic precision and therapeutic strategies. Our analysis revealed distinct proteomic signatures that significantly correspond to the three subtypes, as shown in detailed heat maps and Venn diagrams illustrating subtype-specific protein expression patterns. We selected proteins showing differential expression between tumor and normal tissue in each subtype and validated these distinct proteomic profiles in serum samples from patients with iCC.

B-011 Computational Design of Peptide Inhibitor for Alzheimer's Disease Therapy

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Introduction
The polymorphism of the apolipoprotein E (APOE) gene is a major genetic determinant of late-onset Alzheimer's disease (AD). The APOE ε4 allele is associated with an increased risk, whereas the APOE ε2 allele is linked to a decreased risk, compared to the common APOE ε3 allele. Differences between APOE alleles are distinguished by cystine and arginine residues (apoE2: Cys112/Cys158; apoE3: Cys112/Arg158; apoE4: Arg112/Arg158). These sequence variations may lead to structural differences, potentially resulting in abnormal protein-protein interactions (PPIs). Such abnormalities are implicated in a variety of human diseases. Recent advances in technology have enabled the prediction of protein-protein interaction structure, interaction sites, design peptides to control diseases. Despite these technological advances, designing peptide drugs that control abnormal PPIs remains a significant challenge. In this study, we aim to design peptides that control interactions based on the structural analysis of APOE allele-specific protein complexes using artificial intelligence. Furthermore, we evaluate the designed peptides through docking simulations.

Methods
APOE allele-specific protein-protein interaction complexes were predicted by AlphaFold3-multimer, with interaction site analysis conducted using GROMACS SASA analysis. The backbone design for interaction-inhibiting peptides was achieved using Rfdiffusion, and functional group design was conducted using ProteinMPNN. The designed peptides were evaluated through docking simulations.

Results
We compared predicted structural models of protein complexes specific to APOE alleles by overlapping them to identify structural differences. The APOE E4 protein exhibited distinct folding compared to the APOE E2 and E3 proteins. We quantified differences in surface area using SASA analysis. The structural variations among APOE isoforms E2, E3, and E4 result in distinct interactomes when combined with partner proteins, leading to maladaptive interactions. We designed and synthesized peptides aimed at inhibiting these maladaptive interactions. The peptide design targeted the binding pocket regions of protein-protein interactions as scaffolds. The backbones of the peptides were designed using RFdiffusion, and the functional groups were designed using ProteinMPNN. The synthesis of the designed peptides was evaluated for sequence accuracy using LC-MS (Liquid Chromatography-Mass Spectrometry).

Conclusion
Our study confirms that structural differences in APOE E4 can lead to erroneous protein-protein interactions, potentially serving as a major risk factor for Alzheimer's disease. We propose the design of peptides capable of inhibiting these interactions, guided by artificial intelligence. Our research suggests that such efforts can contribute to the development of targeted therapies using artificial intelligence and structural proteomics.

B. Artificial Intelligence for Proteomics and Biomarker Discovery

B-012 Design of a Novel Peptide Inhibiting the Interaction Among Major Regulators of Parkinson's Disease-Associated Neuroinflammation

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Introduction
The pathological aggregation of α-synuclein (α-Syn) and neuroinflammation are closely associated with Parkinson's disease (PD). However, specific regulatory factors of neuroinflammation triggered by pathological α-synuclein remain unclear. Recent studies have revealed that "protein A/B complexsignaling pathway plays a crucial role in regulating neuroinflammation associated with PD. Pathological α-syn binds to "protein A", causing self-oligomerization and complex formation with "protein B", which leads to"protein B" ubiquitination and the activation of "protein C" and "protein D". Additionally, α-Syn is recognized as a major marker for various brain disorders, including Parkinson's disease, Lewy body dementia, and multiple system atrophy (MSA). We hypothesized that there would be structural differences in α-Syn depending on strain. This study aims to design novel peptide inhibitors that disrupt the interaction between α-Syn preformed fibrils (α-Syn PFF) and the "protein A/B complex", and to evaluate their efficacy.

Methods
The structure of α-Syn preformed fibrils (α-Syn PFF) with the "protein A/B complex" was predicted using AlphaFold23-multimer. Interaction site analysis was conducted with GROMACS SASA analysis. Peptide backbones were designed using Rfdiffusion, and functional groups designed using ProteinMPNN. The designed peptides were evaluated through docking simulations.

Results
Using contributed PDB structure information of α-Syn across different strains as templates, we predicted the structures of α-Syn PFF and the "protein A/B complex"NOD2/RIPK2 complex, discovering PD-specific structural differences. Additionally, we designed and synthesized peptides that inhibit protein-protein interaction, utilizing the binding pocket region of these interactions as a scaffold. The backbone and functional groups of the peptides were designed using RFdiffusion and ProteinMPNN, respectively. The synthesis of the designed peptides was evaluated for sequence accuracy using LC-MS (Liquid Chromatography-Mass Spectrometry).

Conclusion
The identification of the "protein A/B complex" signaling pathway as a key regulator of neuroinflammation in PD provides a new understanding of α-Syn-driven neuroinflammation and neurodegeneration. We propose a novel approach for designing peptides capable of inhibiting PD-specific protein-protein interactions based on artificial intelligence. Our research suggests that these efforts can contribute to the development of targeted therapies using artificial intelligence and structural proteomics.

B-013 Large-scale plasma proteomic profiling of the SARS-CoV-2 infected patients using aptamer- and antibody- based methods

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High-throughput proteomic profiling measuring thousands of protein markers at the same time in plasma have significantly enhanced our understanding of the relationships between diseases and phenotypic markers. While affinity-based plasma proteomic profiling has been performed in large-scale cohorts and clinical studies, it is crucial to understand detailed characteristics of available platforms. In this study, we investigated the proteomic profiles obtained from the SomaScan 7k (N = 7,596 reagents) and the Olink HT (N = 5,416 reagents) platforms using plasma samples obtained from 128 participants, including 14 healthy controls, 13 vaccinated individuals, and 101 COVID-19 infected patients. Following quantile normalization across all platforms, we compared the results of the SomaScan 7k and Olink HT platforms. Among the 2,814 common markers between the two platforms, approximately 11% showed correlations greater than 0.8, while about 50% showed correlations less than 0.2. We integrated these findings with matched scRNA-seq data not only to assess expression dynamics at both transcriptomic and proteomic levels and but also to identify proteomic reagent specificity, providing a comprehensive comparison of large-scale plasma proteomic profiling platforms. Our results offer valuable insights into the investigation of large-scale proteomic profiles using aptamer- and antibody-based methods.

B-014 Deep Learning-Based Method for Differential Analysis in Quantitative Proteomics

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In differential proteomics, the analysis of changes in protein abundance across varying physiological or pathological states is fundamental for the identification of disease biomarkers. Conventional methodologies for this analysis involve a complex sequence of steps: MS1/MS2 XIC extraction, smoothing, de-noising, quantity estimation, and cross-run normalization. often limited by heuristic algorithms and case-specific parameters.
We propose a novel approach that leverages deep learning models derived from computer vision, specifically inspired by Siamese network models used for change detection in satellite imagery. Our deep learning model is designed for the analysis of changes in MS peak maps, significantly simplifying the analytical process by bypassing conventional quantification steps. This model demonstrates improved robustness against ion noise and retention time misalignment, and naturally incorporates peak shapes and other related features.

B. Artificial Intelligence for Proteomics and Biomarker Discovery

B-015 Predictive biomarker for SSRIs treatment effect in major depressive disorders using proteomic approach

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Major depressive disorder (MDD) is the most common mood disorder that affects physical health and is diagnosed when symptoms persist for more than two weeks, including distinct mood swings and various physiological changes such as loss of mood, appetite and sleep disorders. The complex pathogenesis of MDD is still poorly understood, and the heterogeneity associated with the various subtypes may limit our understanding of the pathophysiological mechanisms of depression. Antidepressants are used as the main pharmacological strategy to treat depressive symptoms. The most commonly attempted treatment for depression is SSRI antidepressant treatment, but the predictors of SSRI treatment response and the exact pharmacological mechanism of action are still unclear. For successful treatment of depression using SSRIs, biomarkers that can predict treatment response and effectiveness will provide evidence of molecular changes to understand drug treatment mechanisms and help improve clinical treatment. Therefore, in this study, we investigated serum protein comparisons between patients receiving SSRI treatment and patients who achieved remission through SSRI treatment to identify therapeutic effect predictive biomarkers for SSRI treatment, which are preferentially used in the treatment of depression. Sex hormone-binding globulin increased in the patient group that achieved remission after SSRI treatment and showed a significant difference from the group of depressed patients receiving treatment. The protein has the potential to be a predictive indicator of the therapeutic effect of SSRI antidepressant treatment and could help improve the understanding of the molecular mechanisms of SSRI antidepressant treatment.

B-016 Proteomic changes based on various drug treatments for depression reveals association with immune system networks

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Major depressive disorder (MDD) can present a variety of clinical presentations and has high inter-individual heterogeneity. Multiple studies have suggested various subtype models related to symptoms, etiology, sex, and treatment response. Employing different regimens is common when treating MDD, and identifying effective therapeutics requires time. Frequent treatment attempts and failures can lead to a diagnosis of treatment resistance, and the heterogeneity of treatment responses among individuals makes it difficult to understand and interpret the biological mechanisms underlying MDD. Thus, knowledge of the common mechanisms and changes in biomolecules for different types of medications will help clinicians better understand the medication-induced neurobiological changes in patients with MDD. This will improve our understanding of the pathophysiological mechanisms of drug regimens for MDD. This study explored the differentially expressed proteins and commonly altered protein networks across drug treatments by comparing the serum proteomes of patients with MDD treated with drug regimens and untreated patients. Differentially expressed proteins were profiled in non-drug-treated and drug-treated patients with depression using liquid chromatography-mass spectrometry. Subsequently, common protein networks affected by different types of medications were studied. Twelve proteins were significantly differentially expressed between drug-treated and non-drug-treated patients with depression. Network analysis of these proteins revealed that networks common to various types of drug treatments for depression are related to the complement system and immunity. This study provides information on common molecular and neurobiological mechanisms of action for different types of drug treatments, which will help improve our understanding of the mechanisms of highly heterogeneous MDD.

B-017 A Nonparametric Statistical Test for Hierarchical Mass Spectrometry Data

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Mass spectrometry is used to measure the quantity of proteins by employing a mass spectrometer to break down proteins into peptides and then into fragment ions, and indirectly measure the quantity of proteins and peptides using a bottom-up approach. The data generated through this process exhibits a hierarchical structure due to the decomposition steps. When such hierarchical data is obtained under various experimental conditions, statistical analysis can be performed using mean difference tests at higher levels, such as proteins or peptides. Representative methods include paired t-tests and independent t-tests. However, these methods have limitations: they do not adequately reflect the data structure or they fail to meet the basic statistical assumptions due to small sample sizes. Therefore, this study presents the methods for calculating test statistics when applying these two conventional methods to actual hierarchical data, along with the associated problems. Subsequently, a new statistical approach is proposed to address these issues. This approach calculates test statistics using the variance-covariance matrix based on the lowest level measurements, employing shrinkage estimation methods for the variance-covariance matrix to mitigate problems arising from small sample sizes. Simulation data reflecting the characteristics of actual data is then generated under various conditions to compare the performance of the two existing methods and the newly proposed method. Finally, by applying the three statistical methods to actual mass spectrometry data, the study evaluates the performance and practical applicability of the newly proposed test method, and discusses its potential for further development and extension.

B. Artificial Intelligence for Proteomics and Biomarker Discovery

B-018 Comparative proteome analysis of sputum of pre/post treatment from asthma patients

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As a long-term inflammatory disease of the airways of the lungs, asthma is a complex and heterogenous disease with wide degree of severity. In these days, several immunoglobulin drugs such as mepolizumab or dupliumab have been applied to in asthma treatment with variable mode of actions, but there have been no deep investigation about how these biologics show its effect on patients. Here, sputum of pre-treat me and post treatment (1 month) of biologics were collected from 10 of asthma patients and quantitative proteome analysis was performed using high resolution mass spectrometry with nano-flow liquid chromatography. Totally, 1,301 proteins were identified and differentially expressed proteins (DEPs) between pre-treatment and post-treatment was 252. Principal component analysis indicated that there is quantitative and qualitative proteome change in sputum between pre and post treatment. And following gene ontology analysis showed cytoskeleton reorganization, positive regulation of immune system, chronic inflammation and negative regulation of growth of symbiont in host in post-treatment group. We hope this sputum proteome result can provide possibility of efficacy monitoring biomarker of asthma.

B-019 Serum exosome proteome analysis from obese and diabetic obese patients with bariatric surgery

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Obesity has been a global health problem, and bariatric surgery is one of the safe and helpful long-time treatments. In process of obesity, adipocytes absorb free fatty acids circulating in the blood to reduce insulin concentrations, store them in lipid droplets, and release adipocyte-induced exosomes to communicate with fatty tissue macrophages. So, the study was conducted assuming that the serum exosomes in obese patients could reflect the pathological conditions. We analyzed the serum exosome proteomes of obese (N=18) and obesity diabetics (N=12) before and after surgery. Moreover, 37 sera of normal controls were analyzed. Serum exosomes were isolated through ultracentrifugation and their proteins were digested with peptides quantified by SWATH-MS analysis. The quantified number of exosome proteins was 713. Albumin occupies only 0.25%, and the exosome proteins overlapping with Exocarta were 82%, confirming that the exosomes were well concentrated. Compared to the normal group, we found differential proteins before and after surgery in obese and obesity diabetics. They were related to immune response, leukocyte, lymphocyte, B-cell mediated immunity, complement and coagulation cascades, antioxidant activity, platelet degranulation, negative regulation of lipid catabolic process, vasoconstriction, and protease inhibitor activity

B-020 Discovery of plasma biomarker candidates for canine pancreatitis and lymphoma using SWATH LC-MS platform

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Diagnostic industry for companion canines have been one of important fields nowadays and some blood biomarkers from human disease have been adopted to canine diagnosis such as creatine kinase, serum aspartate aminotransferase (AST), C-reactive protein (CRP). But there have been still unmet needs for more precise and sensitive biomarkers which can be applied on monitoring of companion canines' health. Herein, plasma proteome from healthy canines (33 cases) and canines with pancreatitis (34 cases) or with lymphoma (18 cases) were investigated using high resolution LC-MS platform, called SWATH LC-MS. From 40ul of plasma, 701 proteins were identified and number of DEPs from lymphoma and pancreatitis was 29 and 16, respectively. And combination of two proteins (pentaxin, coagulation factor XIII B chain) showed 100% of sensitivity and 93.9% of specificity for lymphoma classification. Also, 3 protein-panel (PDE5DIP, FGC and SEPPINA3) showed 97% of sensitivity and 84.4% of specificity. Considering that previous blood markers showed low sensitivity and cost burden, this discovery of blood protein biomarkers can be applied on diagnosis. We hope these protein biomarker candidates can be applied on healthcare monitoring as well as diagnosis for companion canines. This study was supported by a cooperative research program of rural development administration (#PJ015336012021).

C. Post-Translational Modifications for Signal Transduction

C-001 Cardioprotection via Tyrosine Phosphorylation of Mitochondrial Creatine Kinase

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Heart failure due to ischemic cardiomyopathy (ICM) is considered as one of the main causes of cardiovascular disease-related deaths worldwide. Patient mortality due to ICM still remains high. Ischemic preconditioning (IPC) has been found as an effective mitigator of ICM. This is done by short-time ischemia is applied before ischemia/reperfusion injury (I/R). The brief time applied for IPC may contribute to a rapid change in protein expression and regulation wherein protein function modulation by post-translational modifications is important. Mitochondria play a significant role in heart disease progression and so, it is a good target for ICM treatment. In this study, we focused on mitochondrial creatine kinase (CKMT2) under I/R injury. Ex vivo Langendorff system on Sprague-Dawley rat hearts were used to simulate normal perfusion, I/R, and IPC conditions and used for phosphoproteomic analysis. In vitro study using human cardiomyocyte AC16 cells were used to determine the cardioprotective role of mitochondrial creatine kinase through overexpression and how CKMT2 site-directed mutagenesis can affect cardioprotection by CKMT2 protein activity, mitochondrial function, and protein expression. CKMT2 was dephosphorylated during ischemia and I/R but remained phosphorylated under IPC conditions. CKMT2 overexpression shows increased cell viability and mitochondrial ATP level against hypoxia/reoxygenation confirming the cardioprotective effect of CKMT2. Conversely, there was decreased cell viability and increased ROS production during H/R when CKMT2 is phosphomutated, specifically in Y368. We also confirmed increased mitochondrial function via the proliferator-activated receptor γ coactivator-1α/estrogen-related receptor-α pathway during CKMT2 overexpression. CKMT2 regulation and phosphorylation may be used for future ICM therapeutics.

C-002 Comprehensive lysine acylome profiling in sepsis-related hepatic injury

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Sepsis is a life-threatening organ dysfunction caused by a dysregulated host response to an infection. Despite the continuous progress in medicine, the specific mechanism of sepsis remains unclear. A key strategy of pathogens is to use post-translational modification to modulate host factors critical for infection. We employed global immunoprecipitation technology for lysine acetylation (Kac), succinylation (Ksu), and malonylation (Kmal) for the first global lysine acylation (Kacy) analysis in the cecal ligation and puncture (CLP) model in mice. This was performed to reveal the pathogenic mechanism of integrative Kacy and the changes in modification sites. In total, 2,230 sites of 1,235 Kac proteins, 1,887 sites of 433 Ksu proteins, and 499 sites of 276 Kmal proteins were quantified and normalized by their protein levels. We focused on 379 sites in 219 upregulated proteins as the integrative Kacy sites of Kac, Ksu, and Kmal decreased on the basis of sirtuins in the CLP group. KEGG pathway analysis of integrative Kacy in 219 upregulated proteins revealed three central metabolic pathways: glycolysis/gluconeogenesis, pyruvate metabolism, and the tricarboxylic acid cycle. These findings reveal the key pathogenic mechanism of integrative PTM alteration in terms of decreased sirtuin levels and provide an important foundation for an in-depth study of the biological function of Kacy in sepsis. Our findings revealed the broad aspects of Kacy substrates and supplied the systemic Kacy profiling database under pathological circumstances.

C-003 Disruption of Cell Adhesion by Alteration of Fibronectin in the Glycated Extracellular Matrix Mediated by Ribose

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Understanding the glycation of extracellular matrix (ECM) proteins is crucial for elucidating the molecular underpinnings of pathologies such as aging, diabetes, and cancer. Glycation, particularly through reactive sugars, significantly alters ECM protein integrity. However, the distinct effects of individual sugars on ECM proteins remain unclear due to ECM complexity and the prevalence of cross-sectional studies. In this study, we used a high-fidelity ECM model to investigate how glycation-mediated changes vary with specific ECM proteins and sugar molecules. Our results identified the top 14 glycated proteins, including fibronectin and type I collagen, which reacted with ribose. We observed temporal patterns of advanced glycation end-product (AGE) formation in each ECM protein. Notably, fibronectin exhibited higher AGE accumulation in arginine and lysine residues compared to type I collagen. Arginine residues in fibronectin showed AGEs like G-H, G-DH, MG-H, and MG-DH, while lysine residues had Amadori, CML, and CEL. Ribose-mediated glycation also altered all RGD sequences, cell-binding sites in fibronectin, impairing cell attachment. These alterations were absent in the glycation of type I collagen or glucose-mediated glycation of fibronectin. These findings enhance our understanding of AGE-mediated disease progression and identify potential therapeutic targets.

C. Post-Translational Modifications for Signal Transduction

C-004 Effects of high-fat diet on global protein acetylation

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It is known that obesity is often linked with protein acetylation and induces intricate changes in post-translational modification, affecting instability in mitochondrion regulations. Redox signaling is critical for maintaining cellular homeostasis. Investigating how the lysine acetylome drives redox signaling elucidates the complexity of the biological networks underlying obesity. High-fat diet-fed mice livers were lysed and immunoprecipitated with lysine-acetyl and lysine-acetoacetyl antibody-conjugated beads, then labeled with isotopic 18O for multiplexing. The twenty-cm homemade column packed with C18 resin was then connected to the Orbitrap Velos MS for tandem MS analysis. A total of 2,282 proteins and over 1,300 acetyl-lysine sites were discovered, herein, 615 sites were novelly discovered. The expressed levels of acetylome were normalized to protein expression, and one-third of acetylome was quantified. Differentially expressed acetylated proteins were annotated by GO analysis, and upregulated proteins belonged to the peroxisome pathway. The three proteins involved in redox regulation, Gstt1, Sod1, and Ephx1, were analyzed to have five-fold higher fold changes at specific sites with acetyl-lysine levels. Our data show that investigating the acetylation pathways can provide insights into the molecular mechanisms driving obesity and offer potential targets for therapeutic intervention.

C-005 Fluctuating O-GlcNAcylation Governs Distant Chromatin Interactions in V(D)J Recombination Throughout Early B Cell Development

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V(D)J recombination, crucial for generating diverse antibody genes during early B cell development, involves complex interactions between regulatory elements and protein factors. O-GlcNAcylation, a type of protein modification, affects various cellular processes, but its role in V(D)J recombination is not well understood. To investigate this, we reduced O-GlcNAcylation in mice using inhibitors or dietary restrictions. Remarkably, decreased O-GlcNAcylation severely disrupted the rearrangement of Ig heavy-chain genes. We found that O-GlcNAcylation directly modifies key factors involved in V(D)J recombination, such as YY1, SMC1, and SMC3, influencing their interactions and DNA binding at the IgH gene locus. Additionally, O-GlcNAc inhibition decreased the expression of DDX5 protein, affecting the association of CTCF with its binding sites on the IgH locus. These findings indicate that O-GlcNAcylation status affects the organization and interactions within the IgH locus, crucial for efficient V(D)J recombination. This study reveals the significance of O-GlcNAc modification in regulating stage-specific proteins during B cell development, offering insights into antibody diversity regulation.in a single page.

C-006 Mitochondrial malate dehydrogenase phosphorylation renders cardioprotection against hypoxia/reoxygenation injury

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Mitochondrial malate dehydrogenase (MDH2) regulates the conversion of malate/NAD+ to oxaloacetate/NADH. Proteomic studies show that MDH2 is involved in cardiovascular diseases wherein the expression of specific mitochondrial proteins is altered under ischemia/reperfusion conditions. Screening of phosphorylation sites of MDH2 revealed several posttranslational modifications occurring in the protein. However, it is still unclear how alterations of these sites lead to the altered activity and function of the system under pathologic models. This study focuses on the importance of MDH2 phosphorylation and how it regulates mitochondrial biogenesis and mitochondrial function. Phosphorylation occurs at various conserved sites, specifically Y56, Y80, Y161 and S246. Phosphorylation mutants based on these sites were manufactured using expression vectors and were transfected into cellular models for analysis. Phosphomutants decreased cell viability, ATP production, and MDH2 activity. Mitochondrial biogenesis marker expressions were also altered by phosphomutants under hypoxia/reoxygenation conditions. The protective mechanism of how MDH2 confers cardioprotection still remains unclear. Further studies on the role of MDH2 phosphorylation in mitochondrial biogenesis can elucidate the importance of MDH2 in cardiovascular disease models and treatment modalities.

C. Post-Translational Modifications for Signal Transduction

C-007 The proteogenomic approaches with nitration in EOGC (Early Onset Gastric Cancer) revealed nitration dependent process.

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Nitration is one of the PTMs (Post translational modification) under the condition of oxidative stress. Peroxinitrite formation is a key contributor to generate 3-nitrotyrosine with NOS, (Nitric oxide synthase) and ROS (reactive oxygen species). Once, the peroxinitrite is generated, MPO (Myeloperoxidase) catalyzes nitration with tyrosine radical to make 3-nitrotyrosine and 3-nitrosotryrosine. Several nitration studies revealed that nitroproteins have roles in inflammation, altered enzymatic activity, reduced cellular siganlling, interruption in phosphorylation pathways and protein degradation. However, there is a hurdle to study the function of nitro-proteins and understand the detailed nitro-signalling. Nitration is a rare PTM comparing to other PTMs such as phosphorylation and glycosylation, which is hard to detect the nitro-proteins even if analyzing with high resolution and high speed mass spectrometry. Fortunately, improvements in mass spectrometry and integration of numerous data from various projects expanded the proteome coverage and enabled to analysis rare PTMs such as nitration. Based on this knowledge, we deeply investigated the nitration in CPTAC (Clinical Proteomic Tumor Analysis Consortium) data which is the open community resource of various cancer. Global proteogenomics data and phosphoproteomics data in EOGC in CPTAC was re-analyzed with nitration search parameters. This revealed the nitration is highly involved in migration, inflammatory process and actin polymerization in EOGC cancer patients. Interestingly, it was not the whole patients that nitration process was activated. Rather than following the dependency of MPO expression, patients who have less MPO showed high nitration in migration and inflammatory process. From this result, we found the interplay between nitration and EOGC across NO2 production.

C-008 PTMOmics Pipeline revealing Protein Modifications through integrated Proteomics

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Post-translational modifications (PTMs) of proteins are key regulators of protein function, significantly contributing to the functional diversity of the proteome. Despite their biological significance, PTM proteomics is often challenging due to the substoichiometric abundance of PTM proteins, resulting in less information compared to global proteomics. To address this issue, we developed the PTMOmics pipeline, which integrates global proteomics with PTM proteomics. Initially, GO network analysis was performed on proteins identified through global proteome analysis. Subsequently, proteins within each GO network were listed and processed through the PTMOmics pipeline, which automatically collects PTM information from open-access protein databases such as UniProt. The pipeline then visualizes the distribution of major PTMs in a GO network and the modified sequence positions of each protein. We applied this approach to investigate PTM-associated relationships and their roles in GO networks identified through global proteomics in colon cancer studies. Global proteomics revealed changes in proteins involved in ECM-related pathways, highlighting glycosylation as a key PTM. We discovered that protein glycosylation patterns were altered in colon cancer.

C-009 Thousands of ubiquitinated proteins can be profiled from dozens of cells using UbiBoost

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Ubiquitination is the essential post-translational modification (PTM) for numerous cellular activities such as degradation of misfolded or damaged proteins. Due to the low stoichiometry of ubiquitinylated proteins, the enrichment process and multiplexing with isobaric labeling tags are necessary for deep-profiling ubiquitome changes. However, there are significant limitations in the conventional method, involving substantial inter-process variability and a significant quantity of peptides, due to the enrichment process for each channel. To address this issue, we presented highly sensitive, and accurate multiplexed strategy by adding boosting channel instead of an enrichment step per channel, termed UbiBoost. For this method, we collected large amounts of enriched ubiquitinated peptides in common cell lines as a boosting channel. Then, the boosting channels and sample channels were combined in an optimized ratio and those mixtures were subjected to analysis using highly sensitive LC-MS/MS equipment with carefully tuned parameter settings. Identification and quantification were carried out using the most suitable profiling pipeline for UbiBoost. Subsequently, post-processing analysis and bioinformatic analysis were conducted using in-house Python code. Here, our results showed that more than 1,000 ubiquitinylated proteins were quantified from less than 50ng of tryptic peptides, corresponding to dozens of cells, from HeLa lysates. In addition, those also indicated that UbiBoost produced comparable quantification results with less amounts of samples and higher accuracy, compared to the conventional methods. After evaluating the accuracy of this methods by mixing yeast peptide with samples, we also demonstrated that the feasibility of UbiBoost for highly multiplexed ubiquitin profiling in a limited amount of biologically perturbated sample. Therefore, the newly proposed method is expected to be able to quantify changes in ubiquitomes of rare samples that were infeasible in the conventional method.

