2024 NYKB
16th ANNUAL CONFERENCE

NEW YORK KOREAN BIOLOGISTS NYKB

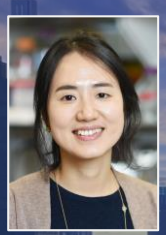
Saturday, April 27th, 9:30 AM – 6:00 PM

Cornell Belfer Research Building 3rd floor
(413 E 69th St, New York, NY, 10021)

Keynote Speakers

Hyung Don Ryoo, Ph.D.
Professor, NYU Grossman School of Medicine

Integrated Stress Response in Drosophila



Minah Kim, Ph.D.
Assistant Professor, Columbia University Irving Medical Center

Unveiling the Role of Angiopoietin-2 in Tumor Immune Evasion and Metastasis

Luncheon Seminar

Richard Somberg, Ph.D.
Director, Promega

Latest tools for cell health, cytokine detection, protein dynamics, and bioluminescence imaging.

NYKB Fellowship Session

NYKB General Session

Meal & Networking

Korean-American Scientists and Engineers Association KSEA · YUHAN · KUSCO KOREA - U.S. SCIENCE COOPERATION CENTER · SK life science a subsidiary of SK biopharmaceuticals · GC Biopharma · COSMAX THE SCIENCE OF KOREAN BEAUTY · SNU MEDICINE · ORUM THERAPEUTICS · MEDICAL STRATEGY GROUP · KASBP 재미한인제약인협회 · LG Chem Life Sciences Company · Promega · PROUD who I am PRESENTABLE how I want to be PROFESSIONAL what I do

Program Preview

NEW YORK KOREAN BIOLOGISTS NYKB

08:30 – 09:30	Registration
09:30 – 09:35	Welcoming
09:35 – 09:40	Congratulatory Remark
09:40 – 10:30	Keynote Lecture I (Prof. Hyung Don Ryoo)
10:30 – 11:40	NYKB Award Fellowship Session I
11:40 – 12:00	Group Photo & Coffee Break
12:10 – 13:00	Luncheon Seminar (Dr. Richard Somberg - Promega)
13:00 – 14:10	NYKB Award Fellowship Session II
14:10 – 15:00	Keynote Lecture II (Prof. Minah Kim)
15:00 – 15:20	Coffee Break
15:20 – 17:40	NYKB Award General Session
17:40 – 18:00	Award & Closing Ceremony
18:00 – 20:00	Dinner & Networking

Contents

Welcome Remark

안녕하세요, NYKB 회원 여러분.

2023-2024 NYKB 회장을 맡고 있는 장민정입니다.

2024년도 제 16회 NYKB 연례 학회에 참석해 주셔서 감사드립니다. 회원분들의 많은 관심과 적극적인 참여 덕분에 NYKB가 더욱 성장해 나가고 있습니다.

이번 NYKB 연례 학회에도 훌륭한 연구를 수행하고 계신 교수님들을 초청 연사로 모시게 되어 큰 영광이며, NYKB fellowship 수상자 분들과 general session 발표자로 선정되신 연구자 분들께도 축하와 감사의 말씀을 전합니다. 뉴욕 근처 지역의 한인 생명과학자들이 한 자리에 모이는 NYKB 연례 학회를 통해 연구에 도움이 될 새로운 아이디어를 얻고, 동료 연구자들과 교류하며 개인적, 학문적으로 더욱 발전하는 계기가 되기를 희망합니다. 점심 시간에는 Promega의 발표가 준비 되어 있으며, 저녁에는 식사와 함께 네트워킹 시간을 충분히 마련하였으니, 참석하셔서 유익한 시간 보내시길 바랍니다.

NYKB의 다양한 행사들은 미국과 한국의 여러 학술 단체, 기업, 개인의 지원을 받아 진행되고 있습니다. 이번 학회에 대한 지원과 응원을 아끼지 않으신 모든 후원자 분들께 깊은 감사의 말씀을 드립니다. 또한, 이번 행사를 준비하시느라 수고하신 NYKB 임원진과 학회 참석자 여러분께도 감사의 인사를 전합니다.

봄의 따뜻함과 함께, 여러분의 연구와 개인적인 삶에서도 큰 성과가 있기를 기원합니다. 앞으로도 저희 NYKB의 활동에 많은 관심과 참여를 부탁드리며, 항상 건강하시길 바랍니다.

제 15대 NYKB 회장 장민정 올림

2023-2024 NYKB Executives

Title	Name	한글 이름	Affiliation
President	MinJung Jang	장민정	Weill Cornell Medicine
Vice President	You-Kyung Lee	이유경	Icahn School of Medicine at Mount Sinai
Vice President	Jung Seung Nam	남정승	Columbia University Medical Center
Secretary-General Director	Jiyeon Hwang	황지연	Albert Einstein College of Medicine
Accounting Director	Yeonoh Shin	신연오	Columbia University Medical Center
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Administration Director	Jiyun Shin	신지윤	New York University
Planning Director	Kwanghoon Park	박광훈	The Rockefeller University
Academic Director	Garam Choi	최가람	Rutgers, the State University of New Jersey
Social Director	Hyomin Jeong	정효민	Stony Brook University
Managing Director	Jin Gyu Cheong	정진규	Weill Cornell Medicine
Advisor	Seungsoo Kim	김승수	Columbia University Medical Center
Advisor	Chul-Hee Lee	이철희	Weill Cornell Medicine

NYKB Affiliations

Albert Einstein College of Medicine

1953년에 Yeshiva University 소속의 의과대학으로 설립된 Albert Einstein Collge of Medicine (AECOM)은 현재 Montefiore Medical Center 소속의 의과대학으로, 미국 뉴욕주 브롱스(Bronx, NY)에 위치해 있습니다. 저희 학교는 1800명 이상의 교수진이 재직 중이며 지역 내에서 가장 큰 Medical research center로 미국 medical school 내에서도 high rank에 소속되어 있습니다.

Columbia University

300년 가까이 오래된 역사와 전통을 자랑하는 컬럼비아 대학교는 101명의 노벨상 수상자를 배출할 정도로 아이비리그에서도 손에 꼽히는 명문 대학교로서 학부생 및 대학원생 27,000명 규모의 대학교입니다. 특히 맨해튼 168가에 위치한 컬럼비아 대학 병원 캠퍼스는 다양한 의생명 관련 연구소로 구성되어 있습니다.

Cold Spring Harbor Laboratory

콜드스프링하버연구소(CSHL)는 미국 뉴욕주 롱아일랜드에 위치한 세계 최정상급 생명과학 연구소이자 교육기관입니다. 분자생물학, 유전학, 그리고 암연구에서 세계 선두를 달리고 있으며, 네이쳐(Nature)지에 의해 연구기관 세계 1위 기관으로 평가받은 바가 있습니다. DNA 이중나선 구조를 발견한 제임스 왓슨 박사를 필두로 8명의 노벨 생리의학상 수상자를 배출하였으며, 매년 전 세계 1만여명의 과학자들이 콜드스프링하버 연구소의 회의나 강좌에 참여하기 위해 방문합니다. 현재도 생물학 분야의 가장 도전적인 문제들을 해결하기 위한 연구가 활발히 진행중입니다.

Icahn School of Medicine at Mount Sinai

1963년에 설립된 Icahn School of Medicine at Mount Sinai (ISMMS)는 Upper East Side, Manhattan에 위치하고 있는 의과대학입니다. 전체 8개의 병원 캠퍼스 (Mount Sinai Beth Israel, Mount Sinai Brooklyn, Mount Sinai Hospital (including Kravis Children's Hospital), Mount Sinai Queens, Mount Sinai Morningside (formerly Mount Sinai St. Luke's), Mount Sinai West (formerly Mount Sinai Roosevelt), New York Eye and Ear Infirmary of Mount Sinai, and Mount Sinai South Nassau)로 구성되어 있으며 5천 명 이상의 교수진이 재직, 2천 명의 학생, 전공의, 전임의가 재학, 임상 수련 중에 있습니다.

Memorial Sloan Kettering Cancer Center

1884 년 뉴욕 맨해튼에 설립된 "메모리얼 슬론-케터링 암센터 (Memorial Sloan Kettering Cancer Center; MSKCC)"는 세계 최고 암 병원/연구소로, 임상-기초 연구진의 긴밀한 협업시스템을 바탕으로, 암 정복을 위한 실제적인 연구가 이뤄지고 있는 곳입니다. 현재 30여 명의 한인 생명과학자가 MSKCC에서 열정적으로 연구를 수행하고 있습니다.

New York University

New York University (NYU)는 1831년에 설립된 사립학교로서 현재 학부과정과 대학원 과정을 교육하는 종합대학이며, 의과대학인 NYU Langone Medical Center, NYU college of Dental, 그리고 Nathan Klein Institute 연구소가 NYU 소속으로 되어있습니다. 각각의 캠퍼스에 위치한 많은 실험실은 bioinformatics부터 neuroscience까지 매우 다양한 연구 분야에 집중하고 있으며, 이를 바탕으로 기초 및 임상 연구가 활발하게 이루어지고 있는 교육/연구 기관입니다.

Rockefeller University

1901년 뉴욕 맨해튼에 설립된 생명과학 연구중심대학으로 모토는 "Science for the benefit of humanity (인류의 이익을 위한 과학)"입니다. 현재까지 26명의 노벨상 수상자를 배출한 저명한 학교이며, 2023년 기준 5명의 노벨상 수상자와 31명의 HHMI investigator들을 포함한 71명의 교수진이 다양한 생명과학 분야의 실험실을 운영 중입니다. 학부 과정은 없으며, 270명의 대학원생, 210명의 박사후 연구원, 그리고 1,325명의 스태프들이 활발하게 생명과학 분야의 연구를 위해 협력 중입니다. 한인 과학자 수는 약 10명으로 NYKB를 통하여 다른 기관의 한인 과학자들과 긴밀하게 교류하고 있습니다.

Rutgers University

1766년 설립된 뉴저지 주립 럿거스 대학교(Rutgers, the State University of New Jersey)는 미국 동부의 뉴저지 주에 위치하고 있고, 250년의 오랜 역사를 지닌 뉴저지 주에서는 가장 규모가 큰 연구 중심의 공립 종합대학입니다. 지리적으로는 New Brunswick, Newark, Camden에 위치한 총 세 개의 캠퍼스로 조직되어 있으며, 북미 지역의 주요 상위권 연구 중심 종합대학교의 연맹체인 AAU(Association of American Universities)에 속해 있습니다. 현재 300여 개의 연구센터 및 기관에서 다양한 연구가 활발하게 이루어지고 있습니다.

Stony Brook University

Stony Brook University는 뉴욕 주립 대학교 소속의 연구 중심 플래그쉽 대학이며 롱 아일랜드에 위치해있습니다. Basic science는 물론 biomedical engineering, bioinformatics, neuroscience 등 다양한 분야에서 매년 혁신적인 연구를 내고 있습니다. Brookhaven National Laboratory, Cold Spring Harbor Laboratory, 그리고 뉴욕주에 위치한 다양한 기관과 기업들과 연구 교류를 맺고 있으며, 미국 전국 순위에 들어가는 스토니 브룩 병원과 협력하에 의학 관련 연구가 특히 활발하게 진행되고 있습니다.

Weill Cornell Medicine

1898년 뉴욕 Manhattan, Upper East Side에 설립된 Weill Cornell Medicine 은 아이비리그 대학 중 하나인 Cornell University 소속 의과 대학으로 미국에서 가장 저명한 의과 대학 중 한 곳입니다. 저희 학교는 약 2000여 명의 Academic staff 들과 400명 이상의 학생들이 U.S. News & World Report's "Best Medical Schools: Research" 랭킹에서 11위를 차지할 만큼 다양한 연구 분야에서 기초 및 임상 연구를 진행하고 있습니다. 또한, 저희 학교는 현재 약 35명 이상의 많은 한인 과학자 분들이 활발하게 연구활동을 하고 있습니다.

