

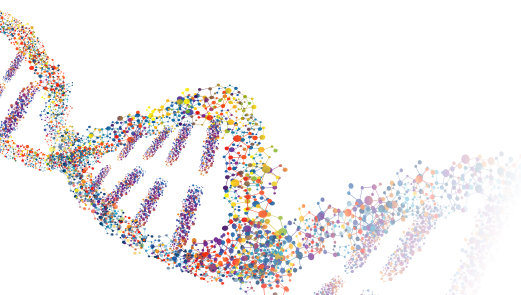
## Plenary Lecture 1

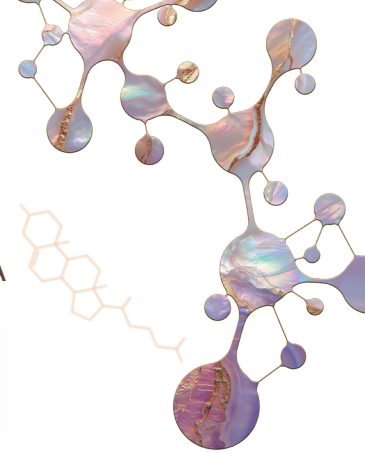
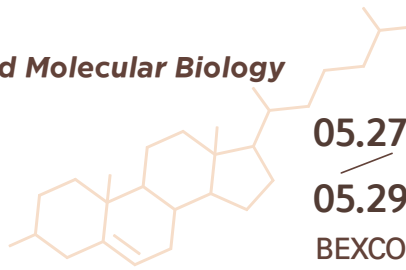
# Spatial omics reveals intra-tumor malignant cell diversity shaped by microenvironmental cues in colorectal cancer

Shyam PRABHAKAR

*A\*STAR, Singapore*

Colorectal cancer (CRC) exhibits extensive intra-tumor heterogeneity that contributes to tumor progression and treatment resistance. To understand the diverse malignant cell states, their spatial organization and microenvironment niches, we employ spatial transcriptomics to generate maps of resected CRC tumors, comprising >10 million cells from 79 samples (Xenium:21, MERFISH:43, GeoMx DSP:15). We identify 16 distinct cellular neighborhoods that reveal disruption of the stereotypic spatial organization of normal colon in cancer. We discover a tumor budding neighborhood comprising invasive malignant cells (IMCs) and inflammatory CAFs at the tumor-normal interface. IMCs upregulate wound healing and cell adhesion programs and predict reduced progression-free survival in an independent cohort. Using in vitro assays on patient-derived organoids, we show that malignant cells adopt the IMC state and become invasive in response to microenvironmental cues. Our integrated spatial and single-cell atlas provides a foundation for understanding and targeting the pathways active in diverse malignant cells in CRC.





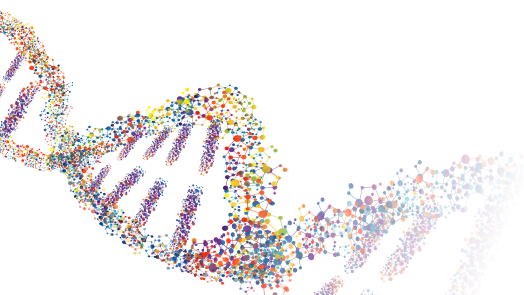
## Plenary Lecture 2

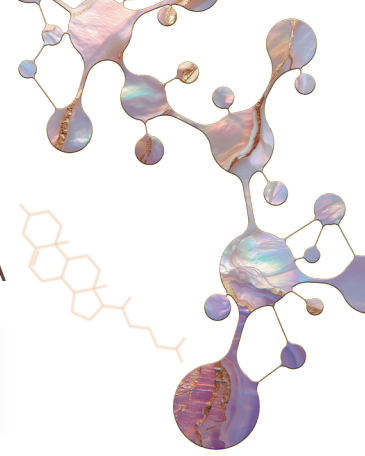
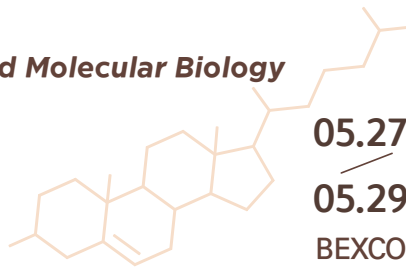
# How to Build Virtual Cell

Bo WANG

*University of Toronto, Canada*

Recent advances in generative AI and large-scale biological data are enabling a new paradigm for understanding living systems. In this talk, I will discuss our efforts toward building “virtual cells”, AI systems capable of modeling and predicting cellular behaviour across diverse biological contexts. I will present our work on scGPT, one of the first foundation models for single-cell biology, which demonstrated how transformer-based architectures trained on millions of cells can learn transferable representations of cellular states and gene programs across datasets and tasks. I will then discuss our recent work at Xaira Therapeutics on X-Cell, a large-scale virtual cell model trained on genome-wide perturbation datasets to predict cellular responses to genetic interventions in unseen biological contexts. X-Cell represents an important step from descriptive biological models toward causal and predictive cellular simulation. Finally, I will introduce emerging directions in biological reasoning systems such as BioReason, which integrate genomic foundation models with large language models to generate interpretable mechanistic hypotheses and support scientific discovery. Together, these efforts point toward a future in which AI-powered virtual cells enable in silico experimentation, accelerate therapeutic discovery, and transform our ability to understand and engineer biology.





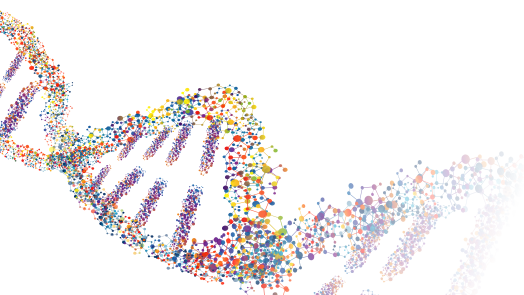
### Ilchun Plenary Lecture 3

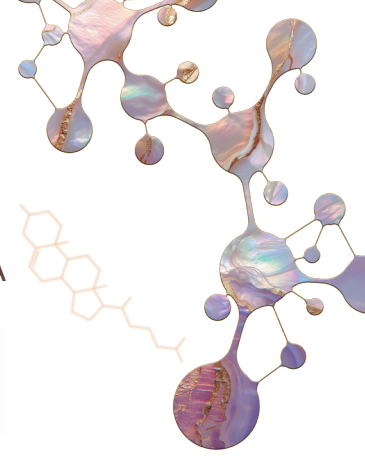
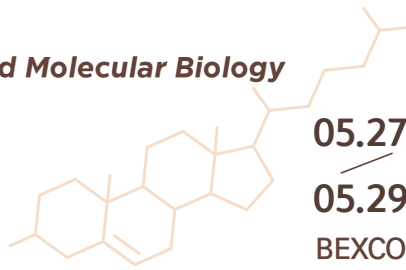
# The ticking DNA clock: How lifelong somatic expansion of a DNA repeat leads to neurodegeneration

Steven McCARROLL

*Harvard Medical School, USA*

Inherited DNA-repeat disorders such as Huntington's disease have long presented fundamental challenges to our understanding: Why do patients enjoy decades of good health before symptoms commence? Why do such disorders profoundly affect certain types of neurons while sparing other types of neurons and other cells? I will describe experiments in Huntington's disease that taught us a surprising answer to such questions: the inherited DNA repeat that causes the disease must undergo decades of somatic expansion – in specific types of neurons – and expand to several times its inherited length before it even begins to cause harm. This surprising model is turning out to explain many long-puzzling features of the illness, such as its tendency to affect different brain areas in ways that had long appeared to have different mechanisms. It also helps us understand how common genetic modifiers of the disease shape its pathogenic trajectory. An interesting possibility is that a similar dynamic may underlie many different DNA-repeat disorders.





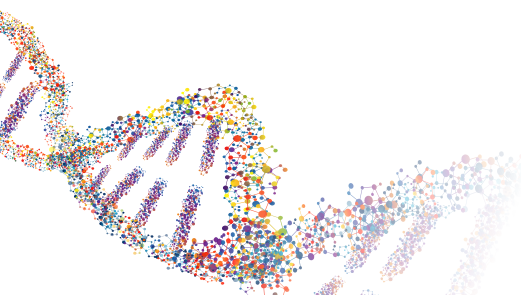
## Plenary Lecture 4

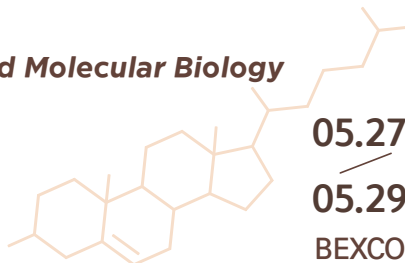
# The intestinal epithelial barrier and neuroimmune network control fatty liver disease pathogenesis

Michael KARIN

*Sanford Burnham Prebys Medical Discovery Institute, USA*

The incidence of non-alcoholic (MASLD) and alcoholic (ALD) fatty liver diseases has grown dramatically in the past 20 years, and their current annual health care costs exceed 150 billion US dollars. Much of the mechanistic investigation of MASLD and ALD pathogenesis had focused on hepatocyte intrinsic metabolic aberrations. However, it has become clear that the gut-liver axis also plays a critical pathogenic and protective roles by serving as a conduit through intestinal microbes and their metabolites, such as endotoxin (lipopolysaccharide, LPS) reach the liver and as a source of anti-microbial peptides (AMP). Starting with RNA-seq analysis of transcriptomic changes that accompany MASLD and MASH development in response to high fructose diet (HFrD) we found pronounced upregulation of Toll-like receptors (TLRs) and their downstream signaling effectors in the diseased liver, suggesting HFrD-induced translocation of intestinal microbes and/or endotoxin. Confirming the existence of diet induced endotoxemia, we also observed signs of barrier disruption and aberrant IL-22 signaling, which contributes to several key aspects of the intestinal epithelial barrier, including AMP induction. Consistent with these findings, administration of recombinant IL-22Fc fusion protein to re-ignite IL-22 signaling resulted in the complete resolution of all MASLD/MASH signs in mice fed HFrD or Western diet (WD). Surprisingly, however, the therapeutic effect was blocked by ablation of IL-22Ra in intestinal epithelial cells (IEC), but was unaffected by its ablation in hepatocytes, indicating that IL-22 acted in the intestine rather than the liver. Further investigation indicated that IL-22Fc treatment inhibited the diet-induced expansion of absorptive enterocytes, thereby minimizing the absorption of dietary fats and sugars. IL-22 signaling was also found to protect the liver from ALD, whose pathogenesis is strongly dependent on gut-to-liver bacterial translocation. Together with our collaborations Drs. Cristina Llorente and Bernd Schnable at UCSD we found that extensive alcohol consumption in mice and humans results in the downregulation of muscarinic acetylcholine receptor 4 (M4), which is specifically expressed in goblet cells. Accordingly, M4 induction and activation provided complete protection from both ALD and MASLD through the stimulation of IL-22 dependent anti-microbial immunity. Collectively, these studies indicate that the intestinal epithelial barrier and the mucosal neuroimmune network play instrumental roles in the pathogenesis, as well as resolution, of non-alcoholic and alcoholic fatty liver diseases.

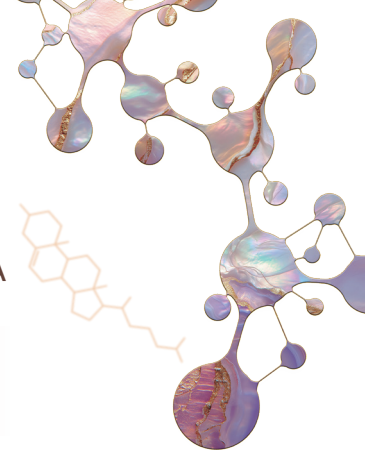




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BEXCO, BUSAN, KOREA



FROM MOLECULES TO MEGABYTES:  
AI AND BIG DATA TRANSFORMING LIFE SCIENCE

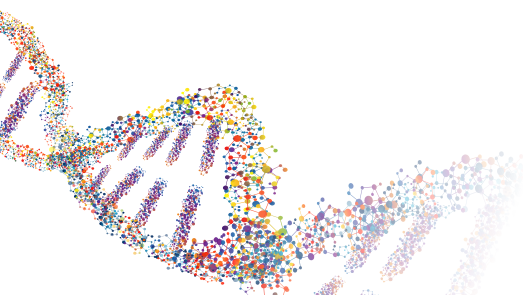
## Plenary Lecture 5

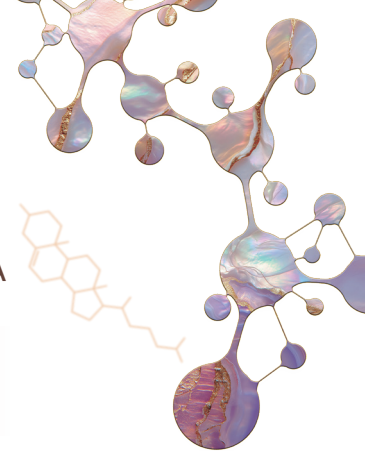
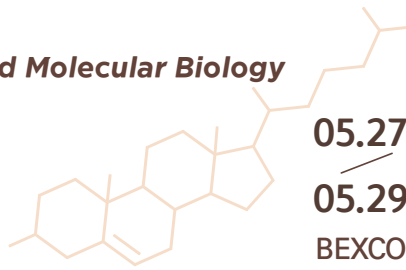
# New Pathways in Lipid Metabolism

Peter TONONZOZ

*University of California, Los Angeles, USA*

Lipids are key signals controlling gene expression in the enterohepatic axis. Our long-term objective is to reveal fundamental mechanisms by which lipid signals orchestrate cellular and systemic lipid homeostasis. The flux of cholesterol and fatty acids through liver and intestine is an important determinant of tissue and systemic metabolism. Excess lipid accumulation in the enterohepatic axis is linked to diabetes and gastrointestinal diseases, including Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD), intestinal inflammation, and atherosclerosis. We have characterized a family of mammalian proteins (Aster-A, -B and -C) that play an important role in nonvesicular cholesterol transport from plasma membrane to ER. Asters are integral ER proteins that are recruited to the plasma membrane in response to excess cholesterol. We have defined important roles for Aster proteins in liver and intestinal metabolism. We have shown that hepatic Aster-C and Aster-A play key roles in reverse cholesterol transport (RCT) and fasting in liver, and that Aster-B and Aster-C are important for dietary cholesterol absorption and chylomicron production by the intestine. We have also validated small molecule Aster inhibitors as tool compounds for the study of Aster function. Collectively, our findings to date establish the Aster pathway as a physiologically important and pharmacologically tractable node in systemic lipid metabolism.