D. Glycoproteomics

D-001 A machine learning model for site-classification of N-glycoprotein fucosylation using HCD mass spectrometry

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Protein glycosylation is known to be involved in biological progresses such as cell recognition, growth, differentiation, and apoptosis. Fucosylation of glycoproteins refers to the attachment of fucose residues to N-glycans, O-glycans, and glycolipids and plays an important role in the structural stability and function of glycoproteins. Here, we report on the use of tandem mass spectrometry (MS/MS) and machine learning algorithms such as deep neural networks (DNN) to classify different types of fucosylation in N-glycoproteins. The HCD MS/MS spectra of N-glycopeptides were analyzed to calculate the relative intensities of different oxonium ions, and the training set and test set of the machine learning method consisted of 433 and 393 GSMs, respectively. The best model were selected from machine learning methods sith different hyper parameters and a test set data from standard proteins of IgG and AGP, where the N-glycopeptide spectra were analyzed with IQ-GPA analysis. In this study, human plasma samples were tested to classify fucosylation pattern of the N-glycopeptides. A total of 82 N-glycopeptides, including 54 core fucosylation types, 24 external fucosylation types, and 4 double fucosylation types from 54 glycoproteins, were classified by DNN model. Specifically, external fucosylation was found to be predominant in three-antenna and four-antenna N-glycoproteins, while core fucosylation was found to be predominant in single-, double-antenna, and hybrid types of N-glycoproteins in human plasma. As a result, the DNN model was demonstrated to be able to effectively classify fucosylated N-glycopeptides from a variety of plasma glycoproteins. Thus, the machine learning methods can be combined with MS/MS to distinguish between different isoforms of fucosylated N-glycopeptides.

D-002 Glycoproteome Similarity Assessment of Biotherapeutics with N- and O-Glycosylation Sites by Sequential Intact Mass Spectrometry

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Glycosylation is a crucial attribute of biotherapeutics with significant impacts on quality, safety, and efficacy. Therefore, ensuring consistent glycosylation requires a systematic review of biotherapeutics including diverse glycan structures (micro-heterogeneity) and variable occupancy of individual sites (macro-heterogeneity), from drug design to upstream and downstream bioprocessing. Various methods have been employed for glycome characterization at different levels-glycan, glycopeptide, and intact protein. In particular, intact protein analysis is considered a facile and rapid glycoform monitoring approach used throughout the product development lifecycle to determine suitable glycosylation lead candidates and reproducible product quality. However, intact glycoproteome characterization of diverse and complex biotherapeutics with multiple N- and O-glycosylation sites can be very challenging. To address this, a robust analytical platform that enables rapid and accurate characterization of biotherapeutics with highly complex multiple glycosylation using two-step intact mass spectrometry has been developed. We used darbepoetin alfa, a second-generation EPO bearing multiple N- and O-glycosylation sites, as a model biotherapeutics to obtain integrated information on glycan heterogeneity and site occupancy through step-by-step MS of intact protein and enzyme-treated protein. In addition, we performed a comparative assessment of the heterogeneity from different products, confirming that our new method can efficiently evaluate glycosylation equivalence. This new strategy provides rapid and accurate information on the degree of glycosylation of a therapeutic glycoprotein with multiple glycosylation, which can be used to assess glycosylation similarity between batches and between biosimilar and reference during development and production.

D-003 In-Depth Glycomic and Proteomic Characterization of Cell-Based Therapeutics

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Cell-based therapeutics offer promising alternatives for treating diseases previously deemed incurable such as cancer and autoimmune diseases. However, these therapeutics can lead to side effects like carcinogenicity and immunogenicity, necessitating comprehensive characterization. Specifically, glycosylation of cell surface proteins significantly influences cellular interactions crucial for recognizing target cells in cell therapeutics. Despite their significance, membrane glycans and glycoproteins in these therapeutics are not well understood. This study unravels the glycomic landscape and proteomic profiles as novel approaches to characterizing cell therapeutics. We thoroughly analyzed the glycan compositions and structures on cell membranes across different types of cell therapeutics. Our findings show distinct glycosylation patterns: fibroblasts predominantly exhibited paucimannosylation, a simpler glycosylation type; natural killer (NK) cells were marked by bisecting glycans and neutral, highly branched glycans; induced pluripotent stem cells (iPSCs) displayed highly fucosylated and high mannose-type glycans. Interestingly, cardiomyocytes, derived from iPSCs, showed significant glycosylation alterations, with the presence of bisecting and acidic, highly branched glycans, highlighting further glycosylation modifications during cell differentiation. It was observed that changing the culture conditions with TGF-β or interleukins to enhance the cellular activity of fibroblasts and NK cells did not significantly affect the glycosylation patterns. Hierarchical analysis and principal component analysis (PCA) revealed cell-specific glycosylation mapping with distinct differences between cell lines. The proteomic analysis of cell membrane proteins has led to identify proteins with crucial functional roles and their interactions within each cell type. For instance, glycoproteins implicated in cell developmental processes, including ALT1, EPHA1, EPH4, and GPM6B, were uniquely identified in induced pluripotent stem cells (iPSCs), while glycoproteins associated with cardiac development, such as SLIT2, LTBP1, TGFB2, WNT11, and FZD1, were specifically detected in cardiomyocytes. Although the specific relationship between glycan expression patterns and cellular glycoproteins requires further investigation, these initial findings provide a foundation for future research. In conclusion, the integration of glycomics and proteomics approaches will enhance our understanding of cellular mechanisms and support the definition of specific molecular markers, ultimately improving the quality characterization of cellular therapeutics.

D. Glycoproteomics

D-004 Proteome and Glycoproteome Characterization of Gastric Cancer-Derived Extracellular Matrix

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Gastric cancer commonly occurs in Asian countries, including Republic of Korea, Japan, and China. It is one of the solid tumors that consists not only of tumor cells but also of extracellular matrix (ECM), stromal cells, and vasculatures. In particular, the ECM plays a principal role in the tumor microenvironment. The tumor ECM is stiffer and denser than normal ECM. Matrix stiffness triggers mechanotransduction in tumor cells, inducing changes in morphology, proliferation, and invasiveness. Meanwhile, many recent studies have been conducting PTM proteomic analyses along with tumor proteomics. PTMs play crucial roles in determining the structure and function of proteins. Some studies have also shown the involvement of glycoproteins in cancer progression and metastasis. In this study, we analyzed proteome and glycoproteome in the ECM of gastric cancer tumors. When unsupervised clustering was performed based on glycopeptide analysis data, ECM was divided into tumor and normal groups. In addition, glycopeptides up-regulated in tumor tissues showed increased expression of complex type with sialic acid and high mannose type. Additionally, though there was no difference in protein levels, a statistically significant increase in the expression of glycopeptides with sialic acid was observed in tumor ECM, especially for COL6A2 and BGN. This study discovered notable alterations in the glycosylation environment of gastric cancer ECM, suggesting that glycosylation characteristics in the tumor microenvironment could potentially facilitate advancements in future cancer treatments.

D-005 Utilization of tandem mass spectrometry data for predicting the enrichment of post-translational modificated peptides

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A post-translational modification (PTM) is a naturally occurring chemical modification of a protein. Many of these modifications, such as phosphorylation, are known to play pivotal roles in the regulation of protein function. PTM perturbations have been linked to diverse diseases like cancer and diabetes. Despite the significant interest in biology, PTMs are found in substoichiometric abundance and therefore require enrichment to improve their detection by mass spectrometry. Phosphorylated peptides are usually enriched using immobilized metal affinity chromatography (IMAC) or titanium dioxide. Acetylated peptides are enriched using antibodies directed against the acetylated epsilon amino group of lysine residues, K(Ac). Glycopeptides can be enriched using hydrophilic interaction chromatography (HILIC). To evaluate the efficiency of each PTM enrichment, we usually calculate the ratio of the number of PTM peptides to the total peptides resulting from peptide identification. Here, we introduce a method to rapidly predict the existence of PTM peptides without peptide identification by utilizing tandem mass spectrometry data. We selected PTM-specific fragment ions for each PTM and examined their distributions in tandem mass spectrometry, which could represent the presence of PTM peptides in samples. This method rapidly provides information on the distribution of PTMs in a proteome sample without the need for a database search.

D-006 Comparative Glycoproteomics between Human and Transgenic Porcine Erythrocytes for Enhanced Xenotransfusion Compatibility

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Recent advancements in xenotransplantation highlight the potential of using porcine red blood cells (pRBCs) as substitutes in blood transfusions. This study addresses the immunogenic challenges posed by xenoglycan antigens such as NeuGc, Sda, and terminal α-gal, which are significant contributors to immune reactions due to their presence in varying levels across and within species. These antigens are primarily associated with proteins and lipids, underscoring the importance of examining glycoprotein variations between species and in genetically modified animals lacking these antigens. Here, we explored micro- and macro-heterogeneity on various glycoproteins, including the core glycoprotein band 3, essential for anion exchange and membrane integrity maintenance in RBCs. Using red blood cells from humans, wild-type (WT), and triple knockout (TKO) porcine specimens provided by Optipharm Inc., we isolated cell membranes after lysing RBC samples to remove hemoglobin interference, followed by digestion with trypsin and Glu C. Subsequently, glycopeptides were selectively enriched using ERLIC-SPE and were analyzed with a Q Exactive orbitrap mass spectrometer. Glycopeptides containing immunogenicity-related glycans (α-gal, NeuGc, and Sda antigens) expressed in porcine were measured using glycan oxonium ions. In the human RBC band 3 protein observed at the glycopeptide level, two glycosylation sites (Asn593_NSSYFPGK, Asn642_VSNSSAR) were identified, while porcine was identified with a single site (Asn654_LSVPSGFTVSNSSAR). More than 30 glycopeptides were observed in the band 3 protein of both humans and porcine (WT). The majority of these were complex-type glycopeptides containing sialic acid. In humans, the Asn642 site showed a higher glycan occupancy rate compared to Asn593 and exhibited micro-heterogeneity. In porcine, glycopeptides containing α-gal, Sda antigens, NeuGc, and NeuAc were present, indicating a greater diversity of micro-heterogeneity compared to humans. Immunogenicity-related glycopeptides were detected in only TKO porcine. Interestingly, we found differences in glycosylation sites and glycan types despite identical protein expression. Additionally, we determined that the glycosylation pattern can vary within the same species due to genetic modifications. These results may help develope methods to minimize immune responses by understanding changes in glycosylation patterns, which could eliminate or modify immunogebeicity-related proteins and improve compatibility between porcine blood and humans.

E. Chemoproteomics for Drug Development

E-001 Chemical proteomics analysis to identify the underlying molecular mechanisms of autism spectrum disorders.

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Autism spectrum disorder (ASD) is a complex neurodevelopmental condition characterized by deficits in social communication and interaction, repetitive behaviors, and varying degrees of intellectual impairment in children. The intricate interplay between genetic predispositions and environmental influences contributes to the susceptibility of individuals to ASD. Among the environmental factors implicated in ASD pathogenesis is prenatal exposure to valproic acid (VPA), a medication commonly employed as either a monotherapy or adjunctive therapy for managing complex partial seizures. However, prenatal exposure to VPA has been associated with the manifestation of an ASD-like phenotype in offspring. Our previous research demonstrated that in-utero administration of VPA in a mouse model disrupts Wnt signaling pathways by inhibiting the activity of glycogen synthase kinase-3 beta. This inhibition results in the aberrant translocation of β-catenin into the nucleus, which regulates the transcriptional activation of downstream Wnt signaling-related genes, consequently impacting the neurodevelopmental processes associated with ASD. The present study aims to elucidate the underlying molecular mechanisms through which VPA alters molecular signaling events relevant to ASD pathogenesis. To do so, we employed multi-proteomic methodologies such as interaction proteomics using biotinylated VPA, chemical proteomics utilizing the CESTA method, target screening using a proteome microarray, and a combined global proteomic and phosphoproteomic analysis. These advanced techniques facilitate the identification of the proteins comprising the VPA interactome and elucidate the associated signaling pathways. Our research findings significantly enhance the understanding of ASD pathogenesis. We believe that integrating multilayered proteomics will aid in developing targeted therapeutic interventions for ASD in the near future.

E-002 Echinochrome A derivatives show Cardiomyocyte protection against doxorubicin toxicity

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A naphthoquinoid pigment from sea urchins, echinochrome A has been known to possess antioxidant effect against ROS-generating environment. We produced 12 echinochrome A derivatives by replacing its potentially reactive groups. In this study, we investigated the cardiomyocyte protective role of echinochrome derivatives in the presence of doxorubicin (Adriamycin, Rubex), an anticancer drug with cardiotoxicity. We found that echinochrome A derivatives protected cardiotoxicity of doxorubicin by reducing reactive oxygen species (ROS) in AC16 cells, isolated human cardiomyocytes. We also found that echinochrome A derivatives protect cardiomyocytes in high glucose condition and cobalt chloride addition which could induce endoplasmic reticulum (ER) stress. Among these derivatives, SpD (2, 3, 5, 6, 8- pentahydroxy-1, 4-naphthoquinone) showed the most significant effect by reducing ROS stress in AC16 cells. We demonstrated that SpD increased ATP ratio and oxygen consumption rate (OCR) from mitochondria. Our study might give light on protecting cardiomyocytes against cancer drugs with severe cardiotoxicity by reducing their ROS generation.

E-003 Label-free small molecule target profiling reveals novel protein target of clinical antihypertensive drug

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Target identification of small molecules is a primary step in understanding the underlying mechanism of action of the compound. The quantitative proteomics approach based on LC-MS/MS allows us to explore the unknown molecular world of the cell comprehensively and without bias. Drug TMS is the widely used FDA-approved hypertension drug, whose safety and stability have been empirically proven. CETSA (CEllular Thermal Shift Assay) is a label-free small molecule-based method for target identification by monitoring the protein-small molecule binding resulting from thermal denaturation. Here, we combined CETSA and quantitative proteomics using TMT labeled LC-MS/MS and constructed a targetome (target proteome) of the drug TMS with the evidence of its known target. Using our targetome database with open bioinformatics database such as CMAP or STRING, we successfully analyzed the target proteome at the subcellular level and identified novel target protein related to the bioactivity of the drug TMS. Furthermore, we proposed a novel mechanism of action of the drug TMS at the molecular cellular level involving such novel target proteins. In conclusion, this study demonstrated that 'targetome' profiling based on CETSA-LC-MS/MS analysis of clinical drugs has great potential for drug repositioning and its underlying unknown mechanisms.

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E. Chemoproteomics for Drug Development

E-004 Neuroprotective and anti-inflammatory effects of E11 in an in vitro Parkinson's disease model

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Drug repurposing not only has several advantages over traditional drug development strategies but also offers new therapeutic alternatives for incurable diseases, including Parkinson's disease, which is characterized by dopaminergic neuronal death. E11 is an antiplatelet agent used to treat acute coronary syndrome as an irreversible P2Y12 ADP receptor antagonist by ADP binding. E11 possesses antioxidant properties in atherosclerotic disease and inhibits pro-inflammatory T-cell response in humans. However, little is known about its potential antioxidant and anti-inflammatory effects in neuronal cells. This study aimed to investigate whether E11 has neuroprotective and anti-inflammatory effects in primary cortical neurons and BV-2 microglial cells. Proteomic analyses showed that various signaling pathways related to apoptotic cell death and neuroinflammation were altered by E11 treatment in 1-methyl-4-phenylpyridinium-treated primary cortical neurons and lipopolysaccharide-treated BV-2 microglial cells. In vitro studies demonstrated that E11 exerts neuroprotective and anti-inflammatory effects by inhibiting the mitogen-activated protein kinase signaling pathway. In addition, E11 ameliorated ROS production and mitochondrial dysfunction in primary cortical neurons. Therefore, this study proposes that E11 has neuroprotective and anti-inflammatory effects in an in vitro Parkinson's disease model.

Keywords: Parkinson's disease, Proteomics, Neuroprotection

E-005 PROTAC discovery strategy of MDM2 protein using proteomics-based site-specific covalent ligand screening

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Targeted protein degradation (TPD) technology has emerged and is gaining attention because of its potential to target undruggable proteins. One of the most representative methods of TPD technology reported thus far is the proteolysis-targeting chimera (PROTAC). To establish the PROTAC discovery strategy of MDM2 protein coupled with proteomics technology, LC-MS/MS analysis method was applied for efficiently screening site-specific covalent binding between electrophilic compounds and nucleophilic residues in target MDM2 protein. 500 MDM2-targeted binding compounds were selected by virtual screening and divided into 50 groups of 10 compounds each. Each group of 10 compounds with MDM2 (M62C) was incubated and digested wit trypsin followed by LC-MS/MS analysis. 379 of 500 hits were identified by MS/MS spectra of peptides containing covalent compounds and 267 of 379 hits were quantified by the intensity of precursor ions and within 30% of coefficient variation in triplicates analyses. To list 267 covalent compounds in the order of binding affinity to hMDM2 (N3–V109) M62C protein, the relative binding affinity (RBA) was calculated by dividing the peak area of each compound-bound peptide by that of the reference peptides. Subsequently, three peptides commonly produced by trypsin digestion of the hMDM2(N3–V109) M62C protein were selected as reference peptides. The sum of the peak areas of the three peptides was then calculated. Finally, 39 compounds corresponding to 80 % of the sum of the RBA were selected as strong binders. To apply the selected hits to the PROTAC approach, two-dimensional (2D) nuclear magnetic resonance (NMR) experiments were performed to evaluate the reversible binding of their analogs without covalent warheads. Western blot analysis showed that newly synthesized PROTACs, incorporated reversible analogs of screening hits, affected degradation in a dose- and time-dependent manner. This methodology makes it possible to use PROTAC technology to exploit previously undruggable proteins for TPD.

F. Immunopeptides and ImmunOthersapy

F-001 ImmunoResource: Noncanonical MHC-I associated peptide database compounded by proteogenomic analysis of immunopeptidome data

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MHC class I-associated peptides (MAPs) play a crucial role in cancer by presenting tumor antigens to cytotoxic T lymphocytes (CTLs), thereby initiating immune responses against cancer cells.

In particular, non-canonical MHC-associated peptides (ncMAPs), resulting from aberrant transcriptional or translational events like alternative splicing, are often discovered in immunopeptidome data. These ncMAPs are predominantly tumor-specific antigens (TSAs) and hold promise as potential candidates for the development of cancer vaccines.

In this study, we developed a proteogenomic pipeline, which integrates RNA-sequencing and de novo peptide sequencing, to identify non-canonical MHC Class I associated peptides (ncMAPs).

Using our pipeline, we conducted extensive analysis on hundreds of raw files spanning over 50 publicly available immunopeptidome data sets, successfully identifying hundreds of thousands of canonical MHC-associated peptides (cMAPs) and unearthing thousands of noncanonical MHC-associated peptides (ncMAPs). It is observed that, consistent with previous research findings, most ncMAPs sourced from 5'-untranslated regions (UTRs), 3'-UTRs, frame shifts, and non-coding RNAs.

We constructed a new comprehensive MAP database obtained from our analysis results. This database is expected to provide cancer epitopes that can be potential targets for cancer immunotherapy and disease research.

F-002 Integrated Analysis of the Proteome, Phosphoproteome, and N-glycoproteome for Immuno-Oncology Biomarker Discovery in Cervical Cancer

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Cancer Immunotherapy has revolutionized treatment by leveraging the body's immune system to target and eliminate cancer cells. Despite its remarkable success in some patients, responses to immunotherapy can vary significantly, highlighting the need for robust biomarkers to predict patient outcomes and guide treatment decisions. In this study, we conducted an integrated analysis employing liquid chromatography-tandem mass spectrometry (LC-MS/MS) to interrogate protein expression, phosphorylation, and N-glycosylation profiles in serum samples from two cervical cancer patients exhibiting divergent drug responses. Samples were collected at nine distinct time points throughout the course of immunotherapy. Our analysis identified potential biomarker candidates characterized by aberrant patterns of protein expression, phosphorylation, and N-glycosylation. These findings underscore the utility of multidimensional proteomic profiling in augmenting our understanding of cancer biology and facilitating personalized therapeutic interventions. In conclusion, our study demonstrates the power of integrating proteome, phosphoproteome, and N-glycoproteome profiling in unraveling the complexity of immuno-oncology biomarkers. The identified biomarker signatures hold promise for improving patient stratification, predicting treatment responses, and guiding the development of immunotherapeutic strategies, ultimately enhancing clinical outcomes in cancer patients.

F. Immunopeptides and ImmunOthersapy

F-003 Quantitative Proteome Analysis Reveals Distinct Mechanisms of Bacterial and Viral Infections in Mouse Models

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Infection by bacteria and viruses involves complex mechanisms crucial for effective therapeutic development. Despite recognition of the differing infection pathways between bacteria and viruses, a comprehensive understanding of their detailed mechanisms, particularly in relation to the infection route, remains elusive. In this study, we employed a quantitative proteomic analysis to elucidate the distinct infection mechanisms associated with bacterial and viral infections in mice. We collected bone marrow washing fluid, bronchoalveolar lavage fluid (BALF), and plasma exosomes from mouse models infected with bacteria and viruses, respectively. Employing an advanced quantitative proteomic approach, we identified and quantified protein expression profiles in these samples. In bone marrow washing fluid, 405 differentially expressed proteins (DEPs) were identified in bacterial infection compared to controls, while 197 DEPs were observed in viral infection. Similarly, in bronchoalveolar lavage fluid, 668 DEPs were discovered in bacterial infections compared to controls, and 602 DEPs in viral infections. Additionally, in plasma exosomes, 460 DEPs were identified in bacterial infection and 322 DEPs in viral infection, both compared to controls. Pathway analysis using Enrichr further elucidated the underlying biological processes associated with these DEPs, highlighting differences in pathways between viral and bacterial infection. This study represents a significant advancement in understanding the variances between bacterial and viral infections, providing valuable insights that may guide the development of targeted therapeutic interventions. Furthermore, our quantitative proteomic approach serves as a powerful tool for dissecting the molecular mechanisms underlying infectious diseases, paving the way for future investigations aimed at enhancing our understanding of host-pathogen interactions.

F-004 Simultaneous detection method of muscle developing monoclonal antibodies with using LC-MS/MS from Dried Blood Spots and Plasma

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Current treatments aim to slow muscle degeneration through diet, while manipulating TGF-β family pathways, such as myostatin, activin A, and GDF-11, offers potential for addressing muscle wasting. However, the use of inhibitors to enhance athletic performance is prohibited by WADA. This study developed a method to detect monoclonal antibodies such as Landogrozumab, Domagrozumab, and Bimagrumab, specifically targeting the TGF-β superfamily. To confirm assay stability, we included Dulaglutide as an internal standard. Utilizing Both Dried blood spots and Plasma, antibodies were purified using protein G magnetic beads to minimize interference, followed by LC-MS/MS analysis. The validation was conducted specificity, selectivity, linearity, precision, recovery, matrix effect. All targeted monoclonal antibodies were below the limit of detection <0.5 μg/ml. The assays showed strong linearity (R2=0.99). No interfering signals were detected that could affect the detection of the targets and Carryover was not detected. Since the matrix effect for most monoclonal antibodies is nearly 100%, using both samples in this multiplex analysis approach is appropriate. Though anti-TGF-β superfamily antibodies lack clinical approval, detecting prohibited compounds is essential for doping control. Also, using DBS for doing analysis offers a fast, safe, and stable process for athletes and analysts. We aimed to develop and validate a multiplex method for detecting prohibited monoclonal antibodies in plasma and DBS.

Keyword: Anti-doping, Monoclonal antibody, Muscle developing, Multiplexing, LC-MS/MS, Immuno-affinity Purification

F. Immunopeptides and ImmunOthersapy

F-005 Analysis of plasma cytokine levels in severe COVID-19 patients identified distinct endotypes based on the Delta and Omicron variants.

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The ongoing COronaVIrus Disease 2019 (COVID-19) pandemic, caused by the novel coronavirus Severe Acute Respiratory Syndrome CoronaVirus-2 (SARS-CoV-2), has triggered significant public health and economic challenges. As the virus continues to evolve, numerous new strains have emerged. However, a comprehensive understanding of how these strains impact immune response remains elusive. Investigating these differences could yield novel and innovative insights for developing targeted therapies, enabling precision treatment strategies and more precise patient classification. This study compared cytokine profiles in 31 severely ill COVID-19 patients infected with either the Delta (n=17) or Omicron (n=14) strain. Cytokine levels were quantified using the Olink Target 96 platform and analyzed using advanced statistical methods. Significant differences in immune response were observed between the variants. Seven cytokines were increased in Delta patients, while three were elevated in Omicron patients. Interestingly, some of these increased cytokines are known markers of disease severity. Additionally, the study identified variant-specific cytokines associated with death in patients infected with each strain: Protein P, Protein Q (lower in the deceased Delta group) and Protein W, Protein Z (lower in the deceased Omicron group). This study reveals distinct cytokine profiles associated with Delta and Omicron variants, identifies potential diagnostic markers, and variant-specific cytokines associated with death for further investigation. These findings could contribute to the development of improved COVID-19 management strategies to improve patient outcomes.

F-006 Impact of LPS Exposure on Immune Responses in LDLR KO Mice: Insights from Proteomic Analysis

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Ldlr knockout (Ldlr-/-) mice demonstrate distinct responses to lipopolysaccharide (LPS) exposure compared to wild-type (WT) mice, impacting their susceptibility to inflammation and immune-related ailments. In this study, we explored the effects of LPS exposure on bone marrow-derived macrophages (BMM) from Ldlr-/- mice and control WT mice using a proteomic approach. BMM samples were digested using the suspension trapping (S-Trap) method, and quantitative proteome analysis was conducted using the Vanquish Neo UHPLC system coupled to an Orbitrap Eclipse mass spectrometer with FAIMS Interface. As a result, 6,577 proteins were identified, with 99 and 77 differentially expressed proteins (DEPs) observed in LPS-treated WT mice and LPS-treated Ldlr-/- mice, respectively. Gene ontology analysis revealed that LPS-treated WT mice exhibited regulation of virus-related processes, while this was not evident in LPS-treated Ldlr-/- mice. This suggests that genes observed in LPS-treated WT mice may have a more direct involvement in virus infection-related processes. The DEPs identified in LPS-treated WT mice were enriched in responses associated with virus infection, whereas those in LPS-treated Ldlr-/- mice seemed to activate pathways linked to T cells and Toll-like receptors in the immune system. This indicates that genes deficient in LPS-treated Ldlr-/- mice may play a more crucial role in immune regulation. The observed differences in protein expression imply altered immune and inflammatory responses in Ldlr-/- mice, suggesting a potential role of Ldlr in modulating these processes. Further exploration of the identified DEPs and their associated pathways could offer valuable insights into the mechanisms underlying the susceptibility of Ldlr-/- mice to inflammation and immune-related diseases.