NYKB Conference Sponsors

NEW YORK KOREAN BIOLOGISTS NYKB

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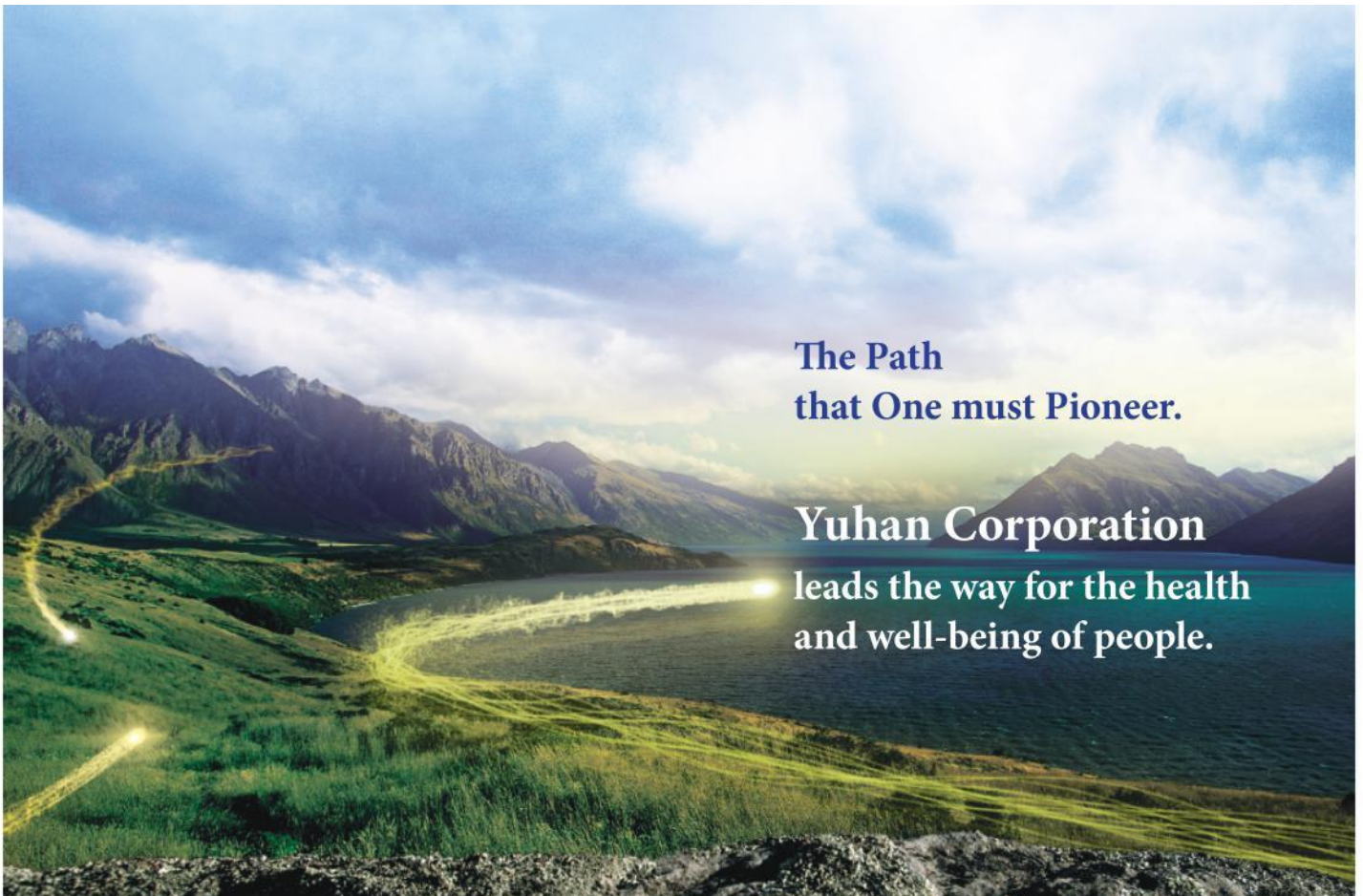


The Way of Yuhan

Yuhan Corporation, a group loved by the people and grown together with the people
For the last 90 years, the corporate culture of honesty and integrity,
and the strong beliefs in social responsibility are what made Yuhan what it is today.

Looking back on the path that we moved on and thinking of the path ahead,
Yuhan will make the leap as a global pharmaceutical company through innovative new drug development,
and by enabling healthiness and happiness for all the people in the world.

In the next 100 years, Yuhan Corporation will follow the noble spirit of our founder, Dr. New Ilhan,
and write the history of challenge and development moving forward.

Our challenge has already begun.

YUHAN

KUSCO
KOREA-U.S. SCIENCE COOPERATION CENTER

The Korea-U.S. Science Cooperation Center (KUSCO) is a non-profit organization established in Vienna, Virginia, founded in 1997, to accomplish two major missions: to enhance cooperative efforts in S&T between Korea and the U.S. and to support Korean - American scientists & engineers in the United States.

VISION & MISSION

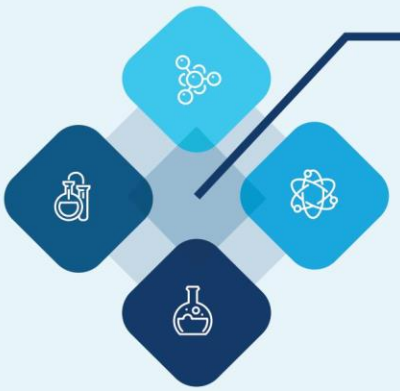
The vision of KUSCO is *"Advancement of the S&T collaborations between Korea and the U.S."*
To realize its vision, KUSCO pursues the mission of becoming a premium center for S&T cooperation and Exchanges by pursuing three goals as follows:

- To strengthen S&T cooperation portfolio between Korea and the U.S.
- To broaden global exchange programs
- To support and leverage Korean-American scientists and engineers

MAJOR ACTIVITIES

- Enhance scientific and technological development of both Korea and the U.S.
- Support mutual cooperation and initiate joint programs with U.S. and Korean scientific and engineering societies, academic universities, and other institutions
- Assess significant trends in scientific research and technological developments affecting Korea and the U.S.
- Assist young Korean-American and other scientists in developing and maintaining networks addressing matters of scientific and technical interest to the two countries

PROGRAMS



KUSCO has 4 different categories of S&T program as follows: US-Korea Joint Program, Korean-American Scientists Support Program, Human Resources Exchange and Development Program and S&T Information Exchange Program.

1 ***US-Korea Joint Program*** *aims at promoting scientific collaboration between Korea and the United States, and it has 2 different subprograms as follows:*

NOAA-MOF Joint Program

NOAA (National Oceanic and Atmospheric Administration)-MOF (Ministry of Oceans and Fisheries) Joint program aims to assist in enhancing cooperation through joint research and exchange of researchers between Korea and the US, covering coastal management, sea grant, fisheries, aquaculture, etc.

US-Korea S&T Forum

This program is to further empower the cooperation platform for scientists and engineers from both countries by focusing on any types of S&T field seeking for the long-term collaboration between the U.S. and Korea.

2 ***Korean-American Scientists Support Programs*** *is to promote Korean-American scientists and engineers to expanding its specialties and network through following programs;*

US-Korea Conference

The US-Korea Conference is one of the largest S&T conferences between the U.S. and Korea. This annual conference provides valuable opportunities for cooperation between two countries via symposiums, forums and workshops to cover broad areas of science and technology, including but not limited to basic science, applied science, engineering, entrepreneurship and science policy.

KSEA Chapter Meetings

This program supports local & regional chapters of the KSEA for developing and maintaining the regional S&T network among Korean-American researchers.

KSEA Professional Association Meetings

This program is to support Korean American Professional Association meetings, which are focused on specific topic related to science and technology in order to promote S&T network among Korean-American professionals.

Graduate Scholarship

This program is to recognize outstanding graduate students who demonstrate excellent talent in the fields of science & engineering. KUSCO selects 20 students per year. These awardees are invited to the US-Korea Conference for the ceremony.

Young Generation Technology Leadership Conference/ Ygnite

YGTLC is a premiere conference for scientists and engineers with a demonstrated interest in Korean heritage. This conference welcomes participation from 1st-generation, 2nd-generation and 3rd-generation Korean-American scientists and engineers, including those from mixed-race and adopted communities, as well as those who are non-ethnically Korean.

3 ***Human Resource Exchange and Development Program*** *is to promote personnel training programs designed to enhance professional capabilities and to work successfully in an international environment.*

NRF-KUSCO R&D Workshop is to provide an opportunity for Korean participants to understand and to enhance the global practices of R&D management, U.S. S&T policies. This workshop aims to enhance the capacities of R&D managers in Korea through the case studies of S&T policies, technology transfer, international cooperation as well as visiting some of advanced U.S. S&T institutes.

4 ***S&T Information Exchange program*** *is to strategically collect information on the latest R&D in the U.S., S&T policies, and venture company support trends for exchanging S&T information between the U.S. and Korea. KUSCO publishes around 300 reports per year and distributes in S&T communities in Korea via NRF.*

KUSCO
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SK Biopharmaceuticals Is Aiming to Become A Global Biotech Company

We are developing treatments that are changing the future of central nervous system disorders and cancer care.

SK Biopharmaceuticals is proud to be the first Korea-based company to discover, develop, and commercialize a molecule from inception through FDA approval.

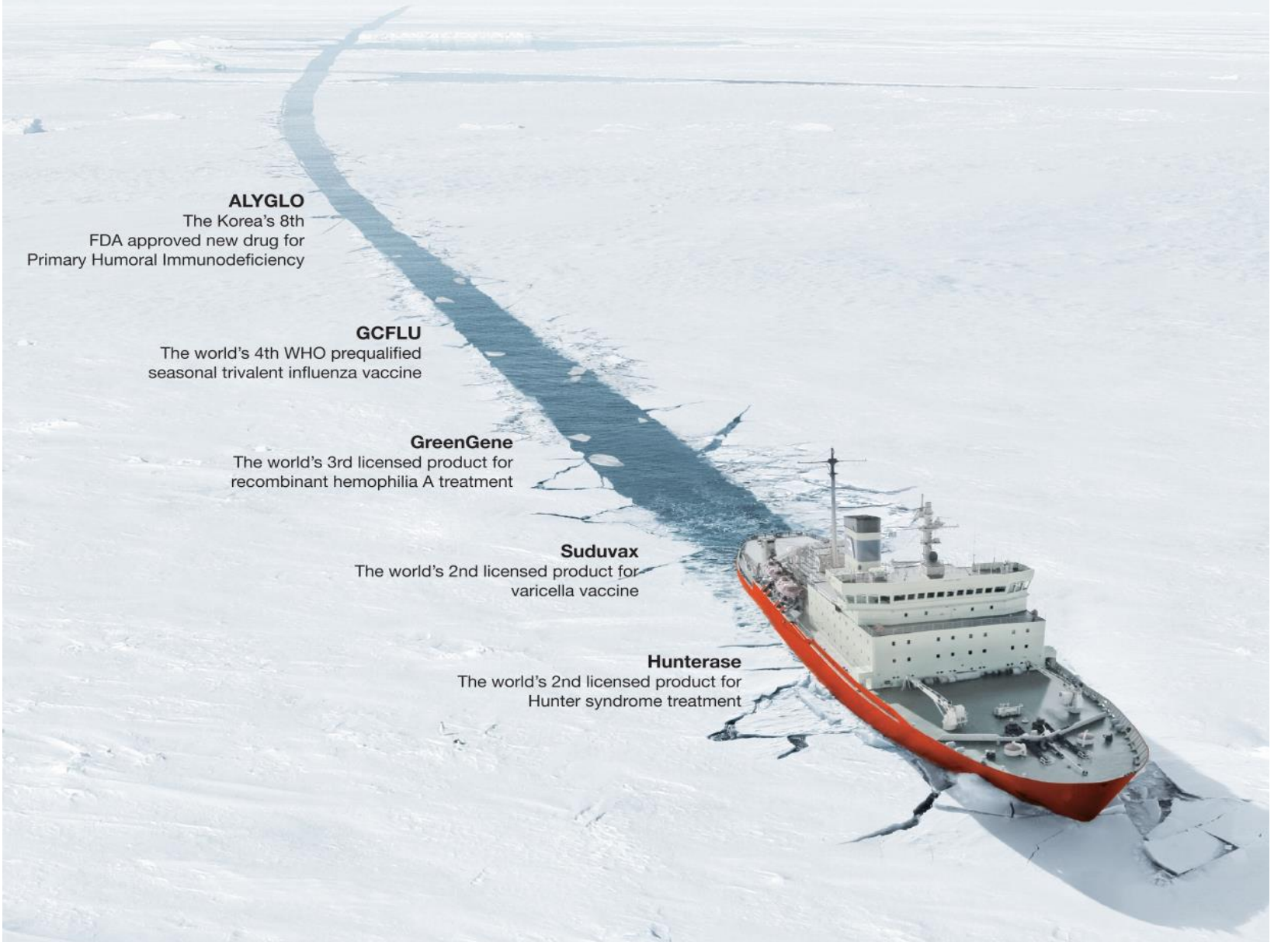
In 2024, over 100,000 patients in the U.S., the U.K., Europe, Switzerland, Canada, and Israel have been treated with our first product. Additionally, the treatment is being developed in over 30 markets through our licensing partners.