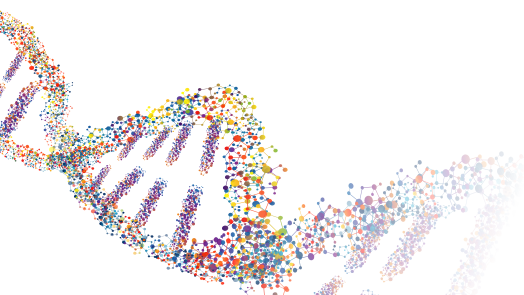
## Plenary Lecture 6

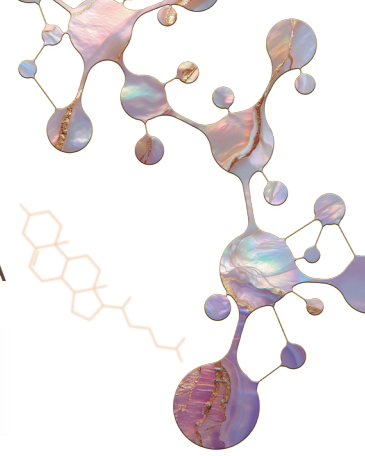
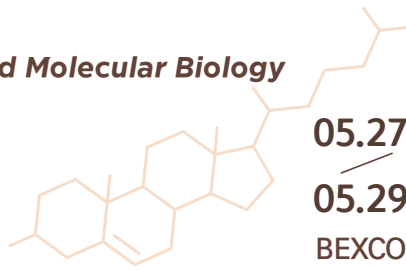
# Meningeal Lymphatics: A Novel Pathway for Brain Clearance

Gou Young KOH

*IBS/KAIST, Korea*

Cerebrospinal fluid (CSF) clearance of neurotoxic proteins—including amyloid- $\beta$  and tau—alongside cellular debris and metabolites, is fundamental to central nervous system (CNS) homeostasis. Undergoing three to five complete turnovers daily through tightly regulated influx and efflux, CSF circulation is essential for sustained brain health. Impaired CSF drainage has been increasingly implicated in age-related cognitive decline and neurological disorders such as Alzheimer's disease, Parkinson's disease, stroke, hydrocephalus, and traumatic brain injury, underscoring the therapeutic potential of strategies that enhance CSF outflow and brain waste clearance. The rediscovery of meningeal lymphatics as a key CSF drainage route—pioneered by the groups of Kari Alitalo and Jonathan Kipnis in 2015—reinvigorated this field. Building on this foundation, our group systematically mapped the principal meningeal lymphatic networks and their anatomical interconnections governing CSF outflow. More recently, we identified a novel, direct CSF egress pathway through a discontinuous arachnoid membrane at the cribriform plate, with significant implications for brain waste clearance and immune surveillance. In this lecture, I will discuss these discoveries in the context of neurodegenerative disease pathophysiology and CNS immune surveillance. Special emphasis will be placed on the anatomical and functional axis spanning the olfactory bulb, cribriform plate, and olfactory mucosa of the nasal cavity—an underappreciated yet critically important brain-periphery interface—as well as adrenergic regulation of cervical lymphatics in CSF outflow.





## Kyung-Ahm Lecture

# Unexpected roles of interleukin-17 and identification of its target cells

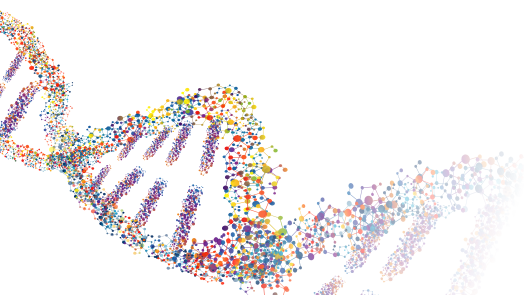
Jun R. HUH

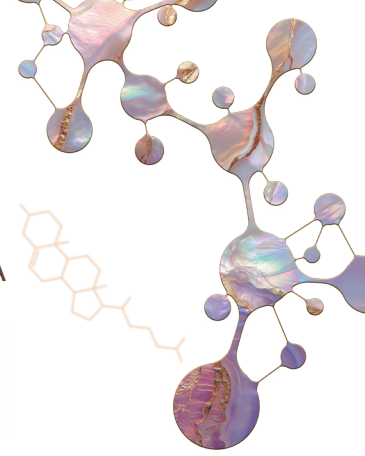
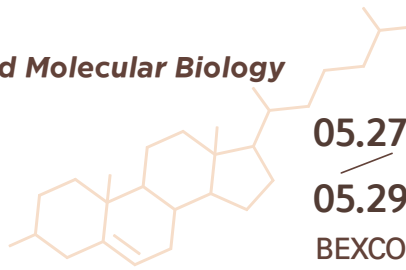
*Department of Immunology, Harvard Medical School, Boston, MA, USA*

Maintaining equilibrium between inflammatory Th17 cells and anti-inflammatory regulatory T cells (Tregs) is critical for supporting intestinal barrier function and tissue homeostasis. Nuclear hormone receptors (NHRs) have been shown to play crucial roles in the development and function of key immune cells, including Th17 and Treg cells. Our earlier work using the *Drosophila* system led to the identification of the first small-molecule inhibitor of ROR $\gamma$ t, a cardinal driver of the Th17 cell program. Building on this work, I hypothesized that microbial metabolites may modulate T cell differentiation and function by binding to NHRs. Using mass spectrometry-based screening approaches, we identified human gut bacteria and their corresponding enzymes that produce immune-modulatory bile acids. We further demonstrated that both these bile acids and the bacterial enzymes required for their biosynthesis are significantly reduced in patients with inflammatory bowel disease.

Beyond its role in mucosal immunity, IL-17 possesses a unique structure distinct from any other known cytokine and modulates neurological function. In the final part of this lecture, I will discuss our ongoing efforts to understand how immune signaling pathways control immune function as well as how they orchestrate behavioral and mood changes in the brain.

**Keywords:** Th17 cell, Interleukin-17, Neuroimmunology, cytokine





## Special Lecture

# Digital Healthcare 2026: The Era of Generative AI

KoonHo RHA

*NAVER CARE, Korea*

### The Integration of Healthcare and Generative AI

Healthcare system is currently facing two pivotal shifts: the transition into a super-aged society and the dawn of the Generative AI era. Digital Healthcare 2025-2026 is defined as the period where Generative AI is fully integrated into clinical settings to secure both operational efficiency and long-term sustainability. While traditional AI (ML, CV, NLP) relied primarily on labeled data, Generative AI holds the potential to solve fundamental inefficiencies in healthcare by proposing and creating new forms of output based on large-scale datasets.

### Enhancing Clinical Efficiency through Generative AI

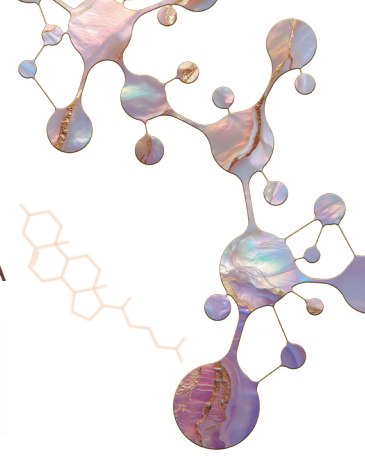
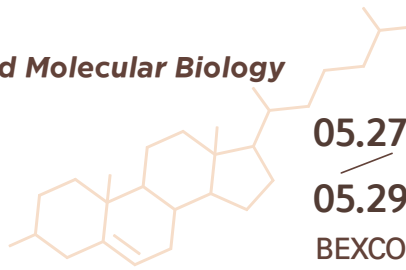
One of the primary factors undermining the sustainability of medical institutions is the excessive administrative burden on clinicians, leading to high rates of burnout. A significant number of practitioners report moderate to high levels of exhaustion. Generative AI addresses this challenge through the following specialized functions:

- Automated Clinical Support: Voice technology is applied to recognize patient-doctor conversations in real-time and automatically record them into Electronic Health Records (EHR).
- Administrative Burden Reduction: AI supports back-office automation by drafting insurance appeals, creating patient education materials, and summarizing vast medical records to extract key information for audits.
- Patient Journey Management: By integrating and automating solutions for symptom triage, automated response systems, and remote monitoring, AI enables patient-centered services built on the vertical integration of healthcare, insurance, and nursing care.

### The Future Direction of Digital Healthcare

The global transition toward a super-aged society is increasing the importance of chronic disease management and caregiving, extending the scope of healthcare into “Life Logs”—the data of daily life outside the hospital. Naver’s daily health-focused content and features, such as the Health Page and Pedometer, are representative examples of this digital health management in everyday life. Moving forward, AI-based Clinical Decision Support (CDS) tools will become increasingly universal and sophisticated.





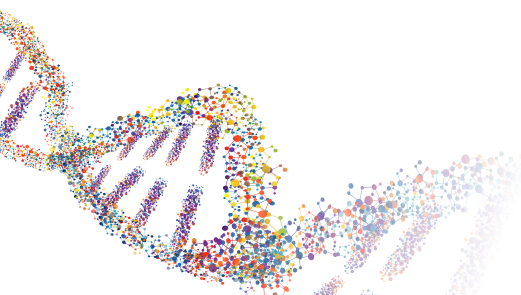
## Special Clinical Session 1

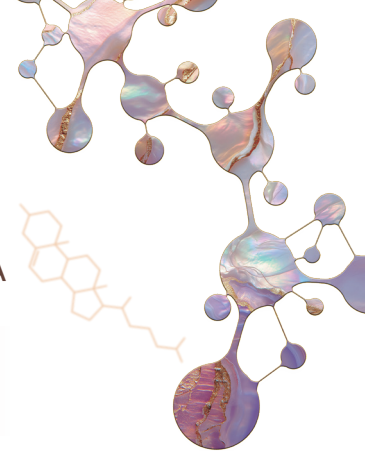
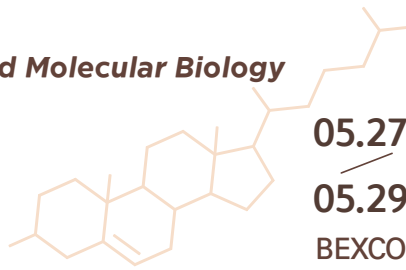
# Striving for a Quantum Leap on Molecular Residual Disease (MRD) Clinical Development: Insights from CIRCULATEJAPAN & SCRUM-MONSTAR

Takayuki YOSHINO

*National Cancer Center Hospital East, Japan*

Circulating tumor DNA (ctDNA) is the fraction of cell free DNA in patient blood that originates from a tumor. Advances in DNA sequencing technologies and our understanding of the molecular biology of tumors have increased interest in exploiting ctDNA to facilitate detection of molecular residual disease (MRD). Analysis of ctDNA as a promising MRD biomarker of solid malignancies has a central role in precision medicine initiatives exemplified by our CIRCULATEJapan project involving patients with resectable colorectal cancer. Notably, the project underscores prognostic significance of the ctDNA status at 4 weeks postsurgery and its correlation to adjuvant therapy efficacy. This substantiates the hypothesis that MRD is a critical prognostic indicator of relapse in colorectal cancer. Despite remarkable advancements, challenges endure, primarily attributable to the exceedingly low ctDNA concentration in peripheral blood, particularly in scenarios involving low tumor shedding and the intrinsic error rates of current sequencing technologies. These complications necessitate more sensitive and sophisticated assays to verify clinical utility of MRD across all solid tumors. Whole genome sequencing (WGS)-based tumorinformed MRD assays have recently demonstrated the ability to detect ctDNA in the parts-per-million range. We have recently showed pan-cancer implementation of WGSbased personalized ctDNA detection, achieving universal baseline sensitivity and ultrasensitive MRD detection across tumor types, including those traditionally challenging to assess by whole exome sequencing (WES)-based tumorinformed MRD assays. This presentation highlights current landscape of MRD assays, highlighting WGSbased approaches as the forefront technique in ctDNA analysis. Additionally, it introduces our upcoming endeavor, WGS-based pan-cancer MRD detection, in our SCRUM-Japan MONSTARSCREEN-3.