G. Cancer Proteogenomics

G-001 Activity-based protein profiling and global proteome analysis reveal MASTL as a potential therapeutic target in gastric cancer

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Gastric cancer (GC) is a prevalent malignancy in recent times; however, the therapeutic options for advanced GC still remain limited. To explore novel targets for targeted GC therapy, in this study, we profiled HSP90 client kinases by mass spectrometry-based activity-based protein profiling (ABPP) using a desthiobiotin-ATP probe, in combination with sensitivity analysis of HSP90 inhibitors in a panel of GC cell lines. We identified four kinases—MASTL, STK11, CHEK1, MET—exclusively as HSP90-regulated kinases in HSP90 inhibitor-sensitive cells. Among these, microtubule-associated serine/threonine kinase-like (MASTL) was found to be upregulated in GC and was associated with poor prognosis in patients with GC. Consequently, MASTL knockdown decreased the migration, invasion, and proliferation of GC cells. To investigate the mechanism underlying the tumor-promoting function of MASTL, we profiled global proteomic alterations following MASTL knockdown; bioinformatics analysis revealed the pathways modulated by MASTL in GC. NEDD4-1—one of the proteins whose expression was reduced by MASTL knockdown—was also found to be upregulated in GC and was associated with poor prognosis. Similar to MASTL inhibition, NEDD4-1 knockdown suppressed migration, invasion, and proliferation of GC cells. Our multi-proteomic analyses suggest that targeting MASTL could be a therapy for advanced gastric cancer potentially through reduction of tumor-promoting proteins including NEDD4-1.

G-002 Characterization of PROSER2 as a new cancer prognostic marker from functionally uncharacterized proteome (uPE1) of intrahepatic cholangiocarcinoma

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Intrahepatic Cholangiocarcinoma (iCCA) is an aggressive and malignant liver cancer originating from the bile duct epithelium, with a poor prognosis due to its propensity for invasion and metastasis. iCCA currently has no prognostic biomarkers used in the clinical setting, necessitating more innovative research and unconventional approaches to identify new molecular targets. The functionally unannotated protein (uPE1) can potentially be studied as a new molecular marker candidates, as its function has not yet been identified. This study aims to identify new molecular targets for CCA from uPE1 using proteome analysis from CCA patient tissues. We selected uPE1s from the LC-MS/MS database, focusing on those with the significant spectral differences between tumor and normal tissue. Among them, proline and serine-rich 2 (PROSER2) has a high C-score on GO terms related to intracellular and membrane-bounded organelles. Furthermore, PROSER2 showed a good prognosis with higher expression in 5-years of survival rates from clinical information of patients. To elucidate the function of PROSER2, we used overexpression and knockdown of PROSER2 according to the expression level in iCCA cell lines. Overexpression of PROSER2 significantly reduced the metastatic ability and proliferation of SNU-1196 cells, while its suppression had the opposite effect. Additionally, we confirmed that PROSER2 reduced tumor growth in subcutaneous tumor models. To elucidate the mechanism of PROSER2, we analyzed proteins associated with PROSER2 using STRING analysis in PROSER2-expressing cell lines, confirming that STK25 and PDCD10 are associated with PROSER2. These results were confirmed through immunoprecipitation and immunocytochemistry, demonstrating that STK25 and PDCD10 bind to PROSER2. It is predicted that the STK25/PDCD10 complex is stabilized by interaction with PROSER2, as shown by RT-PCR. We also used STK25 and PDCD10 knockdown systems to confirm that these pathways are related to tumor invasion. As a result, we found that PROSER2 antagonizes tumor progression through the STK25-AMPK pathway and inhibits the PDCD10-YAP pathway. In this study, we discover the new function of PROSER2 that can be a prognostic biomarker with anti-invasion function. Furthermore, the functional annotation of uPE1 proteins could provide a key approach to uncovering new mechanisms underlying cancer progression.

G-003 Comparative Proteomics of ccRCC Cell Lines to Identify Kidney Cancer Progression Factors

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Clear cell renal cell carcinoma (ccRCC) is the most common type of kidney cancer, accounting for approximately 75% of kidney cancers. We performed quantitative global proteomics coupled with Stable Isotope Labeling by Amino Acids in Cell Culture (SILAC) and high-resolution tandem mass spectrometry in kidney-derived cells, such as HEK-293, 786-O (primary ccRCC), and Caki-1 (metastatic ccRCC) cells, to investigate the novel progression factors of ccRCC. In this study, a total of 1,106 proteins were quantified. The Gene Ontology and Kyoto Encyclopedia of Genes and Genomes characteristics were presented for differentially expressed proteins (DEPs) that were increased in ccRCC cells compared to HEK-293 cells. Ultimately, 99 DEPs including 75 upregulated and 24 downregulated proteins that were significantly increased simultaneously in both ccRCC cells were selected. Among DEPs, vimentin was identified as the most significantly changed protein, and its increased expression in ccRCC was verified through immunoblot in ccRCC cell lines and immunohistochemistry in kidney tumors. Herein, from the global proteome data in ccRCC, we propose 99 DEPs including vimentin as progression factors.

G. Cancer Proteogenomics

G-004 Development of Diagnostic Multimarkers for Glioblastoma at Early Stages Using Quantitative Proteomic Method

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Glioblastoma multiforme (GBM) is a fast-growing glioma that develops from star-shaped glial cells supporting the health of the nerve cells within the brain. And it can be very difficult to treat and a cure is often not possible. So glioblastoma cancer-specific biomarker is need due to the lack of specific method for early screening, diagnosis, and prognosis of the patients with glioblastoma. In this study, we have conducted a comprehensive proteome study using human brain tissue from patients with glioblastoma (Grad 1 - Grade 4). In the discovery stage, we have identified 10,910 glioblastoma-specific proteins (Protein Groups), where 2,886 proteins (ANOBA test, P value < 0.01) were quantitated using Tandem Mass Tag (TMT) method. In order to select reliable biomarker candidates, we have carried out the clustering analysis based on the expression pattern in 5 groups, whrere 5 clusters were showed. In the verification stage (Selected target proteins: 159), we developed quantitative targeted method using stable isotope standards (SIS) peptide such as multiple reaction monitoring (MRM) assay which are capable to target peptide fragments very selective and sensitive in complex sample. The expression of 4 proteins were significantly differed between Normal (N: 22) and cancer (G1&G2: 34). Further, we performed a multiplex assay using logistic regression and the 4-protein marker panel (Kbio 1, Kbio 2, Kbio 3, Kbio 4) was constructed, which resulted in a merged AUC value of 0.910. Although we acknowledge that the model requires further validation in a large sample size, the 4-protein marker panel can be used as baseline data for the discovery of novel biomarkers of the glioblastoma.

G-005 Dissecting the Role of ATP6AP1 in Triple Negative Breast Cancer

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Triple Negative Breast Cancer (TNBC) is a type of breast cancer known for its high potential for metastasis and poor prognosis. However, the understanding of effective anti-cancer targets for TNBC remains limited. NCL overexpression and its increased localization at the plasma membrane have been found in several tumors, including TNBC. We found that nucleolin (NCL) is a potential driver of TNBC cell growth and migration. Further, profiling of the global proteomics revealed that the NCL-targeting aptamer AS1411 leads to a significant reduction in the expression of the protein ATPase H+ transporting accessory protein 1 (ATP6AP1) in TNBC cells. ATP6AP1 is known to be overexpressed in breast cancer, but the mechanisms through which it regulates tumorigenesis have yet to be clarified. We found that ATP6AP1 promotes TNBC cell migration and proliferation, while no significant changes in normal breast epithelial cells, indicating ATP6AP1 could be an effective target for the treatment of TNBC. To gain mechanistic insights into tumor promoting role of ATP6AP1, we performed global proteome analysis to profile altered proteome induced by loss of ATP6AP1. The mass spectrometry(MS) analysis revealed a total of 1949 proteins, with 1496 of them quantified. Pathway enrichment analysis for DEPs (differentially expressed proteins) showed that ATP6AP1 could be involved in the RNA metabolism, which is reportedly linked to DNA damage response. Notabley, we found that ATP6AP1 knockdown led to reduced expression of Poly[ADP-ribose] polymerase 1 (PARP1), collectively suggesting a potential role of ATP6AP1 in DNA damage response. Functional validations for selected proteins are under progress. Updated works will be presented.

G-006 Identification of m6A modification-associated proteogenomic subtypes in various cancer types

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N6-methyladenosine (m6A) is the most prevalent internal modification found in the messenger RNA of eukaryotic cells. Growing evidence indicates that m6A RNA methylation significantly affects RNA metabolism, and disruptions in m6A modification and its associated components—writers, erasers, and readers—are commonly observed across various cancer types. Despite this, the clinical implications of m6A interactive genes on these cancers and their prognostic relationships remain largely undefined. In this study, we analyzed the m6A modification patterns across 10 different cancer types by integrating genomic, transcriptomic, proteomic, and phosphoproteomic datasets. We calculated an m6A score for each patient using 21 m6A regulator genes to indicate prognostic value in predefined subtypes of these cancers. This approach enabled us to identify cancer subtypes associated with distinct m6A profiles and elucidate related pathways. Our findings suggest potential strategies for targeting m6A regulators as a therapeutic approach and underscore the prognostic significance of m6A-related subtypes in cancer.

G. Cancer Proteogenomics

G-007 Nuclear phosphorylation of CDK7 promotes TMZ-resistance of glioblastoma through regulating hypoxia-related functions

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Glioblastoma multiforme (GBM), the most prevalent and aggressive primary brain tumor, presents significant treatment challenges, with patients typically surviving only 15 months post-diagnosis. The standard treatment protocol—maximal surgical resection followed by radiotherapy and chemotherapy—is often initially successful; however, approximately 90% of cases recur locally within two years, predominantly at or near the initial tumor site. This recurrence is notably characterized by resistance to conventional therapies, including Temozolomide (TMZ), a cornerstone DNA alkylating agent used in chemotherapy since the 1940s. Additionally, a significant factor influencing treatment resistance is transcriptional dysregulation, particularly in GBM cells with an IDH1 mutation, which display a G-CIMP signature due to the accumulation of (R)-2-hydroxyglutarate, leading to global changes in the epigenome and transcriptome. Despite TMZ's initial efficacy, its impact is significantly limited by the intrinsic resistance mechanisms of the tumor, particularly due to the role of MGMT, an endogenous DNA repair enzyme. Therefore, we have conducted research through proteogenomics to understand the molecular mechanisms of drug resistance in GBM.
Cyclin-dependent kinase 7 (CDK7) is a key player in both cell cycle regulation and transcription. Alongside cyclin H and MAT1, it forms the CDK-activating kinase (CAK), critical for activating CDKs 1, 2, 4, and 6, essential for cell cycle progression. Additionally, CDK7-mediated phosphorylation modulates various transcription factors, emphasizing its dual role in cell cycle control and transcription regulation. THZ1, a specific CDK7 inhibitor, shows promise in preclinical models of cancers, including glioblastoma (GBM), by targeting transcription factor dysregulation. However, further research is needed to fully understand THZ1's therapeutic mechanisms and efficacy in GBM treatment.
Here in, we investigated the molecular characteristics of CDK7 and its impact on GBM TMZ resistance through proteogenomic analysis. We identified the significant influence of CDK7 phosphorylation under hypoxic conditions on TMZ-resistant GBM.

G-008 Pan-cancer proteogenomic landscape of whole-genome doubling reveals putative therapeutic targets in various cancer types

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Whole-genome doubling (WGD) is prevalent in cancer, driving tumor development and chromosomal instability. Recent studies have reported driver mutations in mitotic cell cycle genes and cell cycle upregulation as major molecular underpinnings of WGD tumors. Despite such efforts, questions remain about underlying genomic signatures and regulatory networks underlying gene transcription and kinase-phosphorylation. In this study, we performed a pan-cancer proteogenomic analysis to decipher a comprehensive molecular landscape underlying WGD tumors. For this, we compared 10 cancer types by integrating genomic, transcriptomic, proteomic, and phosphoproteomic datasets. Our study delineated distinct copy-number signatures characterizing WGD tumors into three major groups: highly unstable genome, focal instability, and tetraploidy. Furthermore, the analysis reveals heterogeneous mechanisms underlying WGD across cancer types, with specific structural variation patterns identified. Contrary to previous studies, the upregulation of the cell cycle and downregulation of the immune response were found to be specific to certain WGD tumor types. Transcription factors (TFs) and kinases exhibited cancer-type-specific activities, emphasizing the need for tailored therapeutic approaches. The study introduces an integrative approach to identify potential TF targets for drug development, highlighting BPTF as a promising candidate for head and neck squamous cell carcinoma. Additionally, drug repurposing strategies were proposed, suggesting potential drugs for treating WGD-associated cancers. These findings offer insights into the heterogeneity of WGD and provide implications for precision medicine approaches in cancer treatment.

G. Cancer Proteogenomics

G-009 Plasma proteomic profiling of breast cancer patients according to age group

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Backgroud
Breast cancer (BC) is one of the most common mlignancies in world. Although young breast cancer has been known poor prognosis, plasma proteomes profiling of this group has not been well investigated. In this pilot study, we compared plasma protein between young and old patient with BC.
Method
We analyzed nine BC patients (n=3; young, <= 40 years old, n=6; old) plasma using Olink platform. Total of 5421 proteins were measured and protein extension assay data was processed using the OlinkAnalyze package in R (version 4.2.2). Prior to statistical analysis, mass spectrometry data was log2 transformed and p-value < 0.05 was considered statistically significant.
Results
Comparison of young vs. old BC patients, 174 proteins (3.2%) were represented difference. Of these, 47 proteins were associated with immune response and cytokine regulation pathway. High rank proteins which were increased in old BC patients were CTCS, DPEP1, ANOS1, and PON1 and cytokines including IL-3, IL-16, IL-9R, FLT4, and RFX5.
Conclusions
Though this pilot study represented several immune and cytokine related proteins were increased in older breast cancer patients, follow-up analysis and validation would be needed to understand aggressive mechanism.

Key words: Breast cancer, biomarker, Proteomics

G-010 Proteogenomic Characteristics of Recurred HER2-Positive Breast Cancer Patients

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Breast cancer accounts for the largest proportion of 21.5% of the approximately 117,300 cases of cancer in Korean women in 2021, showing a steady increase of about 4.8% per year on average from 2008 to 2021. HER2, a major therapy determining biomarker for anti-HER2 therapies, which have been developed in antibody-based therapeutics or tyrosine kinase inhibitor. Here we conducted a multi-omics study involving mass spectrometry-analyzed proteomes and transcriptomics, on a total of 62 HER2 positive breast cancer patient samples. After cryopulverization of tissue samples, TMT 11-plex labeled peptide samples were anlyzed using Q Exactive HF-X hybrid quadrupole-orbitrap mass spectrometer. Raw data were processed for identificaiton and quantification search using FragPipe equipped with MSFragger. Total RNA was converted into a cDNA library using the Illumina TruSeq Stranded mRNA Sample Prep Kit, cDNA synthesis using SuperScript II reverse transcriptase and DNA Polymerase I, followed by adapter ligation using the Illumina kit components. The libraries were then quantified using KAPA Library Quantification Kits and sequenced on an Illumina NovaSeq platform. We conducted an omics analysis to investigate the molecular characteristics of 10 reccurent HER2-positive breast cancer patients treated with herceptin, by comparing them with 52 other patients. In comparing analysis process, we used gene set databases such as Hallmarks, KEGG, Reactome, and Gene Ontology to identify the functions of differentially expressed genes by transcriptome and proteome for 1,000 permutations using Gene Set Enrichment Analysis. Functional analysis of recurred group revealed increased expression of genes involved in oxidative phosphorylation, ribosomal metabolism, and mitochondrial metabolism, which are crucial for energy production (p-value <0.05). Genes that were commonly highly expressed in both proteomic and transcriptomic analysis include MBTPS2, CCDC117, YIPF5, ST3GAL1, IDH2, PRKCD, CHMP2B, GGPS1, NUCKS1, WARS2, BCL2L1, FOXA1, and GPRC5C. Among these, BCL2L1, IDH2, PRKCD and WARS2 are genes specific to the mitochondrial metabolism and IDH2 is a key gene in oxidative phosphorylation and serves as a potential inhibition target within this pathway. Additionally, PPARG transcription factor target genes are up-regulated, playing a role in activating lipid metabolism. Though this study was performed limited number of patients, we would continue to validate by further analysis using open dataset.

G. Cancer Proteogenomics

G-011 Proteogenomic Insights and Biomarker Discovery in Resected Extrahepatic Cholangiocarcinoma from the Phase 2 STAMP Trial

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Extra-hepatic cholangiocarcinoma (eCCA), encompassing perihilar (50-60%) and distal CCA (20-30%) and excluding intrahepatic forms, represents the predominant forms of bile duct cancer, characterized by a 5-year survival rate of less than 20%. Through the STAMP clinical trial, which explored the prognosis of capecitabine (CAP) versus gemtabine plus cisplatin (GemCis) chemotherapy in patients with eCCA, 93 tumor formalin-fixed paraffin-embedded (FFPE) tissues (46 in the CAP group and 47 in the GemCis group) and 21 adjacent normal tissues (NoR) were obtained and whole exome sequencing and bottom-up proteomic analysis were performed. Somatic mutation profiling of eCCA differs from iCCA, with frequent TP53 (63%), SMAD4 (20%), and KRAS (18%) mutations. In the adjuvant GemCis group, KRAS somatic mutations were associated with poor disease-free survival (DFS) and overall survival (OS) (log-rank p=0.004 for DFS and p=0.003 for OS). In global proteomic analysis, when seen through the 50 hallmark genesets in eCCA compared to NoR, interferon alpha and gamma signals were high in tumor, and KRAS signals were low. In addition, when cell typing was performed based on the public scRNA-seq results, the population of cholangiocyte, endothelial, and smooth muscle cells in tumor was low, but the proportion of immune cells was high. As a result of quantitative comparative proteome analysis according to the presence or absence of KRAS mutation, it was confirmed that RDC2 protein, which reacts directly with KRAS and capecitabine, was low in this mutation group. This indicates the prognostic results depending on which drug is administered. Proteogenomics research is poised to redefine clinical diagnostics and therapeutics by mapping intricate protein-genome interactions, offering a more comprehensive approach to understanding disease mechanisms and improving patient outcomes.

G-012 Proteomic Characterization of MUC18 in Gastric Cancer

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MUC18 is a transmembrane glycoprotein associated with epithelial-mesenchymal transition (EMT), immune escape, and poor prognosis in cancer. Yet, the molecular mechanisms underlying MUC18's role in gastric cancer (GC) progression remain elusive. In this study, we aimed to elucidate the function of MUC18 in GC. MUC18 knockdown reduced the migration and proliferation of GC cells, while it marginally affected the downstream signaling pathways of receptor tyrosine kinases (RTK). To uncover novel underlying mechanisms of MUC18 in GC progression, we conducted a global proteome analysis to profile proteome alteration induced by MUC18 knockdowin in GC cells, identifying a total of 1463 proteins with 1104 quantified. Pathway analyses for differentially expressed proteins by MUC18 knockdown indicated that MUC18 could be implicated in cancer metabolism. Among downregulated proteins by MUC18 knockdown, GLUT1 (SLC2A1), SAM68 (KHDRBS1), and SERPINA3 are linked to tumorigenesis and altered metabolism in cancer. Our results suggest that MUC18 could drive GC progression through cancer metabolic reprogramming. Furthermore, we found that MUC18 is also expressed in gastric cancer-associated fibroblasts (CAF) and are currently investigating the role of MUC18 in CAF activation. Updated works will be presented.

G-013 Proteomic Characterization of NEDD4 in Gastric Cancer

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Gastric cancer is one of the cancers with a high incidence in worldwide, and the basic treatment currently remains in surgical treatment and chemotherapy prescription. Neural Precursor Cell-expressed Developed Down-regulated 4 (NEDD4) is known to be involved in various steps of cancer signaling pathways, such as PTEN/Akt, however its role in tumorigenesis is still controversial. The purpose of this study is to investigate the mechanism of NEDD4 in gastric cancer (GC). To investigate the role of NEDD4 in migration, survival, and proliferation of GC cells, transwell migration, wound healing and clonogenic assays were conducted. Silencing of NEDD4 in NEDD4 high expressing GC cells (AGS, SNU216, SNU668) resulted in decreased cell migration, proliferation and survival. Conversely, NEDD4 overexpression in NEDD4 low expressing GC cells (MKN1 and SNU601) promoted cell migration and proliferation. Furthermore, while NEDD4 is known to decrease PTEN, thereby activating p-AKT signaling, we found that inhibiting NEDD4 in gastric cancer cells did not lead to significant changes in the expression of PTEN or activation of p-AKT signaling, indicating that the phenotypes observed upon NEDD4 inhibition could be mediated by other signaling pathways. To gain novel mechanistic insights into tumor promoting role of NEDD4, we profiled global proteome alteration followed by NEDD4 knockdown through mass spectrometry-based proteomics analysis. The proteomics analysis identified a total of 3586 proteins, with 2793 proteins quantified. The results of the pathway network analysis using the Metascape tool showed that among the downregulated proteins, the most significantly enriched pathways were vesicle-mediaed transport pathways. We also present potential proteins whose expressions are i) regulated by NEDD4 and ii) correlated with prognosis of GC patients. Functional validations for selected proteins are under progress. Updated works will be presented.

G. Cancer Proteogenomics

G-014 Proteomic heterogeneity of the extracellular matrix identifies histologic subtype-specific fibroblast in gastric cancer

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Gastric cancer (GC) is a highly heterogeneous disease regarding histologic features, genotypes, and molecular phenotypes. Here, we investigate extracellular matrix (ECM)-centric analysis, examining its association with histologic subtypes and patient prognosis in human gastric cancer. We performed quantitative proteomic analysis of decellularized GC tissues that characterizes tumorous ECM, highlighting proteomic heterogeneity in ECM components. We identified 20 tumor-enriched proteins including four glycoproteins, serpin family H Member 1 (SERPINH1), Annexin family (ANXA3/4/5/13), S100A family (S100A6/8/9), MMP14, and other matrisome-associated proteins. In addition, histopathological characteristics of GC reveals differential expression in ECM composition, with the poorly cohesive carcinoma not otherwise specified (PCC-NOS) subtype being distinctly demarcated from other histologic subtypes. Integrating ECM proteomics with single-cell RNA sequencing, we identified crucial molecular markers in the PCC-NOS-specific stroma. PCC-NOS-enriched matrisome proteins (PEMs) and gene expression signatures of adipogenic cancer-associated fibroblasts (CAFadi) are closely linked, both associated with adverse outcomes in GC. Using tumor microarray analysis, we confirmed the CAFadi surface marker, ATP binding cassette subfamily A member 8 (ABCA8), predominantly present in PCC-NOS tumors. Our ECM-focused analysis paves the way for studies to determine their utility as biomarkers for patient stratification, offering valuable insights for linking molecular and histologic features in GC.

G-015 Regulatory Mechanism of Recurrence based on Extracellular Kinome Network in Oral Squamous Cell Carcinoma

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Oral squamous cell carcinoma (OSCC) is an aggressive cancer characterized by early and high recurrence rate of 30-40% within 2 years. However, patients at high risk of recurrence have few treatment options due to the high heterogeneity and the absence of molecular subtype and driver mutation gene. Therefore, we attempted to understand the mechanism of recurrence by extending extracellularly. Liquid biopsy is emerging as an alternative to tissue biopsies reflecting the tumor microenvironment in the clinical management of malignant diseases. Here, we tried to analyze plasma of patient with OSCC to understand comprehensively tumor microenvironment (TME). From LC-MS-based secretome analysis for thirty-four patients' plasma (recurrence, n=15 vs w/o recurrence, n=19). 295 phosphorylation sites were identified for 113 proteins and phosphorylated proteins were predominantly associated with lipid binding, complement system, extracellular matrix, and calcium binding. When phosphoproteins were classified into three groups based on their secretion level, we observed that subtype cluster 3, which exhibited the poorest prognosis for recurrence, showed increased phosphorylation of FAM20C substrates according to phosphorylated motif enrichment analysis. The FAM20C (family of proteins with sequence similarity to 20-member C) is a novel secreted kinase that phosphorylates ER/golgi-localized secretory proteins or an ectodomain of membrane proteins containing an S-x-E/pS motif such as OPN, FGF. In TCGA data, the group with high FAM20C expression had low overall survival or progression free survival. Additionally, we confirmed that FAM20C can be derived not only from cancer cells but also from CAFs from single-cell analysis data. Moreover, the expression or secretion of FAM20C was increased in patients with recurrence in patient-derived organoids or cancer associated fibroblast libraries established in our NCC cohort. Moreover, we found that the expreesion of EMT markers and cancer stem cell (CSC)-related genes and cellular invasiveness were increased by FAM20C when we validated them using FAM20C-overexpressed or knock-down oral cancer cell line. Collectively, we discovered a novel regulatory mechanism of recurrence mediated by crosstalk between secreted kinases FAM20C and TME. Furthermore, we propose it as a new biomarker for predicting the prognosis of OSCC.

Keywords: Oral Squamous Cell Carcinoma, Phosphoproteome, Secretome, liquid biopsy

G. Cancer Proteogenomics

G-016 Subgroup-Specific Responses in Medulloblastoma Unveiled by Targeted Therapies and Proteomic Profiling

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Medulloblastoma (MB), one of the most frequent pediatric malignant brain tumors, exhibits molecular heterogeneity, contributing to its challenging prognosis. Despite advances in current standard therapy, recurrent cases pose clinical hurdles due to treatment-induced morbidity. Recent genomic profiling has delineated MB into four distinct molecular subgroups; Wingless (WNT), Sonic hedgehog (SHH), Group 3 and Group 4. In this study, I aimed to investigate the efficacy of MET and proteasome inhibitors across medulloblastoma cell lines, focusing on subgroup-specific responses. Utilizing representative cell lines of SHH subgroups and Group 4, I examined drug sensitivity through MTT assays, determining IC 50 values. Additionally, employing LC-MS/MS-based proteome analysis, I characterized global and phospho-proteomic alterations induced by the inhibitors. Our findings revealed differential sensitivity patterns and unique proteomic profiles among medulloblastoma subgroups. Notably, MET and proteasome inhibition demonstrate promising efficacy with Group 4, suggesting their potential as novel therapeutic targets for this subgroup. Taken together, this study provides critical insights into the molecular mechanisms underlying medulloblastoma pathogenesis, emphasizing the potential of subgroup-specific treatments for personalilsed therapeutic interventions.

G-017 Transglutaminase 2/ Hippo Signaling Pathway is associated with Epithelial-Mesenchymal Transition in Glioblastoma

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Glioblastoma (GBM) is the most common aggressive tumor of the brain with median survival rates under 14.6 months. Despite conventional treatments, approximately 90% of GBM patients have experienced local recurrence within 2 years. The poor prognosis of GBM is largely due to the invasion of GBM cells into the surrounding tissue. EMT has been pointed as one of the biological processes that confer this invasive property on GBM cells. EMT is known as a crucial inducer that leads GBM cells to gain more mobility and resistance to conventional therapy in vivo and clinical study. Although EMT is a common issue in GBM, only a few studies have unveiled the association between EMT-inducing factors and GBM progression. Transglutaminase 2 (TGM2) is one of the important regulators in triggering the mesenchymal transition of GBM cells by regulating transcription factors. However, the molecular mechanisms of TGM2 affect ETM in GBM have not been elucidated. Here, I aimed to identify cellular signaling changes by TGM2 overexpression and possible targets correlated with acquiring invasive capability in GBM. First, I selected the down-regulated proteins under overexpression of TGM2 by proteomic analysis. Then, to identify which cellular processes are regulated by TGM2, I conducted diverse pathway analyses using the Enrichr program. The result disclosed that the Hippo signaling pathway was significantly associated with TGM2 expression. Especially, LATS1, the activator of the kinase cascade in the Hippo signaling pathway by restricting YAP/TAZ expression, was polymerized by TGM2. Knockdown of TGM2 decreased YAP/TAZ expression and invasive ability. Furthermore, a TGM2 inhibitor 383 increased LATS1 and suppressed cell proliferation and invasion ability of GBM cells. Collectively, these results indicate that inhibition of TGM2 prevents mesenchymal transition and provides a potential therapeutic target for MES-GBM by regulating Hippo signaling pathway activation.