SK biopharmaceuticals

SK Biopharmaceuticals and its subsidiaries, SK Life Science, Inc. and SK Life Science Labs, are part of SK Group, one of TIME's 100 Most Influential Companies of 2023.

Please learn more about SK Biopharmaceuticals by visiting www.SKBP.com, or go to www.SKLifeScienceInc.com or www.SKLSLabs.com for more information about our subsidiaries in the United States.

GC Biopharma to the world right now!
We bring new hope to patients around the world



A global leader in the healthcare industry

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08:30 – 09:30 **Registration**

09:30 – 09:35 **Welcome Remark**
MinJung Jang, Ph.D.
President of NYKB, Weill Cornell Medicine

09:35 – 09:40 **Congratulatory Remark**
Seongsoo Kim, Consul
Consulate General of the Republic of Korea

Keynote Lecture I

Chair : Jung Seung Nam, Ph.D.

09:40 – 10:30 **Hyung Don Ryoo, Ph.D.**
Department of Cell Biology, NYU Grossman School of Medicine
Integrated Stress Response in Drosophila

NYKB Award Fellowship Session I

Chair : Kwanghoon Park, Ph.D.

10:30 – 11:05 **Chiho Kim, Ph.D.**
Department of Molecular Pharmacology and Therapeutics, Columbia University Irving Medical Center
Overcoming PARPi resistance for human malignancies by targeting a novel PARP1 trapping pathway: Druggability of RNF114-dependent mechanism and its inhibitor, the nature product nimbolide

11:05 – 11:40 **Sung-Min Hwang, Ph.D.**
Obstetrics and Gynecology, Weill Cornell Medicine
Cytoskeletal regulation of T cell lipid metabolism and anti-tumor function

11:40 – 12:00 **Group photo & Coffee Break**

Luncheon Seminar (Promega)

Chair : Chul-Hee Lee, Ph.D.

12:10 – 13:00 **Richard Somberg, Ph.D.**
Director – Pharma Biotech SBU, Promega
Latest tools for cell health, cytokine detection, protein dynamics, and bioluminescence imaging

NYKB Award Fellowship Session II

Chair : Jiyun Shin, Ph.D.

13:00 – 13:35 **Se-In Lee, Ph.D.**
Helen and Robert Appel Alzheimer's Disease Research Institute, Weill Cornell Medicine
ApoE4, Astrocyte priming, and Alzheimer's disease

13:35 – 14:10 **Gihoon Lee, Ph.D.**
Department of Chemistry, Princeton University
Time-resolved protein synthesis reveals distinct phases of oncogenic signaling and identifies an 'Achilles Heel' of a liver cancer FL-HCC

Keynote Lecture II

Chair : You-Kyung Lee, Ph.D.

14:10 – 15:00 **Minah Kim, Ph.D.**
Department of Pathology and Cell Biology, Columbia University Irving Medical Center
Unveiling the Role of Angiopoietin-2 in Tumor Immune Evasion and Metastasis

15:00 – 15:20 **Coffee Break**

NYKB Award General Session

Chair : Wooseung Lee, Ph.D.

15:20 – 15:37 **Soyoung Kwak, Ph.D.**
Department of Population Health, NYU Grossman School of Medicine
Oral microbiome and subsequent risk for head and neck squamous cell cancer development

15:37 – 15:54 **Soonbum Park, Ph.D.**
Department of Molecular Pharmacology and Therapeutics, Columbia University Irving Medical Center
Precision oncology approach to identify novel treatments for metastatic bladder cancer

15:54 – 16:11 **Charlie Chung, Ph.Dc.**
Cold Spring Harbor Laboratory
Microbial regulation of anti-tumor immunity in colorectal cancer

16:11 – 16:28 **Myeong Joon Kim, Ph.D.**
Department of Medicine , Gastroenterology & Hepatology Division, Jill Roberts Institute for Research in IBD, Weill Cornell Medicine
Deletion of PD-1 in regulatory T cells promotes effective immunity by exacerbating their stability in the tumor microenvironment and autoimmune disease

16:28 – 16:45 **Minwoo Wendy Jang, Ph.D.**
Brain and Mind Research Institute, Weill Cornell Medicine
Molecular and functional characterization of a novel ion channel TMEM43

16:45 – 17:02 **Seohee Ahn, Ph.D.**
Brain and Mind Research Institute, Weill Cornell Medicine
Dendrodendritic connections between inhibitory neurons in the visual thalamus from complex networks

17:02 – 17:19 **Taeju Lee, Ph.D.**
Department of Electrical Engineering, Columbia University
Semiconductor technology for reliable neural activity observation

17:19 – 17:36 **Hyunwoo Kim, Ph.D.**
Howard Hughes Medical Institute, The Rockefeller University
Structural Basis for Mitoguardin-2 Mediated Lipid Transport at ER-mitochondrial Membrane Contact Sites

NYKB Award Ceremony

Chair : NYKB Council

17:40 – 17:50 **Ceremony**

17:50 – 18:00 **Closing Remark**

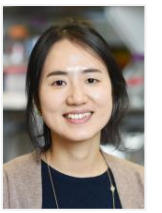
Integrated Stress Response in *Drosophila*

Hyung Don Ryoo, Ph.D.
Department of Cell Biology,
NYU Grossman School of Medicine

The Integrated Stress Response (ISR) refers to signaling pathways initiated by stress-activated eIF2a kinases. Distinct eIF2a kinases respond to different stress signals, including amino acid deprivation and mitochondrial stress. Such stress-induced eIF2a phosphorylation attenuates general mRNA translation and, at the same time, stimulates the preferential translation of specific downstream factors to orchestrate an adaptive gene expression program. My laboratory has been using *Drosophila melanogaster* as a model system to study the ISR signaling mechanisms and their *in vivo* roles. In this organism, there are two eIF2a kinases, GCN2 and PERK, activated in response to amino acid deprivation and endoplasmic reticulum (ER) stress respectively. Once these kinases phosphorylate eIF2a, the transcription factor ATF4 is preferentially induced. We have identified a number of regulators that mediate such ATF4 induction. We have also identified a distinct transcription factor, Xrp1, induced in parallel to ATF4. These transcription factors heterodimerize with other bZIP factors to activate a stress-responsive transcription program. We and others have noted that ISR target genes include many enzymes that mediate the biosynthesis of serine, glycine, and cysteine. Consistently, genetic conditions that suppress ISR reduce many amino acids and their metabolites. In addition, there is an enhanced level of oxidative stress and light-dependent retinal degeneration. These results highlight the importance of ISR signaling in the maintenance of the cellular redox potential and the homeostasis of many vital cell types in an intact organism.

Unveiling the Role of Angiopoietin-2 in Tumor Immune Evasion and Metastasis

Minah Kim, Ph.D.
Department of Pathology and Cell Biology,
Columbia University Irving Medical Center



Together with angiogenesis, vascular destabilization is recognized as a hallmark of tumor growth and metastasis. Importantly, emerging evidence suggests that vascular destabilization can facilitate tumor immune evasion by impairing immune cell infiltration. Angiopoietin-2 (ANGPT2), which binds to the Tie2 receptor tyrosine kinase, is a potent vascular destabilizing factor. While ANGPT2 can serves as both a therapeutic target and a biomarker for cancer due to its frequent upregulation in many cancer types, the mechanism behind ANGPT2-mediated immune escape remains largely unknown. Our study in pancreatic neuroendocrine tumors (PanNET), where nearly half of patients present with liver metastases, showed ANGPT2 as one of the most upregulated angiogenic factors correlating with poor survival rates. Notably, both pharmacologic inhibition and genetic deletion of ANGPT2 in PanNET mouse models slowed the growth of PanNET liver metastases, improving the survival of mice, and promoted T cell infiltration and activation in liver metastases. These changes were accompanied by reduced vascular leakage and improved vascular integrity in metastases. Furthermore, our recent studies in melanoma highlight ANGPT2/TIE2 signaling as a key mediator of T-cell exclusion and a promising target to potentiate immune checkpoint blockade efficacy.

Latest tools for cell health, cytokine detection, protein dynamics, and bioluminescence imaging

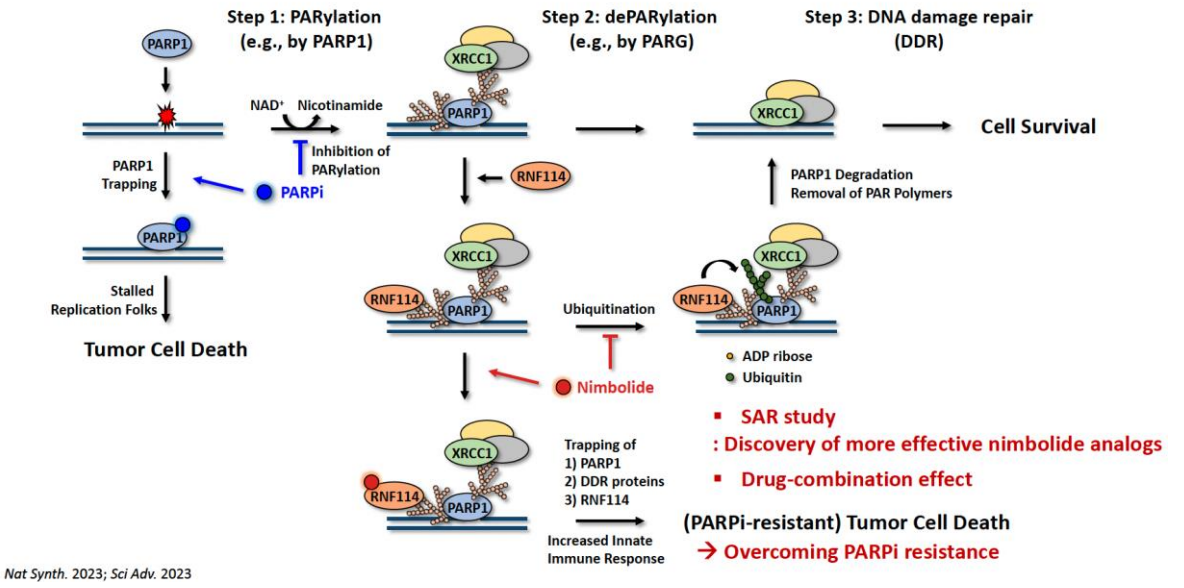
Richard Somberg, Ph.D.
Director – Pharma Biotech SBU, Promega

Learn about the Promega assays to best understand cellular activities for health and disease states, including:

- Viability, apoptosis, metabolism, and proliferation.
- Homogenous cytokine detection.
- HiBiT technology combined with CRISPR knock-in to measure protein levels in real-time.
- GloMax Galaxy, a new instrument for bioluminescence imaging.