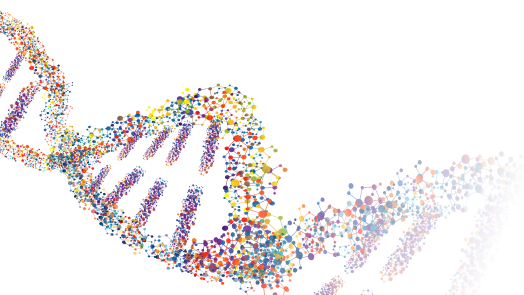
## Special Clinical Session 2

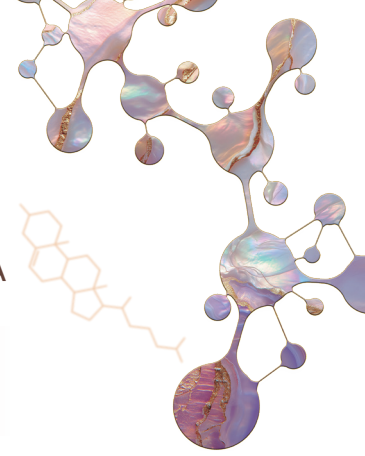
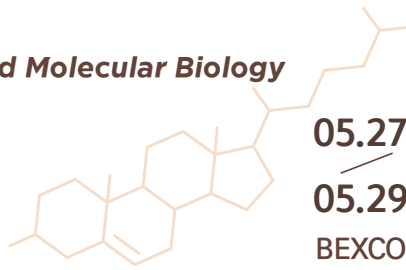
# Changing treatment paradigm of advanced gastric cancer with insights from tumor microenvironment biology

Sun Young RHA

*Yonsei University, Korea*

Precision medicine including targeted and immunotherapy is becoming feasible in gastric cancer(GC), with accumulation of immune-genomic information. Based on TCGA molecular classification, current NGS technology makes it feasible for proper subgrouping toward precision treatment of advanced or metastatic GC. However, the progress of precision immunotherapy in metastatic GC has been slow and somewhat disappointing. The potential reasons for these limitations are tumor heterogeneity and difficulties in proper sample availability for reliable translational researches, and complex clinical behavior with unproven immune-genomic biology behind. Recently, we have increasing data with new technologies such as RNA transcriptomics, single cell genomics and spatial transcriptomics. Even though there is still lack of success in genome stable type GC, now we have more opportunities for precision medicine in GC with novel targets such as claudin 18.2 and various combination treatment with immunotherapy. Also, recent clinical trials data supports changing strategy of systemic treatment for metastatic GC. Here I will share the advances of immunotherapy of GC with more precise stratification of the patients based on tumor microenvironment





**KSBMB Award-Moosa Award Lecture**

# Cereblon: dark past, exciting present and bright future

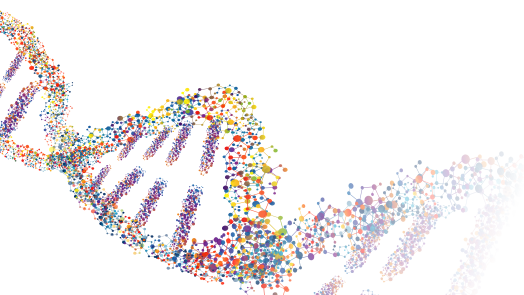
Chul-Seung PARK

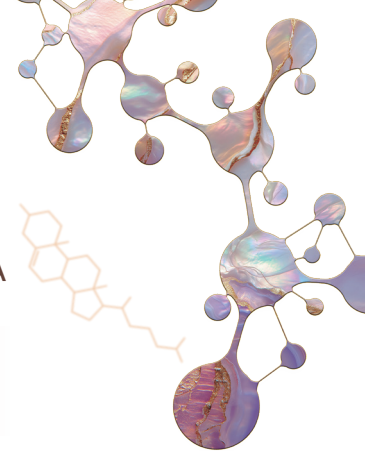
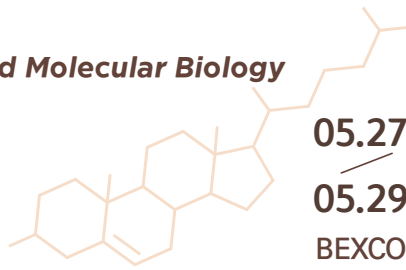
*GIST, Korea*

Cereblon (CRBN) is a substrate recognition component of the E3 ubiquitin ligase complex. The binding partners of CRBN vary across tissues and cell types, enabling it to regulate diverse biological functions. Over the past decade, the identification of novel endogenous CRBN substrates has significantly expanded our understanding of its physiological and pathological roles, as well as its potential as a therapeutic target in a wide range of diseases.

In this lecture, I will introduce CRBN and discuss how CRBN and its endogenous substrates contribute to the regulation of physiological and pathological processes. Recently, we identified molecular chaperones and co-chaperones as endogenous substrates of CRBN, and demonstrated how CRBN modulates the aggregation and toxicity of amyloidogenic proteins, including tau and  $\alpha$ -synuclein. We were able to obtain small peptides that inhibit the recruitment of target substrates to CRBN, thereby preventing their ubiquitination.

Our recent findings imply the therapeutic potential for the specific inhibition of CRBN and its substrates binding and provide novel strategies for preventing or delaying the progression of those neurodegenerative diseases.





**KSBMB Award-Donghun Award Lecture**

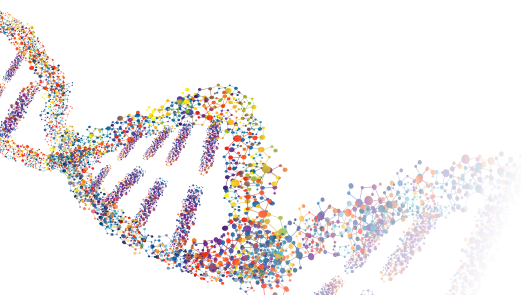
# Antibody engineering and B cell receptor repertoire analysis in Prof. Junho Chung's laboratory

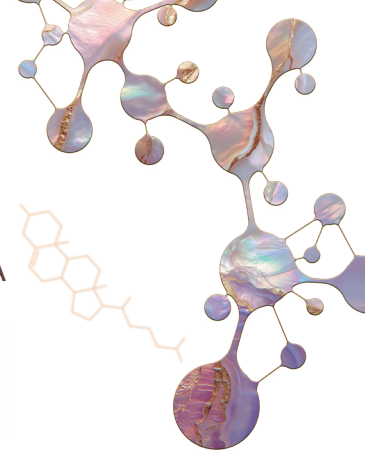
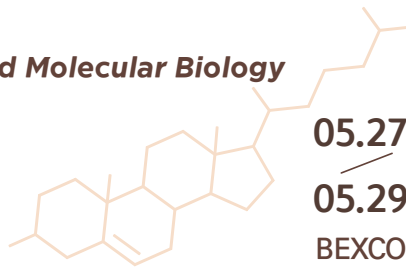
Junho CHUNG

*Seoul National University, Korea*

Research in our laboratory bridges classical antibody engineering and computational B cell receptor (BCR) repertoire analysis to develop next-generation antibody therapeutics. Building on training in recombinant antibody technology with the late Carlos F. Barbas III, we have used phage display, scFv-Fc and scFv-Ck formats, epitope mapping and antibody-drug conjugate design to generate antibodies against soluble ligands, cell-surface receptors and viral antigens. These efforts have produced a clinical-stage pipeline that includes a phase 2 anti-hepatocyte growth factor (HGF) antibody, an anti-CD19 chimeric antigen receptor (CAR) T cell therapy, anti-complement C5, anti-FAM19A and anti-contactin-4 (CNTN4) antibodies, a neutralizing antibody for severe fever with thrombocytopenia syndrome virus, and a universal HER2-targeting CAR-T platform — supported by more than 159 peer-reviewed publications, 30 issued patents and over 20 licensed assets.

In parallel, we have established a computational framework for human and primate BCR repertoire analysis that integrates next-generation sequencing with deep-learning models. We defined the peripheral blood volume required to faithfully reconstitute individual repertoires, developed protein-embedding methods to compare repertoires across donors, and built BCR-SORT, a deep-learning classifier that infers B cell subset identity directly from antigen receptor sequences. Applying this framework to COVID-19 patients and BNT162b2 vaccinees, we identified stereotypic SARS-CoV-2-neutralizing antibodies that pre-exist in naïve repertoires and traced the somatic-hypermutation trajectories that give rise to Omicron-variant-neutralizing antibodies after ancestral-strain vaccination. Together, these complementary lines of work establish a discovery-to-clinic pipeline anchored in repertoire biology.





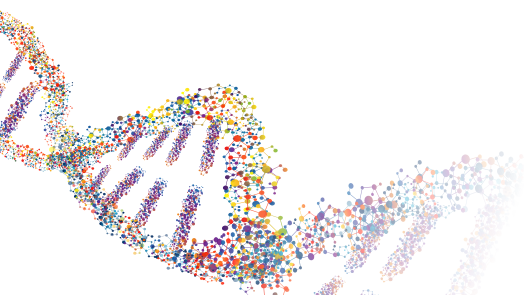
**KSBMB Award-Sasuk Award Lecture**

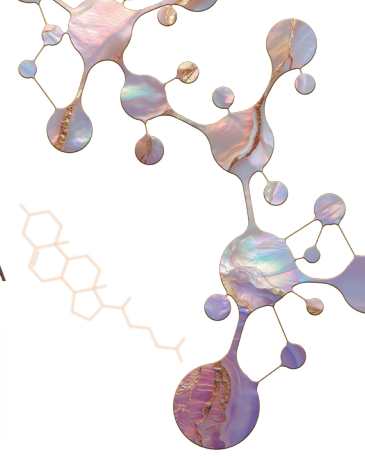
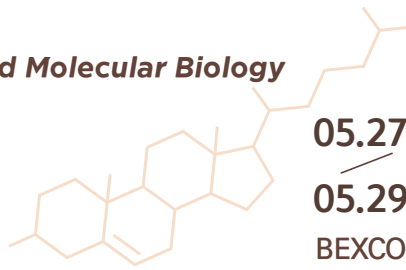
# Next-Generation Genome Editing: Precision, Delivery, and Therapeutic Potential

Kyoungmi KIM

*Seoul National University, Korea*

Recent advances in CRISPR-based genome editing have enabled precise genetic modifications. However, challenges remain in improving accuracy and delivery efficiency. Here, we focus on developing next-generation genome editing technologies that enhance precision while minimizing unintended effects. This work includes innovative delivery strategies, such as virus-like particle (VLP)-based systems, as well as compact CRISPR platforms like Cas12f1 for improved in vivo applications. We also develop advanced editing approaches, including base and prime editing, to achieve precise and efficient genome modification. These efforts aim to advance safe and versatile genome editing technologies and facilitate their translation into therapeutic applications for genetic diseases.





**KSBMB Award-Gong-Wu Nature Award Lecture**

# **Saving lives through ultra-rapid antimicrobial susceptibility testing**

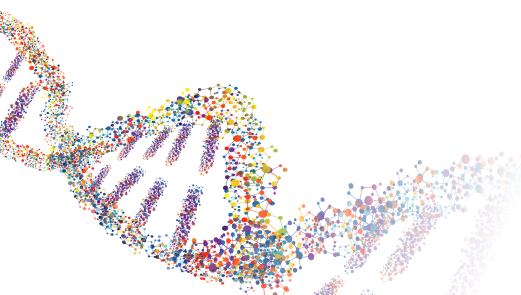
Sunghoon KWON

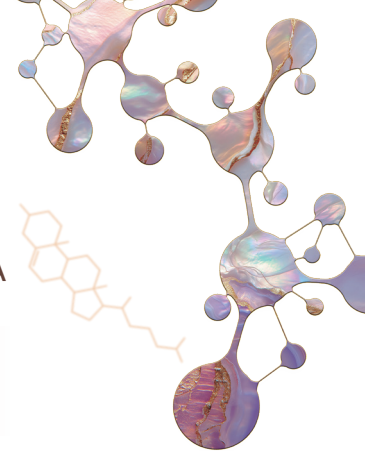
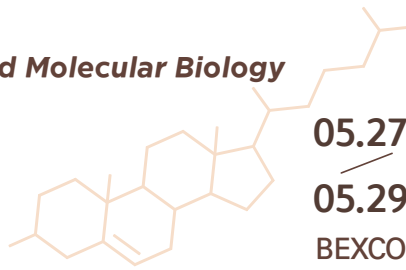
*Seoul National University, Korea*

Sepsis is a life-threatening condition caused by bloodstream infections and requires immediate, targeted antimicrobial therapy. Each hour of delay in administering appropriate treatment increases the risk of mortality. However, current diagnostic workflows are still heavily reliant on time-consuming blood culture processes, which often take more than 48 hours to produce actionable results. Consequently, empirical use of broad-spectrum antibiotics remains common, yet frequently leads to suboptimal clinical outcomes.

To overcome this critical bottleneck, several rapid antimicrobial susceptibility testing (AST) methods have been developed that bypass the need for pure bacterial culture. Among these, our group previously introduced the direct and rapid AST (dRAST) system, which performs phenotypic susceptibility testing directly from positive blood cultures using time-lapse imaging of bacterial growth dynamics. While dRAST significantly reduces turnaround time by eliminating the subculture step, the initial blood culture phase still poses a major limitation to further accelerating sepsis diagnostics.

Here, we present an ultra-rapid AST (uRAST) platform designed to substantially shorten the diagnostic timeline by minimizing reliance on conventional blood culture. This system integrates magnetic nanoparticle-based bacterial enrichment directly from whole blood, species identification via an encoded microdisk library, and rapid phenotypic AST from a low-inoculum bacterial suspension. By combining these technical components, uRAST enables a culture-independent workflow that delivers results over 60 hours faster than standard methods. This advancement represents a significant step forward in the pursuit of truly rapid sepsis diagnostics, with the potential to facilitate earlier targeted therapy and improve patient outcomes in critical care settings.





**KSBMB Award-Kang Hyen Sam Excellence in Research Award Lecture**

# Cellular Senescence: An Inevitable End or a Reversible Pause?

Tae Jun PARK

*Ajou University School of Medicine, Korea*

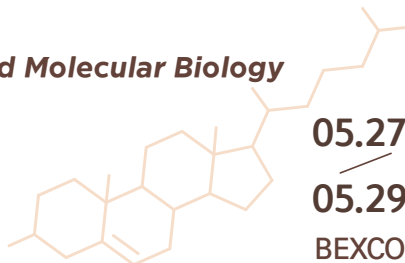
Traditionally, cellular senescence has been viewed as an irreversible growth arrest, serving as a terminal barrier against oncogenic transformation. However, deeper molecular interrogation reveals that senescence is not a monolithic destination but a highly dynamic and heterogeneous process. My research has consistently challenged the notion of “no return” by identifying distinct transitional states within the senescent program.

A pivotal shift in this paradigm emerges from the discovery of ‘mid-old cells,’ a unique intermediate population retaining functional plasticity. Unlike full-senescent cells in a metabolic stalemate, mid-old cells exhibit a remarkable capacity for rejuvenation when exposed to systemic youthful factors or specific pharmacological interventions. This suggests that the aging process contains latent windows for functional restoration, shifting the therapeutic focus from the mere elimination of senescent cells to the sophisticated modulation of their state.

This complexity is further magnified within the tumor microenvironment, where senescence undergoes a profound spatial evolution. Far from being a simple inhibitory mechanism, senescent phenotypes in cancer cells can adaptively transition to promote metastatic progression and remodeling. Such spatial heterogeneity underscores that senescence is a context-dependent, strategic pause utilized for survival and adaptation.