G-018 Unraveling the malignant role of TSTD2 in Breast cancer

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Within the ambitious scope of the Human Proteome Project (HPP), unraveling the functions of proteins is a crucial goal. In the study, we investigated the function of such a protein, Thiosulfate Sulfurtransferase Like Domain Containing 2 (TSTD2), which lack detailed annotations. TSTD2 is a gene located on chromosome 9, belonging to the TSTD family with a domain similar to thiosulfate sulfurtransferase. The role of TSTD2 in cancer is not yet fully understood. We specifically elucidated its relevance to breast cancer. In breast cancer, the expression of TSTD2 is elevated compared to normal breast epithelial cells, showing a negative correlation with overall survival. TSTD2 knockdown significantly suppresses cell proliferation and migration in breast cancer cells. Subsequent mass spectrometry analysis aims to reveal how TSTD2 operates in breast cancer, including its interaction with other proteins. There is hope that TSTD2 could be utilized as a biomarker for breast cancer. Our ultimate goal is to understand the role of TSTD2 in breast cancer.

G. Cancer Proteogenomics

G-019 Using Mass Cytometry to Distinguish Immune Cell Subtypes in Peripheral Blood Mononuclear Cells of Leukemia Patients

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Introduction:
Leukemia, a hematologic malignancy originating in blood-forming tissues such as bone marrow and the lymphatic system, produces an excessive number of abnormal blood cells. Among these, acute myeloid leukemia (AML), the most common leukemia in adults, is characterized by genetic mutations leading to clonal expansion of undifferentiated myeloid precursors, while acute lymphoblastic leukemia (ALL) manifests as malignant tumors of B or T lymphocytes. Accurate diagnosis of these entities and assessment of tumor immunity play pivotal roles in determining the efficacy of immunotherapeutic agents such as immune checkpoint inhibitors. Therefore, we aimed to elucidate immune cell populations in leukemia patients and characterize intratumoral heterogeneity using mass cytometry.

Method:
Using Cytometry by time of flight (CyTOF), we simultaneously identified 17 cell surface markers to characterize of all major peripheral blood cellular subsets. Peripheral blood mononuclear cell (PBMC) samples were analyzed from four healthy individuals, four with acute myeloblastic leukemia (AML), and four with acute lymphoblastic leukemia (ALL) aged 20 to 45. Clustering of multidimensional data was performed using FCS Express software, enabling analysis and visualization of inter-cluster correlations and intra-cluster characteristics by linking metadata information. The abundance of each population was compared with clinical information such as age, gender, complete blood count, and blood chemistry examination.

Results:
In healthy individuals, the sizes of immune cell clusters showed considerable consistency, whereas among leukemia patients significant heterogeneity in distribution was observed. The ALL group showed individual variations in the T/B cell population, with a particularly noticeable reduction in the CD3+ and CD45+ phenotypes, as indicated by Spearman correlation coefficients showing a positive rank correlation with platelet counts. The AML group exhibited high heterogeneity in subclusters CD3-, CD20-, and CD11c+, and correlations were observed with hemoglobin and platelet counts. Analysis of correlations between the size of specific clusters and WBC counts across the entire leukemia patient group enabled the identification of clusters most indicative of a favorable prognosis.

Conclusion:
Immune profiling via mass cytometry underscores the need for personalized therapeutic approaches, revealing distinct populations across different leukemia types, reflecting fundamental differences in tumor immunity. It demonstrates the potential of CyTOF analysis to aid in diagnosis and treatment, indicating the possibility for precise validation and further study of protein interactions in specific cell types with distinctive expression patterns.

G-020 Multi-omics analysis of sex difference in human glioblastoma

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Glioblastoma (GBM) is one of the most prevalent and fatal brain cancers among adults, presenting limited therapy options and bad prognoses. Recent investigations underline the significance considering sex disparities in tumor progression, occurrence, molecular distinctions and remedy responses over various tumors types, including bladder adenocarcinoma, colorectal adenocarcinoma and GBM. This study delves into a comprehensive analysis of extensive multi-omics result data acquired from TCGA and CPTAC databases, aiming to elucidate the molecular and genetic factors contributing to distinct clinical characteristics observed in female and male GBM patients. Our findings reveal some important findings. Complementary analyses of proteomic and phosphor-proteomic data unveiled sex-specific variations in protein expression and phosphorylation activity, such as SPP1 hyperphosphorylation in females and EGFR activation predominantly in males. Furthermore, the identified sex-specific biological marker exhibited prognostic relevance, implicating their potential as treatment targets. In summary, our study offers unparalleled perceptions into the basic drivers of clinical outcomes and cancer progression among female and male patients, paving the way for tailored treatment strategies catering to sex-specific nuances.

G. Cancer Proteogenomics

G-021 Multi-omics Profiling of Glycosylation-Related Genes in Clear Cell Renal Cell Carcinoma

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Background:
Renal cell carcinoma (RCC) is a significant oncological challenge due to its resistance to conventional therapies and limited treatment options. Clear cell RCC (ccRCC) is a prevalent form of kidney cancer with a notoriously poor prognosis. Glycosylation, an epigenetic modification, is implicated in tumor progression across various cancers. However, its role in ccRCC, particularly concerning glycosylation-related genes (GRGs), remains underexplored.

Methods:
We employed publicly available datasets and machine learning approaches to classify clear cell RCC into molecular subtypes, as described by Motzer et al., using transcriptomic data from the Immotion151 trial. By integrating multi-omics data, we conducted enrichment analyses of GRGs and associated pathways within each molecular cluster.

Results:
Our study revealed significant associations between GRGs and tumor subtypes, correlating with differences in clinical outcomes for RCC patients. Multi-omics analysis of RCC tissues elucidated the relationship between GRGs expression and tumor characteristics. Additionally, we identified novel glycosylation genes with potential roles in RCC progression, meriting further investigation.

Conclusion:
The identification of distinct GRGs and enriched pathways in each cluster may lead to new diagnostic biomarkers. This comprehensive approach enhances our understanding of the molecular landscape of RCC and its glycosylation profile across subtypes, offering promising avenues for personalized therapies. Our findings highlight the significance of glycosylation dysregulation in RCC pathogenesis and suggest potential diagnostic and therapeutic targets for further exploration.

G-022 Proteogenomic Characterization Reveals Estrogen Signaling as a Target for Never-Smoker Lung Adenocarcinoma Patients without EGFR or ALK Alterations

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Never-smoker lung adenocarcinoma (NSLA) is prevalent in Asian populations, particularly in women. EGFR mutations and anaplastic lymphoma kinase (ALK) fusions are major genetic alterations observed in NSLA, and NSLA with these alterations have been well studied and can be treated with targeted therapies. To provide insights into the molecular profile of NSLA without EGFR and ALK alterations (NENA), we selected 141 NSLA tissues and performed proteogenomic characterization, including whole genome sequencing (WGS), transcriptomic, methylation EPIC array, total proteomic, and phosphoproteomic analyses. Forty patients with NSLA harboring EGFR and ALK alterations and seven patients with NENA with microsatellite instability were excluded. Genome analysis revealed that TP53 (25%), KRAS (22%), and SETD2 (11%) mutations and ROS1 fusions (14%) were the most frequent genetic alterations in NENA patients. Proteogenomic impact analysis revealed that STK11 and ERBB2 somatic mutations had broad effects on cancer-associated genes in NENA. DNA copy number alteration analysis identified 22 prognostic proteins that influenced transcriptomic and proteomic changes. Gene set enrichment analysis revealed estrogen signaling as the key pathway activated in NENA. Increased estrogen signaling was associated with proteogenomic alterations, such as copy number deletions in chromosomes 14 and 21, STK11 mutation, and DNA hypomethylation of LLGL2 and ST14. Finally, saracatinib, an Src inhibitor, was identified as a potential drug for targeting activated estrogen signaling in NENA and was experimentally validated in vitro. Collectively, this study enhanced our understanding of NENA NSLA by elucidating the proteogenomic landscape and proposed saracatinib as a potential treatment for this patient population that lacks effective targeted therapies.

H. Others

H-001 A global and phosphoproteomic analysis to systematically understand the effect from disturbed proteostasis and seek potential TDP-43-induced toxic compounds in Frontotemporal Dementia

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Frontotemporal dementia (FTD) affects the frontal and temporal lobes of the brain causing difficulty in behavior and language. Previous findings identified toxic accumulation of TDP43 aggregates in the majority of FTD patients, yet the removal of these aggregates alone has not been so successful. Here, an extensive profiling was carried out to systematically understand the effect caused from disturbed proteostasis to search for potential TDP43-induced toxic compounds in FTD. Four replicates of day1(early) and day2(late) stage mouse cell-line samples 1) pAAV-MCS (MOCK), 2) pAAV-MCS-TDP43, two pathogenic mutants of TDP43 3) pAAV-MCS-TDP43(MT1) and 4) pAAV-MCS-TDP43(MT2) were labeled with two 18-plex TMTs for analysis. Comprehensive phospho and global proteome profiling appyling DO-NCFC-RP/RP-MS/MS platform [2016, Lee et al] resulted in total of 64,849 distinct phosphopeptides (44,975 phosphorylation sites, 7,251 phosphoprotein groups) and 199,006 distinct peptides (9,975 protein groups (≥2 hits)). Based on our extensive profiling results, we plan to select potential TDP43-induced toxic compounds to seek hints in drug targets for FTD.

H-002 Application of MALDI-TOF-based diagnostic platform for multiple myeloma diagnosis

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Introduction: In multiple myeloma, malignant plasma cells produce monoclonal immunoglobulins known as M-proteins. Detecting the cancerous M-protein is crucial for treating patients with therapeutic monoclonal antibodies (t-mAbs), However, conventional routine methods such as serum protein electrophoresis (SPEP) and immunofixation electrophoresis (IFE) have limitations in interpretation due to the potential for false positives caused by therapeutic monoclonal antibody (mAb) Daratumumab. Our MALDI-TOF platform enables the determination of Daratumumab (Dara) intake status in multiple myeloma (MM) patients by detecting mass differences where conventional methods fail to provide insight.

Methods: Negative and positive sera diagnosed by the SPEP method were subjected to immunoenrichment using IgG, IgA, IgM, total κ light chains, and total λ light chains nanobodies. The eluates were analyzed by MALDI-TOF, which was parameter-optimized and mass calibrated. Additionally, positive serum with the lowest concentration was diluted with normal pooled serum to determine the limit of detection. Next, the mass spectra were visually inspected using FlexAnalysis software (Bruker Daltonics).

Results: The resulting mass spectra displayed kappa or lambda light chain m/z distributions that were attached to an IgG, IgA, or IgM. Normal serum showed Gaussian curves, whereas positive sera with an M-protein had a spike in the light chain mass range. By analyzing all five spectra from the five immune enrichments, the isotype of the M-protein for each positive sample was identified. Furthermore, in one of the positive samples, the MALDI-TOF MS spectrum from the IgG and kappa-specific purification showed peaks of M-protein and Daratumumab, which were not detected by SPEP. We also found that the M-protein peak was detectable down to 0.008 g/dL.

Conclusion: Immunoenrichment using nanobodies followed by our MALDI-TOF MS platform allows for the identification of M-protein isotypes, as well as the presence of monoclonal antibodies, which cannot be discriminated with current multiple myeloma diagnosis electrophoretic methods (i.e., SPEP, IFE). This implies its potential to replace bone marrow-based analysis, the current minimal residual disease (MRD) testing method, in a less invasive manner.

H. Others

H-003 ARID3C acts as a regulator of monocyte to macrophage differentiation interacting with NPM1

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ARID3C is a protein located on human chromosome 9 and expressed at low levels in various organs, yet its biological function is not elucidated. In this study, we investigated both the cellular localization and function of ARID3C. Employing a combination of LC-MS/MS and deep learning techniques, we identified NPM1 as a binding partner for ARID3C's nuclear shuttling. ARID3C was found to predominantly localize with the nucleus, where it functioned as a transcription factor for genes STAT3, STAT1, and JUNB, thereby facilitating monocyte-to-macrophage differentiation. The precise binding sites between ARID3C and NPM1 were predicted by Alphafold2. Mutating this binding site prevented ARID3C from interacting with NPM1, resulting in its retention in the cytoplasm instead of translocating to the nucleus. Consequently, ARID3C lost its ability to bind to the promoters of target genes, leading to the loss of monocyte-to-macrophage differentiation. Collectively, our findings indicate that ARID3C forms a complex with NPM1 to translocate to the nucleus, acting as a transcription factor that promotes the expression of the genes involved in monocyte to macrophage differentiation.

KEYWORDS: ARID3C, NPM1, LC-MS/MS, Alphafold2, Interactome analysis, Monocyte differentiation, Chromosome-centric Human Proteome Project

H-004 Biomarker Discovery and Pathogenic Insights in Age-Related Macular Degeneration through Proteomic Analysis

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Age-related macular degeneration (AMD) is characterized by progressive degeneration of macular, which can result in significant visual impairment. While dry AMD begins with drusen accumulation, wet AMD is marked by neovascularization beneath the retina, causing hemorrhage and exudation, eventually leading to irreversible fibrosis. Current treatments targeting vascular endothelial growth factor are ineffective against fibrotic retinal cells in late-stage AMD, necessitating the development of novel therapies.
In this study, we aimed to identify AMD biomarkers and explore their expression patterns in related retinal diseases. Proteomic analysis was performed on aqueous humor samples obtained during ocular surgery. Control samples from macular hole (MH) patients were compared to those from patients with wet AMD, epiretinal membrane (ERM), and proliferative diabetic retinopathy (PDR).
Label-based quantitative proteomics techniques, including tandem mass tag (TMT) and data-independent acquisition (DIA) analysis, were employed to identify differentially expressed proteins (DEPs) in each experimental group.
Through proteomic profiling, a total of 763 proteins were identified. Analysis of aqueous humor samples from patients with wet age-related macular degeneration (wAMD) revealed 134 differentially expressed proteins (DEPs) deemed potential biomarkers, consisting of 98 upregulated and 36 downregulated proteins. Similarly, patients diagnosed with epiretinal membrane (ERM) exhibited 97 DEPs, including 15 upregulated and 82 downregulated proteins. Furthermore, in patients with proliferative diabetic retinopathy (PDR), 164 DEPs were identified, with 70 upregulated and 94 downregulated proteins. Angiogenesis-related proteins and fibrosis-related proteins were observed in the aqueous humor of AMD patients, suggesting their potential as biomarkers for AMD diagnosis. In the future, we are planning functional studies and biomarker validation analyses. We believe that this study will contribute to the identification of biomarkers for AMD, which may provide insight into the pathogenesis of AMD and potential therapeutic targets.

Keywords : Age-related macular degeneration (AMD), Macular hole (MH), Wet AMD (wAMD), Epiretinal membrane (ERM), Proliferative diabetic retinopathy (PDR), Aqueous humor, Angiogenesis, Fibrosis, Differentially expressed proteins (DEPs), Tandem mass tag (TMT), Biomarkers, Proteomic analysis

H-005 Cereblon as potential biomarker for diabetic cardiomyopathy in type 2 diabetes-induced mice

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The high incidence of heart failure in patients with type 2 diabetes mellitus (T2DM) can be attributed to myocardial fibrosis, weakening of ventricular function, and damage to myocardial muscles, such as mitochondrial dysfunction. We studied physiological changes in the heart, which are early characteristics of diabetic myocardial disease, using 6- and 8-week old obese T2DM model mice (db/db, BKS.Cg-Dock7m+/+Leprdb/J) and wild type mice. We confirmed mitochondrial dysfunction in 8 weeks old db/db mice, which was not accompanied by any changes in heart function. Metabolomic analysis performed on heart tissues revealed that the levels of 12 metabolites changed substantially. The levels of glucose and leucine increased considerably, and lipid metabolites changed. Protein expression analysis of the blood and heart tissues confirmed a remarkable increase in cereblon (CRBN) levels and a decrease in AMP-activated protein kinase, a negative regulator. Furthermore, in silico studies on data in the blood of diabetic cardiomyopathy (DCM) patients. These results show that an increase in CRBN, without any abnormal heart function, in early T2DM mice roles an important role in the reduction of mitochondrial function and metabolomic changes. Therefore, CRBN level in blood and heart tissues may serve as a diagnostic biomarker for the detection of early DCM.

H. Others

H-006 Characterization of Bacillus-derived Extracellular Vesicles and proteomic profiling.

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Probiotics-derived Extracellular Vesicles (EVs) and proteins are characterized using data from proteomic analysis, which is evaluated and processed using bioinformatics. Proteomics is crucial in microbiome research as it provides information on protein identification, expression levels, and alterations. The proteomics data revealed the identification of various proteins in the Cellular Component and biological processes, along with their gene symbols, protein names, molecular weights, and abundances, facilitating the determination of the immune systems of the Probiotic strain. We investigated the anti-tuberculosis (TB) efficacy of Bacillus strain-derived Extracellular Vesicles (EVs) and proteins. Treatment of Mycobacterium tuberculosis-infected mouse macrophages with Bacillus strain extract resulted in the intracellular killing of Mycobacterium tuberculosis strains and Drug Resistant-Tuberculosis strains, confirming its efficacy in reducing M. tuberculosis bacteria. Additionally, treatment with Probiotic strain extract decreased intracellular NO and ROS levels and increased lysosomes. Further investigation of Probiotic strain-derived EVs revealed their high anti-TB activity. Proteomic analysis of Bacillus-derived EVs identified a high abundance of extracellular protein locations known for their presence in large quantities on the bacterial cell surface. Our study utilized different cultures and conditions compared to previous studies of Lactobacillus-derived EVs isolated in MRS mediums. We employed diverse EV isolation techniques depending on the strain, used an Optimized Medium of safe ingredients, and established conditions suitable for scaling up to animal testing. To date, EVs from Gram-positive bacteria have been studied less than those from cell-derived or Gram-negative bacteria. This MRC project will further investigate probiotic-derived EVs and their mechanisms of action, requiring in-depth and diverse analytical techniques for the potential development of new drugs.

Keywords: Microbiome, Probiotics, Anti-tuberculosis effect, Mycobacterium tuberculosis, Proteomics

H-007 Comparative Analysis of Proteomic Outcomes from Three Distinct Pretreatment Methods Utilizing TimsTOF Pro 2

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Cholangiocarcinoma, the second most common cancer in the liver after hepatocellular carcinoma, involves the bile duct, a pathway for bile secreted from the liver to be discharged into the intestine. The tissue size of the bile duct is relatively small, and it is known that protein extraction from liver bile duct samples is lower compared to other cancers. Although formalin-fixed paraffin-embedded (FFPE) samples have many advantages, they are limited in protein extraction due to cross-linking. In response to this, we aimed to optimize protein extraction from a 5 μm thick FFPE slide with a consistent region of interest size (1 cm x 1 cm) using the Covaris R230 Focused-ultrasonicator. In this experiment, 48 biological triplicate samples were used. Among them, 24 samples were processed three times with the same preprocessing method for reproducibility, and the remaining 24 samples were treated with three different preprocessing methods for the same samples. For comparative analysis, protein was extracted from the FFPE tissue slice using Adaptive Focused Acoustics (AFA) accelerated sonication, and quantified using a BCA assay, yielding an average of 38.7 μg of protein. Subsequently, proteins were digested into peptides using AFA accelerated, Evotip digestion (EVO), and single-pot, solid-phase-enhanced sample preparation (SP3) methods. Peptides were loaded onto Evotip for data independent acquisition (DIA) analysis via LC-MS/MS. Data analysis revealed that the AFA accelerated method yielded the highest number of protein IDs (average: 4,545) than other two methods (average 2,211; SP3 and 2,659; EVO, 20 samples per day method). The highest amount of protein was quantified in 20 out of 24 samples using the AFA acceleration method. Whereas, the reproducibility test results for three biological repeated measurements of 24 samples using the same method were evaluated using the coefficient of variation (CV) of the number of identified proteins. The AFA accelerated method was the most reproducible with a CV of 6.6%, followed by the EVO method with 12.6%, and the SP3 method with 20.6%. In this study, we found that the AFA accelerated method yielded the highest number of protein IDs and was highly reproducible. Furthermore, we anticipate this optimization method to be utilized in other cohort FFPE proteomic studies.

H. Others

H-008 Comparative Analysis of TMT and DIA Methods in Relative Quantification

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In proteomics, comparing protein expression levels is very important, and this can be achieved in mass spectrometry-based methods by employing either labeled or label-free techniques. Label-free methods have attempted to increase the number of quantitative protein groups using DDA-based 24 fraction Master maps, Match between runs, or boxcar acquisition. However, the number of quantitative protein groups with at least two razor+unique peptides is usually around 5,000.
The DIA method requires a spectral library but offers the advantage of fewer missing values compared to DDA-based approaches. Recent software developments allow for the generation of spectra using machine learning, eliminating the necessity for a spectral library and thus making it more convenient to use.
In labeled methods, TMT is commonly used, allowing for the quantification of up to 18 samples simultaneously. However, it is well-known that ratio compression can cause distortions in the comparison of relative quantities.
PROTAC is a technology that utilizes the intracellular ubiquitin-proteasome system to degrade and remove disease-causing target proteins. When the target protein is linked by PROTAC to an E3 ligase, it is ubiquitinated and then degraded by the proteasome.
We conducted multiple tests on a DIA-based quantitative analysis method and applied it to PROTAC research, and compared the differences in target protein-focused results between TMT-based and DIA-based analyses.
The samples were prepared with three each for the control group and PROTAC. Equal amounts of extracted protein from each sample were used for enzymatic reactions. 5 μg of the peptide was used for quantitative analysis based on DIA, and 120 μg of the peptide was used for quantitative analysis based on TMT 10plex. We used the Orbitrap Exploris 240 (Thermo Scientific). DIA data were identified using DIA-nn, and TMT data were identified using MaxQuant. Quantitative analyses for each dataset were performed using Perseus.
The DIA results show that, although the number of protein groups with at least two razor+unique peptides is slightly lower compared to the TMT results, there is an improvement in the fold-change and p-value of the target protein. As DIA analysis software continues to be developed, it is expected that DIA will be increasingly used in relative quantification analysis in the future.

H-009 Comparison of FASP versus S-Trap digestion and Effective Processing Step merging two methods for Bottom-Up Proteomics

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Bottom-up proteomics depends on efficient protein extraction and digestion method for mass spectrometry analysis. Sodium dodecyl sulfate (SDS) is a most commonly used detergent to effectively investigate various proteins, but it is incompatible with downstream mass spectral analysis. There are several filter-based digestion methods for removal SDS and higher digestion efficiency, and the most popular among them are filter-aided sample preparation (FASP) and suspension trapping (S-Trap). Although there have been numerous attempts to compare these two methods, the direction of merging the MS raw data obtained from both methods has not been considered, mainly due to significant disparities of each data. However, because the data obtained from each digestion method cover different information in the samples, combining the data from both methods can provide us with more comprehensive understanding. This integration not only yields more enhanced data than what is obtained from each method individually but also leads to the discovery of new insights. In this study, we compared two well-established digestion methods: FASP versus S-Trap and devised an effective processing step to merge the data obtained each method. This sample composition, with equal amounts of Escherichia coli protein and twofold differences in human protein across samples, aims to validate each digestion method by assessing consistency in coefficient of variation (CV) for E. coli input and accuracy in reflecting the human input according to the given fold change. E. coli BL21 and HeLa cells were lysed, and protein quantification was conducted. Acetone precipitation was performed, followed by denaturation in the same SDS buffer, and then digestion was carried out by FASP and S-Trap digestion protocol. All peptides were desalted using SDB-RPS Stage Tips and analyzed by Q Exactive HF-X mass spectrometer with data-independent acquisition (DIA) method. We observed the differences between two methods by comparing the number of identified proteins, peptides, and the extent of quantification of proteins. Overall, the number of proteins and peptides identified from S-trap was higher than from FASP, with fewer missed cleavages. We performed Gene Ontology (GO) analysis on the differentially expressed proteins (DEP) between two methods to identify the biological functions and cellular components of DEP. Based on these differences, we devised processing steps to integrate the two methods. Through processing steps such as batch effect removal, MS raw data from two different methods can be combined and analyzed at once. In conclusion, this study provided insights into the differences between the two methods and attempted, for the first time, to merge MS raw data obtained through both methods. We demonstrate that same samples prepared using two different digestion methods can be combined through processing steps, and this could be beneficial for proteomics research.

H. Others

H-010 Comparison of Single-pot, Solid-phase-enhanced Sample Preparation (SP3) and Suspension Trapping (S-Trap) Sample Preparation Methods for Deep Profiling of TMT-Multiplexed Proteome

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The most effective option to maximize efficiency of protein extraction from a biological sample is utilization of ionic detergents. Nonetheless, amphipathic nature of detergents is often incompatible with LC-MS analysis and necessitates an extra removal procedure beforehand, which can have a detrimental effect on the quality of the sample. Commonly used single-reactor methods to address this are SP3 and S-Trap methods, which permit the removal of detergent without additional sample transfer. Here, we compare the performance of two methods by deep profiling TMT-multiplexed sample prepared by each method. Through the use of TMT-based quantitation, we were able to determine the reproducibility with high accuracy. Our results revealed the performances between the methods are nearly identical for spectral count, PSM identification rate, quantifiable protein count per channel, and number of proteins located at plasma membrane - 11.67% and 11.59% for SP3 and S-Trap, respectively. S-Trap contained more missed cleavages than SP3 and consequently generating PSMs with charge greater than 4+ by 2-fold. However, S-Trap deemed more reproducible with 20.2% and 9.04% %CV (with and without outliers, respectively) for median protein abundance per channel in constrast to 29.6% and 14.7% for SP3. Overall, we found S-trap more suitable due to simplicity in method procedure and robustness in the outcome.