Overcoming PARPi resistance for human malignancies by targeting a novel PARP1 trapping pathway: Druggability of RNF114-dependent mechanism and its inhibitor, the nature product nimbolide

Chiho Kim, Ph.D.
Department of Molecular Pharmacology and Therapeutics,
Columbia University Irving Medical Center



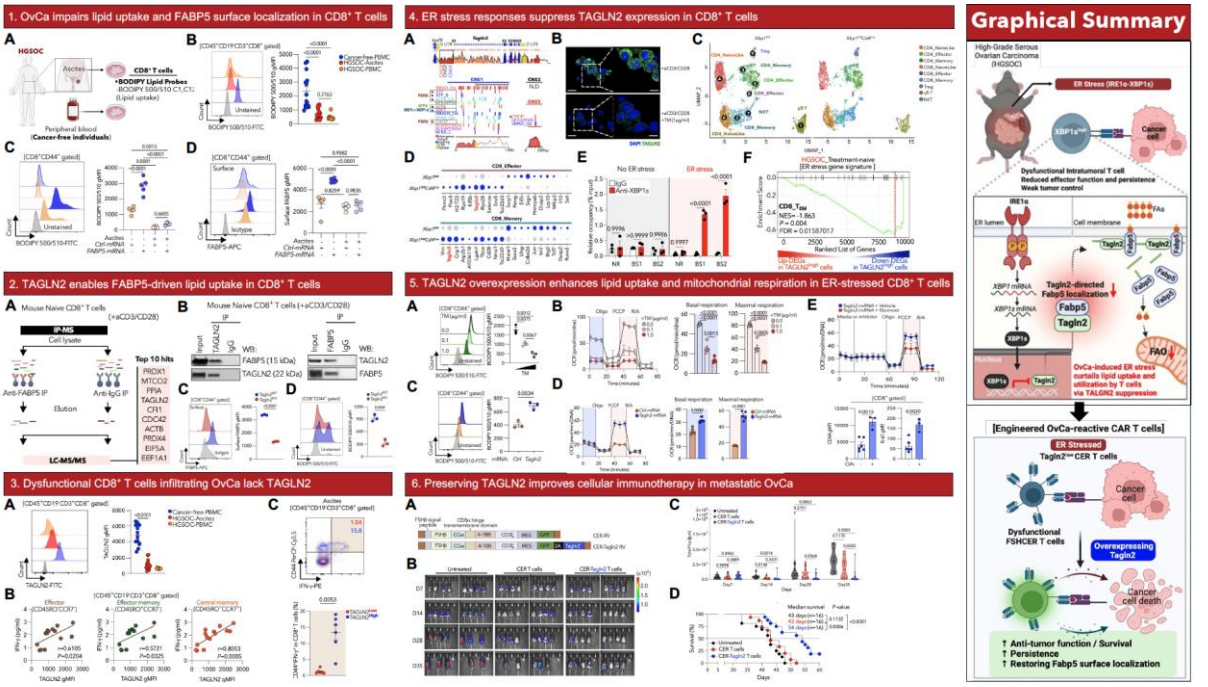
The advent of PARP1 inhibitors (PARPi) has significantly reshaped the therapeutic landscape for human malignancies harboring BRCA mutations. However, the efficacy of PARPi exhibits considerable variability, with intrinsic and acquired resistance posing prevalent challenges in clinical scenarios. To address this, there's an urgent need to deepen our understanding of PARPi mechanisms and devise innovative strategies rooted in synthetic lethality to achieve more robust and enduring therapeutic outcomes in BRCA-mutated cancers. Recent studies have spotlighted PARP1 trapping as a pivotal determinant influencing the anticancer effects of PARPi. In our study, we conducted quantitative proteomic screens utilizing mass spectrometry experiments to dissect the molecular intricacies of PARP1 trapping. This endeavor led to the identification of RNF114 as a PARylation-dependent E3 ligase intricately interwoven with the DNA damage response. Upon DNA damage, RNF114 was recruited to DNA lesions in a PAR-dependent manner, orchestrating the degradation of PARylated-PARP1. Disruption of this pathway impeded the removal of PARP1 from DNA damage sites, resulting in substantial PARP1 trapping. A remarkable aspect of the RNF114-PARP1 pathway lies in its translational potential. Our findings demonstrate that nimbolide, a natural compound, selectively

targeted RNF114, thereby hindering the degradation and removal of PARP1. Unlike conventional PARPi, nimbolide induced the trapping of both PARP1 and PARylation-dependent DNA repair factors, such as XRCC1. This approach induced synthetic lethality in BRCA mutations and effectively overcame the resistance to PARPi through a dominant negative mechanism. Moreover, nimbolide synergized with other DNA-damaging agents, activated innate immune responses, and upregulated PD-L1 expression. Our structure-activity relationship (SAR) study revealed several nimbolide analogs with enhanced cytotoxicity against BRCA-mutated cancer cells, suggesting the potential for developing improved analogs for clinics. In conclusion, our findings unveil promising avenues for targeting the druggable RNF114-dependent mechanism and its inhibitor, nimbolide, along with its analogs, to enhance the treatment outcomes of BRCA-mutated cancers.

Cytoskeletal regulation of T cell lipid metabolism and anti-tumor function

Sung-Min Hwang, Ph.D.

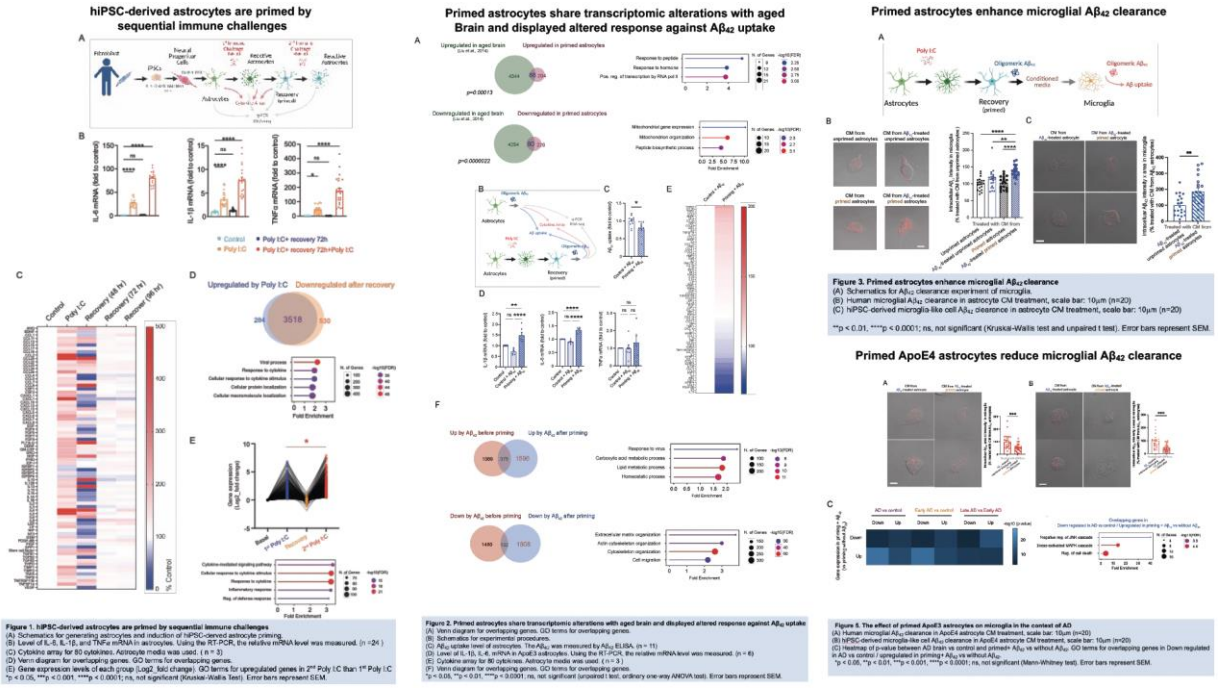
Obstetrics and Gynecology, Weill Cornell Medicine



Mounting effective immunity against pathogens and tumors relies on the successful metabolic programming of T cells by extracellular fatty acids. During this process, fatty-acid-binding protein 5 (FABP5) imports lipids that fuel mitochondrial respiration and sustain the bioenergetic requirements of protective CD8⁺ T cells. Importantly, however, the mechanisms governing this crucial immunometabolic axis remain unexplored. Here we report that the cytoskeletal organizer Transgelin 2 (TAGLN2) is necessary for optimal CD8⁺ T cell fatty acid uptake, mitochondrial respiration, and anti-cancer function. We found that TAGLN2 interacts with FABP5, enabling the surface localization of this lipid importer on activated CD8⁺ T cells. Analysis of ovarian cancer specimens revealed that endoplasmic reticulum (ER) stress responses elicited by the tumor microenvironment repress TAGLN2 in infiltrating CD8⁺ T cells, enforcing their dysfunctional state. Restoring TAGLN2 expression in ER-stressed CD8⁺ T cells bolstered their lipid uptake, mitochondrial respiration, and cytotoxic capacity. Accordingly, chimeric antigen receptor T cells overexpressing TAGLN2 bypassed the detrimental effects of tumor-induced ER stress and demonstrated superior therapeutic efficacy in mice with metastatic ovarian cancer. Our study unveils the role of cytoskeletal TAGLN2 in T cell lipid metabolism and highlights the potential to enhance cellular immunotherapy in solid malignancies by preserving the TAGLN2-FABP5 axis.

ApoE4, Astrocyte priming, and Alzheimer's disease

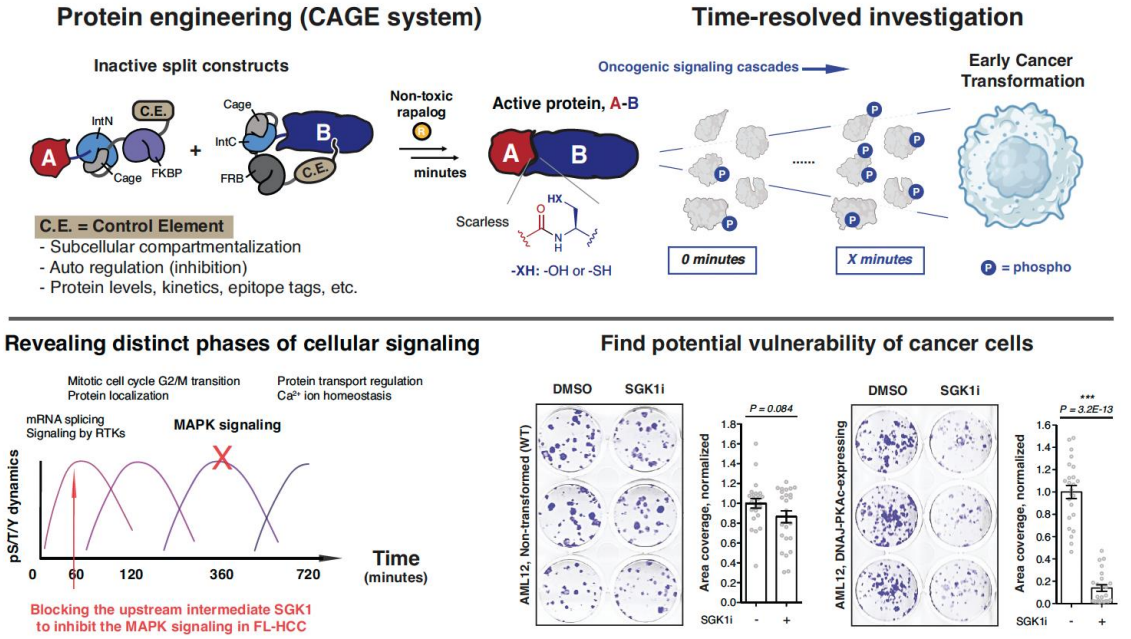
Se-In Lee, Ph.D.
Helen and Robert Appel Alzheimer's Disease Research Institute,
Weill Cornell Medicine