By integrating molecular insights into the systemic impact of senescent secretomes, we uncover a ‘modulable pause’—a biological stasis that can be re-scripted through precise intervention. This lecture illuminates how deciphering this language will define the next frontier of precision anti-aging medicine and oncology.

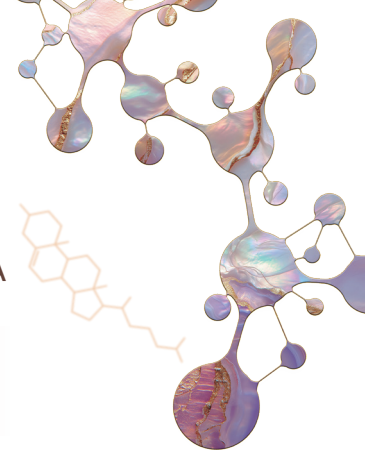




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BEXCO, BUSAN, KOREA



FROM MOLECULES TO MEGABYTES:  
AI AND BIG DATA TRANSFORMING LIFE SCIENCE

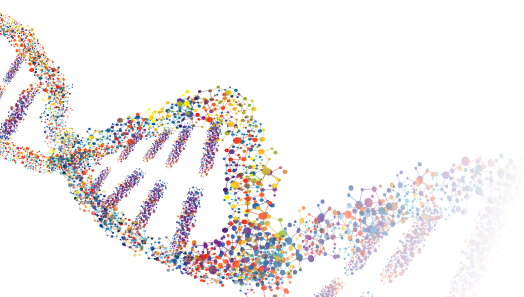
**S1-1 Neuroimmunology in Health and Diseases**

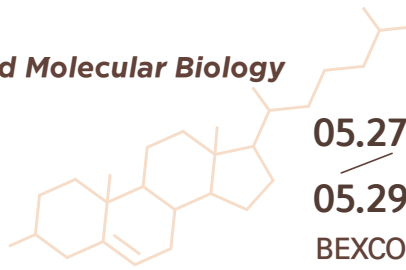
## Regulation of CNS inflammation

Francisco J. QUINTANA

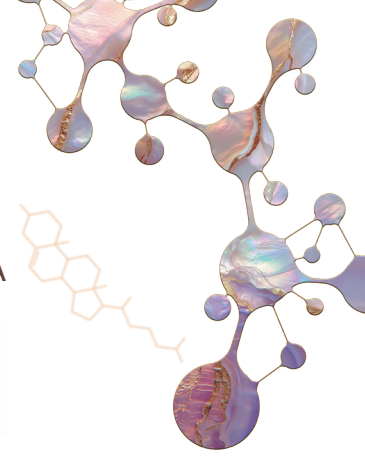
*Brigham and Women's Hospital, Harvard Medical School, USA*

Inflammation in the central nervous system (CNS) is a tightly regulated process that supports host defense and tissue repair but, when dysregulated, contributes to neurodegeneration and neurological disease. Regulation of CNS inflammation involves coordinated interactions among microglia, astrocytes, peripheral immune cells, and the blood-brain barrier that balance pro- and anti-inflammatory signaling to maintain immune homeostasis.

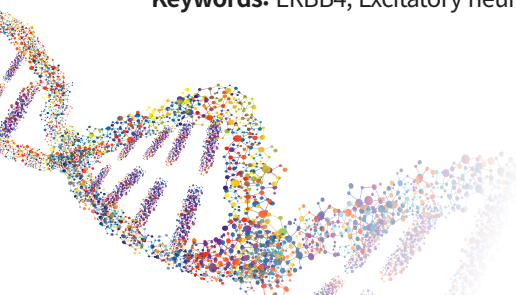


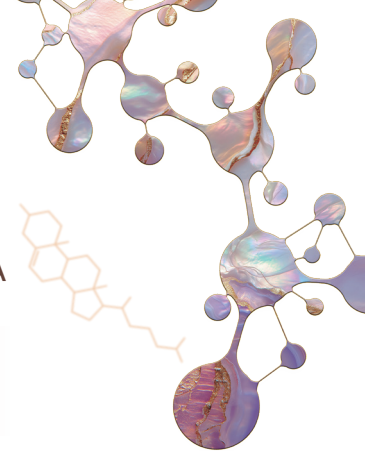
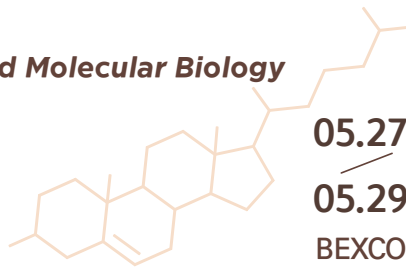
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BEXCO, BUSAN, KOREA

FROM MOLECULES TO MEGABYTES:  
AI AND BIG DATA TRANSFORMING LIFE SCIENCE**S1-2 Neuroimmunology in Health and Diseases****Excitatory Neuronal ERBB4 Promotes Early Pathophysiology of Alzheimer's Disease**Se Young LEE<sup>1,2</sup>, Eunseok PARK<sup>1,2</sup>, Seongbin KIM<sup>2,3</sup>, Yeji YEO<sup>2,3</sup>, Juwon PARK<sup>2</sup>,  
Young-Jin CHOI<sup>1,2</sup>, Kiheon LEE<sup>2</sup>, Ki-Jun YOON<sup>2</sup>, Sanghoon PARK<sup>4</sup>,  
Eunjoon KIM<sup>2,3</sup>, Won-Suk CHUNG<sup>1,2,\*</sup><sup>1</sup>Center for Vascular Research, Institute for Basic Science (IBS), Daejeon 34141, Republic of Korea<sup>2</sup>Department of Biological Sciences, Korea Advanced Institute of Science and Technology (KAIST), Daejeon 34141, Republic of Korea<sup>3</sup>Center for Synaptic Brain Dysfunctions, Institute for Basic Science (IBS), Daejeon 34141, Republic of Korea<sup>4</sup>Illim Therapeutics, Seoul 06376, Republic of Korea

Neuroinflammation and synapse loss are highly associated with cognitive decline in Alzheimer's disease (AD). Although microglial hyper-phagocytic activity has been implicated in synapse loss, the precise mechanisms underlying these pathologies remain obscure. Here, we demonstrated that during AD progression in mice, astrocytes and microglia increase phagocytic elimination of excitatory synapses, while markedly reducing elimination of inhibitory synapses, suggesting neuroinflammation alone may be dispensable for early AD synapse loss. Instead, using single-nucleus RNA sequencing (snRNAseq), we identified the emergence of Early Responsive Excitatory Neurons (ERENs), characterized by ectopic *erb-b2 receptor tyrosine kinase 4 (ErbB4)* expression, as one of the earliest major alterations in AD mouse models. Notably, specific deletion of *ErbB4* in AD excitatory neurons abrogated abnormal neuronal network activities and synapse loss, as well as reactive gliosis, amyloid plaque deposition, and cognitive deficits. Conversely, overexpression of *ErbB4* in wild-type (WT) excitatory neurons recapitulated these core AD phenotypes in the absence of amyloid plaques. Mechanistically, these effects were mediated by mammalian target of rapamycin (mTOR) signaling downstream of ERBB4. Subsequent snRNAseqs following *ErbB4* deletion or overexpression confirm that excitatory neuronal *ErbB4* is both sufficient and necessary to induce EREN and reactive gliosis. Finally, causal modeling of human AD transcriptomic data supports a model in which excitatory neuronal ERBB4 participates in a pathogenic cascade linking amyloid pathology to tau propagation and cognitive decline. Together, these findings reveal that the early pathophysiology of AD arises largely from aberrant *ErbB4* expression in excitatory neurons, and that targeting excitatory neuronal *ErbB4* may represent a therapeutic strategy for mitigating multiple neurodegenerative diseases.

**Keywords:** ERBB4, Excitatory neurons, Synapse loss, Alzheimer's disease



**S1-3 Neuroimmunology in Health and Diseases**

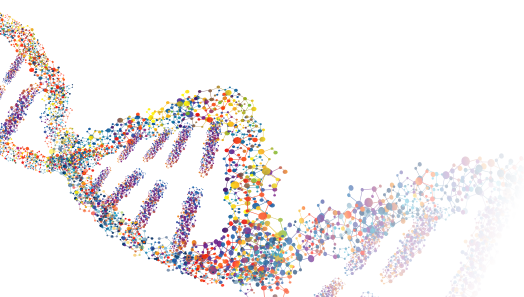
## Brain–body communication underlying complex behavior

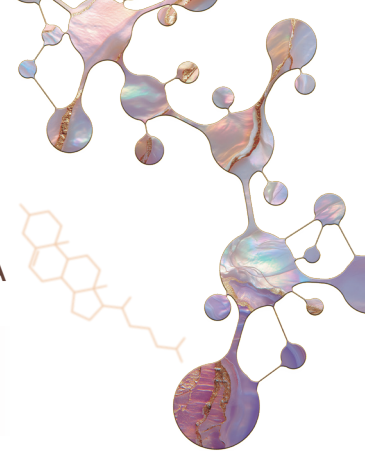
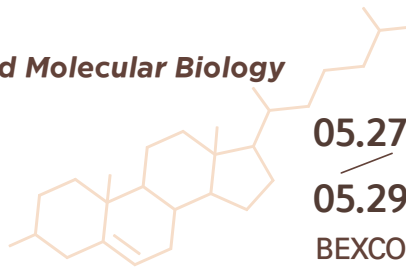
Michael WHEELER

*Harvard Medical School*

Neuroimmune interactions—signals transmitted between immune and brain cells—regulate many aspects of tissue physiology including responses to psychological stress, which can predispose individuals to develop neuropsychiatric diseases (Wheeler & Quintana Nature 2025). Still, the interactions between hematopoietic and brain-resident cells that influence complex behaviors are poorly understood. We recently used a combination of genomic and behavioral screens to demonstrate that astrocytes in the amygdala limit stress-induced fear behavior through EGFR (Chung et al. Nature 2025). Mechanistically, amygdala astrocyte EGFR expression inhibits a stress-induced pro-inflammatory signal transduction cascade that facilitates neuro-glial cross-talk and stress-induced fear behavior through the orphan nuclear receptor NR2F2 in amygdala neurons. We uncovered that, in turn, decreased EGFR signaling and fear behavior were associated with meningeal monocyte recruitment during chronic stress. This set of neuroimmune interactions was therapeutically targetable by psychedelic administration, which reversed monocyte accumulation in the brain meninges along with fear behavior. Moreover, we believe that these principles underlying the anti-inflammatory benefits of psychedelics in the brain are applicable to other tissues, such as peripheral tissues, with potentially similar mechanisms operating during tissue inflammation (Lee & Wheeler Neuron 2026). In the aggregate, these data suggest that psychedelics can be used to target neuroimmune interactions relevant to neuropsychiatric disorders and potentially other inflammatory diseases.

**Keywords:** Neuroimmunology, psychedelics, behavior





**S1-4 Neuroimmunology in Health and Diseases**

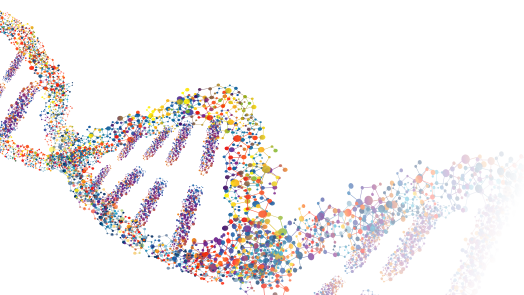
# Monocyte-derived microglia and neurodegenerative diseases

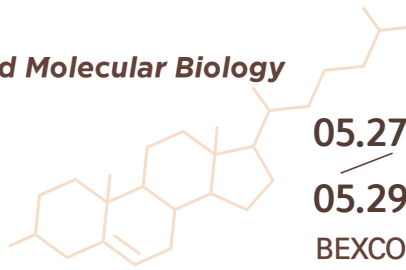
Jung-Seok KIM

*Department of Biological Sciences, Ulsan National Institute of Science and Technology (UNIST),  
Ulsan, 44919, Republic of Korea*

Microglia, the parenchymal brain macrophages, are established during embryogenesis and form a self-containing cellular compartment resisting seeding with cells derived from adult definitive hematopoiesis. We report that monocyte-derived macrophages (MoMF) accumulate in the brain of aging mice with distinct topologies, including the nigrostriatum and medulla, but not the frontal cortex. Parenchymal MoMF adopt bona fide microglia morphology and expression profiles. Unlike embryonic yolk sac-derived cells, monocyte-derived microglia (MoMg) are targets of clonal hematopoiesis (CH) due to their HSC derivation. Indeed, using a chimeric transfer model, we show that hematopoietic expression of DNMT3AR882H, a prominent human CH variant, renders MoMg pathogenic and to promote motor deficits resembling atypical Parkinsonian disorders. Collectively, we establish that MoMg progressively seed the brain of healthy aging mice, accumulate in selected areas, and, when carrying a somatic mutation associated with CH, can cause brain pathology.