H-011 Comprehensive Glycolipid Profiling in Porcine Organs for Xenotransplantation

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Glycolipids ply a critical role in cell recognition and immune responses, which are crucial aspects of xenotransplantation where organ rejection is a significant challenge. Given the high demand and low supply of transplantable organs, xenotransplantation using genetically modified pigs has emerged as an essential alternative. Understanding the glycolipid profiles of pig organs is vital for developing strategies to minimize immune reactions in xenotransplants. To this end, we utilized advanced liquid chromatography-mass spectrometry (LC-MS) techniques for a comprehensive analysis of both acidic and neutral glycolipids in key organs such as the kidney, heart, and pancreas. Using a C18 LC-MS/MS platform, we developed a novel database to identify organ-specific acidic and neutral glycolipids. Our LC-MS analysis revealed differences in ceramide backbones and glycan moieties across these organisms with particular attention to organ-specific variations in glycan moieties linked to Neu5Gc, known for its immunogenic potential. Through multiple reaction monitoring (MRM), we precisely quantified Neu5Gc levels. Our detailed glycolipid analysis identified 62, 41, and 45 acidic glycolipids in the kidneys, hearts, and pancreases, respectively, along with 13, 8, and 9 neutral glycolipids. In all organs, The GD3 structure dominated glycan moiety in more than half of the acidic glycolipids in all examined organs, while ceramide moieties of 40:1, 38:1, and 42:2 was also prevalent. Additionally, we quantified Neu5Gc and Neu5Ac levels and noted that the pancreas has NeuGc levels more than three times higher than Neu5Ac, unlike the other organs. Consequently, this comprehensive analysis underscores the importance of both glycan and ceramide moiety in xenotransplantation organs. Further investigations are in progress to unravel the functions of these specific molecular constituents for a deeper understanding at the molecular level.

H-012 Comprehensive Subproteome Analysis based on Secreted Proteins from ARPE-19

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The subproteome environment refers to a specific organization of proteins associated with particular cellular structures, tissues or pathological states, including secretome, extracellular vesicles, or exosome. It has been emerged as one of the most important fators to discover disease characteristics and appropriate treatments. Among them, secretome associated all the secreted proteins that a cell directly releases into its environment. Furthermore, it also acts a critical role to moderate signaling pathways of diverse diseases such as cancer and chronic diseases. From now on, only 4,045 secreted human proteins were identified in the UniProt database, and it indicated that only about 5% of the human secreted proteomes are identified. Therefore, for in-depth proteomic study, sufficient secretome data were important. In this study, we aim to build secretome database with spectrum library of ARPE-19 cell which is human retinal pigment epithelium cell line and the library is expcted to be utilized within clinical biofluid sample. The ARPE-19 cells were prepared in conditioned media and collected from more than 80% confluency. The collected media was concentrated to obtain serctreted proteins and were tryptic digested by S-trap column. All of the peptides were prepared by HPLC based high-pH fractionation. In order to construct spectrum library, the data dependent analysis (DDA) was performed by Q-Exactive high resolution mass spectrometry and spectrum raw data was searched by Spectronaut 15. Through the library, we were able to identify a larger number of 12,922 peptides and 923 proteins than previous studies. The identified secreted proteins were verified with the secretome prediction database such as SecretomeP, SignalP, or TMHMM. Collectively, the investigation of secreted proteins from ARPE-19 cells and constructed spectrum library would be applied to other source of clinical sample to compare the quality of spectrum data and increase the depth of identified proteins. This research will provide important basic data to understand the pathological mechanisms of retinal diseases and develop new diagnostic and treatment strategies.

H. Others

H-013 Deciphering Structural Diversity and Immunogenicity of Glycans in Transgenic Pig RBCs

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Transgenic pigs are emerging as a new alternative to solving recurring blood shortages by potentially providing compatible blood for human transfusions. For successful xenotransfusion, it is essential to remove pig-specific epitopes such as α-gal, NeuGc, and Sda antigen from the cell surface to prevent hyperacute and acute rejection. While genetic engineering of donor pigs can suppress the expression of these xenoantigens. the glycan biosynthetic process driven by enzymatic reactions unpredictably can increase the expression of pre-existing glycan residues or generate new ones. Previous studies have primarily focused on identifying these known epitopes, resulting in a limited understanding of the structural diversity and immunogenicity of pig-specific glycans, as well as their similarity to human glycans. In this study, we employed Liquid Chromatography/Mass Spectrometry (LC/MS), a powerful tool for glycomic analysis, to characterize glycans in human, pig, and transgenic pig RBCs. We determined the structural diversity of non-human glycans, emphasizing both immunogenic glycans and novel glycans unique to transgenic pigs. We observed that the diversity of immunogenic glycans, which account for more than 90% of total glycans in wild-type pig RBCs, was significantly increased by co-expressing two or more species rather than the three antigens expressed alone. Effective removal of immunogenic antigens in transgenic pig RBCs led to qualitative and quantitative increases in NeuAc-sialylated glycan structures. Furthermore, while human glycan structures often contain blood group H-antigens (Hex-HexNAc-Fucose) on a bisecting backbone, transgenic pigs displayed a distinct pattern with fucose and NeuAc at the termini of glycans from which xenoantigens had been eliminated. Notably, NeuAc was overexpressed in transgenic pigs compared to human RBCs, with specific identification of the tri-NeuAc- sialylated glycan structure, raising concerns about the potential unexpected immune response. Our findings offer new insights into the structural and compositional diversity of immunogenic glycans and suggest potential strategies for mitigating immune rejection in xenotransfusion by precise genetic manipulation of pigs.

H-014 Development of Analysis Method for Isomers of Per- and polyfluoroalkyl Substances (PFAS) using Ion Mobility Mass Spectrometry

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Per- and polyfluoroalkyl substances (PFAS) are compounds used as coating agents in various industries and are pollutants that accumulate in both the environment and humans. Recent studies have demonstrated that exposure to PFAS has adverse effects on the human health. In this study, we developed a method to accurately quantify low levels of PFAS using serum samples exposed to these substances. The PFAS were extracted from serum using protein precipitation method and then PFAS profiling was performed using Ion-mobility high resolution mass spectrometry, TIMS-TOF, coupled with liquid chromatography. The untargeted DDA method of TIMS-TOF successfully detected various types of PFAS compounds. Isomers are typically challenging to separate through liquid chromatography; however, utilizing the ion mobility and Collisional Cross Section (CCS) values of TIMS-TOF enables the detection of peaks with different structures and facilitates the isolation of isomers in shorter run times. The structures of PFOS and PFHxS isomers could be predicted by recognizing them as entirely distinct substances based on CCS values. Furthermore, due to its capability to detect low concentrations of substances, this method is also effective in establishing a threshold for PFAS. These advantages of TIMS-TOF allow for the efficient analysis of PFAS isomers that are typically difficult to separate. The analytical approach employed in this study will significantly contribute to the straightforward quantification and diagnosis of PFAS at low concentrations within the human body.

H-015 Development of Cell surface proteomic analysis using Desthiobiotin-phenol for proximity labeling

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Cell-surface proteins hold significant importance in a multitude of biological processes, such as cell signaling, ion transport, and cell-to-cell communication. As they are located on the surface of the cell and perform critical biological functions, they are considered a prime target for drug development. Therefore, it is essential to develop new proximity labeling techniques that can accurately identify these proteins. We propose a new proximity labeling technique using Desthiobiotin-phenol (DBP) after wheat germ agglutinin – horseradish peroxidase (WGA-HRP) coating. This new technique may contribute to the discovery of new biomarkers and biological metastasis processes. To achieve this, we conducted experiments on HEK293T-rex cells under five different conditions. These were negative, negative with DBP, DBP labeling after WGA-HRP coating, Biotinylation using sulfo-NHS and HRP-TM which express TM protein and label around the protein. We used streptavidin immunoprecipitation to obtain biotinylation and DBP-labeled peptide samples. After we had the peptide samples, we performed liquid chromatography-tandem mass spectrometry (LC-MS/MS) to analyze the peptides using dual online ultrahigh-pressure liquid chromatography (DO-UHPLC) over a 3-hour gradient. The resulting peptide spectrum matches (PSMs) were manually inspected to obtain confident identification of DBP-labeled peptides. Consequently, the method in which DBP labeling after WGA-HRP coating highly enriched protein related to cell surface while the HRP-TM method enriched protein related with endoplasmic reticulum and Golgi. Furthermore, the WGA-HRP method identified more cell-surface proteins than the sulfo-NHS method. These results suggest that using proximity labeling with Desthiobiotin-phenol after WGA-HRP coating on various samples can provide valuable information on cell surface proteins.

H. Others

H-016 Changes of brain glycosylation landscape in Alzheimer's disease (AD) model mouse

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Alzheimer's disease (AD) is a chronic neurodegenerative disorder that seriously endangers the physical and mental health of patients. However, comprehensive molecular-level analyses are still insufficient. The glycosylation patterns of some key AD proteins, such as APP, tau, and transferrin, are altered in AD brains, suggesting a close link between abnormal protein glycosylation and AD. To explore changes in N-glycosylation, nano-LC-MS/MS-based comprehensive glycome analysis was performed for wild-type and 5xFAD AD models in 6-month-old C57BL/6 mice. We investigated altered glycans in five major brain regions, including the cerebral cortex, hippocampus, cerebellum, olfactory bulb, and thalamus. The analysis of N-glycan profiles revealed that the most significant differences in N-glycan expression between AD and control groups were observed in the cerebral cortex. Relative quantitative comparisons were conducted using t-tests, focusing on the expression patterns of N-glycans in various brain regions. From the perspective of the N-glycan pathway, the N-glycans were categorized into high mannose (HM), complex/hybrid (C/H), complex/hybrid-fucosylated (C/H-F), complex/hybrid-fucosyl sialylated (C/H-FS), and complex/hybrid-sialylated (C/H-S) types. Notably, only in the cerebral cortex were changes in N-glycan observed between AD and control groups. The primary N-glycan changes were found in those decorated with fucose, leading to an in-depth analysis focusing on fucosylation differences. Mono- and di-fucosylated neutral N-glycans showed a decreasing trend in AD compared to the control group. In contrast, highly branched N-glycans with a high degree of fucosylation and sialylation exhibited an increasing trend in AD. Given that fucosylation is closely linked with AD, our study underscores the necessity for further investigation into the fucosylation of N-glycans associated with Alzheimer's disease.

H-017 Stability study of angiogenesis-stimulating peptides for infertility treatment of poor ovarian responder targeting ovarian function improvement

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Ovarian stimulation (OS) plays a central role in the success of in vitro fertilization (IVF) cycles. Despite great advances in assisted reproductive technology (ART), the incidence of poor ovarian response (POR) is approximately 9-24% and the proportion continues to increase and is still considered a major challenge in reproductive medicine. Little is known about the potential mechanisms by which the dormant follicles in POR patients are activated. Recently, new treatment strategies are being actively attempted to improve ovarian function by regulating the ovarian microenvironment, such as by promoting ovarian angiogenesis or stem cell activity. In previous study, using computer simulation techniques, we screened two peptides, based on the active site of visfatin with angiogenesis-promoting effects. After performing alanine scanning for stability, we studied the effectiveness of angiogenic activities in human umbilical vein endothelial cells (HUVECs) and response to 17β-Estradiol in MCF-7 cell in vitro. The experimental results showed that the novel peptides promoted endothelial cell migration, tubule formation and microvessel formation and E2 levels in vitro. Our findings suggest that these peptides could be developed into a foundation for developing infertility treatment for POR patients by modulating the critical role of angiogenesis in ovarian function.

Keyword: premature ovarian failure; primordial follicles; angiogenesis; ovarian function; infertility

H-018 Development of routine label-free proteomic pipeline for sample-limited proteomics: Application to spatial proteomics

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Recent advancements in proteomics have made significant strides towards profiling proteomes using smaller sample quantities, even down to individual cells. Obtaining high-quality data from subnanogram (ng) protein samples requires exquisite sensitivity, accuracy, and precision at every stage of the proteomics workflow from sample collection to data analysis. Recently, this has been facilitated by utilizing expensive equipments frequently used in single-cell analysis. However, many proteomics laboratories without access to these instruments face challenges in acquiring stable proteomic data from subnanograms of protein samples, often leading to troubles in understanding the biological context due to the unstable proteomic data. To overcome this limitation, we have established a label-free BoxCar Data-Independent Acquisition (DIA)-based proteomic method without the need for expensive instruments. This method as a pipeline minimizes sample loss by optimizing the entire experimental procedure, from sample preparation to LC-MS analysis. Notably, by utilizing 40 ng of peptide as the starting input for this procedure, equivalent to 200 cells, we quantified approximately 7000 proteins. Based on these inspiring results, we applied this method to spatial proteomics, analyzing regions of interest (ROIs) as small as 0.25 mm2, which comprise an approximately 300 cells, isolated from formalin-fixed, paraffin-embedded (FFPE) breast cancer tissue using spatial laser-assisted cell sorting (SLACS). Through proteomic analyses coupled with bioinformatics, over 2000 proteins were indentified, revealing heterogeneity within the tissue based on their expression levels. This pipeline not only unveils the potential of in-depth proteomics using subnanogram protein samples but also demonstrates its applicability to spatial proteomics in submicroscale tissue pieces, all without requiring expensive instruments commonly used in single-cell analysis. Conclusively, this study highlights universal applicability of our proteomic pipeline enabling in-depth proteomic profiling for sample-limited proteomics.

H. Others

H-019 Development of simple and productive protein extraction methods for proteomic research of human adipose tissue

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White adipose tissue, which plays an important role in whole body energy homeostasis, is the dominant type of adipose tissue, unlike brown adipose tissue. White adipose tissue is also associated with various diseases such as obesity. For this reason, many studies on white adipose tissue have been conducted on proteomic research. But white adipose tissue has a very high proportion of fat, over 50% of the tissue volume, and a protein content of less than 2%, making protein extraction difficult. Therefore, an effective protein extraction method from white adipose tissue is expected to bring more insight into proteomic approaches to discover the pathogenesis of white adipose tissue-related diseases. Acetone and chloroform/methanol protein precipitation methods are mainly used for protein extraction from adipose tissue. However, the number of identified protein of acetone and chloroform/methanol protein precipitation methods in white adipose tissue were not compared. Therefore, we compared lipid removal efficiency, protein digestion yield, and the number of identified protein between two protein precipitation methods. For comparison, human adipose tissue was lysed with lysis buffer using probe sonication. The tissue lysate was centrifuged at 14,000 rpm, RT, 10 min. Protein phase was collected using gel loading tip combined with 1,000 ul tip. Protein solution 100 µl was precipitated using acetone and chloroform/methanol methods. Protein pellet was resuspended with denaturation buffer. Then, to compare lipid removal efficiency, the turbidity of the solution caused by the lipid was compared for the resuspended protein solution. We also compared the digestion yield of two typical digestion methods used in proteomics, S-trap and FASP, for the same amount of protein. Finally, digested peptides are analyzed by mass spectrometer using a data-dependent acquisition method and the number of identified protein in each method was compared. Therefore, we present an effective protein extraction method from white adipose tissue.

H-020 DIA-based quantitative proteomic approach for a comprehensive study of the human lung cancer secretome: A pathway to novel biomarkers

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Lung cancer, a major contributor to global cancer-related mortality, often remains undetected until advanced stages. To address this critical issue, researchers are actively exploring novel biomarkers for early diagnosis. Recent attention has shifted toward analyzing body fluids (such as blood, urine, saliva, and bronchoalveolar lavage fluid) to identify cancer-derived molecules, including potential protein biomarkers. However, the vast dynamic range of secreted proteins in these fluids poses challenges for the comprehensive identification and quantification of low-abundance proteins. The cancer cell secretome, consisting of secreted proteins, holds immense promise for biomarker discovery. Despite previous efforts to decipher the lung cancer secretome, existing studies have been limited by technological constraints, lacking depth and robustness. To overcome these limitations, we present a groundbreaking study utilizing a Data-Independent Acquisition (DIA)-based quantitative proteomic approach. We investigated 15 lung cancer cell lines representing both small and non-small cell types. Remarkably, we identified over 3,000 proteins, establishing the largest lung cancer cell line secretome dataset to date. Bioinformatics analysis confirmed the high reproducibility of our method. Notably, many proteins identified in our study overlapped with secretome datasets from previous research. In addition, functional analysis highlighted enrichment in cancer-related processes, including cell proliferation, cell-matrix adhesion, and angiogenesis. Importantly, this secretome dataset includes nearly all well-known lung cancer tumor antigens and identifies 27 proteins as potential immunotherapy targets based on reviewing current literature. In summary, our comprehensive dataset serves as a valuable resource for future biomarker investigations and hypothesis-driven lung cancer studies. By shedding light on the intricate lung cancer secretome, we pave the way for early detection and improved therapeutic strategies.

H. Others

H-021 Dynamic and Static Changes in Immune Cell Populations in PBMCs During Healthy Aging Observed by Mass Cytometry

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Immune patterns are shaped by genetic and environmental variations. The changes in the immune system associated with healthy aging are significantly influenced by the environmental conditions experienced throughout a person's life. As a result, healthy individuals of the same age may exhibit different immune patterns. Age is a crucial factor as it indicates the duration of exposure to various factors that contribute to accumulating diverse immune features. These variations are observed in healthy blood through aging in different contexts, as seen via cytometry-based approaches. Mass cytometry identifies immune cell types in blood samples using surface and intracellular markers coupled to antibodies conjugated with metal isotopic mass tags. The samples used in this study were peripheral blood mononuclear cells (PBMCs) from 7 healthy individuals aged 22-56 years. Clinical information, including age, gender, BMI, drinking and smoking habits, CBC (Complete Blood Count), and Blood Chemistry Examination, was acquired when the samples were collected. The samples were prepared with a Maxpar® Human PB Phenotyping Panel Kit, 17 Marker (Standard BioTools Inc.), and data were acquired using Helios™ Mass Cytometer (CyTOF, Standard BioTools Inc.). Data were processed using FCS Express 7 (De Novo software). t-SNE was run using default FCS Express parameters for Barnes-Hut Approximation (# of iterations=500, perplexity=30), cofactor=500, and a sample size=30,000 in all analyses. From 11 healthy PBMC samples representing diverse ages, we analyzed a dataset of 1,379,729 live cells that described 14 subpopulations of blood immune cells. The data showed no statistically significant gender differences. However, plasmacytoid dendritic cells demonstrated slightly elevated values in females compared to males, with a p-value of 0.07273using the Wilcoxon Rank-Sum Test. Although this p-value with a sample size of 11 is considered non-significant, the results of each analysis should not be statistically disregarded. CD11c expression was high irrespective of age. In the 30s, some populations revealed different immunological patterns even within the same age group. Consistent with previous studies, the ratio of monocytes in each age group was disproportionate, and the ratios of naïve CD8+ T cells expressing CD45RA decreased with age, with a p-value of 0.108 using Kruskal-Wallis Test. The data also illustrated an age-related increase in the percentage of the NK cell population, with a p-value of 0.04037 obtained using the Kruskal-Wallis test. We demonstrated changes in age-associated subpopulations using specific markers from the antibody panel in CyTOF. Static changes were observed in monocyte populations between age groups, and dynamic changes were noted in naïve CD8+ T cells and NK cells. To accurately identify immune system patterns, large-scale immune profiling should be conducted to collect extensive data. This study represents the beginning of immune profiling of Korean PBMC samples. By monitoring changes in the immune system, it will be possible to ascertain the immune stage of each individual and promote the effective development of personalized medicine.

H-022 Effective sample digestion for bottom-up proteomics

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Proteomics is an increasingly utilized approach to gain insights into biological systems. However, the primary obstacles in proteomic analysis is the lengthy low reproducibility and potential for sample loss and contamination caused by multi-step sample preparation. This study aims to establish effective sample preparation for mass spectrometry-based bottom-up proteomics by comparing and validating three different trypsin digestion methods. the traditional overnight digestion, rapid digestion, and digestion using spin column methods. Proteins from commercially available serum were prepared with triplicates for each method and each sample was analyzed by tandem mass spectrometer equipped with liquid chromatography. The digestion efficiency, the quality of identified and quantified data of three methods were compared. Traditional method requires the longest time (over 16 hr) but incurs the lowest cost. In contrast, the rapid trypsin and digestion spin method can save the time, reducing enzyme incubation to less than one hour but at a cost more than 1.5 times that of the traditional method. The compromised best methodological samle process for the specific research such as clinical research using hundreds of samples that need short sample preparation could improve the effeciveness of cohort study.

H. Others

H-023 Essential Resources for Curated Immune Markers and Antibody Panels in Cytometry Analysis

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Single-cell analysis, evolving from bulk-cell analysis, is utilized across multiomics fields such as genomics, transcriptomics, and proteomics. The immune system, playing a crucial role in these fields, is analyzed at the single-cell level using high-dimensional data from Flow cytometry (FACS, Fluorescence-Activated Cell Sorting) and Mass Cytometry (CyTOF, Cytometry by Time of Flight). The antibody panels used in cytometry analysis should include targeted markers that classify target cells and be designed based on reliable information. Valuable markers with well-estabilished discriminatory power in multiple studies enable the identifdication and characterization of different immune cells. We have developed a database featuring information on cell markers and antibody panels studied to date, accessible via a Python-based Graphical User Interface called ImapDB (Immune cell Marker and Panel Database). The information on cell markers in this program is sourced from cell marker guidebooks produced by biology-related companies and review papers from various journals to ensure verified data. To aid in searching for or customizing a panel that suits specific research needs, the database includes information on commercially available products and panels designed by researchers as detailed in research papers. Our program can display custom panels used in prior studies and commercial panel products, offering a validated approach to target analysis. It also organizes information from previous studies about cell markers and includes curated data on antibody panels and immune cell markers used in mass cytometry and flow cytometry. The current version of the program focuses on the normal states of human immune cell, not disease phenotypes. For instance, if a user wishes to search for markers of naïve CD8+ T cells, they can do so by selecting from three comboboxes in the Immune Cell Marker dialog: first Lymphocyte, then CD8+ T cell, and finally naïve. This program allows users to search for cell surface markers and antibody panels used in diversity research through a comprehensive database, therby enhancing the efficiecy of immune cell assays. We aim to provide a tool that simplifies immune profiling assays, similar to how maps are used to navigate. By serving as a repository of immune information, we anticipate that it will facilitate easy access to essential data for cytometry analysis and support immune profiling analysis.

H-024 Evaluating the Efficiency of Protein Precipitation Across Various Conditions to Optimize Analysis of Specific Proteins

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Introduction
In proteomics, pre-processing proteins through precipitation is essential to purify or concentrate specific proteins. Liquid Chromatography-Mass Spectrometry (LC-MS) is used to analyze complex compounds, determining their molecular composition and concentrations. Although protein precipitation enhanced the analysis suitability, appropriate metrics for evaluating specific proteins are lacking. This study employs LC-MS to optimize the precipitation procedure under various conditions by creating a molecular library.

Method
This study evaluates the efficiency of protein precipitation using Acetone, Ethanol, and Methanol/Chloroform. Proteins extracted from were lysed using 50 mM Tris Buffer (pH 8.0) and sonicated with a Bioruptor Pico (Diagenode). Precipitated proteins, under different conditions were analyzed by on-column injection of 10 µg into LC-MS.

Result
Qualitative and quantitative analyses of proteins precipitated under various conditions revealed significant differences in their molecular compositions. We optimized precipitation under three specific conditions using LC-MS and constructed a library representing the precipitated results.

Conclusion
This study confirms that the composition of protein compounds varies with each precipitation condition. The findings enhance the efficiency of protein precipitation for specific proteins, aiding researchers in proteomics. Additionally, the developed library advanced protein analysis techniques and sets the groundwork for further studies using novel conditions.

H. Others

H-025 Exploring Ganglioside Modulation in Alzheimer's Disease Model Mice

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Alzheimer's disease (AD) is a complex degenerative brain disorder where new insights are crucial for understanding its underlying mechanisms and developing effective treatments. Recent studies have highlighted the potential role of gangliosides that constitute less than 1% of the brain but are critical for nerve growth, neurotransmitter transport, and cell survival. In this study, we not only profiled but also investigated the qualitative and quantitative changes in ganglioside composition across five distinct brain regions in both AD model mice and their normal counterparts using UPLC/Q-TOF-MS. We used 6-month-old mature adult mice, specially 5xFAD models, which exhibit characteristics similar to AD. By leveraging an in-house ganglioside compound database and library program, we characterized approximately 80 ganglioside compounds from five key brain regions. Our findings revealed that the hippocampus exhibited the most pronounced ganglioside profile differences among the examined regions, indicating its potential as a focal point for understanding AD pathophysiology. In particular, significant variations in ganglioside compositions were observed, in the expression levels of GD1 isomers, which correlate with changes in the biosynthetic pathways previously cataloged in our databases. This analysis pinpointed notable quantitative differences in ganglioside distribution across the hippocampus, cortex, olfactory bulb, thalamus, and cerebellum in the AD models. These findings offer fresh insights into the pathophysiology of Alzheimer's disease and suggest new pathways for therapeutic intervention based on ganglioside modulation.

H-026 Exploring hepatotoxicity mechanism induced by time dependent and dose dependent allethrin exposure based on quantitative proteomics

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Allethrin exposure has been associated with immunosuppressive effects, reproductive issues, and carcinogenic effects with long-term exposure. Additionally, it has been linked to various toxicological effects in mammals, including hepatotoxicity. Despite its widespread use, the detailed mechanisms underlying Allethrin-induced liver damage remain poorly understood. Therefore, it is important to identify the basis of hepatotoxic effects, which can provide deeper insights into the correlation between Allethrin and liver damage. By systematically evaluating the proteomic alterations at different time points and doses post-exposure, this study seeks to identify temporal patterns of protein expression changes and uncover the progressive molecular events leading to liver toxicity, employing tandem mass tag labeling combined with nano LC-MS/MS analysis. The study reveals significant alterations in protein expression, with common characteristics among differentially expressed proteins (DEPs) associated with cytosol, cytoplasm, nucleoplasm, RNA binding, and metabolic pathways. Hierarchical clustering analysis identifies clusters of proteins showing regulation increasing from downregulated to upregulated with treatment duration and dose associated with key metabolic pathways. Further analysis of significant DEPs highlights the upregulation of lanosterol 14-alpha demethylase, implicating its role in cholesterol metabolism and potential involvement in Allethrin-induced hepatotoxicity.

H-027 Exploring the relationship between cellular doses of silver ions and multiple protein responses at the single-cell level

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Silver nanoparticles are widely used across various fields, including biomedical applications, due to their unique antimicrobial properties. The high surface area of metal-based nanoparticles enhances the possibility of metal ions being released from them. The cellular accumulation, release, and cytotoxic effects of silver ions have been studied at the bulk level, while studies at the single-cell level have received less attention. Considering the heterogeneous nature of both cells and ion interactions, it is crucial to monitor multiple protein responses to the cellular dose of silver ions at the single-cell level. In this study, we used single-cell mass cytometry to investigate how a monocyte cell line (THP-1) interacts with silver ions. This technique allowed us to measure the cellular dose of silver ions for each cell and analyze the associated intracellular protein responses. We observed dose-dependent cytotoxic effects and specific protein responses, including fluctuating levels of thioredoxin, pERK, cleaved PARP, and cleaved caspase 3, indicating oxidative stress and apoptosis. Our findings revealed that even within a phenotypically homogeneous cell line, individual cells displayed diverse protein response profiles and underwent different biological processes in response to silver ion exposure. This study provides the foundation for future single-cell-based research using a broader range of nanoparticles or ions and cell lines, ultimately contributing to the safe and sustainable use of nanoparticles or ions in biomedical applications.