Apolipoprotein E4 (ApoE4) is one of the most substantial risk factors for Alzheimer's disease (AD). Previously, we showed that human-induced pluripotent stem cells (iPSCs)-derived astrocytes carrying APOE4 isoform nicely recapitulate some AD-related phenotypes such as impaired amyloid-beta clearance and intracellular cholesterol accumulation. An exaggerated immune response of astrocytes is another well-known common pathology of AD, but whether/how ApoE4 affects immune response in astrocytes has not been defined yet. We identified a primed status in human iPSCs-derived astrocytes after recovery from immune stimulation, displaying an exaggerated immune response to a subsequent immune challenge. Primed astrocytes displayed altered transcript profiles similar to those from the brain of the elderly. We observed that primed astrocytes reduced their phagocytotic activity against Aβ but increased the secretion of cytokines known to influence microglia. Indeed, conditioned media from Aβ-treated primed astrocytes increased Aβ clearance by microglia. Interestingly the comparison between isogenic ApoE3/E4 hiPSC-derived astrocytes revealed that stimulation-induced priming in ApoE4 astrocytes was significantly attenuated compared to ApoE3 astrocytes. We further observed that secretory factors from Aβ-treated primed ApoE4 astrocytes significantly reduced microglia-dependent clearance of Aβ. Our study elucidates the role of astrocyte priming in AD pathogenesis and how ApoE4 impacts this process.

Time-resolved protein synthesis reveals distinct phases of oncogenic signaling and identifies an 'Achilles Heel' of a liver cancer FL-HCC

Gihoon Lee, Ph.D.
Department of Chemistry, Princeton University



Cellular processes are regulated by dynamic alterations in protein activity. As such, dysregulation of proteins involved in cell transformation leads to diseases. Understanding the propagation of these changes through associated molecular pathways necessitates tools that can operate effectively within relevant timescales, which can often be in the minute range. Here, we report the development of a versatile and high-precision approach, the 'CAGE system,' for seamlessly manipulating protein structure and function at the post-translational level (1). The technology exploits genetically 'caged' split intein pairs for time-resolved protein trans-splicing. By integrating the caged split inteins with a diverse array of control elements, we enable posttranslational synthesis of intracellular proteins, facilitating alterations in their cellular localization and activity in response to a small molecule trigger in a dose and time-dependent manner. The efficacy of this platform has been demonstrated across multiple targets, including five distinct native oncofusion proteins with varying sizes and functions. The temporal control afforded by our CAGE system allowed us to monitor acute changes in cellular signaling that occur following the allosteric activation of the kinase oncofusions BCRABL and DNAJ-PKAc through the time-resolved quantitative phospho-proteomics. Distinct phases of protein phosphorylation were unveiled, with a

particularly new discovery being the identification of transient phosphorylation events within the first few hours following activation. In the case of DNAJ-PKAc, we find a role for the protein kinase SGK1 as an upstream intermediate, bridging DNAJ-PKAc activity to the MAPK pathway in fibrolamellar hepatocellular carcinoma (FL-HCC), and as a novel therapeutic target of cancer cells shown by selective inhibition of DNAJ-PKAc-expressing AML12 cells growth by pharmacological SGK1 blocking. In conclusion, our study illustrates the power of the CAGE system for studying molecular pathways of fusion oncoproteins associated with the initial stages of cell transformation and discovering upstream intermediates as novel targets for cancer therapeutics.

Reference

1. Lee, G., & Muir, T. W. (2023). Distinct phases of cellular signaling revealed by timeresolved protein synthesis. BioRxiv. 2023.07.10.548208

Oral microbiome and subsequent risk for head and neck squamous cell cancer development

Soyoung Kwak, Ph.D.

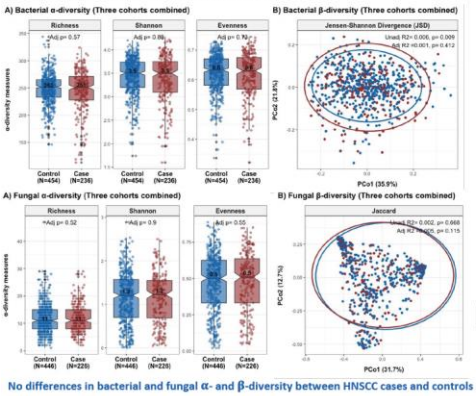
Department of Population Health,
NYU Grossman School of Medicine

Table 1. Participants characteristics

	ACS CPS-II		PLCO		SCCS	
	Case (N=55)	Control (N=106)	Case (N=71)	Control (N=138)	Case (N=110)	Control (N=214)
Age (mean)	71.2	71.4	62.7	63.3	54.5	54.5
Male (%)	72.7	72.6	81.7	81.9	72.7	72.9
White (%)	100	100	93.0	93.5	25.5	26.2
Smoker (%)	**27.3**	2.8	**35.2**	5.1	**62.7**	36.9
Drinker (%)	**61.8**	58.5	**70.4**	63.8	**67.3**	58.4
HPV-positive (%)	**7.3**	0.9	**9.9**	0.7	-	-

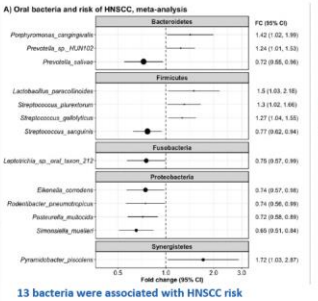
Matching factors did not differ by HNSCC status
HNSCC cases tended to be more smokers, drinkers, and HPV-16 positive

Figure 2. bacterial and fungal diversity

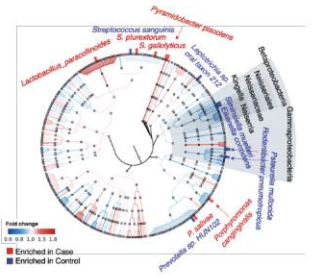


No differences in bacterial and fungal α- and β-diversity between HNSCC cases and controls

Figure 3. Bacterial association with HNSCC

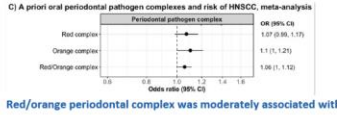


13 bacteria were associated with HNSCC risk



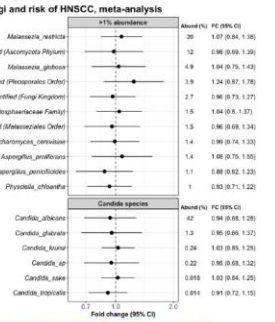
Species belonging to *beta-* and *gamma-proteobacteria* showed decreased risk of HNSCC

Figure 4. Bacterial complex association with HNSCC



Red/orange periodontal complex was moderately associated with HNSCC

Figure 5. Fungal association with HNSCC



No fungal taxa were associated with HNSCC risk

Table 2. Microbial risk score with HNSCC risk

	OR (95% CI)
$MRS_{ANCOM-BC}$	**1.29 (1.05, 1.59)**
MRS_{red}	**1.34 (1.09, 1.65)**
MRS_{orange}	1.22 (0.99, 1.51)
$MRS_{red/orange}$	**1.40 (1.13, 1.75)**
$MRS_{ANCOM-BC\ \&\ red/orange}$	**1.50 (1.21, 1.85)**

The summary MRS for 22 bacteria was associated with a 50% increase in HNSCC risk

Background: The oral microbiota may be involved in head and neck squamous cell cancer (HNSCC) etiology, yet current evidence is largely limited to bacterial 16S amplicon sequencing or small retrospective case-control studies. We tested whether oral bacteria and/or fungi influence the subsequent risk of HNSCC development.

Methods: We conducted a prospective case-control study nested within three epidemiological cohorts: the ACS-Cancer Prevention Study-II Nutrition Cohort (ACS-CPS-II), the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial (PLCO), and the Southern Community Cohort Study (SCCS). Among 159,840 cohort participants who provided oral samples, 236 individuals developed HNSCC during an average of 5.1 years of follow-up, and 485 controls who remained HNSCC-free were selected by 2:1 frequency matching on cohort, age, sex, race/ethnicity, and time since mouthwash collection. We characterized the oral bacterial microbiome, using whole-genome shotgun sequencing, and the oral fungal microbiome, using ITS sequencing. Association of bacterial and fungal taxa with HNSC was assessed by ANCOM-BC analysis. Association with “red” and “orange” oral pathogen complexes was tested by logistic regression. A microbial risk score (MRS) for HNSCC risk was calculated from all risk-associated microbes.

Results: Overall microbiome diversity at baseline was not related to the subsequent risk of HNSCC; however, we found that 13 oral bacterial species were differentially associated with development of this disease, including newly identified *Prevotella salivae*, *Streptococcus sanguinis*, *Leptotrichia sp*, and several species belonging to *Beta*- and *Gamma-proteobacteria*. The 'red/orange' periodontal pathogen complex was moderately associated with HNSCC risk (OR=1.06, 95% CI=1.00-1.12). Each standard deviation in the 22 bacteria summary MRS was associated with a 50% increase in HNSCC risk (OR=1.50, 95% CI=1.21-1.85). We did not identify any fungal taxa associated with HNSCC risk.

Conclusions: Our prospective study yields compelling evidence that oral bacteria are a risk factor for HNSCC development. The identified bacteria and bacterial complexes hold promise, with other risk factors to identifying high-risk individuals for personalized prevention of HNSCC.

Precision oncology approach to identify novel treatments for metastatic bladder cancer

Soonbum Park, Ph.D.

Department of Molecular Pharmacology and Therapeutics,
Columbia University Irving Medical Center

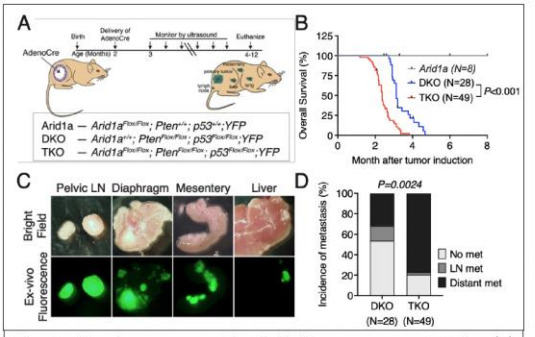


Fig. 1. Novel mouse model of bladder cancer metastasis. (A) Experimental design. (B). Kaplan-Meier analysis. *P-value*: two-tailed log-rank test. (C) Representative images of metastasis. (D) Incidence of metastasis (N=23 DKO and N=43 TKO). *P-value*: Two-sample Fisher's exact t-test.

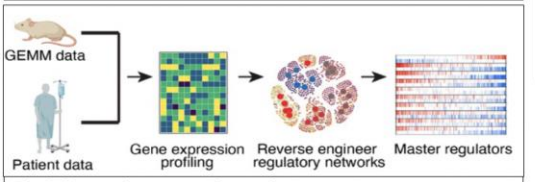


Fig. 2. Strategy for cross-species analyses.