**Keywords:** Microglia, clonal hematopoiesis, monocyte, Parkinsonian disorders

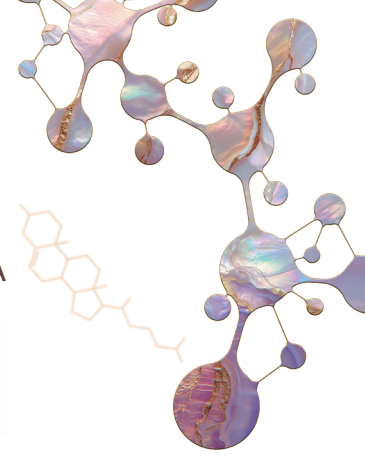




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FROM MOLECULES TO MEGABYTES:  
AI AND BIG DATA TRANSFORMING LIFE SCIENCE

**S2-1 Genome Engineering I: Advances in Functional Genomics Technology**

# Curing SDS disease: Prime Editing of SBDS and Precise Long-Read Assessment by CRISPRLungo

Gue-Ho HWANG<sup>1</sup>, Jing ZENG<sup>2,3</sup>, Haarika KATHI<sup>2,3</sup>, Timothy BARRY<sup>2,3,4,5</sup>,  
Akiko SHIMAMURA<sup>2,3</sup>, Luca PINELLO<sup>4,5\*</sup>, Daniel BAUER<sup>2,3\*</sup>

<sup>1</sup>Chemistry, Hanyang University, South Korea 04763, Korea

<sup>2</sup>Hematology/Oncology, Boston Children's Hospital, Boston 02115, USA

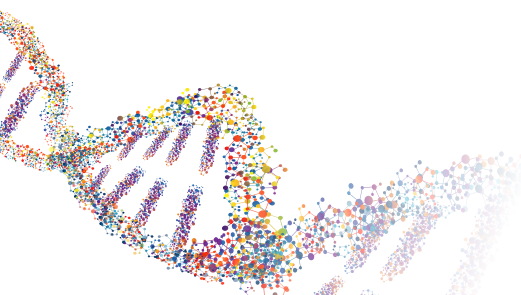
<sup>3</sup>Pediatrics, Harvard Medical School, Boston 02115, USA

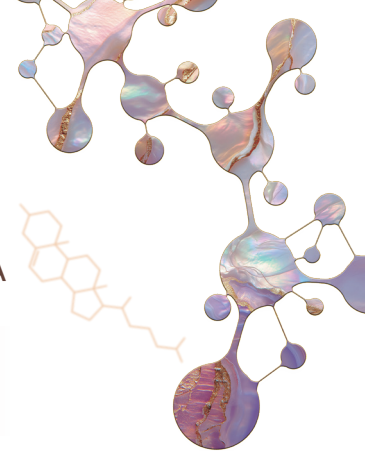
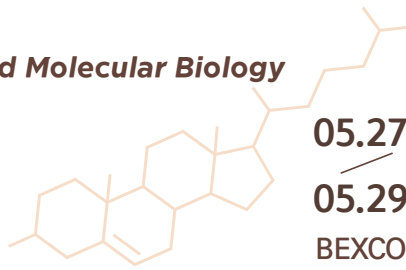
<sup>4</sup>Molecular Pathology, Massachusetts General Hospital, Boston 02114, USA

<sup>5</sup>Pathology, Harvard Medical School, Boston 02115, USA

Shwachman-Diamond syndrome (SDS) is an inherited bone marrow failure disorder primarily driven by the SBDS c.258+2T>C mutation. Here, we developed a Prime Editing (PE) strategy to precisely correct this mutation. To comprehensively evaluate editing efficiency, product purity, and structural variations, we utilized CRISPRLungo, a specialized long-read sequencing analysis pipeline. In engineered cells and patient-derived fibroblasts, PE achieved highly efficient correction (up to 68%), rescuing SBDS expression and ribosome biogenesis. Deep profiling via CRISPRLungo confirmed an exceptional precise edit-to-indel ratio without unintended massive structural variations. In patient-derived CD34+ hematopoietic stem cells (HSPCs) harboring somatic TP53 clones, ex vivo PE yielded 30% initial editing. Upon transplantation into NBSGW mice, edited cells demonstrated a profound survival advantage, with edit frequencies enriching to 78% in engrafted bone marrow. Importantly, SBDS correction effectively restored multilineage hematopoiesis and counter-selected against the engraftment of TP53 mutant clones. Conclusively, validated by the rigorous long-read assessment of CRISPRLungo, this PE approach demonstrates near-universal efficacy and high product purity, offering a precise and safe therapeutic strategy to restore hematopoietic function in SDS patients.

**Keywords:** CRISPR therapy, Shwachman-Diamond syndrome, Long-Read analysis





**S2-2 Genome Engineering I: Advances in Functional Genomics Technology**

# Building a Genome-wide Functional Genomics Atlas at Single-Cell Resolution

Byungjin HWANG<sup>1\*</sup>

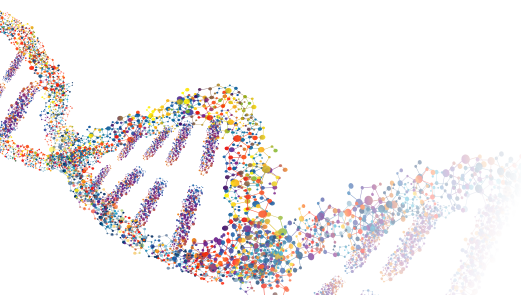
<sup>1</sup>*Department of Biomedical Sciences, Yonsei University, Seoul 03722, Korea*

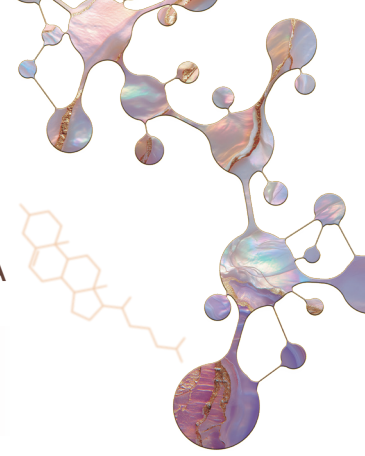
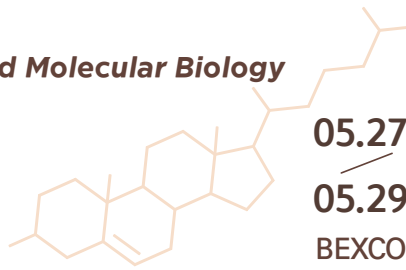
Genome-wide single-cell CRISPR screens have emerged as a powerful approach for mapping causal genes for specific phenotypes. Recent advances integrating CRISPR perturbations with single-cell profiling has created opportunities to further map causal regulatory networks at scale, but they have relied almost exclusively on transcriptomic readouts. As a result, the regulation of cell-surface protein phenotypes—which define immune cell identity, delineate functional subsets, and are primary targets for immunotherapy—remains largely unmapped at the same genome scale.

Here, we present SCITO-Perturb-seq, an ultra-high-throughput platform that integrates SCITO-seq combinatorial indexing (a droplet-based two-step combinatorial indexing method enabling single-cell measurement of hundreds of protein readouts across >10 cells per reaction) with genome-wide CRISPR activation to enable single-cell protein-level phenotyping at genome scale. Instead of profiling the entire transcriptome, SCITO-Perturb-seq focuses the readout on a targeted panel of surface proteins, reducing sequencing cost by orders of magnitude while maintaining massively parallel phenotyping across up to ~500,000 cells per 10x Chromium reaction.

Decomposition of the perturbation matrix by semi-NMF further revealed five phenotypic modules that coherently bridged pathway-annotated gene clusters and baseline surface protein co-expression groups, providing an integrated framework for interpreting how genetic regulators coordinate T cell surface phenotypic programs.

**Keywords:** Functional Genomics, CRISPR, Single-Cell Atlas





**S2-3 Genome Engineering I: Advances in Functional Genomics Technology**

# Functional Genomics–Driven Identification of ROS-Mediated Synthetic Lethality Between PTEN Loss and NRF2 Pathway Inhibition to Enable Biomarker-Guided Clinical Development

Kyuho HAN

*MEDiC Life Sciences Inc.*

High clinical attrition in oncology is often driven by insufficient efficacy and narrow therapeutic windows arising from inadequate patient selection. Although precision biomarkers hold promise, scalable and systematic approaches to identify robust genetic predictors of response remain limited.

We developed MCAT™, a high-throughput functional genomics platform integrating 3D tumor modeling with CRISPR-based engineering to generate a million-scale library of defined tumor variants. This system enables unbiased identification of synthetic lethal interactions, sensitivity determinants, and resistance mechanisms for therapeutic candidates.

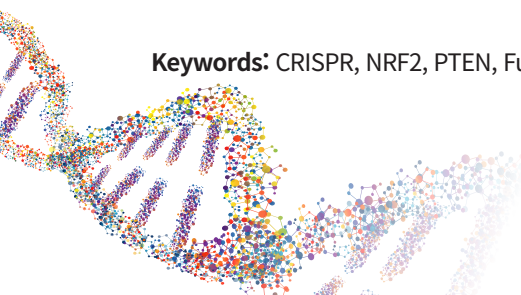
Applying MCAT™ to SLS-X, a clinical-stage NRF2 pathway inhibitor, we identified PTEN loss as a strong synthetic lethal biomarker. Mechanistically, PTEN-deficient tumors exhibit increased metabolic flux and mitochondrial oxidation, resulting in elevated basal reactive oxygen species (ROS). NRF2 inhibition by SLS-X suppresses antioxidant defenses, driving ROS beyond the viability threshold selectively in PTEN-loss tumor cells. This ROS-mediated cytotoxicity was not observed in PTEN-wildtype tumors or normal cells, supporting a tumor-selective mechanism.

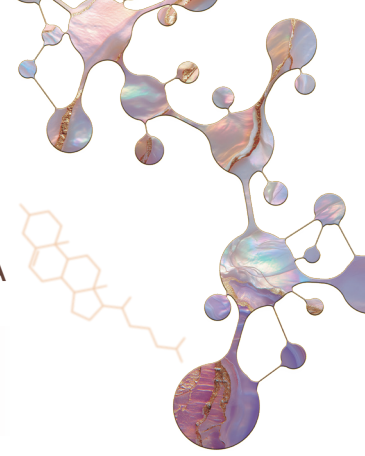
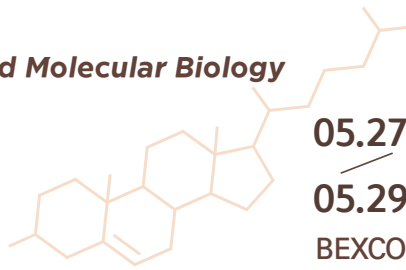
In vivo validation across a diverse panel of patient-derived xenograft models demonstrated robust tumor growth inhibition in PTEN-loss tumors with minimal activity in PTEN-intact models, confirming biomarker-dependent efficacy.

Given that PTEN is one of the most frequently altered tumor suppressors in solid malignancies and lacks targeted treatment options, these findings provide a strong biological rationale for biomarker-guided clinical development. A Phase 1b open-label basket study of SLS-X in PTEN-loss solid tumors is being initiated to prospectively evaluate safety, preliminary efficacy, and translational biomarkers.

Collectively, these results demonstrate the utility of scalable functional genomics to enable precision oncology and support SLS-X as a targeted therapy for PTEN-loss cancers.

**Keywords:** CRISPR, NRF2, PTEN, Functional Genomics, Biomarker





**S2-4 Genome Engineering I: Advances in Functional Genomics Technology**

# Systematic alignment of regulatory and functional prior knowledge with single-cell perturbation landscapes

Hyungtai SIM<sup>1,2#</sup>, Junha PARK<sup>2#</sup>, Byungjin HWANG<sup>1,3\*</sup>

<sup>1</sup>Department of Biomedical Sciences, Yonsei University College of Medicine, Seoul 03722, Korea

<sup>2</sup>Department of Medicine, Yonsei University College of Medicine, Seoul 03722, Korea

<sup>3</sup>Brain Korea 21 Project, Yonsei University College of Medicine, Seoul 03722, Korea

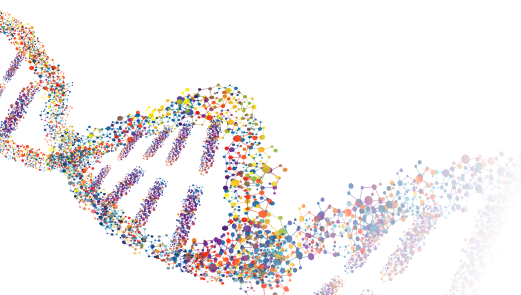
Predicting cellular responses to genetic perturbations remains a fundamental challenge in functional genomics. Recent linear models that incorporate prior knowledge have shown promise for perturbation-response prediction; however, the sources of predictive power within these knowledge-driven priors remain unclear.

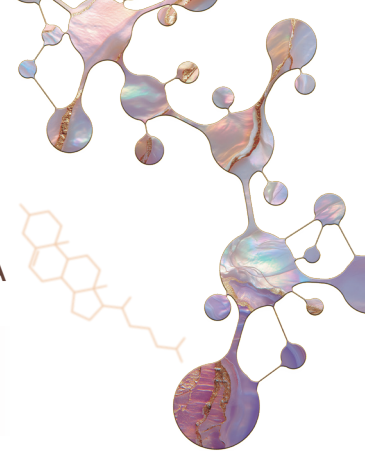
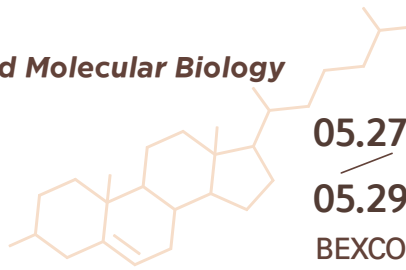
Here, we systematically analyze the predictability of prior knowledge based on pairwise gene relationships and assess the contribution of gene-intrinsic features to perturbation responses. We compare 10,875 genes shared across eight prior knowledge sources spanning networks, gene-level profiles, and neural network embeddings, and encompassing expression, regulation, and functional evidence. This comparison reveals both shared and distinct structures of pairwise gene relationships across sources.

This approach enables the linear transfer of biological knowledge onto three axes of perturbation profiles—co-expression, co-regulation, and co-function—and allows us to map sources of predictive power across prior knowledge types, disentangling biological signal from measurement effects and gene-intrinsic contributions.

We formalize this linear transferability into a gene-wise predictability rubric that forecasts performance across models and highlights biological factors linked to systematic prediction failures. Together, this study clarifies the structure of prior knowledge sources, identifies the origins of predictive power in linear perturbation-response models, and provides practical guidance for selecting and integrating prior knowledge in predictive frameworks.