H. Others

H-028 Extracellular Matrix Proteome of Aging-Specific Fibrotic Niche Cells in Mouse Liver Tissue

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The extracellular matrix (ECM) is a complex network comprising hundreds of proteins, serving not only a structural role in shaping multicellular organisms but also participating in signaling processes. Moreover, the ECM exhibits high tissue specificity and undergoes significant alterations with aging progression. We analyzed the proteome of ECM produced by liver aging-specific fibrotic niche cells in old mice to obtain an age-related proteome profile. Our analysis revealed the identification of 714 quantifiable proteins, with 126 classified as matrisome proteins according to the matrisome database. Notably, proteins significantly upregulated in the ECM of liver aging-specific fibrotic niche cells indicated characteristics reminiscent of ECM formation (Eln, Mfap4, Lox, Tgfb2, Thbs2) and immune cell recruitment (Cxcl12), akin to those originating from fibrotic regions. Our findings suggest that this study may contribute to elucidating heightened fibrotic characteristics associated with the aging process.

KEYWORDS: LC-MS/MS based proteomics, tandem mass tag, senescence, extracellular matrix

H-029 Hepatoprotective effects of empagliflozin in type 2 diabetes db/db mice

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Type 2 diabetes mellitus (T2DM) is considered one of the major risk factors for the faster progression of nonalcoholic fatty liver disease to nonalcoholic steatohepatitis (NASH), advanced fibrosis or cirrhosis. Studies have suggested that empagliflozin (EMPA), a sodium-glucose cotransporter 2 inhibitor and a new type of oral antidiabetic drug, may also have a beneficial effect on NASH in patients with T2DM. However, the mechanisms underlying this effect remain unclear. We aimed to investigate how the EMPA prevent NASH in T2DM mouse model. Diabetes and obese db/db mice were administered EMPA (10 mg/kg/day) daily by oral gavage for 10 weeks. Db/db control mice and C57BLKS/J as wild-type (WT) mice received equal amounts of the vehicle. After treatment, serum was collected to determine ALT and AST levels. Liver triglyceride level was measured. Hepatic fibrosis was analysed using Masson's trichrome stain. In addition, the expression of main target proteins and mRNA genes relating to liver steatosis, fibrosis and inflammation were checked using immunohistochemistry, Western blot and real-time PCR analysis. In this report, we provide preliminary results on the effects of EMPA on diabetic liver disease in db/db mice. Results showed that treated db/db mice with EMPA significantly decreased serum ALT and AST levels, reduced hepatic lipid accumulation via ameliorating CD36 protein expression and triglyceride level. Moreover, EMPA attenuated hepatic fibrotis molecules (collagen 1 and 3 and Smad 2 phosphorylation). Furthermore, EMPA inhibited NF-κB/IL-1β, IL-18 and enhanced IL-10 expression attenuating liver inflammation compared to the control group. These findings indicate that the empagliflozin is a promising agent for the prevention of liver steatosis/fibrosis/inflammation in type 2 diabetic mice. However, future studies will be required to identify the main target of EMPA activity in protecting nonalcoholic fatty liver disease.

Keywords: nonalcoholic fatty liver, SGLT2 inhibitor, steatohepatitis, hepaic fibrosis and inflammation

H-030 THS-1793 protects C2C12 cells from oxidative stress through mitochondrial function regulation

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HS-1793, a novel analogue of resveratrol, was previously determined to be more potent at lower dosages by improving mitochondrial function and increased mitochondrial biogenesis-related proteins. In this study, we focused on targeting the mitochondria to address muscle wasting with HS-1793 by measuring mitochondrial mass, mitochondrial membrane potential (Δψm), reactive oxygen species (ROS) level, and mitochondria biogenesis-regulated genes and proteins to determine the effects on mitochondrial biogenesis upon HS-1793 treatment. Results show HS-1793 reduced ROS generation and regulated mitochondrial function by increasing cellular and mitochondrial ATP synthesis function, stabilizing Δψm and decreasing ROS. More importantly, these dysfunction in these parameters were ameliorated by HS-1793 in a simulated oxidative stress model with tBHP. We also observed increase in mitochondrial mass and upregulation in vital mitochondrial biogenesis-related gene PGC1-α as a response to HS-1793 treatment. Phosphorylation of AKT and mTOR proteins, considered as regulators of skeletal muscle function were also increased during the treatment. HS-1793 also demonstrated protective effects against cisplatin-induced skeletal muscle cell injury by increasing expression of mitochondrial biogenesis-relate markers. Overall, it shows the viability of HS-1793 as a compound that can restore mitochondrial function and render protection in skeletal muscle cells, especially during high oxidative stress levels.

Keywords: reactive oxygen species, mitochondria, resveratrol, skeletal muscle, oxidative stress

H. Others

H-031 Immunoproteasome inhibition induces apoptosis in senescent cells in combination with ABT-737

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Cellular senescence, an irreversible arrest of cell proliferation, naturally occurs during aging process but also can be triggered by various stressors. Senescent cells exert beneficial effects on such as tumor suppression, while their accumulation contributes to aging and age-related diseases, making their removal as an interesting anti-aging approach. Immunoproteasome is a specialized form of the proteasome that is primarily involved in processing antigens for presentation by major histocompatibility complex (MHC) class I molecules. Immunoproteasome substitutes the constitutive proteasome's catalytic β subunits (β1, β2, β5) with the interferon-gamma (IFN-γ) inducible subunits β1i (LMP2), β2i (MECL-1), and β5i (LMP7). We found that following IFN-γ treatment, the level of immunoproteasome subunits is less pronounced in senescent cells when compared to non-senescent cells in several cell types and under various senescence conditions. Additionally, the decrease in constitutive proteasome expression is not much observed in senescent cells compared to non-senescent cells. Interestingly, while the immunoproteasome specific inhibitor ONX-0914 alone does not induce apoptosis in senescent cells, its combinatorial treatment with ABT-737, a potent senolytic agent that selectively inhibits anti-apoptotic Bcl-2 family proteins, more effectively eliminates senescent cells at lower doses than the one for non-senescent cells. These results may suggest that the reduced induction of immunoproteasome in senescent cells may result in higher vulnerability to immunoproteasome inhibition along with ABT-737. Our study underscores the complexity of immunoproteasome regulation during cellular aging and may suggest a potential therapeutic option for seletively targeting senescent cells in age-related pathologies.

Keywords: cellular senescence, immunoproteasome, apoptosis, ONX-0914, senolytic, ABT-737

H-032 Integrative multi-proteomics approach reveals new molecular targets to treat drug-resistant cancer

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Cancer is one of the highest mortality worldwide. Despite therapeutic advances based on understanding molecular mechanisms, resistance to chemo-therapy drugs inevitably occurs, resulting in invasion and metastasis. Overcoming drug resistance is the most important clinical challenge in cancer therapy. To discover new molecular signatures for drug-resistant cancer, we analyzed proteomic profile changes of Drug-1-resistant and Drug-2-resistant cancer using a highly reliable multi-proteomic analysis method. Based on our finding for relatively higher similarities between two drug-resistant proteomes, we further found that commonly changed signaling modules according to AI-based data science analysis. In particular, eight molecular targets in the signaling modules were newly discovered for treating drug resistance by in-depth analysis based on multi-dimensional criteria. Finally, we found X, a known Y inhibitor, suppressed cell proliferation in all cell lines including drug resistant cancer. In mouse xenograft models, X inhibited the growth of tumors made from Cell-A and Cell-A-Drug-1-resistant cell lines by more than 50%.

H-033 Integrative proteomics approach for AD progression in PS19 model mice reveals new signaling modules

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Alzheimer's disease (AD) is a progressive neurodegenerative disease associated with cognitive, functional, and behavioral impairments. It is characterized by the accumulation of extracellular amyloid-β plaques, and formation of intracellular neurofibrillary tangles by accumulating hyperphosphorylated-tau protein. Changes in neurotransmitter function, such as dopamine, are also significant in AD, leading to impaired neurotransmission. While the association between neurotransmitter alteration and AD pathology is recognized, in-depth profiling about neurotransmitters and their related proteomic changes still needs to be studied. Thus, we conducted a study to profile and integrate proteomes and neurotransmitters using seven brain regions of PS19 (Tau P301S) mice according to AD progression. We found notable changes in canonical pathways, including metabolic abnormalities, depending on the brain regions though proteomic analysis. Additionally, alteration of six neurotransmitters were identified under AD progression via profiling neurotransmitters. By integrating the proteomic and neurotransmitters profiles, we found that several specific neurotransmitter-related signaling modules are AD progression-dependently associated to the neurotransmitter changes, especially in the hippocampus and cerebellum. This integrative approach could offer new signaling modules to help understand AD progression.

H. Others

H-034 Is Phylotranscriptomics as Reliable as Phylogenomics?

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Phylogenomics, the study of phylogenetic relationships among taxa based on their genome sequences, has emerged as the preferred phylogenetic method because of the wealth of phylogenetic information contained in genome sequences. Genome sequencing, however, can be prohibitively expensive, especially for taxa with huge genomes and when many taxa need sequencing. Consequently, the less costly phylotranscriptomics has seen an increased use in recent years. Phylotranscriptomics reconstructs phylogenies using DNA sequences derived from transcriptomes, which are often orders of magnitude smaller than genomes. However, in the absence of corresponding genome sequences, comparative analyses of transcriptomes can be challenging and it is unclear whether phylotranscriptomics is as reliable as phylogenomics. Here, we respectively compare the phylogenomic and phylotranscriptomic trees of 22 mammals and 15 plants that have both sequenced nuclear genomes and publicly available RNA sequencing data from multiple tissues. We found that phylotranscriptomic analysis can be sensitive to orthologous gene identification. When a rigorous method for identifying orthologs is employed, phylogenomic and phylotranscriptomic trees are virtually identical to each other, regardless of the tissue of origin of the transcriptomes and whether the same tissue is used across species. These findings validate phylotranscriptomics, brighten its prospect, and illustrate the criticality of reliable ortholog detection in such practices.

H-035 Method Development and Optimization of Single-Cell Proteomics to Study Drug Resistance Mechanism

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Cancer cells have exhibited distinguishing biological features as compared to normal cells and tissues. Since tumors are composed of a diverse collection of cells including cancer cells, fibroblast, endothelial cells among others, it is very important to study their spatial interactions for a fundamental understanding of cancer. Previous studies have repeatedly found that anti-cancer drug resistance is associated with cancer cell clonal evolution and their heterogeneity, leading to research focus on investigating tumors' resistance at the single-cell level using single-cell RNA sequencing technologies. This study focuses on the development of single-cell proteomics technology that can accurately measure changes in protein expression at the single-cell level. Several pre-analytical parameters including lysis, digestion, TMT labeling, and mass spectrometry were tested towards the best practice for the single-cell proteomics. Cancer cells were treated with anti-cancer drugs and single cell proteomes were analyzed at the single cell level. Large variation was observed among these drug-treated cancer cells indicating cancer cells' diverse responses to anti-cancer drug. Therefore, by developing a single-cell proteomics technology and optimizing various parameters that can maximize the depth of protein analysis, we may contribute to a deep understanding of detailed mechanisms of how cancer cell heterogeneity is related to drug resistance.

H-036 NovoCert: Statistical validation of de novo peptide sequencing

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De novo peptide sequencing via tandem mass spectrometry can be useful to discover novel, unknown peptides. Yet, its practical application is hampered by a lack of statistical validation. We introduce NovoCert, a novel method leveraging semi-supervised learning and statistical techniques to validate peptide spectrum matches (PSMs) inferred from de novo sequencing. NovoCert can independently validate high-confidence peptides, reducing reliance on scores from specific de novo peptide sequencing tools. Initially, PSMs were acquired by de novo peptide sequencing tandem mass spectra. The 'exact' group was determined by aligning de novo results with the reference protein sequences. For each PSM in the exact group, we generated a corresponding decoy PSM by de novo sequencing a 'reverse-shifted (RS)' spectrum: (1) a decoy peptide is produced by reversing each target peptide; (2) the target spectrum is converted into a decoy spectrum by adjusting the positions of its fragment ions to align with the computed m/z values expected for the decoy peptide. A 1% false discovery rate (FDR) for the exact group was estimated using Percolator. NovoCert's efficacy was assessed using the ProteomeTools synthetic peptide dataset (PXD004732), employing Comet for database search, and PEAKS, Novor and Casanovo for de novo peptide sequencing. We compared the distributions of XCorr, Delta Mass, Peptide length, Spectral angle, and Delta retention time between results of searching target spectra using DecoyDB (reversed human protein sequences) and results from searching decoy spectra generated by RS method against TargetDB (reference sequences of homo sapiens). The similarities in these distributions support the effectiveness of decoy PSMs generated by de novo sequencing of decoy spectra obtained by applying the RS method. Utilizing PEAKS, NovoCert identified 70% of PSMs (92.2% at the peptide level) within the exact group (2,438,270 total PSMs) at 1% FDR. Novor recognized 67% of PSMs (85.8% at the peptide level) from 1,652,688 total PSMs, and Casanovo discerned 67% (92.7% at the peptide level) of 3,209,531 PSMs, both at 1% FDR. To ascertain these results' reliability, we compared them with the existing FDR estimation method for de novo sequencing, which involves matching the de novo results with a reversed protein sequence DB. This decoy PSM generation method yields very limited decoy counts thus is insufficient for accurate FDR estimation. This is evident because an FDR of 1% encompasses over 99% of target peptides when applied to ProteomeTools dataset, suggesting a high false-positive rate. NovoCert demonstrated its effectiveness by improved identifications in terms of spectral angle, delta retention time, and the scores provided by the de novo peptide sequencing tools.

H-037 Optimization of NanoLC and UPLC Systems for Selected Reaction Monitoring and Validation of Peak Separation in Multiple Heart-Cutting

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Introduction
Quantitation of multiple target proteins across a wide range of samples has been facilitated by Selected Reaction Monitoring (SRM) equipped with Triple Quadrupole Mass Spectrometry (QqQ). Furthermore, NanoLC and UPLC systems have been integrated into a single module. Particularly, SRM analysis, combining very slow flow rates such as hundreds of nanoliters per minute with QqQ, has been applied to discover and validate biomarkers in complex proteome. Recently, a QqQ with an enhanced Electrospray Ionization (ESI) source and NanoLC system has been tested for protein quantitation. A new method employing Multiple Heart-Cutting (MHC) 2D-LC has been developed, where UV-based peaks detected in one-dimensional separation are heart-cut and transferred to a second-dimensional device with different selectivity for further separation.

Method
This study compares the optimization of parameters and spectrum intensity between the UPLC ESI source and the Nano ESI Source of the Agilent 6495C triple quadrupole mass spectrometer by analyzing a Standard Peptide Reference. Peak separation performance of MHC was validated using hyaluronic acid polymers to confirm peak overlap, analyzed with the Agilent 1290 Infinity 2D-LC.

Result
When compared to the UPLC system using the same sample amount, NanoLC showed an improvement in spectrum intensity by over 100 times, highlighting the advantage of detecting trace amounts of samples when combining the Nano ESI Source with the NanoLC system. The peak separation performance of MHC in complex matrices was validated by confirming the separation of hyaluronic acid tetramer [M+H] peaks in a polymer mixture. The potential for improving SRM performance in QqQ instruments equipped with optimized ESI sources and NanoLC systems through stepwise optimization of source-related parameters is demonstrated, evidenced by serial labeling with multiple stable isotopes across 30 different quantities of peptide mixtures.

Conclusion
It is anticipated that the optimization of QqQ using NanoLC within the same system will lead to enhanced SRM results, particularly in the context of biomarker development. This study demonstrated that through the analysis of 30 peptide mixtures, each labeled with multiple stable isotopes and varying in quantities, significant SRM performance improvement is achievable in QqQ instruments equipped with optimized ESI sources and NanoLC systems. Utilizing the excellent separation performance of the MHC system in complex matrices, precise separation of target moleclues from biological samples is expected to be achievable.

H-038 Potential utility of ANOS1 as a prognostic marker associated with tamoxifen resistance in Luminal B breast cancer

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Breast cancer, a major health issue worldwide, is predominantly treated with tamoxifen, a selective estrogen receptor modulator, in hormone receptor-positive cases. Despite its efficacy, tamoxifen resistance emerges as a critical challenge, undermining treatment success and leading to poorer patient outcomes. This study focuses on ANOS1 (KAL1), a gene encoding the glycoprotein anosmin-1, which is implicated in neuronal development but less understood in the context of breast cancer and tamoxifen resistance.

Our research examined ANOS1 expression in breast cancer datasets and cell lines, revealing higher ANOS1 levels in the disease, particularly linked to adverse outcomes in tamoxifen-treated patients. Elevated ANOS1 was also detected in tamoxifen-resistant cell lines, prompting an exploration of its role in cancer progression and resistance mechanisms. The study underscores the potential of ANOS1 as a biomarker for predicting tamoxifen response and as a therapeutic target.

These findings establish a connection between ANOS1 expression and tamoxifen resistance, offering insights into its role in breast cancer. Understanding ANOS1's impact on tamoxifen resistance could enhance treatment personalization and patient outcomes, advocating for further research into its mechanistic influence and clinical relevance.

Keywords: ANOS1; KAL1; breast cancer; tamoxifen resistance; prognosis

H. Others

H-039 Protective effects of β-lapachone on isoproterenol-induced cardiac hypertrophy and dysfunction model

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This study aimed to explore the potential therapeutic benefits of β-Lapachone in a model of hypertrophy and heart failure induced by isoproterenol. Isoproterenol (ISO) was used to induce cardiac hypertrophy and fibrosis in 8 weeks old and male C57BL/6 mice with a dose of 100 mg/kg/day for 2 consecutive weeks after one week of β-Lapachone -pre-treatment with 2 different doses of 20 mg/kg/day and 80 mg/kg/day. β-Lapachone was given during ISO injection and maintained until 15 weeks of age. Body weight was checked every week and cardiac function was evaluated by echocardiography. After the treatment, a blood sample was collected, and followed heart tissue analysis. β-Lapachone treatment effectively improved cardiac function and alleviated hypertrophy and fibrosis in mice with isoproterenol-induced heart failure. Interestingly, blood levels of creatine, AST, and ALT were not affected by isoproterenol or HK660S treatment, though there was a slight decrease in body weight. Additionally, HK660S treatment was associated with enhanced mitochondrial function through the activation of NQO1 and the AMPK/NRF2/HO-1 signaling pathway. Moreover, HK660S treatment attenuated isoproterenol-induced cardiomyocyte apoptosis. Furthermore, β-Lapachone protected against isoproterenol-induced heart failure by activating and phosphorylating the CaMKK2/CaMK4/CREB signaling pathway. In current study demonstrates that β -Lapachone improves cardiac function in ISO-induced heart failure model by reducing cardiac fibrosis and mitochondrial dysfunction via activating NQO1 and CaMKK2/CaMK4/CREB signaling pathway. These findings suggest that β-Lapachone is expected to be a promising agent against cardiac fibrosis and heart failure.

Keywords: β-Lapachone, cardiac hypertrophy, NQO1

H-040 Protein damage drives the cellular senescence by compromising proteostasis

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Cellular senescence is a permanent growth arrest, defined by naturally occurring cell division cessation or triggered by various aging-associated stress. During the aging process, it is known that the proteome integrity, maintained by protein quality control system, is progressively compromised. But there is no conclusive evidence to prove that proteostasis decline by protein damage can be a driver of cellular senescence. Here we propose a new cellular aging model, protein damage-induced cellular senescence (PDIS). We showed that protein damage inducers, including amino acid analogs (AAAs), can induce the cellular aging phenotypes in both non-immortalized and immortalized fibroblast cell lines that were characterized by cell growth arrest, enlarged cell size and senescence-associated autofluorescence or β-galactosidase staining. Cells exposed to AAAs showed increased ubiquitin conjugate levels and decreased autophagic flux, reflecting the cellular protein damage and high burden to the protein quality control system. Transcriptome analysis of IMR-90 fibroblast cells chronically exposed to AAAs indicated that PDIS displays highly distinct gene expression profiles from other known senescence models. In PDIS transcriptome, differentially expressed genes (DEGs) are rarely found in protein quality control pathways, suggesting that PDIS is likely driven by global proteome disintegrity and proteostasis failure. Quantitative mass spectrometry analysis of PDIS cells showed enriched senescence-associated pathways like cell cycle regulations, lysosomal proteins, and ER stress responses, supporting that PDIS is a senescence phenotype. Importantly, protein damage-induced cellular aging process can be partially recovered by the treatment with proteasome activity-enhancing compounds. Moreover, AAA feeding dramatically decreased the lifespan and autophagic activity of flies, and this was also rescued by proteasome activity-enhancing compounds. Our research reveals a direct functional link between protein damage and cellular senescence, which may provide a fundamental basis for understanding cellular aging based on proteostasis.

H-041 proteoCHIP EVO 96 – Evotip PureTM – timsTOF SCP: A powerful Trio for Single Cell Proteomics

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In recent years, Single Cell Proteomics (SCP) has become a meaningful tool to investigate cell heterogeneity. Technical advances both in liquid-chromatography mass spectrometry (LC-MS) and in sample preparation have led to improvements in analysis depth and robustness. Advances in sample preparation were mainly focused on reducing the total reaction volume to a minimum to maximize recovery of peptides for MS analysis and on technology that interfaces sample preparation to LC-MS. Here we present the proteoCHIP EVO 96, a substrate for processing up to 192 single cells in parallel within the cellenONE nL-volume liquid handler and cell isolation robot. The proteoCHIP EVO 96 allows for easy and fast transfer of single cell digests to Evotips PureTM via centrifugation for peptide separation on the Evosep ONE LC system. Based on this workflow, 96 HeLa cells were isolated based on four cell size bins ranging from 18 to 30 µm in diameter. Samples were digested, diluted and directly transferred to Evotips for LC separation with the Whisper 40 SPD method. Samples were analysed on the timsTOF SCP using diaPASEF. On average, 3,500 Protein groups were identified for all cell size groups, with some analytical runs yielding over 4,400 identifications. Principal component analysis shows clear separation of the two smaller and the two bigger cell size bins. Additionally, ANOVA analysis reveals more than 2,500 proteins being significantly regulated between those two clusters. Here we present an end-to-end workflow for SCP sample preparation using the proteoCHIP EVO 96 in combination with Evotips PureTM for separation on the Evosep One and for data acquisition on the timsTOF SCP.

H. Others

H-042 Proteomic analysis of menstrual blood as dried blood spots for discovery of proteins specific to endometriosis and adenomyosis

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With the average age of pregnancy and childbirth increasing, many women are exposed to uterine disorders before giving birth. Endometriosis is a chronic condition occurring in the female reproductive system, typically when the endometrial tissue grows outside the uterus. Adenomyosis is a condition where endometrial cells, which normally line the inside of the uterus, invade the muscular layer of the uterus. These diseases affect fertility; however, many women with these conditions are unaware of the increasing severity of their symptoms. While vaginal ultrasound is commonly used for diagnosis, using menstrual blood for diagnosing uterine disorders presents a promising alternative. Menstrual blood samples can be collected non-invasively and consist of a mixture of endometrial tissues, blood, and secretions that may contain specific markers indicative of uterine disorders, offering potential diagnostic value. In the present study, menstrual blood samples are collected as dried blood spots on protein saver card, facilitating non-invasive collection, transport and storage of the samples from normal controls and patients with endometriosis and adenomyosis We first optimized extraction processes of proteins from the DBS spots on the cards and pursued proteomic analyses using liquid chromatography-tandem mass spectrometry (LC-MS/MS) coupled with tandem mass tag (TMT) labeling in order to find the proteins specific to endometriosis and adenomyosis, respectively.

H-043 Proteomic analysis of periodontal tissues and gingival crevicular fluid to identify potential periodontal disease biomarkers

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Periodontitis, a progressive inflammatory condition affecting periodontal tissues, involves complex interactions influenced by genetic variations in inflammatory proteins such as IL-1 and TNF-alpha. To reveal significant mechanism and protein biomarker related periodontitis, we analyzed periodontal tissue and gingival crevicular fluid (GCF) samples from patients, identifying biomarkers for diagnosing and understanding the pathology of periodontitis.
The sample preparation protocol for periodontal tissues and GCF included focused-ultrasonication, in-solution digestion, and desalting using C18 spin column. The digested peptides were analyzed using by LC-MS equipped an UltiMate 3000 RSLC nano LC system coupled to a Q-Exactive mass spectrometer. Then, data analysis was conducted with both approaches, qualitative and quantitative analysis using by Proteome Discoverer™ software.
In qualitative analysis, we identified 3,803 proteins in periodontal tissues group and 910 proteins in GCF group, respectively. In addition, 775 proteins common between periodontal tissues and GCF, underscoring significant overlaps in inflammatory and immune response pathways. Notably, the proteins like S100A12, CARD19, and APOE were significantly identified, suggesting to key inflammatory processes and potential systemic effects such as cardiovascular and metabolic diseases.
In quantitative analysis between periodontal tissues and GCF group, we perfomed several statistical analyses like Partial Least Squares-Discriminant Analysis (PLS-DA) and differentially expression analysis, and identified differential expression patterns and 1,244 differentially expressed proteins (DEPs, 1,117 upregulation and 127 downregulation) including RPL5, RPL11, RACK1, APOA1, APOE, MPO, and HP. Finally, we revealed that these results reflect distinct physiological and pathological states, with significant proteins suggesting connections to other systemic conditions.
This comprehensive proteomic approach confirms the utility of GCF and tissue analysis in revealing the local and systemic dimensions of periodontitis, proposing novel biomarkers and therapeutic targets that bridge periodontal and systemic health.

H-044 Proteomic analysis of three-dimensional lung spheroids exposed to urban particulate matter over an extended duration

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Urban particulate matter (UPM) poses a significant public health risk, underscoring the need to investigate its long-term cytotoxic effects. We optimized a three-dimensional (3D) spheroid culture platform with human lung fibroblasts to assess the cytotoxic effects of prolonged exposure to UPM. The UPM source in the current study is Certified Reference Material 109-02-004, a standard material developed by the Korea Research Institute of Standards and Science. Over a period of one month, the lung spheroids were exposed to various concentrations of UPM to evaluate cytotoxic responses across different exposure durations and concentrations. Subsequent proteomic analysis using liquid chromatography-tandem mass spectrometry (LC-MS/MS) coupled with tandem mass tag (TMT) labeling was conducted to identify cellular protein changes induced by prolonged UPM exposure, helping to enhance the understanding of the molecular mechanisms associated with the long-term exposure of UPM.

H. Others

H-045 Proteomic Analysis of Tissues in Mice Following Acute Inhalation Exposure to Key Compounds of Cannabis Oil via Vaping

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With the recent surge in addiction issues associated with cannabis oil, there is an increasing need to assess its harmful effects on the human body. However, the exact molecular pathways through which components of cannabis oil trigger pathological conditions in humans are not yet well understood. This study aims to investigate the proteomic changes across various mouse organs, including the brain, lung, and liver, resulting from cannabis oil vaping, and therefore to identify unique protein signatures associated with cannabis oil exposure. In this study, mice were exposed to 50 mg of Δ9-tetrahydrocannabinol (THC) and cannabidiol (CBD), the main bioactive constituents of cannabis oil, respectively. Vaping was performed with a 2-second puff (vaping) followed by a 10-second rest, repeated for 20 sets with a 6-minute break afterward. The procedure was conducted for a total duration of 30 minutes. While control groups were exposed only to the base oil without cannabis components, mice exposed to acute cannabis oil were sacrificed on the days 1 and 14 post-exposure for proteomic analysis of the brain, lung, and liver tissues. Proteomic analyses was are being conducted using liquid chromatography-tandem mass spectrometry (LC-MS/MS) in combination with tandem mass tag (TMT) labeling, which enables simultaneous comparisons of relative protein abundances of multiple samples, in order to find proteins that are specifically changed in response to exposure of THC and CBD in the mouse organs. Identification of proteins with notable changes is expected to illuminate organ-specific biological responses to cannabis oil constituents, providing a crucial foundation for understanding their pathophysiological roles and functional impacts.