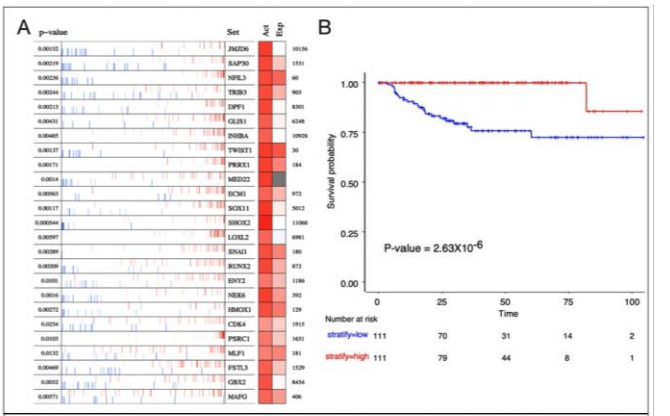


Fig. 3. Conserved master regulators of metastasis. (A) Conserved MRs showing up-regulated MRs. Shown are the integrated p-values for each MR based on Stouffer's method. Relative activity (act) and expression (exp) are shown by the colored boxes; red is up and blue is down. (B) Kaplan-Meier survival analyses based on the Lund dataset, showing the combined activity levels of the Up conserved MRs. *P*-values show two-tailed log-rank test.

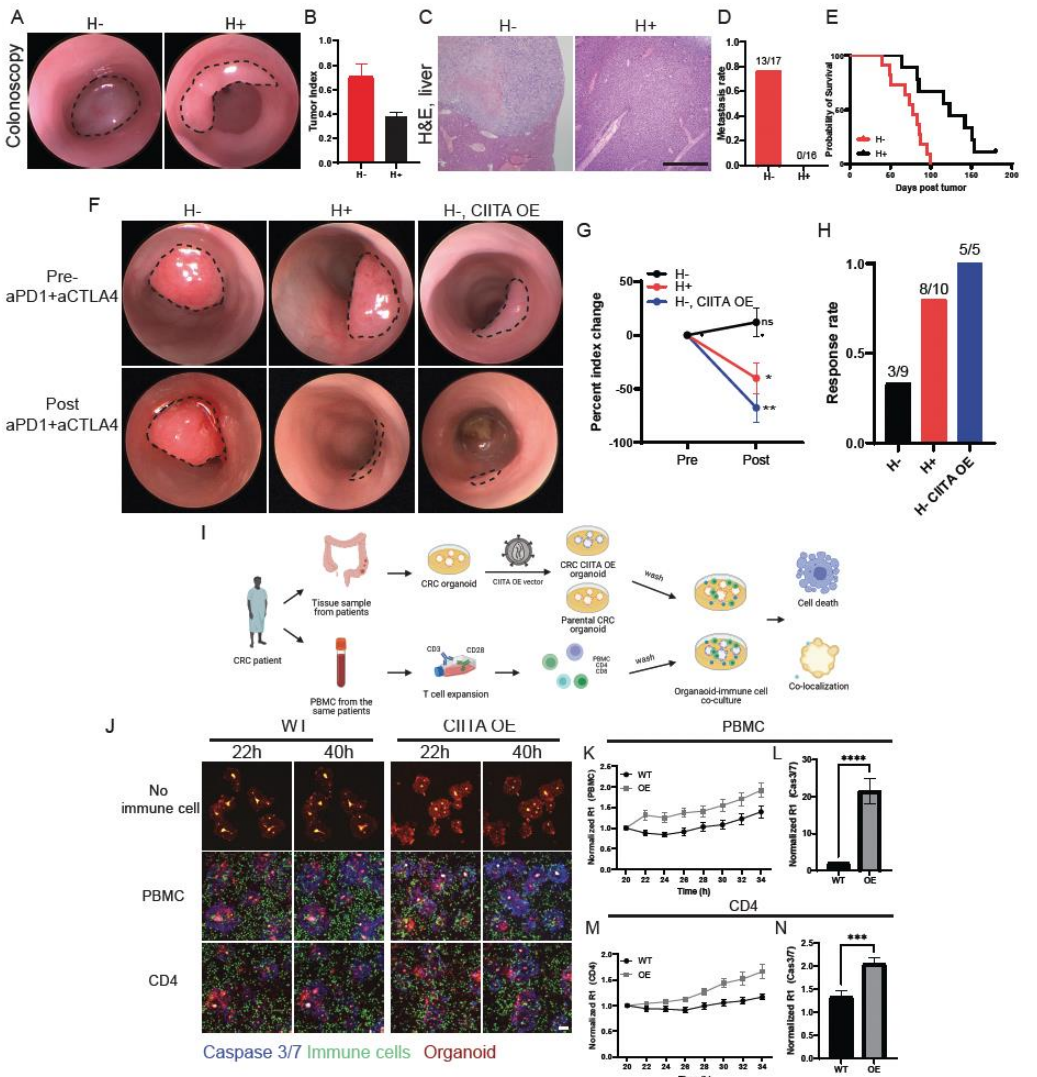
Although there have been notable advancements in treating locally invasive cancers, metastatic cancer remains a significant challenge, particularly in cases like bladder cancer where the transition to metastasis drastically worsens outcomes. Despite poor outcomes associated with metastatic bladder cancer, the standard-of-care, namely systemic chemotherapy, results in a median progression-free survival of less than one year. While promising treatment options are emerging, none of the current therapies are curative. The urgent need for novel treatment options underscores the importance of gaining a deeper understanding of the underlying mechanisms driving metastatic progression in bladder cancer, which can help to inform new interventions to improve patient outcomes. Until now, a significant challenge in studying metastatic bladder cancer has been the lack of suitable *in vivo* models that enable investigations of metastatic progression as occurs de novo during tumorigenesis in the context of the native tumor microenvironment. A major innovation of my work involves the utilization of two independent approaches to accelerate metastasis progression in a genetically engineered mouse model (GEMM). Complementing these efforts to model bladder cancer *in vivo*, I have implemented state-of-the-art systems biology approaches to identify mechanistic determinants—master

regulators (MRs)—driving metastatic progression in GEMMs and I have shown that MRs enriched in metastatic tumors in the mice exhibit remarkable conservation in human bladder cancer. Cross-species analysis comparing the mouse signatures with human patient data identified the MRs of metastatic progression that are conserved with human bladder cancer. Most notably, these conserved MRs include key regulators of bladder cancer and its luminal phenotype such as Pparg and Shh, and those know to be associated with lineage plasticity, such as Sox11. Accordingly, integrating conserved MRs with drug perturbation profiles, we had identified drugs that target lineage plasticity mechanisms, which we are now evaluating in our mouse and patient-derived organoid models.

Microbial regulation of anti-tumor immunity in colorectal cancer

Charlie Chung, Ph.Dc.

Cold Spring Harbor Laboratory



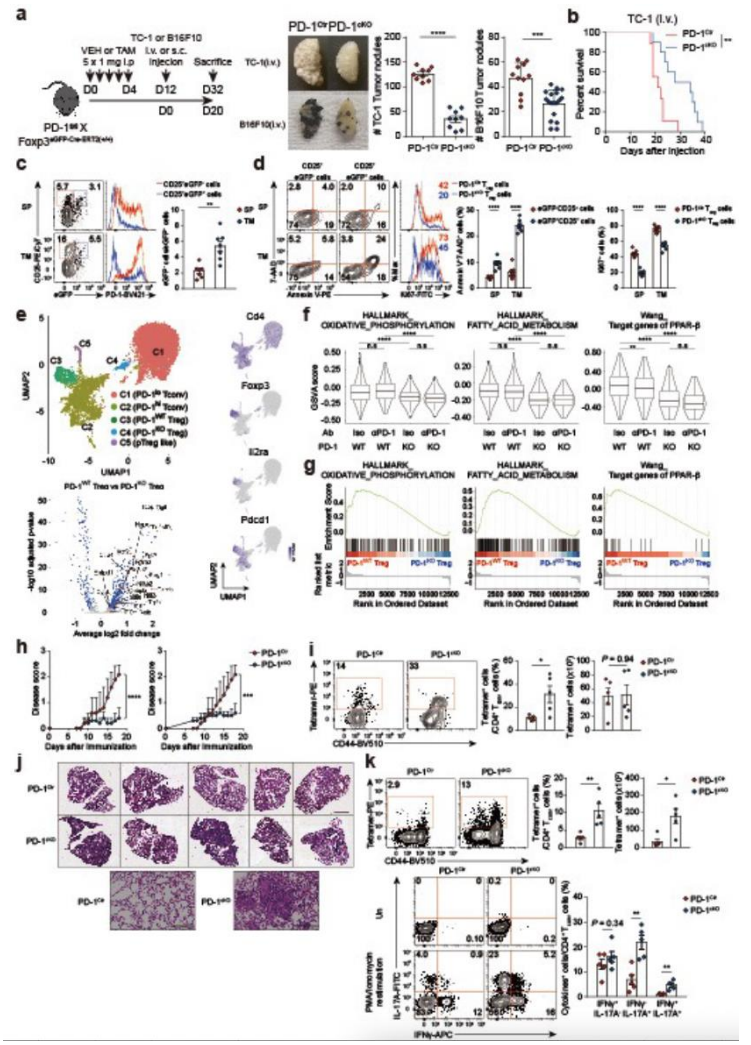
(A-E) Representative colonoscopy images of colon tumors (A) and associated tumor index (B), and H&E or liver metastasis (C) and associated metastasis rate (D) induced by AKPS organoids in H- and H+ mice, and corresponding survival rate (E). Scale bar = 500 μm. (F-H) Representative colonoscopy images of tumors in H- or H+ mice induced by either WT or CIITA overexpressing AKPS, and associated tumor index changes upon immunotherapy and the response rate. (I) A schematic depicting the experimental flow of autologous human CRC organoid-immune cell co-culture. (J) Representative images of syngeneic cell co-culture using either parental or CIITA overexpressing MSS CRC organoids with autologous PBMC or CD4 T cells. Scale bar = 70 μm. (K-N) Co-localization of organoids and PBMC (K) or CD4 T cells (M) over the time of imaging and associated end point viability of organoids measured by cas3/7 signals from the organoids in PBMC (L) and CD4 T cell co-culture (N).

Colorectal cancer (CRC) is a leading cause of cancer-related mortality worldwide, with a concerning increase in incidence among individuals under 50 years old and a high mortality rate in patients with metastatic disease. Despite the revolutionary impact of immunotherapies in cancer treatment, their effectiveness is limited in CRC, particularly in patients with microsatellite stable (MSS) tumors and metastasis. The microbiome, known for its extensive role in influencing host physiology including immune responses, presents a largely unexplored area in its potential to affect anti-tumor immunity in MSS and metastatic CRC. Here, we identify commensal microbes that inhibit tumor progression and metastasis, thereby extending survival in three distinct metastatic CRC models across various mouse strains. These microbes exert tumor-suppressive effects by reprogramming the tumor immune microenvironment. This results in improved fitness and increased infiltration of T cells into MSS CRC, transforming nonimmunogenic, 'cold' tumors into immunologically active, 'hot' ones. We demonstrate that the MHC-II antigen presentation pathway in MSS cancer cells is necessary and sufficient for mediating the anti-tumor effects of the microbiome, and enhanced MHC-II on MSS CRC tumors improves the efficacy of immunotherapy. Furthermore, enhancing MHC-II expression on human MSS CRC organoids significantly improves interactions between cancer and immune cells, leading to more effective cancer clearance in autologous patient-derived organoid-immune cell co-cultures. These findings suggest that gut microbes which promote MHC-II antigen presentation on CRC cells can boost anti-tumor immunity and potentially improve the response to immunotherapies in patients with MSS and metastatic CRC.

Deletion of PD-1 in regulatory T cells promotes effective immunity by exacerbating their stability in the tumor microenvironment and autoimmune disease

Myeong Joon Kim, Ph.D.