**Keywords:** Perturb-Seq, Single-Cell, Gene expression prediction





**S2-5 Genome Engineering I: Advances in Functional Genomics Technology**

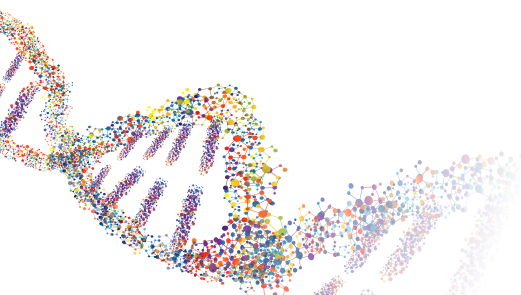
## **Bifunctional lncRNA SNHG16 with antagonistic RNA and peptide functions in colorectal cancer malignancy**

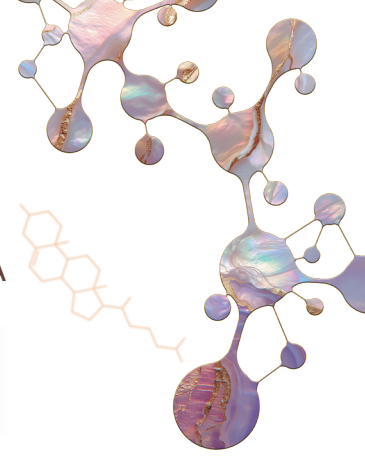
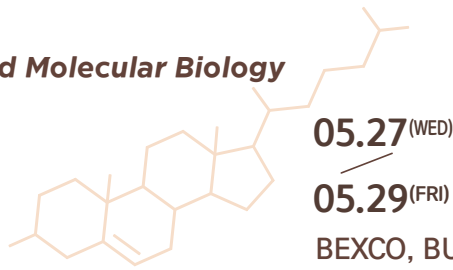
**Minwook LEE<sup>1#</sup>, Sang-Ho YOON<sup>1#</sup>, Yeongwon KIM<sup>1#</sup>, Junho CHO<sup>1\*</sup>, Jin-Wu NAM<sup>1\*</sup>**

*<sup>1</sup>Department of Life Science, Hanyang University, Seoul 04763, Korea*

Long non-coding RNAs (lncRNAs) are emerging as key regulators of gene expression with cell type-specific functions, yet their roles in colorectal cancer (CRC) remain poorly defined. Bulk RNA-sequencing obscures cell-level heterogeneity, and the bifunctionality of lncRNAs, as both regulatory transcripts and sources of functional peptides, has been largely overlooked. Here, we integrated TCGA bulk RNA-seq with single-cell transcriptomes from Korean and Belgian CRC patients, and applied long-read sequencing, ribosome profiling, and functional assays to resolve isoform- and cell type-specific lncRNA functions. Among 20,971 novel lncRNAs, SNHG16 was enriched in malignant cells and encoded two micropeptides (MP20 and MP33). These isoforms localized to light polysomes and showed translation potential. Functional studies revealed that MP33 enhanced migration, invasion, and tumor growth, while untranslated SNHG16 RNA suppressed these traits. Inserting stem-loop structures abolished translation-dependent effects, confirming the functional role of the peptides. Furthermore, SNHG16 expression was upregulated by JAK/STAT3 signaling from tumor-associated macrophages. Collectively, these findings redefine SNHG16 as a bifunctional lncRNA with opposing roles at the RNA and peptide levels, highlighting the need to resolve lncRNA isoform-specific functions. This work provides a framework for investigating lncRNA bifunctionality and developing isoform- or peptide-targeted therapies in cancer.

**Keywords:** lncRNA, Colorectal cancer, Tumor microenvironment





**S2-6 Genome Engineering I: Advances in Functional Genomics Technology**

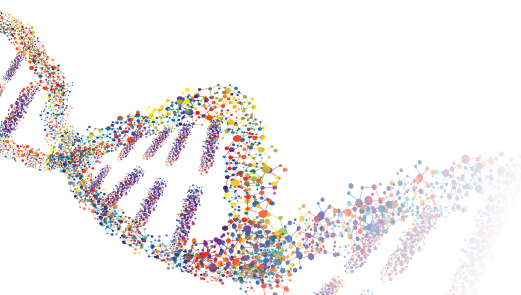
# A High-Efficiency Target Enrichment Platform for Long-Read Sequencing-Based Variant Detection in Single-Cell CRISPR Screening

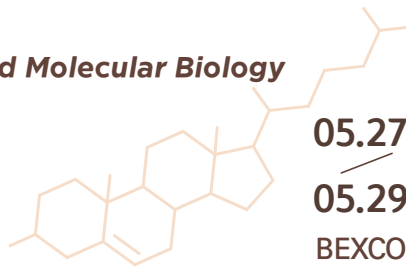
Seong-Ho PARK<sup>1</sup>, Heonseok KIM<sup>1\*</sup>

<sup>1</sup>Department Of Life science, Hanyang University, Seoul 04763, Korea

Understanding the functional impact of genetic variations is essential for the advancement of precision medicine. While single-cell CRISPR screening offers the potential to integrate genetic perturbations with phenotypic changes, it primarily relies on indirect inference via gRNA. Recently, to overcome this limitation, direct variant detection methods based on long-read sequencing have been introduced. However, since all single-cell-cDNA molecules share a common Read 1 sequence (containing cell barcodes and UMIs), conventional PCR-based enrichment often leads to significant non-specific amplification, resulting in reduced target recovery and increased sequencing costs. In this study, we developed a novel affinity-based enrichment method to address these technical challenges. Unlike conventional PCR-based approaches, our method minimizes non-specific signals by physically isolating target cDNAs from complex library pools. Consequently, we achieved up to a 1,200-fold increase in the target enrichment rate compared to existing methods. By maximizing enrichment efficiency, our approach significantly enhanced the recovery of cell barcodes from long-read sequences with a high error rate, ensuring precise assignment of each read to its cell of origin. This platform provides a cost-effective and precise solution for large-scale single-cell variant screening and is expected to facilitate the direct mapping of genetic variants to transcriptional responses.

**Keywords:** Long-Read sequencing, Single-Cell sequencing, CRISPR screening

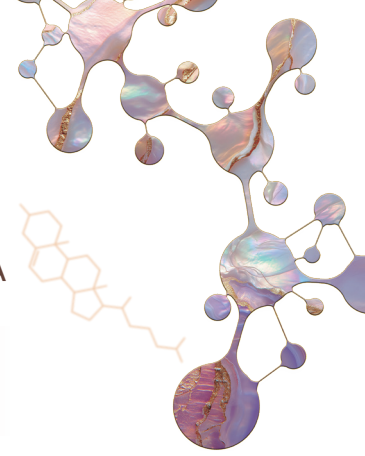




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FROM MOLECULES TO MEGABYTES:  
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**S2-7 Genome Engineering I: Advances in Functional Genomics Technology**

# Hijacking and recording intracellular RNAs in human cells using eukaryotic reprogrammed tracrRNAs

Seok-Hoon LEE<sup>1#</sup>, Junho PARK<sup>1#</sup>, Yejun CHO<sup>1</sup>, Chanju JUNG<sup>1</sup>, Sangsu BAE<sup>1,2,3,4\*</sup>

<sup>1</sup>Department of Biomedical Sciences, Seoul National University College of Medicine, Seoul 03080, Korea

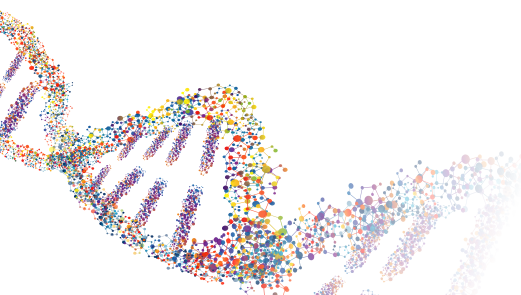
<sup>2</sup>Genomic Medicine Institute, Seoul National University College of Medicine, Seoul 03080, Korea

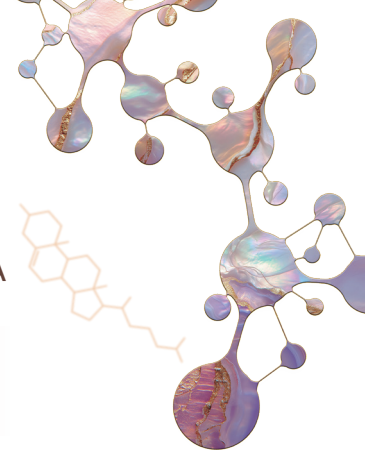
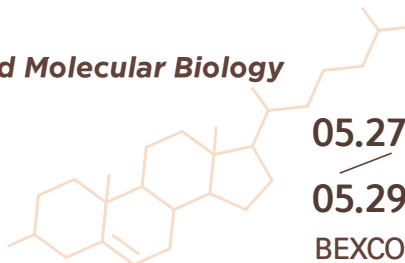
<sup>3</sup>Cancer Research Institute, Seoul National University College of Medicine, Seoul 03080, Korea

<sup>4</sup>Institute of Molecular Biology and Genetics, Seoul National University, Seoul 08826, Korea

Recording intracellular RNA expression events is critical for understanding cell states and biological processes, but no method is currently available to directly capture intracellular RNAs in mammalian cells. Here, we determined the sequence formula of eukaryotic reprogrammed tracrRNA, named euRptr, which can hijack intracellular RNAs to make a complex with CRISPR-associated tools. By leveraging the programmability of euRptr, we devised the system called “CHEETAH” and successfully recorded the appearance by hijacking exogenous viral RNA fragments and endogenous non-coding RNAs on a dedicated DNA reporter. Through CHEETAH, we could record the dynamic expression events of endogenous RNA transcripts under heat-shock condition. We further demonstrated that CHEETAH selectively records two similar viral RNA fragments on different DNA reporters using base editors with a shared-euRptr, and that CHEETAH enables multiplexed, time-resolved recording of viral RNAs on a DNA Tape using prime editors, providing a new avenue for investigating intracellular RNA in eukaryotes.

**Keywords:** CRISPR, Eukaryotic reprogrammed tracrRNA, Mammalian RNA recording





**S2-8 Genome Engineering I: Advances in Functional Genomics Technology**

## High-resolution functional mapping of androgen receptor variants

Yoojin CHANG<sup>1#</sup>, Hyeong-Cheol OH<sup>1,2#</sup>, Jihye PARK<sup>1</sup>, Yumin CHEONG<sup>3</sup>, Kwang Seob LEE<sup>1</sup>, Hyunho HAN<sup>4</sup>, Hyongbum Henry KIM<sup>1\*</sup>

<sup>1</sup>Department of Pharmacology, Yonsei University College of Medicine, Seoul 03722, Korea

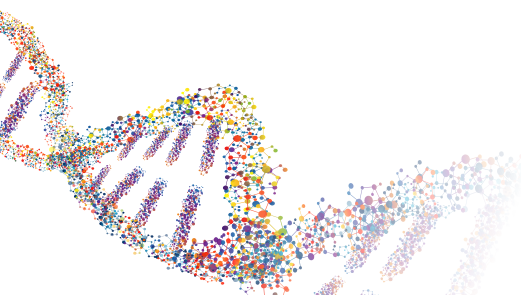
<sup>2</sup>Department of Neurosurgery, Yonsei University College of Medicine, Seoul 03722, Korea

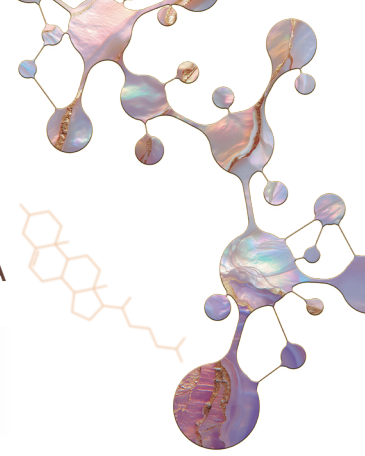
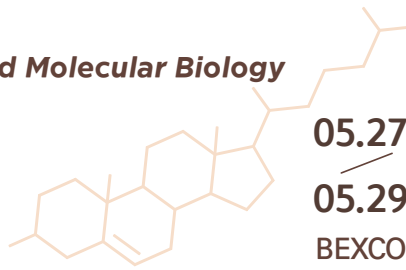
<sup>3</sup>College of Medicine, Yonsei University, Seoul 03722, Korea

<sup>4</sup>Department of Urology, Severance Hospital, Urological Science Institute, Yonsei University College of Medicine, Seoul 03722, Korea

The androgen receptor (AR) plays a central role in the progression and therapy resistance of prostate cancer, the most common cancer in men. While AR signalling inhibitors such as enzalutamide are key treatments, their efficacy is often compromised by drug-resistant AR variants. In addition, mutations leading to germline loss of AR function cause androgen insensitivity syndrome, yet most AR variants are of uncertain significance. Here we use advanced prime editing to generate and assess 2,765 AR variants, covering 99.95% of all possible single amino acid variants encoded by single nucleotide variants in the ligand-binding domain. This mapping identified 755 new non-functional AR variants and revealed 225 and 40 new variants resistant to enzalutamide and bavdegalutamide, an AR degrader, respectively. Our findings also enabled prognosis prediction for patients with prostate cancer based on AR mutation profiles. The broader implications of the study include improved androgen insensitivity syndrome diagnosis, better prostate cancer prognosis prediction and precision treatments for patients with prostate cancer.

**Keywords:** Genome engineering, Functional genomics, Androgen receptor





**S3-1 mRNA Vaccine and RNA Therapeutics**

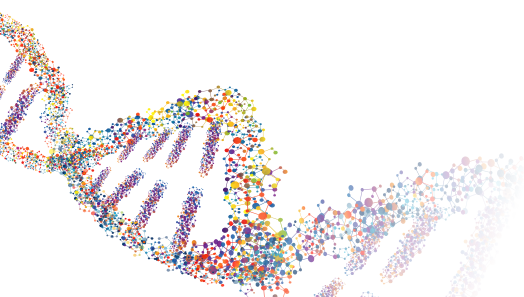
# Language AI for Viruses, Vaccines, and Drugs

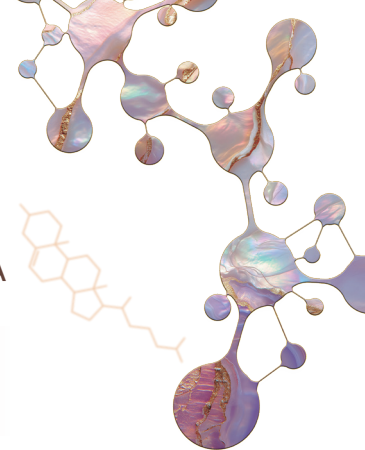
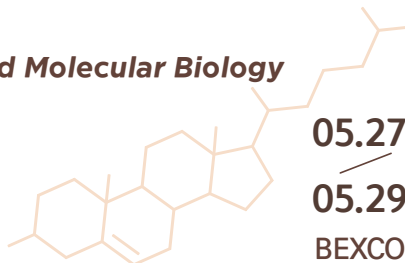
Liang HUANG

*Oregon State University and Coderna.ai*

Believe it or not, linguistics and biology are two sides of the same coin, and language AI can be used not only to understand but also to design de novo biological systems. For example, our Nature (2023) paper designed highly stable and efficient messenger RNA (mRNA) vaccines using natural language processing techniques. Experiments on COVID and another virus show that our designs dramatically improves mRNA half-life, protein expression, and in vivo antibody response, compared to the standard method used by Pfizer/BioNTech and Moderna. Nature News reported our work as a “remarkable AI tool” for mRNA design. Time permitting, I will also present some other recent work on RNA design.