H-046 Proteomic Changes in Three Tissues of Mice in Response to Diesel Exhaust Particle Exposures

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Particulate matter (PM) is a mixture of solid particles and liquid droplets in the air, varying in particle size and shape. Among these, PM2.5, with a diameter of less than 2.5 micrometers, can penetrate deep into the lung and even enter the bloodstream. PM has attracted special attention due to its potential to induce various diseases, particularly the confirmed association with cancer. Diesel exhaust particles (DEPs) are a major component of urban air pollution with PM2.5. Exposure to DEP is associated with airway inflammatory responses and respiratory weakening. However, there is a shortage of studies focusing on the precise mechanisms involved. Furthermore, research on in vivo tissues such as the upper respiratory tract is lacking, as is research from a proteomics perspective. In this study, we conducted tandem mass tag (TMT)-based proteomics analysis using mass spectrometry to identify protein changes in three respiratory-related tissues: the larynx, nasal cavity, and tongue, in response to DEP exposure. The mice (n = 3 in each group) were exposed to DEPs at concentrations of 100 μg/m3 for 1 hour per day, 5 days a week, from 4 to 8 weeks in a closed-system chamber attached to an ultrasonic nebulizer with an output of 1 mL/min and particle sizes ranging from 1 to 5 μm. The three tissues were isolated, lysed, and then proteins were precipitated with acetone. Subsequently, protein digestion was performed using the filter-aided sample preparation method, and the resulting peptides were labeled with 8-plex TMT reagents. After desalting the labeled peptides using an OASIS HLB column, reverse-phase high-pH fractionation was conducted using an Agilent 1290 bioinert HPLC system. LC-MS/MS analysis was performed using a Q Exactive HF-X Hybrid Quadrupole-Orbitrap Mass Spectrometer coupled with an Ultimate 3000 RSLCnano system. MS raw files were processed by Proteome Discoverer version 3.0. Statistical analysis was performed using Perseus software version. Using six sets of TMT 8-plex, a total of 8,636, 8,484, and 8,061 proteins were quantified in the larynx, nasal cavity, and tongue tissues, respectively, with the protein and peptide level false discovery rate (FDR) below 1% (FDR Q-value < 0.01). We hypothesized that the changes in protein expression induced by DEP exposure would also depend on the duration of the exposure. A two-way ANOVA in the exposure condition (control vs. DEP) and exposure time (4 weeks vs. 8 weeks). As a result, 202, 465, and 962 proteins were identified as differentially expressed in the larynx, nasal cavity, and tongue in response to DEP (p-value < 0.05). Hierarchical clustering was performed using these proteins, followed by gene ontology analysis for proteins exhibiting similar expression patterns influenced by DEP treatment. Through this analysis, we confirm that proteins related to response to stress, transport, and cellular component organization are differently expressed across the three tissues. Terms related to respiratory and immune responses were prominently identified in the larynx. Nerve-related terms were identified in the nasal cavity and tongue. In particular, the nasal cavity showed terms associated with mitochondrial function, whereas the tongue exhibited numerous terms related to metabolic processes and responses to hypoxia. In summary, proteomics analysis of three respiratory-related tissues in response to DEP exposure helps us understand how it affects the body and its functions.

H. Others

H-047 Proteomic profiling of cysteamine-mediated anti-fibrosis in human kidney tubular epithelial cells

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Cysteamine is a potential inhibitor targeting transglutaminase 2 (TG2), which is an enzyme dependent on a calcium ion that serves multiple functions, including catalyzing protein crosslinks and various post-translational modifications. TG2 overexpression by recombinant transforming growth factor-β (rTGF-β) in kidney tubular epithelial cells (TECs) contributes to kidney failure, enhancing the extracellular matrix (ECM) accumulation and apoptosis. However, cysteamine-mediated specific down-stream regulation of TG2 in kidney fibrosis remain incompletely understood. To mimic fibrotic kidney failure and identify effects of cysteamine, TECs underwent treatment with rTGF-β (2 ng/mL) over either a 24 h or 48 h, alongside cysteamine (2 mM) for TG2 inhibition. Proteins extracted from harvested TECs were digested through s-trap column with Trypsin/LysC enzymes. Subsequently, a comprehensive analysis of the global proteome was conducted using a tandem mass tag 16-plex approach, Peptides were analyzed by the Orbitrap Exploris 480 instrument employing data-dependent acquisition mode. The resulting MS raw data underwent analysis via Protein Discovery software, while the proteome datasets were further analyzed using Perseus software and gene ontology enrichment analysis. In-depth proteome analysis led to the quantification of about 9,000 proteins. Expectedly, inhibition of TG2 decreases the expression of kidney fibrosis markers like fibronectin. Integrated proteomic analyses showed significant differential expressed proteins (DEPs) by cysteamine in the fibrotic kidney model. These DEPs are related to the ECM-receptor interaction, apoptosis, inflammatory response, and oxidative stress that are significantly related with progression of kidney fibrosis. Specifically, upregulated-fibrotic proteins (COL1A1, COL4A1, ITGB6, SV1, and THBS1) and APAF1-mediated apoptosis by rTGF-β were inhibited in the cysteamine-treated TECs. Also, cysteamine mediated alternated expression of TGFβ receptors (TGFBR1 and TGFBR2) and down-regulated SMAD2/3 and C-X-C motif chemokine (CXCL5 and CXCL6), blocking activation of inflammation. In addition, ROS-induced downstream pathway such as MAPK and PI3K-AKT signaling pathways (GRB2, HRAS, NRAS, and AKT3) were suppressed by cysteamine. Collectively, we newly discovered overall cysteamine-mediated alteration of proteins and these data could potentially explain the specific anti-fibrotic effect of cysteamine.

H-048 Quantification of KPC-2 protein in carbapenem-antibiotics resistance strains using LC-MS/MS system

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Introduction:
Carbapenemase-producing Enterobacteriaceae (CPE) resistant to carbapenem class antibiotics are causing serious infection problems all over the world. CPE isolates first need to be identified by MALDI-TOF analysis and to be further confirmed using antimicrobial susceptibility tests (AST) such as MIC and DISK diffusion method. Since the AST tests are indirect and time-consuming, it is required for more direct and rapid tests. Here, as a model test system, we selected a method direct measuring active enzymes (e.g., KPC-2) responsible for bacterial cell's resistance using LC-MS/MS system. We also analyzed how the correlation between the abundance in cells and the AST results in each isolate.

Method:
EUCAST's antibiotic susceptibility testing standards were applied to classify the results as antibiotic-free, antibiotic-susceptible, and resistant. Same number of bacterial cells from clinical isolates were used to LC-MS/MS analysis after normalized by optical density or protein concentrations. The cells were lysis through our OS lysis method and the supernatant fraction was digested with trypsin. Quantification of KPC-2 protein was performed by the LC-MS/MS system with stable-isotope-code heavy standard peptides. Correlation analysis between AST and LC-MS/MS was further performed.

Result:
Three types of antibiotic-resistant strains (antibiotic-free, antibiotic-susceptible, and resistant) classified by EUCAST's testing standards were used for quantitative analysis. Our normalization strategy regarding same number of cells showed more accurate quantitative results in LC-MS/MS system rather than simple colony picking. Direct quantitative analysis revealed a high level of active KPC-2 protein in antibiotic-resistant strains (antibiotic-susceptible and resistant), whereas KPC-2 was not detected in antibiotic-free strains as we expected. In the case of antibiotic-resistant strains, KPC protein expression gradually increased upon the AST level.

Conclusion:
KPC-2 quantification using the LC-MS/MS system may be more direct and effective method than current antibiotic susceptibility test, since it detects the exact enzyme responsible for the antibiotics (i.e. carbapenems). In addition, we expect that the quantity of KPC peptide can be converted to the antibiotic inhibitory concentration in CPE and it suggests drug dosage or administration method according to the results. As another application, we expect that, if we apply this to direct detection of carbapenemases upon MALDI-TOF platform, we can make a more shorten and more affordable assay.

H. Others

H-049 SGLT2 inhibition with empagliflozin attenuates cardiac fibrosis and mitochondrial dysfunction in diabetes mice.

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Diabetic cardiomyopathy (DCM) is one of the major causes of end-stage heart failure (HF), which brings about mortality and morbidity in type 2 diabetes mellitus patients. Empagliflozin (EMPA), a sodium-glucose cotransporter 2 inhibitor (SGLT2i), showed cardioprotective effects against DCM but its molecular mechanism remains unclear. We investigated whether EMPA prevents cardiac dysfunction by reducing fibrosis and mitochondrial dysfuntion in obese db/db mice. Male C57BL/6J mice were set as the control and male db/db mice were treated with or without EMPA (10 mg/kg/day) for up to 10 weeks. Treated db/db mice with EMPA reduced body weight and blood glucose level. EMPA improved both systolic and diastolic functions and reduced myocardial hypertrophy and fibrosis in db/db mice. Especially, EMPA reduced lipid accumulation and improved mitochondrial function via the NRF2/OXPHOS signaling pathway. Our data suggest that EMPA might be of benefit to cardiac fibrosis patients with type 2 diabetes and obesity.

Keywords: diabetic cardiomyopathy, SGLT2 inhibitor, empagliflozin, fibrosis, mitochondria dysfunction

H-050 Statistical Analysis of Daughter Ion Mass Errors in MS2 to Distinguish N-Terminal Methylation from Near-isobaric Modifications

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α-N-terminal methylation is an understudied post-translational modification with presumed functions involving protein-protein and/or protein-DNA interaction. The covalent addition of mono-, di-, trimethyl groups to free α-amino group has proven to be difficult to profile globally by mass spectrometry due to trace endogenous amount and interference from near-isobaric modifications such as Nt-acetylation, even after N-terminome enrichment. To address this problem, we assume that in each MS2 spectrum b-ions will have a different mass error distribution compared to y-ions if the spectrum is falsely assigned to near-isobaric Nt-modification and exploit this statistically to correct the Nt-modification, a procedure we name as mass error test (MET). We confirmed that MET worked well by manual inspection on chemically methylated BSA peptides. MET was further confirmed by comparing physiochemical properties between Nt-methylation and Nt-acetylation in chemically modified cell lysates. We apply MET to potentially Nt-methylated spectra from repurposed dataset and assign correct Nt-modification without further validation experiment. This indicates that MET is a useful tool for detection of Nt-methylated proteins in complex proteomes. We performed MET to deep profiled Nt-enriched sample from our previous work and found a novel Nt-methylation substrate, SSR3, which contains canonical motif and both di- and tri-methylation.

H-051 The Bacteroides fragilis proteome library for deep proteome profiling and comparing between non-enterotoxigenic and enterotoxigenic bacteria

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Bacteroides fragilis (B.fragilis) is a gram-negative, rod-shaped anaerobic bacteria, and it accounts at most 2% of the healthy human colonic microflora. B.fragilis is divided into non-enterotoxigenic B.fragilis (NTBF) and enterotoxigenic B.fragilis (ETBF) depending on a secreted enterotoxin, Bacteroides fragilis toxin (BFT). BFT, zinc-dependent metalloprotease, is a specific virulence factor for ETBF and it is highly associated with acute diarrheal disease, inflammatory bowel disease and colorectal cancer. ETBF forms biofilm for colonisation in human large intestine and produce toxin which can lead to chronic intestinal inflammation. But intracellular processing of inflammatory reactions by ETBF have not been discovered yet. Also, proteomic profiling of Bacteroides fragilis and between NTBF and ETBF was not fully understand were proceeded. Therefore, comprehensive proteome analysis of Bacteroides fragilis is important to identify BFT-mediated diseases. In this study, for NTBF and ETBF proteome library, 3-replicate of ETBF and NTBF bacterial pellet were obtained. These samples were lysed with 4% SDS-DTT-Tris buffer and the amount of extracted protein was determined by Compatible BCA assay. After acetone precipitation, bacterial proteins were digested by filter aided sample preparation method. Peptides were desalted using OASIS HLB cartridges and analysed by Q-Exactive plus mass spectrometer with data-dependent acquisition method. For comparison of overall proteins between ETBF and NTBF, peptides were analysed by Q-Exactive plus mass spectrometer with data-independent acquisition method. In this study, about 20,000 peptides and 3,000 proteins of ETBF and NTBF were identified. These proteins were expressed in ETBF and NTBF, first confirmed through proteome analysis. Also, to elucidate the differential expression of proteins between ETBF and NTBF, we performed bioinformatics analysis for comparing two different strains based on B.fragilis genomic data and proteome library. There were significant differences between proteomes of ETBF and NTBF. Collectively, we established comprehensive proteome libraries for both ETBF and NTBF, which can be useful method for in-depth protein profiling of ETBF and NTBF.

H. Others

H-052 USP14 regulates TDP-43-induced toxicity by influencing its stability and localization

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Amyotrophic lateral sclerosis (ALS) is one of the fatal neurodegenerative diseases characterized by the progressive loss of motor neurons in spinal cord and motor cortex. Transactive response DNA-binding protein 43 (TDP-43)-induced neurotoxicity is currently well recognized as a main contributor to the ALS pathology, and the aberrant cytoplasmic accumulation of TDP-43 has also been observed in other neurodegenerative diseases, such as frontotemporal lobar degeneration (FTLD) and Alzheimer's disease (AD). Therefore, prevention of TDP-43 accumulation coupled with its clearance is emerging as ALS-associated therapeutic intervention. Recent studies revealed that the ubiquitin-proteasome system (UPS) plays a pivotal role in removal of TDP-43 through protein quality control. Deubiquitinating enzymes (DUBs), the key components of the UPS, have also been implicated in TDP-43 proteinopathies. However, the underlying mechanisms of TDP-43 regulation by DUBs in ALS pathology remain elusive. In this study, we investigated USP14 – a key proteasomal DUB, as a crucial regulator for TDP-43 stability and localization. Overexpression of USP14 showed a remarkable accumulation of TDP-43, while inhibition or depletion of USP14 significantly reduced TDP-43 levels. In addition, we revealed that USP14 regulated TDP-43 mislocalization to cytosol, which may modulate the TDP-43-induced neurotoxicity. Moreover, USP14 colocalized, interacted and deubiquitinated TDP-43 on protetasome via K48-linked ubiquitin chains. USP14 knockdown also performed a noticeable protective effect in TDP-43-induced model. Thus, our study may define USP14 as potential drug targets for the therapeutic treatment of TDP-43 proteinopathies based on protein degradation machinery.

* Keywords: Amyotrophic lateral sclerosis, USP14, TDP-43, ubiquitin-proteasome system, TDP-43 proteinopathy, neurodegenerative diseases

H-053 USP14 Regulates the Aggrephagy by Facilitating the Aggresome Formation under Proteotoxic Stress

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Ubiquitin-specific protease 14 (USP14) is one of the major proteasome-associated deubiquitinating enzymes (DUB) that is known to regulate proteasomal degradation by checking proteasome activity while hindering the degradation of ubiquitinated proteins by eliminating ubiquitin chains from its substrates. Recent studies showed that in addition to proteasome regulation, USP14 is also involved in regulating autophagy, which may initiate when proteasome function is inhibited. Here we report that USP14 regulates aggresome formation in the aggrephagy pathway under proteotoxic stress. USP14 localizes in the aggresomes containing misfolded proteins when the proteasome is inhibited. Exogenous expression of USP14 in USP14 knockout cells shows an increase in the number and size of ubiquitin-positive aggresomes. By contrast, cells lacking USP14 fail to eliminate misfolded protein aggregates by aggresome, and exhibit increased susceptibility to stress caused by misfolded proteins, ultimately leading to apoptosis. Interestingly, the same behaviour is also demonstrated by catalytically inactive USP14, indicating that regulation of aggresome relies on the non-catalytic role of USP14. Since the aggresome is an essential transit centre for aggrephagy critical for cell survival in proteinopathies, USP14 may serve as a vital player in managing misfolded protein-induced stress at the junction of proteasome and aggrephagy pathways.

H-054 Evaluation of the serum proteome using column chromatography for depletion of abundant proteins

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Serum is the body fluid most frequently used in biomarker discovery. Due to its wide dynamic range of protein concentrations among biological samples, novel and creative separation techniques have been required. Albumin, the most abundant serum protein, and a dozen other abundant proteins contribute to more than 95% of the serum protein content. Therefore, the removal of these highly abundant proteins, such as albumin and immunoglobulins, is necessary as the first step in proteome analysis for biomarker discovery. The Multiple Affinity Removal System (MARS) column was employed to remove 14 highly abundant proteins in a single analysis and was applied to over 300 serum samples. We developed a screening method to assess the suitability of serum samples for proteome analysis in biomarker discovery.

H. Others

H-055 Global proteome analysis of optogenetic C. elegans ALS model

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Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease that causes damage to motor neurons in the central nervous system. TDP-43 is a key protein implicated in the onset and progression of ALS, as overexpression and aggregation of this protein is observed in over 90% of ALS patients. Aggregation of TDP-43 occurs due to its mislocalization in the cytosol, which leads to liquid-liquid phase separation and neuronal damage. While human ALS models are limited, C. elegans is a useful platform for studying neuronal changes due to its well-characterized nervous system and genomic homology to human. The aim of this study was to identify differentially expressed proteins in an optogenetic C. elegans ALS model, where TDP-43 fused to Cry2olig is designed to form oligomers and aggregates upon exposure to blue light. For proteome quantification, LC-MS analysis was performed using an EASY-nLC 1000 HPLC coupled to the Orbitrap Eclipse Tribrid mass spectrometer. As a result, a total of 8,027 proteins were identified. We observed 16 up-regulated and 24 down-regulated proteins in the optogenetic C. elegans ALS model. Functional annotation analysis of these proteins using DAVID revealed that 28 proteins were related to phosphorylation. Especially, 10 proteins were annotated to be located in the cytoplasm and involved in metabolic and modification process. Through KEGG and Reactome pathway analysis, up-regulation of motor proteins CENPE, TUBB3, and MYL2, and down-regulation of ubiquitylation proteins USP7, UBA1, and PEX14 were confirmed during the initial stage of TDP-43 aggregation. In addition, we observed up-regulation of HSPB1 and TUBB3, and down-regulation of RLIM, UBA1, and UBP7, which is in line with the previous observation in the ALS patients and mouse models. Through further functional validation of the differentially expressed proteins, we expect to provide a clear snapshot of the biological processes altered in the early stages of ALS.

H-056 Optimization of Data-Independent Acquisition Mass Spectrometry coupled with FAIMS interface for Highly Quantitative Proteomic Analysis

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DIA (Data Independent Acquisition) analysis is utilized to accurately identify and quantitatively measure proteins and other biological molecules in large-scale biological samples. It provides a more comprehensive and in-depth analysis, offering rapid and precise information in complex biological systems. Moreover, the FAIMS (high-field asymmetric waveform ion mobility spectrometer) interface reduces chemical noise and improves signal-to-noise ratios, particularly benefiting proteomics. To enhance the utility of DIA in the diagnostic field, we aimed to couple it with a FAIMS interface to maximize protein identification in human serum and optimize quantitative comparative analysis. Initially, we validated the effectiveness of DIA analysis before applying it to human serum and conducted CV (compensation voltage) optimization. Subsequently, we confirmed whether these results were consistent in human serum and compared the quantitative results of DIA-FAIMS with or without depletion of high abundant proteins. By integrating multiple results, we established an optimized method for human serum analysis that maximizes effectiveness.

H-057 Unravelling the Consequences of Sam2 Knockout through Integrative Proteomics and Metabolomics Analysis in Autism Spectrum Disorders

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Introduction
S-Adenosylmethionine (Sam2) plays a pivotal role in various cellular processes. Deficiencies in Sam2 have been linked to behavioural abnormalities, such as fear and anxiety responses in evolutionarily conserved models, including zebrafish and mice. These models are associated with heterogeneous neurodevelopmental diseases like autism spectrum disorders (ASD). This research seeks to deepen our understanding of the molecular changes resulting from Sam2 knockout (KO) by employing proteomics and metabolomics approaches using liquid chromatography-mass spectrometry (LC-MS) and identifying novel potential biomarkers.
Methods
We acquired three samples each of Sam2 KO and wild type (WT), totalling six mouse blood plasma samples. Initially, metabolomics analysis was performed using LC-QTOF MS on crude samples. Samples were processed using Top14 high abundance protein depletion columns, followed by BCA analysis for protein quantification. Subsequent steps included protein digestion and peptide collection, which were then desalted offline and dried using a speed vacuum. Quantitative proteomics analysis was performed separately via LC Orbitrap MS. Data analysis involved bioinformatics techniques such as PCA, OPLS-DA, Volcano plots, and Venn diagrams to differentiate between KO and WT in both proteins and metabolites. Statistical analysis was conducted in R using the Student's t-test for proteins and the Mann-Whitney U test for metabolites, with significance set at P-value less than 0.05. Integrative analysis of identified proteins and metabolites was also performed to detect any significantly metabolic pathways
Results
We identified 102 significantly altered peptides, of which 39 were upregulated and 63 were downregulated. GO enrichment analysis identified two significant proteins, Protein A and Protein B, where Protein A was upregulated and Protein B was downregulated. Untargeted metabolomics identified 15 significant metabolites; 9 were upregulated and 6 were downregulated. Integrated analysis of identified proteins and metabolites unveiled two significantly dysregulated metabolic pathways.
Conclusion
This comparative study investigates the impact of Sam2 gene knockout in a mouse model, providing significant insights into the intricate relationship among genetic modifications, metabolic pathways, and the onset of autism spectrum disorder (ASD). Through the integration of LC-MS proteomics and metabolomics analyses, notable alterations in proteins and metabolites were identified, enriching our understanding of the Glycolysis/Gluconeogenesis and Glycerophospholipid metabolism pathways. This comprehensive analysis contributes to a deeper comprehension of the interplay between genetic factors and metabolic dysregulation, setting a foundation for future investigations and therapeutic interventions in ASD research.

H-058 The automated sample preparation to increase reproducibility for enhancing proteome analysis

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In proteomics research, effective desalting of samples is crucial, especially following serum depletion using MARS column chromatography and subsequent sample preparation steps involving protein denaturation, reduction, alkylation, and digestion. These processes introduce high salt concentrations that can impede further analyses. To overcome this obstacle, we developed an automated desalting protocol utilizing the Tecan Resolvex A200 system. Optimized for high-throughput analysis, this protocol ensures sample integrity while minimizing preparation time and contamination risks. The system demonstrates excellent reproducibility and simplifies sample handling. The achieved recovery rates were 55.9% to 76.6% for tryptic peptides in bovine serum albumin (BSA) and 55.6% to 78.2% for depleted human serum using the MARS column. Notably, the Tecan Resolvex A200 system efficiently processes up to 96 samples in approximately 20 minutes, demonstrating increasing advantages as sample numbers scale up. Implementing this automated desalting protocol could significantly enhance the throughput and accuracy of proteomic studies, promising more robust and reproducible research outcomes in proteomics.

H. Others

H-059 A Platform Development for Engineering Antibody Production: Integrating Mass Spectrometry-Based De Novo Sequencing with a Specific Bacterial Expression System for Monoclonal Antibodies

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Introduction: The production of monoclonal antibodies (mAbs) is a key area of biotechnological innovation, driving advances in therapeutics and diagnostics. Producing mAbs in large quantities using bacterial systems is challenging but essential for achieving high sensitivity and low costs in diagnostics. We present a novel approach to enhance mAb properties and production.

Methods: We combinesd mass spectrometry-based de novo sequencing with a specific bacterial expression system. With the sequence information, we constructed a recombinant DNA format that allows the variable region (VR) of mAb`s light and heavy chains to be replaced as a gene cassette. And, we cloned the mAb gene into plasmid DNA, then the recombinant plasmid harvouring mAb gene was transformed in the specific bacteria system for mAb protein expression. A specific bacterial system that facilitates proper folding and disulfide bridge formation in cytosolic compartment was used for our mAb expression.

Results: The optimal mAb was selected from multi-dimensional screenings. The mAb was fully sequenced at the single amino acid level using multiple proteolysis and high-resolution mass spectrometry (100% coverage). The expressed protein from the recombinant DNA was confirmed through various biochemical assays, including mass spectrometry.

Conclusion: we expect that our platform for mAb production is cost-effective and promising for accelerating mAb modifications, leading to improved efficacy and specificity.

H-060 Proteomic landscaping of high-grade serous ovarian carcinoma identifies stearoyl-CoA desaturase 5 as a potential predictive biomarker for poly(ADP-ribose) polymerase inhibitor response

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High-grade serous ovarian carcinoma (HGSOC) has shown high recurrence and mortality rates despite treatment comprising cytoreductive surgery and chemotherapy. However, the recent introduction of poly(ADP-ribose) polymerase inhibitors (PARPi) in the management of HGSOC significantly improved the prognosis. As more HGSOC patients receive PARPi treatment, accurately predicting the treatment response becomes crucial. In this study, we first establish the proteomic landscape of ovarian cancer according to PARPi response. Protein signatures were validated in the independent cohort, and preliminarily investigated their potential roles in PARPi resistance. To identify protein signatures associated with PARPi resistance, we conducted an in-depth quantitative proteomic analysis of formalin-fixed paraffin-embedded (FFPE) cancer tissues (n = 24) from platinum-sensitive recurrent HGSOC patients using a tandem mass tag (TMT) 10-plex quantification strategy. According to PARPi treatment response, a total of 187 differentially expressed proteins (DEPs) were identified ($p < 0.05$, $|\text{fold-change}| > 1.2$), with 54 and 133 exhibiting higher expression in the good and poor response groups, respectively. Next, we conducted feature selection with leave-one-out cross-validation to identify protein signatures that stratify the response to PARPi. Machine learning algorithms yielded lists of top proteins selected by each respective algorithm. Among these, we identified three common proteins: stearoyl-CoA desaturase 5 (SCD5), NUDT4 and GRP107 which were upregulated in the poor response group. For validation, we performed data-independent acquisition-based proteomics using an independent set of FFPE tissues (three good and seven poor responders). The SCD5 showed high predictive performance in identifying poor responders (area under the receiver operating characteristic curve, 0.952). From a clinical viewpoint, for HGSOC patients who are identified as at high risk of showing poor response to PARPi maintenance therapy via pretreatment proteomics analyses, physicians may deter the use of PARPi, maximize the effect of PARPi combined with other therapy, or recommend intensive surveillance during PARPi maintenance to detect recurrence earlier. Our findings broaden biological insights into predicting PARPi responses.

H. Others

H-061 LC-MS analysis to identify the drug binding of antibody-drug conjugates

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An ADC (antibody-drug conjugate) is a drug in which a cytotoxic small molecule drug (payload, a cytotoxic anticancer agent) is covalently conjugated to an antibody that binds to a specific target antigen on the surface of cancer cells through a linker. It is one of the next-generation anticancer drugs that can increase treatment effectiveness and minimize side effects by selectively targeting only cancer cells using the target selectivity of the antibody and the strong killing activity of the drug. The ADC binds to the target antigen of cancer cells by an antibody and is internalized into the cell. The antibody is degraded in the lysosome, a cell organelle, and the drug is released into the cytoplasm and kills the cancer cell by acting on the drug's target. Stable ADC binding is closely related to the reproducibility of the drug effect, so it needs to be precisely controlled. The ADC used in this study was produced by treating IgG1 with TCEP to break the interchain disulfide bond and then conjugating the drug to cysteine of IgG1. The produced ADC was analyzed by LC-MS/MS to confirm the binding of the drug to site specific cysteine in IgG1. We validated by MS spectrum that the drug had successfully bound to the predicted site on IgG1.