Department of Medicine, Gastroenterology & Hepatology Division,
Jill Roberts Institute for Research in IBD, Weill Cornell Medicine



a. Experimental scheme (left). Tumor tissues of PD-1^{Ctr} and PD-1^{cKO} mice. Quantification of the tumor nodules in the lungs of PD-1^{Ctr} and PD-1^{cKO} mice at day 20 post-intravenous injection with TC-1 cells and B16F10 cells (right). b. Survival in PD-1^{Ctr} and PD-1^{cKO} mice injected intravenously with TC-1 cells. (c, d). Representative flow cytometry plots and histograms of T_{reg} cells isolated from the spleen and tumor of PD-1^{Ctr} and PD-1^{cKO} mice at day 20 post-intravenous injection of TC-1 cells. e. UMAP dimensions based on single-cell transcriptome profiles in TI CD4$^+$ T_{conv} cells and Treg cells in isotype- and PD-1 antibody-treated Pdcd1$^{f/f}$ X Foxp3$^{eGFP\text{-}Cre\text{-}ERT2(+/-)}$ PD-1$^{Cre+/-}$ mice. UMAP plot of expression of *Cd4, Foxp3, Il2ra* and *Pdcd1* in TI CD4$^+$ T cells indicated by colors ranging from gray (low expression) to blue (high expression). Volcano plot of the genes upregulated and downregulated in PD-1^{WT} T_{reg} cells compared to PD-1^{KO} T_{reg} cells in isotype-treated PD-1$^{Cre+/-}$ mice. f. Violin plot of the GSVA scores for the indicated gene sets within each TI T_{reg} cell subset. g. GSEA plot for the indicated gene sets in PD-1^{WT} and PD-1^{KO} T_{reg} cells in isotype-treated PD-1$^{Cre+/-}$ mice. h. The disease score of PD-1^{Ctr} and PD-1^{cKO} mice immunized with MOG peptide in CFA emulsion at day 12 post-tamoxifen treatment.

i. Representative flow cytometry plots of CD4$^+$ T_{conv} cells and quantification of the percentages and absolute number of Tetramer$^+$CD4$^+$ T_{conv} cells in the spinal cord of PD-1Ctr and PD-1^{cKO} mice as in h. j. Images of H&E staining of the lung of PD-1^{Ctr} and PD-1^{cKO} mice as in h. k. Representative flow cytometry plots of Tetramer$^+$CD4$^+$ T cells and quantification of the percentage and absolute number of Tetramer$^+$CD4$^+$ T cells in the lung of PD-1^{Ctr} and PD-1^{cKO} mice as in h. Representative flow cytometry plots of CD4$^+$ T_{conv} cells and quantification of the percentage of IFNγ$^+$ and/or IL-17A$^+$ cells in CD4$^+$ T_{conv} cells in the lung of PD-1^{Ctr} and PD-1^{cKO} mice as in h.

Regulatory T cells (T_{reg} cells) have an immunosuppressive function and highly express the immune checkpoint receptor PD-1 in the tumor microenvironment (TME). However, the function of PD-1 in tumor-infiltrating (TI) T_{reg} cells remains controversial. Here, we showed that conditional deletion of PD-1 in T_{reg} cells delayed tumor progression. In *Pdcd1*$^{fl/fl}$*Foxp3*$^{eGFP\text{-}Cre\text{-}ERT2(+/-)}$ mice, in which both PD-1-expressing and PD-1-deficient T_{reg} cells coexisted in the same tissue environment, conditional deletion of PD-1 in Treg cells resulted in impairment of the proliferative and suppressive capacity of TI T_{reg} cells. PD-1 antibody therapy reduced the TI T_{reg} cell numbers, but did not directly restore the cytokine production of TI $CD8^+$ T cells in TC-1 lung cancer. Single-cell analysis indicated that PD-1 signaling promoted lipid metabolism, proliferation, and suppressive pathways in TI T_{reg} cells. These results suggest that PD-1 ablation or inhibition can enhance antitumor immunity by weakening T_{reg} cell lineage stability and metabolic fitness in the TME. Interestingly, in experimental autoimmune encephalomyelitis model, we found that deletion of PD-1 resulted in ameliorated disease score. Contrary to relieved disease symptoms, central nervous system-infiltrating $CD4^+$ T cells were more activated by the T_{reg} cell-specific PD-1 deletion. This discrepancy was caused by unexpected inflammation in the lung tissues. We identified that PD-1 deletion of Treg cells prevented autoantigen-specific $CD4^+$ T cells from migrating the CNS. Taken together, we suggest that PD-1 plays an important role in the stability of T_{reg} cells in the TME and autoimmune disease.

Molecular and functional characterization of a novel ion channel TMEM43

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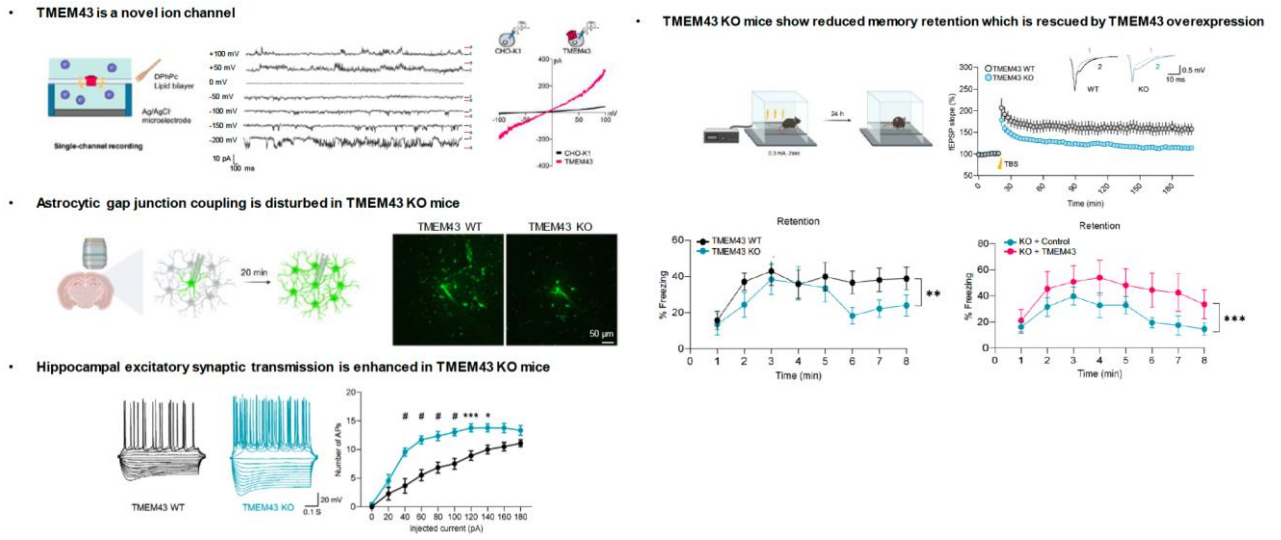
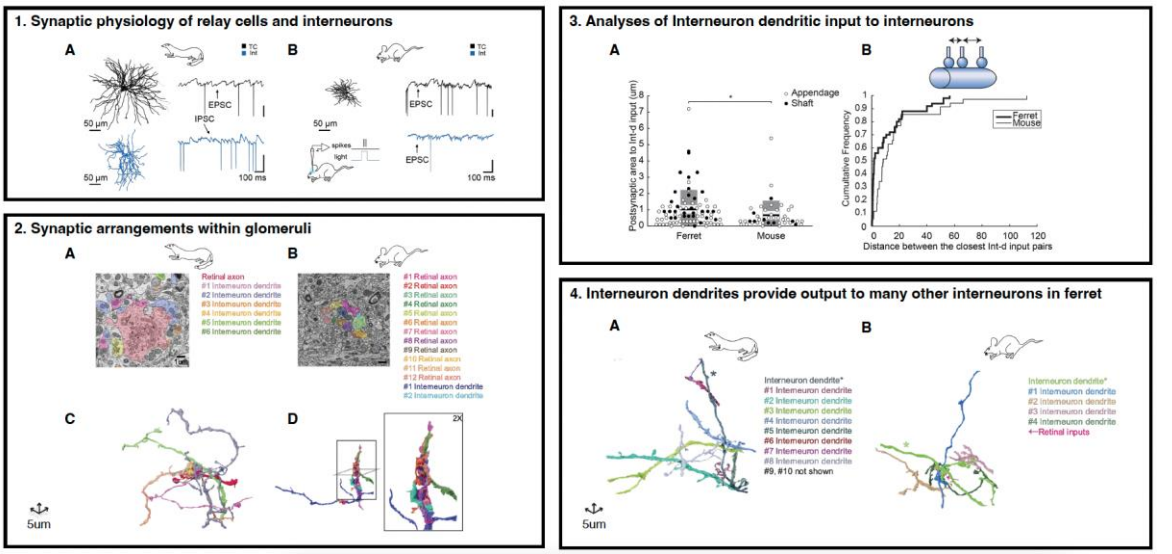
Brain and Mind Research Institute, Weill Cornell Medicine



The *TMEM43* gene has been reported to play supportive but critical roles in human diseases, including cancer, arrhythmogenic right ventricular cardiomyopathy (ARVC), and auditory neuropathy spectrum disorder (ANSD). However, direct characterization of the TMEM43 protein and its role in the brain remain unexplored. In this study, we demonstrated that TMEM43 confers ion channel activities via the lipid bilayer reconstitution of purified TMEM43 protein. We further characterized TMEM43 as a pH-sensing cation channel in the heterologous expression system. TMEM43 was shown to conduct transjunctional potentials between adjacent cells, further facilitating electrical couplings of the gap junctions. In the hippocampus of TMEM43 knockout (KO) mice, we observed decreased astrocytic dye diffusion and potassium buffering, increased neuronal excitability, and alterations in AMPA/NMDA ratio and LTP. The electrophysiological changes in the KO mice led to a disturbance in memory retrieval, which was rescued with TMEM43 overexpression. These results indicate that TMEM43 actively participates in gap junction networks of the hippocampus to prevent neurons from hyperexcitability, which is critical for memory retrieval. Together, our study elucidates the molecular and functional identities of TMEM43 and underscores its role in memory retrieval.

Dendrodendritic connections between inhibitory neurons in the visual thalamus from complex networks

Seohee Ahn, Ph.D.
Brain and Mind Research Institute, Weill Cornell Medicine



Local interneurons in the lateral geniculate nucleus of the thalamus supply feedforward inhibition to both relay cells and each other and, thus, have a powerful impact on visual signals traveling from retina to cortex. Previously, we showed that recordings from carnivore interneurons comprise trains of inhibitory postsynaptic currents (IPSCs), each preceded by transient depolarization, suggesting dendrodendritic synapses between interneurons. By contrast, recordings from mouse interneurons feature trains of excitatory postsynaptic currents (EPSCs). Thus, we were motivated to use serial block-face electron microscopy to study inhibitory networks across species. We first explored glomeruli--synaptic clusters in which dendrodendritic synapses are often embedded. Although glomeruli contained dendrodendritic connections between interneurons in both species, they were vastly different in structure. In ferret, glomeruli involved a large, central retinal bouton encircled by dendritic appendages of interneurons and relay cells. The situation in mouse was almost the inverse, numerous small retinal boutons surrounded one or two dendritic segments. This result suggests that a single retinal ganglion cell can activate undiluted and strong feedforward inhibition from one interneuron to another in ferret, whereas single afferents have a weaker impact in mouse. Further, interneuron dendritic inputs were made mainly onto shafts and postsynaptic dendrites were thicker in ferret, suggesting that many IPSCs can travel for long distances. Moreover, interneuron dendritic inputs to interneurons were closer to each other in ferret, suggesting stronger spatial summation of IPSCs. Finally, we discovered specialized lengths of interneuron dendrites in ferret that contacted many other interneuron segments but did not receive retinal input, a further indication of the importance of dendrodendritic communication among interneurons in this species. In sum, our work reveals a previously unappreciated feature of thalamic circuity--complex networks of dendritically coupled interneurons whose density and power appear greater in higher visual animals, carnivore, than in lower visual animals, rodent.