**Keywords:** AI, mRNA vaccine, RNA design, RNA folding, biophysics





**S3-2 mRNA Vaccine and RNA Therapeutics**

## Efficient In Vitro Synthesis of Circular RNA Using RtcB Ligase

Daegi AN<sup>1#</sup>, Do-Hyung KIM<sup>2#</sup>, Yoon-Seob KIM<sup>2#</sup>, Saebyeol LEE<sup>1</sup>, Chan Kyoung KIM<sup>1</sup>, Dongjin KIM<sup>1</sup>, Ho-Young KANG<sup>2\*</sup>, Hak Kyun KIM<sup>1\*</sup>

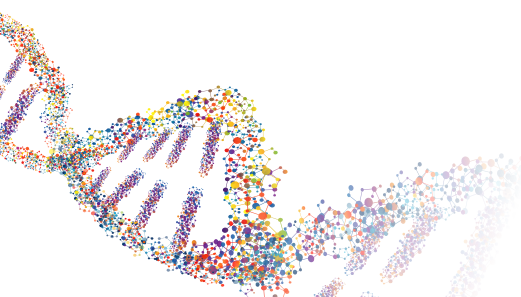
<sup>1</sup>Life Science, Chung Ang University, Seoul 06974, Korea

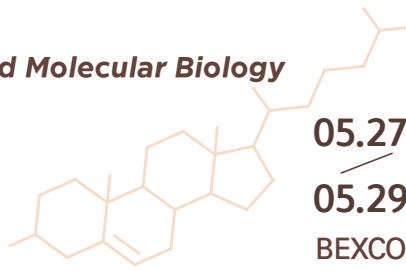
<sup>2</sup>Drug Discovery Center, NuclixBio, Seoul 08377, Korea

mRNA therapeutics, including vaccines and drugs, have rapidly advanced as a major platform for preventing infectious diseases and treating rare disorders. However, conventional linear RNA is limited by intracellular instability and the potential to trigger innate immune responses, requiring modified nucleotides and a 5' cap structure for therapeutic use. These requirements increase both manufacturing complexity and cost. In contrast, circular RNA (circRNA), because of its closed-loop structure, is more resistant to exonuclease degradation and can reduce innate immune activation without nucleotide modification. When combined with an internal ribosomal entry site (IRES), circRNA can also support cap-independent protein translation, highlighting its promise as an alternative RNA therapeutic format.

In this study, we developed a ribozyme-phosphatase assisted circRNA synthesis method, termed rpcRNA, using purified *E. coli* RtcB ligase. This strategy generates preRNA substrates with a 5' hydroxyl group and a 3' 2',3'-cyclic phosphate, enabling efficient RtcB-mediated circularization. rpcRNA showed comparable or improved circularization efficiency relative to existing in vitro methods. HPLC-purified rpcRNA displayed low immunogenicity and sustained protein expression in cells. Moreover, circRNA-mediated ornithine transcarbamylase expression restored enzyme activity in an OTCD mouse model, supporting the therapeutic potential of this platform.

**Keywords:** Circula RNA, RtcB ligase, MRNA therapeutics

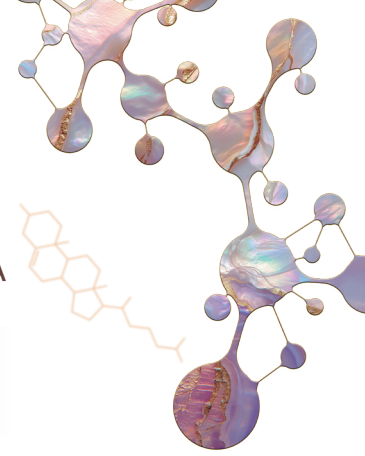




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05.29<sup>(FRI)</sup>

BEXCO, BUSAN, KOREA



FROM MOLECULES TO MEGABYTES:  
AI AND BIG DATA TRANSFORMING LIFE SCIENCE

**S3-3 mRNA Vaccine and RNA Therapeutics**

## RNA stability enhancers for durable base-modified mRNA therapeutics

Soo-Jin JUNG<sup>1,2,4#</sup>, Jenny J SEO<sup>1,2#</sup>, Sunghan LEE<sup>1,2#</sup>, Seong-In HYUN<sup>1,2</sup>, Ji-eun LEE<sup>1,2</sup>, Sojeong LEE<sup>1,2</sup>, Yeji LEE<sup>3</sup>, Hyeshik CHANG<sup>1,2</sup>, Hyukjin LEE<sup>3</sup>, Jin-Hong KIM<sup>2</sup>, V.Narry KIM<sup>1,2\*</sup>

<sup>1</sup>Center for RNA Research, Institute for Basic Science, Seoul National University, Seoul 08826, Korea

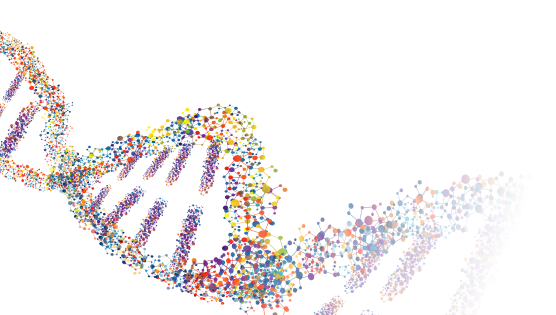
<sup>2</sup>School of Biological Sciences, Seoul National University, Seoul 08826, Korea

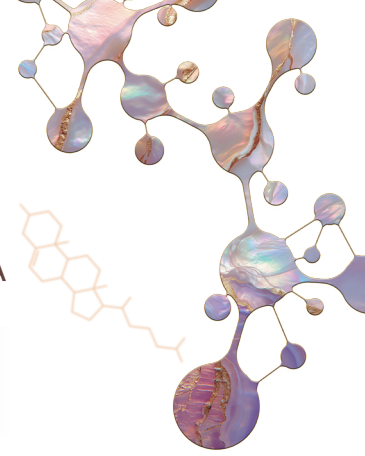
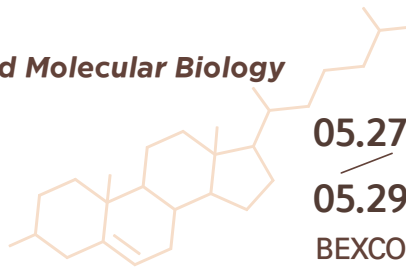
<sup>3</sup>College of Pharmacy, Seoul National University, Seoul 08826, Korea

<sup>4</sup>Life Science, Sogang University, Seoul 04107, Korea

The limited stability of mRNA in vivo remains a major challenge for vaccines and therapeutics. While alternative RNA formats such as circular RNA or self-amplifying RNA offer greater durability, these modalities often suffer from low translation, modification incompatibility and difficult manufacturing. To overcome these limitations, we screen 196,277 viral sequences and identify eleven elements that strongly enhance mRNA stability and translation. Mechanistically, they recruit TENT4 to extend the poly(A) tail, preventing deadenylation. Five of them are compatible with N1-methylpseudouridine, which improves mRNA efficacy and reduces immunogenicity. An element named A7 demonstrates particularly robust performance across cell types, delivery methods, modifications and coding sequences, making linear mRNA as stable as circular RNA while achieving higher translation efficiency. In mouse liver, A7-containing linear mRNA exhibits substantially higher protein levels than circular RNA, with sustained expression lasting for over 2 weeks. These RNA stability enhancers enable robust linear mRNA platforms that combine high and durable expression, low immunogenicity and simple manufacturing

**Keywords:** RNA therapy, mRNA vaccine, Viral genomics





**S3-4 mRNA Vaccine and RNA Therapeutics**

# Targeting microRNA-mediated metabolic reprogramming to attenuate chondrocyte senescence in osteoarthritis

Soy KIM<sup>1,2</sup>, Soojin PARK<sup>1</sup>, Jianhong CHING<sup>3</sup>, Jin-Hong KIM<sup>1,2\*</sup>

<sup>1</sup>Department of Biological Sciences, Seoul National University, Seoul 08826, Korea

<sup>2</sup>Center for RNA Research, Institute for Basic Science, Seoul 08826, Korea

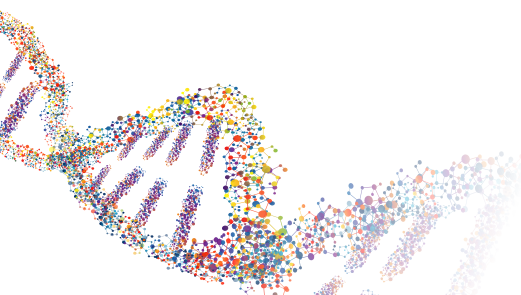
<sup>3</sup>Cardiovascular and Metabolic Disorders, Duke-NUS Medical School, Singapore 169857, Singapore

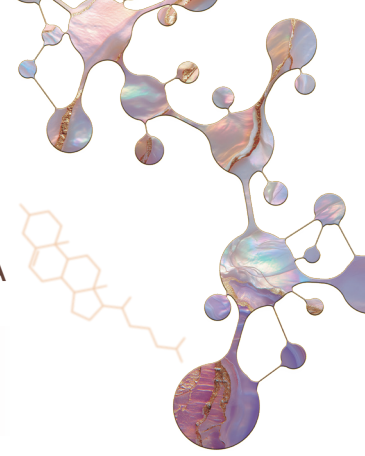
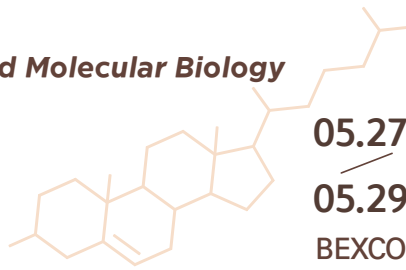
Chondrocyte metabolic homeostasis is fundamental to the structural integrity of articular cartilage, and its disruption serves as a primary driver of osteoarthritis (OA) pathogenesis. Here, we identify a “metabomiR” that orchestrates pathological metabolic reprogramming in OA. This identified microRNA is upregulated in human and murine OA cartilage, inversely correlating with key metabolic target genes.

Integration of transcriptomic and metabolomic data demonstrates that this metabolic regulator induces a loss of metabolic plasticity by co-targeting NADPH and CoA biosynthetic pathways. This multi-targeted inhibition precipitates “metabolic hibernation,” driving chondrocytes toward irreversible pathological senescence. These findings indicate that the modulation of a single microRNA can elicit metabolic shifts that dictate cellular fate, establishing this RNA species as a potent therapeutic target.

For therapeutic translation, we developed a cartilage binding peptide (CBP)-conjugated antisense oligonucleotide (ASO) targeting this pathological driver. Intra-articular administration of this ASO attenuated cartilage degradation in surgical OA models. Notably, the ASO exhibited remarkable cartilage homing even upon systemic delivery. These findings identify the microRNA as the metabolic rheostat in chondrocytes. By demonstrating that RNA-based metabolic reprogramming can be achieved through both local and systemic ASO delivery, this study provides a new therapeutic paradigm for treating degenerative joint diseases

**Keywords:** Metabolic hibernation, OA, ASO (Antisense-Oligonucleotide)





**S4-2 Global Horizons in Biochemistry and Molecular Biology: The IUBMB–FEBS  
Joint Spotlight**

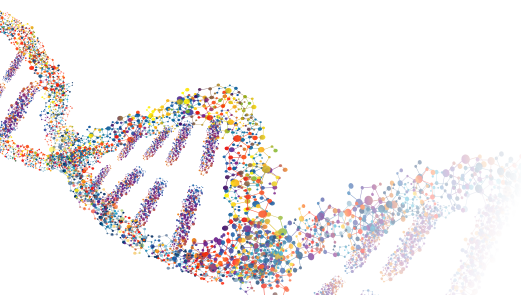
## IUBMB and Understanding LRRK2 and its role in Parkinson's disease

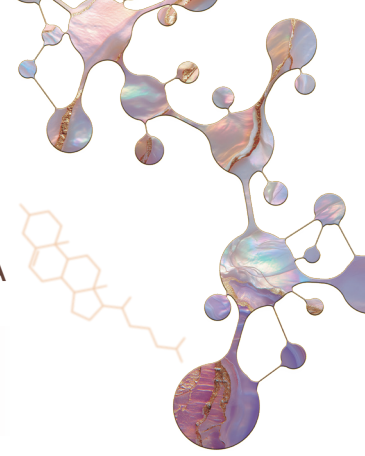
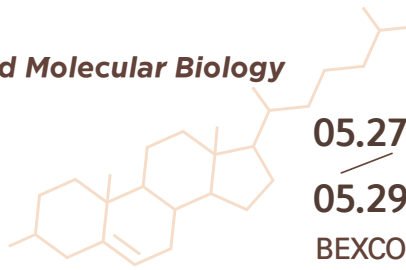
Dario R ALESSI

*MRC Protein Phosphorylation and Ubiquitylation Unit, Faculty of Life Sciences, University of Dundee*

In this presentation, I will provide a brief overview of the IUBMB and how we support the international scientific community through education and training fellowships, as well as by advancing global research via our academic journals. I will then highlight our research on autosomal dominant missense mutations in LRRK2, which destabilize its inactive conformation and lead to kinase hyperactivation a common cause of inherited Parkinson's disease. This has led to the development of LRRK2 inhibitors, which are currently being evaluated in clinical trials. I will discuss how LRRK2 phosphorylates a subset of Rab GTPases within their Switch-II motif, thereby modulating their interactions with novel effectors such as RILPL1. I will also describe the role of "recruiter" Rabs, in targeting LRRK2 to specific organelles and vesicles, where it becomes activated. Finally, I will present evidence that endolysosomal dysfunction triggered by Parkinson's-linked VPS35 mutations or lysosomal stress drives LRRK2 recruitment and activation on lysosomal membranes. This enhances kinase activity and promotes pRab–RILPL1 interactions with downstream partners. These findings provide new mechanistic insights and highlight promising avenues for the development of targeted therapies for Parkinson's disease.