H-062 Proteomic biomarker profiling for discovering muscle, bone, and fat cross talk from elite athletes

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The health benefits of physical activity are widely acknowledged and impact various organ systems as promoting overall resilience and longevity. Following the research of discovering signaling molecules that are released in response to exercise from various organs such as skeletal muscle, heart, neurons, and adipose tissue exerting their effects through endocrine, paracrine, or autocrine pathways, numerous functional molecules caused by physical activity have been identified. However, controversial issues persist inconsistencies between responses to acute and chronic exercise, and differences observed between human and animal exercise models. Therefore, to understand the precise molecular mechanisms responsible for these benefits, and provide robust ground for future advancements in exercise biomarker research, well-structured biomarker profiling analysis with controlled sampling methods from elite athletes is essential. In this study, we identified various proteomic biomarkers from elite athletes and the suggested proteins showed promising relationships with enhancing cardiovascular, metabolic immune, and neurological health, suggesting potential applications in treating cardiovascular disease, type 2 diabetes, obesity, and promoting healthy aging. In addition, this study emphasizes the significance of using a meticulous sampling strategy to yield precise findings on functional molecules triggered by exercise.

H-063 Exercise alleviates cisplatin-induced toxicity in the hippocampus of mice by inhibiting neuroinflammation and improving synaptic plasticity

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Chemotherapy-induced cognitive impairment is recognized as the most typical symptom in patients with cancer that occurs during and following the chemotherapy treatment. Recently many studies focused on pharmaceutical strategies to control the chemotherapy side effects, however it is far from satisfactory. There may be a need for more effective treatment options. The aim of this study was to investigate the protective effect of exercise on cisplatin-induced neurotoxicity. Eight-week-old C57BL6 mice were separated into three group: normal control (CON, n=8); cisplatin injection control (Cis-CON, n=8); cisplatin with aerobic exercise (Cis-EXE, n=8). Cisplatin was administered intraperitoneally at a dose of 3.5 mg/kg/day. The Cis-EXE group exercise by treadmill running (14~16m/min for 45 min daily, 3 times/week) for 12 weeks. Compared to the CON group, the cisplatin injection groups showed significant decrease in body weight and food intake, indicating successful induction of cisplatin toxicity. The Cis-CON group showed significantly increased levels of pro-inflammatory cytokines including IL-6, IL-1β, and TNF-α in the hippocampus, while the Cis-EXE group was significantly decreased in the expression of IL-6, IL-1β, and TNF-α. In addition, compared to the CON group, the levels of synapse-related proteins including synapsin-1 and -2 were significantly reduced in the Cis-CON group, and there was a significant difference between the Cis-CON and Cis-EXE groups. Antioxidant and apoptosis factors were significantly improved in the Cis-EXE group compared with the Cis-CON group. This study suggest that exercise could be meaningful approach to prevent or improve cisplatin-induced cognitive impairment.

Keywords: Cisplatin; Hippocampus; Exercise; Inflammation; Synaptic plasticity

H. Others

H-064 Age and ethnic-driven molecular and clinical disparity of East Asian breast cancers

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Breast Cancer (BC) is a complex disease with profound genomic aberrations. However, the underlying molecular disparity influenced by age and ethnicity remains elusive. In this study, we aimed to investigate the molecular properties of 843 primary and metastatic BC patients enrolled in the K-MASTER program. By categorizing patients into two distinct age subgroups, we explored their unique molecular profiles. Additionally, we leveraged large-scale genomic data from the TCGA and MSK-IMPACT studies to examine the ethnic-driven molecular and clinical disparities. The K-MASTER patients were mainly comprised of triple-negative breast cancer (TNBC) and HER2-positive tumors, while the TCGA and MSK-IMPACT cohorts exhibited a predominance of hormone receptor-positive (HR+) subtype. We observed a high prevalence of PI3KCA mutations in K-MASTER HER2+ tumors, particularly in older patients. Moreover, we identified increased mutation rates in DNA damage response molecules, including ARID1A, MSH6, and MLH1. Importantly, GATA3 mutations were less frequently observed in East Asian patients, which correlated with poor clinical outcomes. In addition to characterizing the molecular disparities, we developed a gradient-boosting multivariable model to identify a new molecular signature that could predict the therapeutic response to platinum-based chemotherapy. Our findings collectively provide unprecedented insights into the significance of age and ethnicity on the molecular and clinical characteristics of BC patients.

H-065 Comparative Proteomics Analysis of Elite Athletes Across Various Sporting Disciplines

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Regular physical activity typically causes significant transformations across different bodily tissues and organs. Similarly, elite athletes experience substantial alterations in proteins due to their rigorous training regimens. As a result, the adoption of 'Omics' techniques in the domain of sports science is increasingly prevalent. These approaches offer valuable insights into how exercise type, intensity, and duration influence phenotypic alterations. In this study, our aim is to analyze the blood proteomic profiles of elite. We conducted proteomic analysis on serum samples collected from 320 elite athletes representing 32 different sports disciplines, as well as 10 control subjects. The athletes participated in elite sports events and tested negative for doping in anti-doping laboratories. We employed a data-independent analysis (DIA)-MS approach to perform the proteomic profiling. The variances in proteomic levels between each sports discipline and the control group were evaluated using the student t-test. Differentially expressed proteins were verified using the parallel reaction monitoring (PRM)-MS approach. Using data-independent analysis (DIA), we were able to quantify an average of over 400 proteins based on an in-house library containing 3,802 proteins. Furthermore, we developed an 18-minute analysis method capable of analyzing 80 samples per day. We identified 147 differentially expressed proteins when comparing 32 sports disciplines to the control (Benjamini-Hochberg FDR < 0.01). Of these, 45 proteins were verified through PRM-based target analysis. The exercise-related biomarkers discovered are expected to contribute to the development of systematic training programs for athletes and personalized physical management in the future.

Keyword: Sportsomics, proteomics, LC-MS, high-throughput sample preparation, DIA, PRM

H-066 Unraveling KLF4-Mediated Cellular Diversity Using Single-Cell Proteomics

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KLF4, a member of the Krüppel-like family of transcription factors, is known to regulate expression of numerous target genes involved in various cellular processes. While its role as a key regulator of pluripotency in stem cells is well-established, however, the functional significance of KLF4 in non-pluripotent cell types remains poorly understood. In this study, we aim to investigate the impact of KLF4 expression on human cancer cell (HeLa) and kidney cell (HEK-293) using single-cell proteomics. KLF4 overexpression was achieved through transfection of a KLF4-EGFP fusion vector, and its expression was confirmed via fluorescence microscopy. Additionally, KLF4-expressing single cells were isolated using the CellenONE system, enabling real-time monitoring of their expression through the presence of fluorescent signal. We found that considerable heterogeneity in the expression and subcellular localization of KLF4 across individual cells, suggesting that its expression is modulated by distinct intra- and extracellular signaling cues in a cell-to-cell manner. Notably, cells exhibiting elevated KLF4 expression displayed upregulation of housekeeping proteins, such as ribosomal proteins (RPL11, RPL18). This increase in housekeeping protein levels was associated with an increase in cell size, potentially reflecting enhanced translational capacity induced by KLF4 overexpression. The observed cellular heterogeneity in KLF4 expression patterns and the concomitant changes in the expression of fundamental cellular machinery highlight the complex regulatory roles of this transcription factor in modulating cellular phenotypes.

H. Others

H-067 Data Collection, Preprocessing, and Quality Control of Time-Series Multi-Modal Dataset from SARS-CoV-2 Infected Patients

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To understand dynamic immune responses after SARS-CoV-2 infection, leveraging multimodal data—such as clinical information, medical images, and omics—can significantly aid in managing current and emerging virus-mediated pandemics. In this study, a time-series multimodal dataset from 559 COVID-19 patients and 161 healthy controls was collected. The dataset included clinical information, medical images (lung CT and chest X-ray), and multi-omics data, such as single-cell RNA sequencing, TCR and BCR sequencing at both single-cell and bulk resolution, and Luminex-based profiling for 191 cytokines from the initial COVID-19 diagnosis to discharge. Additionally, whole genome sequencing (WGS), HLA typing, laboratory testing, and COVID-19 viral genome sequencing were obtained at the initial diagnosis. All datasets are publicly available via the National Biobank of Korea (NBK) under prior approval. Preprocessing steps include handling missing values, outlier removal, filtering out low-quality data, normalization, and batch effect correction, highlighting the importance of quality control. We expect hat these comprehensive multimodal datasets from COVID-19 patients can enhance our understanding of the biological interactions essential to virus-mediated infections and support the development of new techniques for COVID-19 diagnosis and treatment.

H-068 Impact of CCNH Deletion on Homologous Recombination Deficiency and Chemotherapy Sensitivity in High-Grade Serous Ovarian Cancer

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High-grade serous ovarian cancer (HGSOC) constitutes the predominant subtype of ovarian cancer, characterized by marked chromosomal aberration and TP53 mutation. Initial treatment typically involves chemotherapy, with homologous recombination deficiency (HRD) serving as a predictive marker for therapeutic response. However, the scarcity of reliable HRD markers beyond BRCA1/2 mutations necessitates exploration. Herein, we present a comprehensive multi-omics analysis encompassing whole-exome sequencing (WES) and RNA sequencing of 158 HGSOC patients. Our investigation reveals CCNH deletion as a notable determinant significantly influencing HRD score variations, surpassing the impact of other genomic alterations. Validation using The Cancer Genome Atlas (TCGA) data corroborates the association between CCNH alteration, HRD score discrepancies, and survival outcomes. Notably, consistent elevation of HRD scores in concordance with CCNH deletion is observed across diverse tumor regions within individual patients. Elastic-Net model based on transcriptome unveils the association between CCNH expression and HRD, with BRCA1 expression. Furthermore, functional enrichment analysis demonstrates the activation of chemotherapy-sensitive pathways upon CCNH deletion, suggesting its potential as a biomarker for treatment stratification. Further mechanistic exploration elucidates the interaction between CCNH and CDK7, a pivotal regulator of transcription and DNA repair. Modulation of CDK7 activity, either through inhibitor treatment or in synergy with CCNH, results in the downregulation of diverse DNA repair pathways. Consequently, the identification of CCNH deletion as a determinant of HRD in HGSOC underscores its utility in identifying patients with proficient BRCA wild-type chemotherapy responses, with potential implications for enhancing treatment efficacy, particularly in combination with CDK7 inhibitors.

H-069 The features of formalin-fixed, paraffin-embedded (FFPE) tissue for comparative proteome analysis

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Formalin-fixed, paraffin-embedded (FFPE) tissue is a sample that is widely used in clinical research, and has been mainly used in immune-based experiments such as IHC. Recently, many efforts have been made to extract proteins from FFPE and use them in mass spectrometry-based proteomic studies. In recent years, various protein extraction methods for proteomic studies have been suggested, but the number and quantitative characteristics of proteins found differ according to the method. The protein extraction method using the recently published Adaptive-Focused Acoustics (AFA) ultrasonication method discovered the number of proteins similar to flash frozen samples compared to the previously proposed methods. Although, protein modification caused by fixation remains a challenge in quantitative analysis using FFPE samples. We extracted proteins from breast cancer FFPE samples by the method using the recently proposed AFA, discovered proteome through mass spectrometry, and discovered various modifications using open search to review protein modifications. Through this information, modifications to be considered in the analysis of proteome in FFPE samples and properties of proteome are suggested to be helpful in clinical proteomic studies using FFPE. This study was supported by a grant from the National Research Foundation (NRF) funded by the Korean government (MSIT) (NRF-2019M3E5D3073567).

H. Others

H-070 Cardiac-specific Cereblon Deletion Promotes Cardiac Hypertrophy, Senescence, and Fibrosis through AMPK Hyperactivation

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Cereblon (CRBN), a substrate receptor of the E3 ubiquitin ligase complex, has been known to regulate AMPK activation negatively. Previous studies showed that cardiac-specific CRBN knockout (CRBN cKO) mice in 8 weeks exhibit enhanced cardiac contractility through calcium signaling. However, it is unclear whether sustained cardiac-specific depletion of CRBN continues to be a beneficial effect. In the present study, we investigated cardiac-specific CRBN knockout mice (αMHC-Cre+/-; CRBNflox/flox) at 37 weeks. CRBN cKO mice in 37 weeks showed cardiac hypertrophy and cardiac dysfunction in the heart. Notably, CRBN cKO mice in 37 weeks induce alterations in lipid metabolism by AMPK hyperactivation in the heart, leading to impaired mitochondrial function. Moreover, we revealed that sustained CRBN cKO in 37 weeks mice increased cardiac senescence and fibrosis. In conclusion, we suggest that CRBN is essential for metabolic homeostasis in the heart.

H-071 Proteomic analysis of SARS-CoV-2 variants infected cells reveals molecular insights into COVID-19 pathogenesis

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COVID-19 has emerged as a severe infectious disease with significant impacts on global public health and the economy. COVID-19, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), gives rise to variants through genetic mutations, some of which exhibit increased transmissibility, immune evasion, and reduced vaccine efficacy. Notably, the Delta and Omicron variants have caused global concern due to their high transmissibility and resistance to existing defenses. However, these variants have not yet been comprehensively characterized through proteomic analysis. In this study, we infected human Calu-3 cells with nine different COVID-19 variants and performed proteomic analyses to identify and quantify variant-specific proteins. Using two biological replicates and one pooled sample, we obtained triplicate samples, which were then divided into two batches for labeling with TMT 18-plex. Subsequent identification and quantification were conducted. As a result, we identified 10,203 and 10,110 proteins in each batch, respectively, with no empty channels remaining unquantified. Notably, we compared the protein quantification data of the BA.1 variant, which is included in the Omicron lineage, with previously known GO analysis results of SARS-CoV-2 Omicron miRNA target genes. We found overlapping terms in the GO analysis between proteins downregulated in BA.1 compared to the mock and the miRNA target genes. These findings provide insights into the proteomic changes associated with different SARS-CoV-2 variants and underscore the importance of integrating multi-omics data to understand the molecular mechanisms underpinning COVID-19 pathogenesis. Further studies are needed to validate these observations and explore their potential implications for therapeutic strategies.

H-072 Ultrasensitive and robust profiling of metabolome for spatiotemporal mapping of protein-metabolite interaction

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A single -ome does not function individually; rather, each -ome induces biological phenomena through close interactions with others. Contemporary, interact-omics studies are elucidating the intricate relationships between various -omes, particularly between proteins and metabolites such as co-enzymes. In order to unveil their interactions, it is essential to construct individual analysis platforms; however, unlike the well-developed proteomic analysis platforms that use highly sensitive nano-liquid chromatography, the development of low-flow metabolomic analysis systems remains insufficient due to their molecular properties. As a demand, the objective of this study was to lower the flow rate to a minimum threshold while maintaining the retention time (RT) reproducibility that is significant in metabolite analysis. We screened flow rate within the range of 200 μL/min to 450 nL/min while choosing the inner diameter of columns to keep linear velocities. Through this study, we have discovered an RP particle with low back pressure, allowing us to create long 50 cm columns, which exhibit the narrowest LC peak width (FWHM) and excellent capability to separate nearly identical isomers. Additionally, due to the high carbon percentage of the particle, we were also able to effectively retain hydrophilic metabolites with phosphate derivatives. Through meticulously controlled column QC procedures, we have standardized reproducible custom home-packed columns with retention time variability below 0.5% CV, enabling us to secure a library spectrum for 200 chemical compounds. Consequently, using flow rate of 1 μL/min, we achieve 100 average fold signal enhancements for 45 metabolite derivatives compared to conventional flowrate (200 μL/min). In conclusion, this study achieved comparable sensitivity to proteomics analysis platforms using nano-flow LC.

H. Others

H-073 Multiplexed bulk and single-cell proteomic analysis of nitric oxide effects on neuroblastoma

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Nitric oxide (NO) can exhibit dichotomous roles in cancers by interacting with other free radicals and molecules to generate genotoxic metabolites or induce post-translational modifications termed S-nitrosylation. The conflicting tumouricidal and tumour-promoting effects of NO are dependent on its concentration, source of synthesis, and cancer type. Previous investigations have demonstrated the effectiveness of utilizing NO as an anti-tumour therapy for neuroblastoma. However, the proteome-wide dynamics and cellular signaling overview upon NO exposure remain unexplored. Utilizing multiplexed LC-MS/MS and single-cell proteomics, we quantitated the changes in protein expression in a neuroblastoma cell line and the heterogeneity within their population in response to NO in a concentration-dependent manner.

We first assessed the differentially expressed proteins and their concomitant alterations in signaling pathways using bulk proteomics. Neuroblastoma SK-N-SH cells exposed to an NO donor (DETA NONO-ate) at concentrations of 0 μM, 10 μM, and 100 μM were digested by trypsin and labelled with TMT-10plex and subjected to offline fractionation into 24 fractions prior to analysis by QE Orbitrap. As a result, each treatment exhibited distinct proteome landscapes. Notably, treatment with 100 μM NO decreased the levels of proteins associated with cell apoptosis, IL2/STAT5, and mTORC1 signaling. To further scrutinize the subpopulations of neuroblastoma cells and their responses to the same treatment, we conducted single-cell proteomics experiments. Cells were isolated on the ProteoCHIP and processed by CellenOne machine and labelled with TMT-16plex. As expected, heterogeneous protein levels were observed even within the same conditions, including control samples. Preliminary data also showed that cells treated with 1 mM NO exhibited increased cell diameter compared to other treatments and transformed into a more spherical shape. Notably, previous studies suggest that mammalian cell size is controlled by the mTOR pathway, prompting us to perform further analysis to elucidate this aspect. However, no correlation was found between cell size and protein expression patterns. Our study suggests that the regulation of the neuroblastoma proteome changes significantly depending on NO levels. Our data also indicated that mTOR signaling was suppressed at high concentrations of NO donor. On the other hand, single-cell proteomics revealed cellular heterogeneity in neuroblastoma, which may harbor different responses to NO flux.

In conclusion, our study demonstrates that neuroblastoma's proteome regulation is highly dependent on NO levels. The data indicated suppression of mTOR signaling at high NO donor concentrations. Single-cell proteomics revealed cellular heterogeneity in neuroblastoma, suggesting that different subpopulations may respond differently to NO. Nonetheless, as single-cell proteomics is still in its nascent stage, inferring explicit biological pathways remains challenging. Further investigations are necessary to explore the subpopulations of neuroblastoma based on their proteome and their respective responses to NO, thus tailoring appropriate synergistic treatments

H-074 Multiplexed quantitative proteomics reveals proteomic alterations in two rodent traumatic brain injury models

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Traumatic brain injury (TBI) is accompanied by a disorder in cognitive, emotional, and behavioral functions without notable surface wounds after a physical impact on the head. Every year, 1.5 million people experience TBI from traffic accidents, falls, violence, etc. Currently, TBIs are classified into mild, moderate, and severe grades according to the consciousness status assessed by the Glasgow Coma Scale. In the case of mild TBI, injury in cranial nerves recovered after sufficient rest, however, it is difficult to expect a natural recovery in TBIs above the moderate level. Thus, molecular components involved in the recovery are deemed to be significantly different between mild TBI and moderate-to-severe TBI. Yet, studies that investigate what molecules or pathways are relevant to the recovery phase of TBI are rare, especially for proteomic approaches. In this study, the prefrontal cortex tissues of mice undergone mild/severe TBI were collected over periods of recovery, then their proteome was analyzed using LC-MS/MS. We performed quantitative analysis using 10-plex TMT, identifying about 300 proteins of which expression levels were temporally altered. We also discovered molecular pathways activated or inhibited under TBI conditions through bioinformatics analysis. As a result, we found that the sirtuin signaling pathway was gradually inactivated over the phase of recovery and that the proteins involved in the lipid metabolism were stably up-regulated till two weeks from TBI. These findings will help to uncover molecular mechanisms leading to recovery from TBI. Furthermore, the biomarkers that play an important role in the recovery of mild TBI can be used as a target of drug intervention intended for severe TBI patients.

H-075 HK660S (β-lapachone) Ameliorates Diabetic Cardiomyopathy by Enhancing Mitochondrial fuction and energy expenditure through activation of NQO1

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Objectives: This study aimed to investigate the effects of the drug HK660S, a natural compound and newly developed β-lapachone analogue that increases mitochondrial function, mitochondrial intergrity, energy expenditure and antioxidant capacity in various tissues, on DCM and explore its underlying mechanisms. Methods: To evaluate the effect of HK660S on mitochondrial function in the in vitro ***treatment:*** mitochondrial isolation and fiber permeabilization from heart tissue of C57BL/6 eight weeks male mice and four types of intact cell A549, HepG2, AC16, H9C2 were treated with different dose of drug to measure mitochondrial respiratory capacity then checked and compaired the NQO1 expression in different cell types and heart tissue. In the in vivo treatment: C57BL/6 seven weeks male mice were used high-fat diet (HFD) and low- dose streptozotocin 40 mg/kg/day (STZ) to established diabetic mouse modal. Mice were randomly divided into six groups: WT (wild type mice), WT+HK80, DM (diabetic mouse), DM+HK20, DM+HK80 and DM+Met (mice were fed HK660S 20mg/kg/day (HK20), 80mg/kg/day (HK80) and Metformin 200 mg/kg/day (Met) combined with HFD treatment for 10 weeks, STZ intraperitoneal (ip) injection for 5 consecutive days after 2 weeks of treatment to study the protective effect of HK660S on DCM.
Results: In the in vitro treatment, HK660S ameliorates mitochondrial function. In the in vivo models, HK660S-treated DM mice reduced heart and body weight, food and water intake, blood glucose levels and HbA1C, enhanced cardiac function and Insulin resistance (IR). In addition, treated-DM mice showed increased mitochondrial respiratory capacity and calorimetries. Furthermore, HK660S reversed the decrease in phosphorylated AMPK expression, altered the levels of proteins associated with mitochondrial biogenesis, increased mitochondrial content and antioxidant ability.
Conclusions: These data suggest that HK660S is at least partially cardioprotective. Mitochondrial function is important for cardiomyocyte survival in DCM, and mitochondrial dysfunction is a critical factor in DCM. HK660S restored impaired mitochondrial biogenesis and improved mitochondrial activity, content, and function in cardiomyocytes. Therefore, HK660S has the potential to serve as a novel therapeutic agent for the prevention and treatment of DCM.
Key word: Diabetic Mellitus, Diabetic Cardiomyopathy, Mitochondria function, Beta- lapachone

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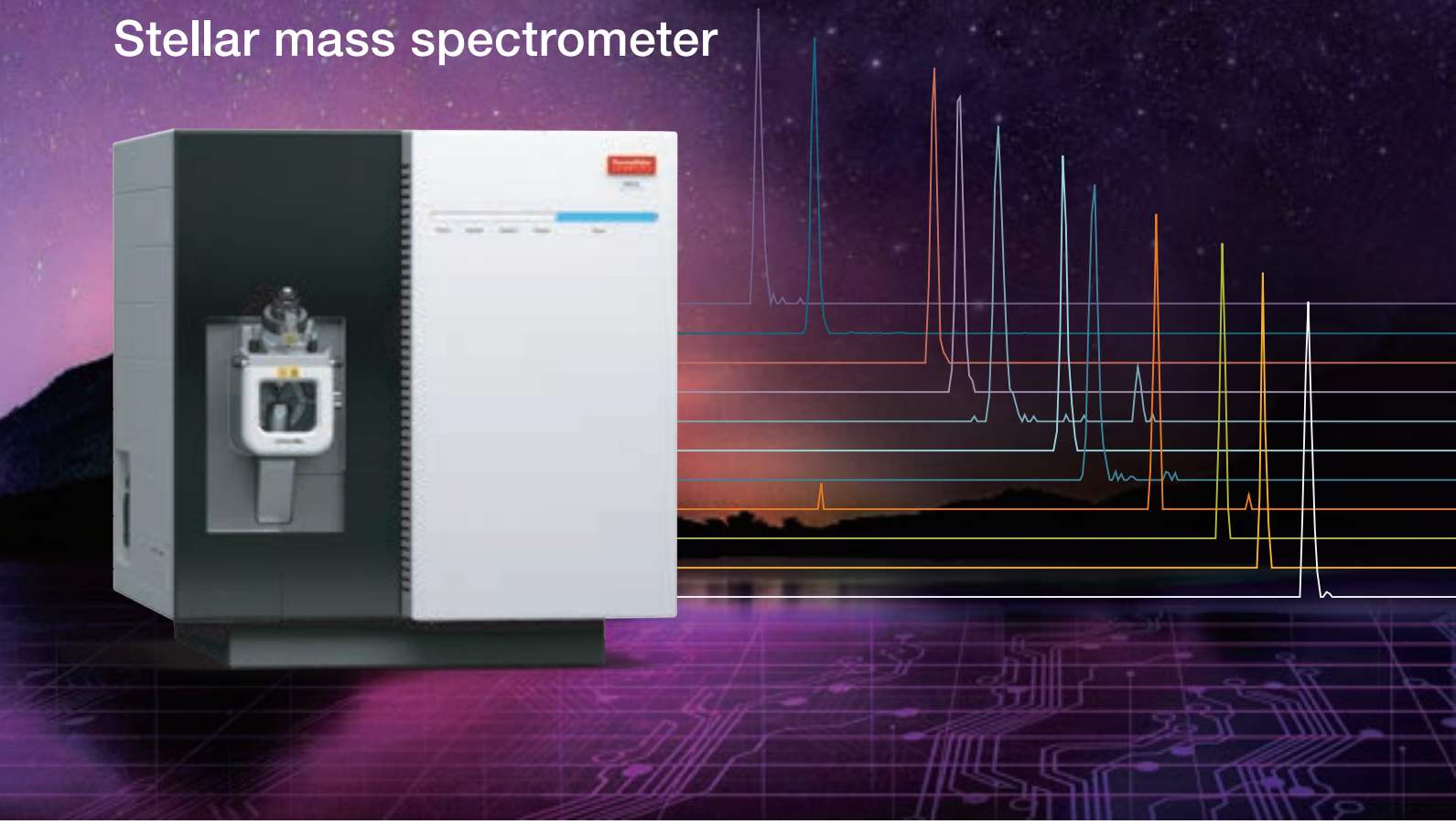
Stellar mass spectrometer



Moving biomarker candidates from discovery to validation more efficiently, confidently, and at lower cost requires breakthroughs in sensitivity, specificity, and throughput at scale. Designed to verify more biomarkers in less time, the Thermo Scientific™ Stellar™ mass spectrometer introduces revolutionary technology combined with robust quantitation. Enhance certainty with the specificity of rapid full-scan MS^n acquisition and detection with single ion sensitivity. Streamline high-throughput generation of high-quality data with automated multi-analyte method creation and dynamic instrument control. Compared to other technologies, the instrument delivers 10X sensitivity when targeting 5X more analytes using faster gradients, accelerating the transition from research to clinical trials.

Learn more at **thermofisher.com/stellar**

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