Semiconductor technology for reliable neural activity observation

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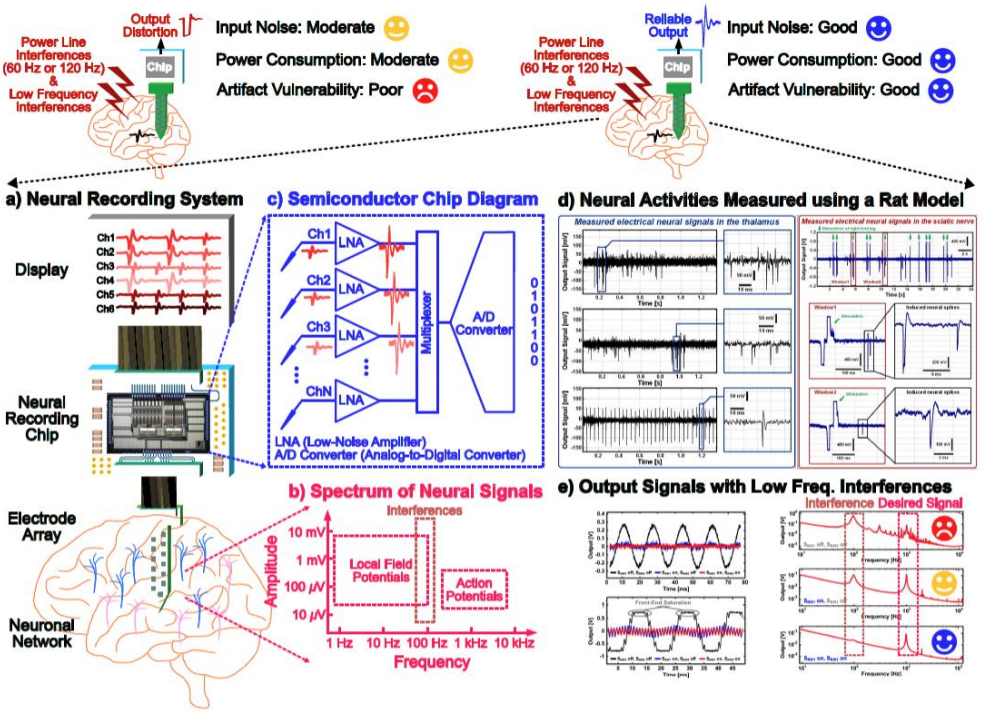
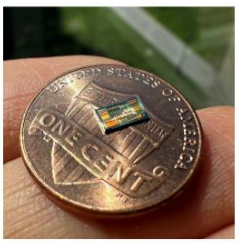
Department of Electrical Engineering, Columbia University





Chip Summary

Chip Size: 4.8 mm × 2.8 mm

Number of Channels: 16

Key Features
- **Reliable neural recording robust to interferences**
- **Low power and low noise operation**
- **Digital output**

Applicable Fields
- **Brain connectivity study**
- **Neural prosthetic device, e.g., brain-computer interface**
- ***In-vitro* cell monitoring platform**

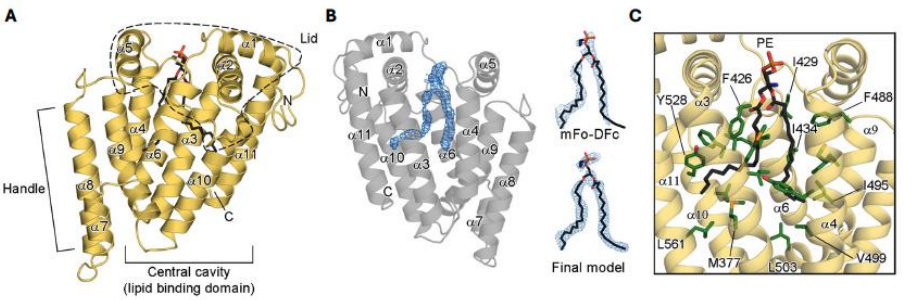
Since the 1970s, semiconductor technology has made significant progress, leading to advances in neuroscience and neural prosthetic devices. Advanced semiconductor technologies have enabled high-resolution neural activity observation, from single neuron activity to multiple neuronal harmonics. In this study, the semiconductor chip that monitors action potential (APs) and local field potentials (LFPs) is presented, and the verification results of the chip are presented using a rat model. The proposed semiconductor chip consists of 16 recording channels and produces digital output through amplification and digitization of APs and LFPs. When observing neuronal activity through calcium imaging, reliable monitoring of APs is essential because neuronal spikes are correlated with the rate of calcium ion release. Therefore, the proposed chip provides the ability to record neural

activity while minimizing signal distortion of APs due to out-of-band interferences. Compared to conventional neural recording chips, the proposed chip is designed to be robust to power line interferences (60-Hz or 120-Hz) and low-frequency interferences (e.g., motion artifacts), which significantly suppresses the distortion of APs due to interferences. Accordingly, the proposed chip can be used as a useful tool in the neural connectivity study by providing reliable neural information to neuroscientists and biologists even in the presence of various electrical interferences, e.g., 60-Hz, 120-Hz, and motion artifacts. The proposed chip is developed using a 180-nm complementary metal-oxide-semiconductor (CMOS) technology and the chip size is 4.8 mm Å~ 2.8 mm. The power consumption is 2 μW per channel and the input noise of a channel is achieved as 2.9 μV_{rms}. Finally, in the thalamus and sciatic nerve of a rat model, the chip functionality is verified by monitoring reliable neural activity even in the presence of interferences. This chip can be applied to a variety of neural recordings in multiple brain regions by providing distortion-free neural activity.

Structural Basis for Mitoguardin-2 Mediated Lipid Transport at ER-mitochondrial Membrane Contact Sites

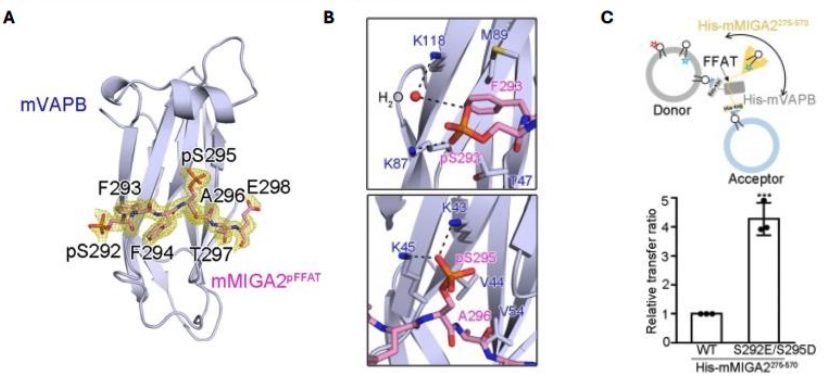
Hyunwoo Kim, Ph.D.
Howard Hughes Medical Institute, The Rockefeller University

Fig 1. Overall structure of Mitoguardin-2 LD targeting domain



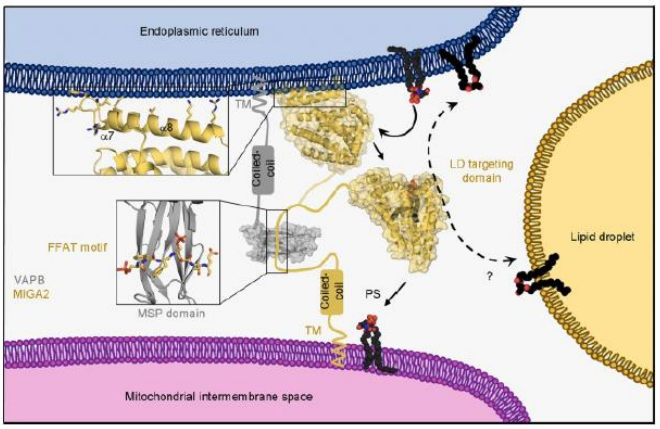
A) Overall structure of MIGA2 LTD. B) Lipid density and C) Lipid binding interface of MIGA2 LTD.

Fig 2. MIGA2 interacts with VAPB via the phosphorylated FFAT motif



A) Overall structure and B) binding interfaces of VAPB-MIGA2 FFAT motif complex.
C) Lipid transfer ratio when both the His-mMIGA2$^{275–570}$ and His-mVAPB are associated with the membranes.

Fig 3. Putative working model of MIGA2 at the ER-Mitochondria Membrane Contact Sites



The endoplasmic reticulum (ER)-mitochondria contact site (ERMCS) is crucial for exchanging biological molecules such as phospholipids and Ca2+ ions between these organelles. Mitoguardin-2 (MIGA2), a mitochondrial outer membrane protein, forms the ERMCS in higher eukaryotic cells. Here, we report the crystal structures of the MIGA2 Lipid Droplet (LD) targeting domain and the ER membrane protein VAPB bound to the phosphorylated FFAT motif of MIGA2. These structures reveal that the MIGA2 LD targeting domain has a large internal hydrophobic pocket that accommodates phospholipids and that two phosphorylations of the FFAT motif are required for tight interaction of MIGA2 with VAPB, which enhances the rate of lipid transport. Further biochemical studies show that MIGA2 transports phospholipids between membranes with a strong preference for binding and trafficking phosphatidylserine (PS). These results provide a structural and molecular basis for understanding how MIGA2 mediates the formation of ERMCS and facilitates lipid trafficking at the ERMCS.

Venue

NEW YORK KOREAN BIOLOGISTS NYKB

Cornell Belfer Research Building 3rd floor
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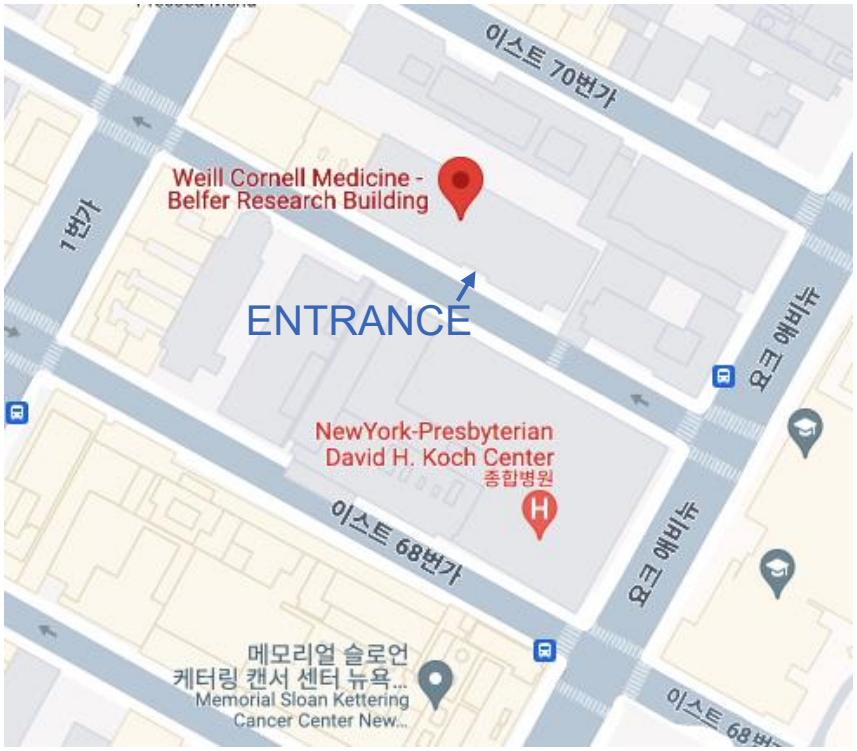

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