**Keywords:** LRRK2 signaling, Rab GTPases, Endolysosomal dysfunction, Parkinson's disease therapeutics, Global scientific training and collaboration (IUBMB)





**S4-3 Global Horizons in Biochemistry and Molecular Biology: The IUBMB–FEBS  
Joint Spotlight**

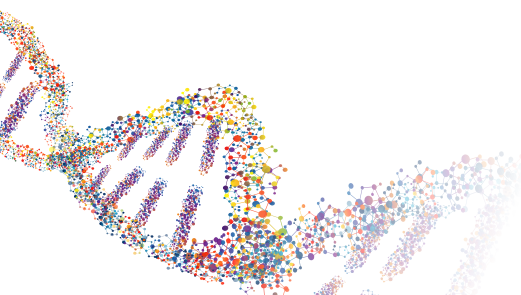
## Protein Kinase C Unbalanced: Dysregulated Signaling in Disease

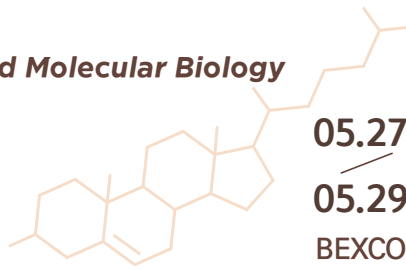
Alexandra C. NEWTON

*University of California, San Diego*

Protein kinase C (PKC) isozymes transduce the myriad of signals that cause lipid hydrolysis. These enzymes are maintained in a tightly autoinhibited conformation until transiently activated by the second messengers diacylglycerol and  $\text{Ca}^{2+}$ . PKC isozymes have historically been considered oncoproteins. This stems in large part from the discovery in the early 1980s that PKC is directly activated by tumor-promoting phorbol esters. Yet three decades of clinical trials using PKC inhibitors in cancer therapies not only failed, but in some cases worsened patient outcome. Why has targeting PKC in cancer eluded successful therapies? Our recent findings reframe PKC isozymes as generally having tumor suppressive function and suggest that therapeutic strategies should focus on restoring, rather than inhibiting, PKC activity in cancer. In striking contrast, enhanced activity of PKC is associated with degenerative diseases, with gain-of-function variants in PKC $\alpha$  identified in Alzheimer's disease and PKC $\gamma$  in cerebellar Ataxia Type 14, suggesting that inhibitors for PKC could be repurposed for neurodegenerative diseases. Understanding the molecular mechanisms that control PKC, including by upstream regulators such as mTORC2 and the phosphatase PHLPP, inform on how to effectively target this ubiquitous family of kinases in disease.

**Keywords:** Phosphorylation, protein kinase C, signaling

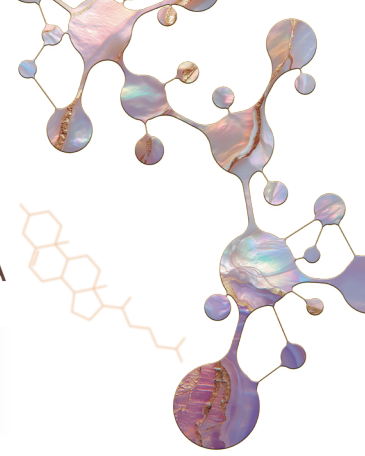




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BEXCO, BUSAN, KOREA



FROM MOLECULES TO MEGABYTES:  
AI AND BIG DATA TRANSFORMING LIFE SCIENCE

**S4-4 Global Horizons in Biochemistry and Molecular Biology: The IUBMB–FEBS  
Joint Spotlight**

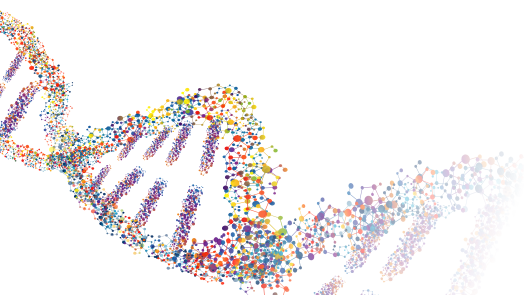
## Gut reactions and gut instincts: the role of cGMP

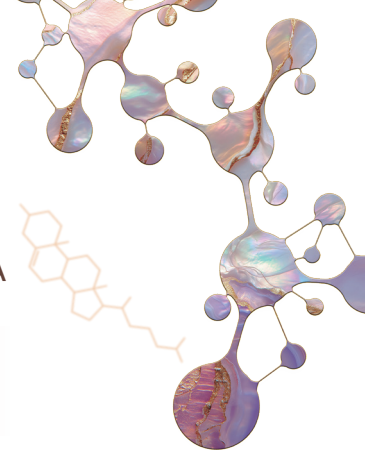
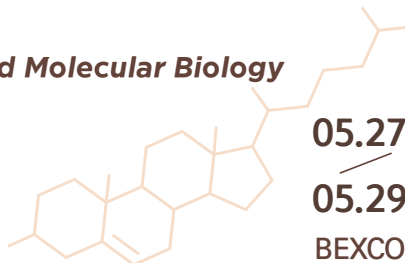
Sandhya S. VISWESWARIAH

*Indian Institute of Science, Bangalore, India*

Diarrhoeal disease and inflammatory bowel disease (IBD) are the most common disorders of the gut. In this talk, I will focus on the role of a receptor guanylyl cyclase, GC-C, the product of the *GUCY2C* gene. GC-C is the target of gastrointestinal hormones guanylin and uroguanylin, as well as bacterial heat-stable enterotoxins, which are a major cause of watery diarrhoea. Mutations in *GUCY2C* are associated with familial secretory diarrhoea that manifests in symptoms that mimic Crohn's Disease and ulcerative colitis. I will summarise our findings on the biochemistry and biology of GC-C in the context of intestinal epithelial cell signalling and in mouse models.

**Keywords:** Receptor guanylyl cyclase C; cGMP; inflammatory bowel disease; intestinal epithelial cell; microbiome





**S4-5 Global Horizons in Biochemistry and Molecular Biology: The IUBMB–FEBS  
Joint Spotlight**

## **Integrated Functional, Transcriptomic and In Silico Analysis Reveal the Anticancer Mechanisms of Maslinic Acid in MCF-7 cells**

Soon Yan TAN<sup>1</sup>, Chai Nien FOO<sup>2</sup>, Foong Leng NG<sup>3</sup>, Chee Hong TAN<sup>5</sup>, Yang Mooi LIM<sup>1,4\*</sup>

<sup>1</sup>Department of Pre-clinical Sciences,

<sup>2</sup>Department of Population Medicine,

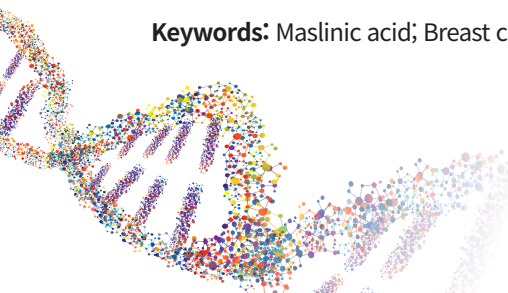
<sup>3</sup>Department of Chinese Medicine,

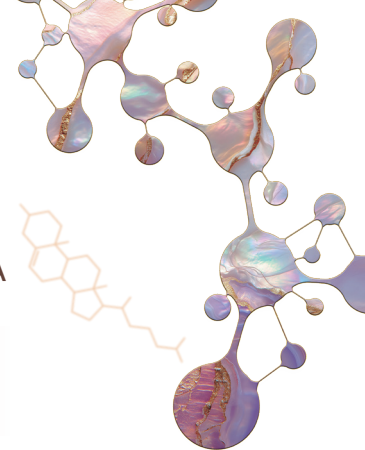
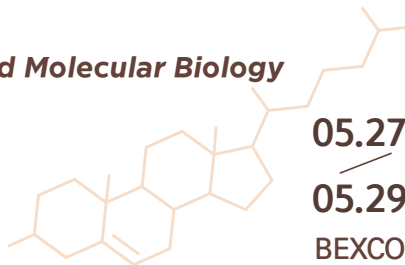
<sup>4</sup>Centre for Cancer Research, M. Kandiah Faculty of Medicine and Health Sciences,  
Universiti Tunku Abdul Rahman, Bandar Sungai Long, Cheras 43000, Kajang, Selangor, Malaysia

5Quiliniq Lifesciences Sdn. Bhd, Unit 1-2, Menara Oval Damansara, Taman Tun Dr. Ismail. 60000, Kuala Lumpur, Malaysia

Breast cancer remains a leading cause of mortality globally, indicating the need for alternative therapeutic strategies. This study aims to investigate the anticancer effects and underlying molecular mechanisms of Maslinic acid (MA) in MCF-7 breast cancer cells. Cell viability KSBMB demonstrated significant growth inhibition with an IC<sub>50</sub> value of 40.96 μM at 72 hours. Cell cycle analysis revealed an increase in the G0/G1 phase (22.19%) and reductions in the S phase (67.28%) and G2/M phase (40.37%), indicating cell cycle arrest. Apoptosis assay further showed a significant increase in late apoptotic cells compared to the control. NanoString gene expression profiling was performed across three time points. Results show that MA treatment induced an early cellular stress response by upregulation of MAPK-related genes and significant downregulation of key regulators of DNA replication, DNA repair, and cell cycle progression, including CDC6, CDK2, CCNE2, MCM family members, and PCNA, indicating suppression of proliferation. Prolonged treatment shows significant downregulation of key genes involved in DNA replication (CDC6, MCM2/5/7, PCNA), cell cycle progression (CDK2, CHEK1), and receptor tyrosine kinase signalling (EPHA2, RET). Besides, the upregulation of DDIT3 suggested activation of ER stress-mediated apoptotic pathways. Molecular docking was performed on the key targets (CDK2, RET, and IRE1), demonstrating favourable binding interactions. These interactions were validated by molecular dynamics simulations, which show stable protein-ligand complexes. In conclusion, MA exhibits potent anticancer effects in MCF-7 cells by inhibiting proliferative signalling, DNA replication, and inducing ER stress-mediated apoptosis. These findings highlight MA as a promising candidate for breast cancer therapy.

**Keywords:** Maslinic acid; Breast cancer; Cell cycle arrest; ER stress-mediated apoptotic pathway; Dynamic stimulation





**S4-7 Global Horizons in Biochemistry and Molecular Biology: The IUBMB–FEBS  
Joint Spotlight**

## Global Connections in Biomolecular Science: Korea–Europe Partnerships

Miguel A. De la ROSA

*FEBS, Secretary General*

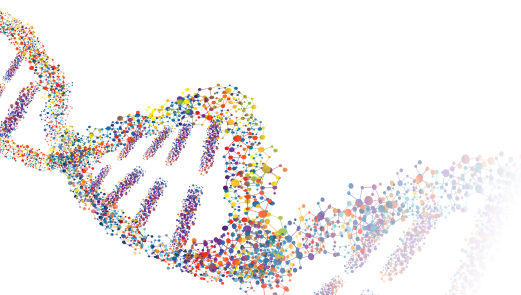
The Federation of European Biochemical Societies (FEBS) Strategic Plan 2024–2028 prioritizes strengthening ties with other countries and continents, thereby fostering global scientific exchange and collaboration. Enhancing links between biomolecular research communities in Korea and Europe exemplifies this goal, leveraging complementary expertise in life sciences to accelerate discovery and translational impact.

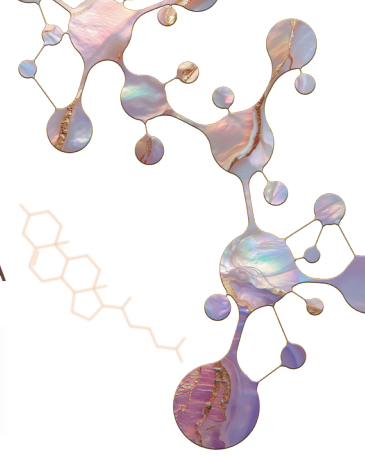
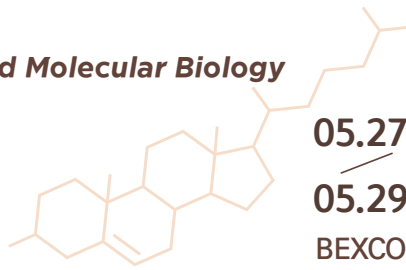
Recent developments highlight the growing intensity of this collaboration. Approximately 150 Korean researchers attend FEBS Congresses each year, reflecting strong international engagement. At the 2025 Congress in Istanbul, a formal agreement between KSBMB and FEBS was signed to establish reciprocal speaker exchanges between Korean and European conferences, while FAOBMB and FEBS concluded a similar agreement to reinforce interregional ties. Building on this momentum, a joint symposium will be held at the upcoming FEBS Congress in Maastricht next July, providing a high-visibility platform for scientific exchange. In Busan, FEBS delegates are invited to attend the KSBMB Congress, further strengthening direct engagement between the two communities.

At the global level, IUBMB plays a central role as a facilitator of collaboration, as exemplified by this joint IUBMB–FEBS session. In 2024, in Milan, the leaders of IUBMB and the four continental federations (FEBS, FAOBMB, PABMB, and FASBMB) signed the Milan Declaration, emphasizing the essential role of science in addressing global challenges and highlighting the shared responsibility of scientists, policymakers, and citizens worldwide.

By reinforcing institutional ties, promoting researcher mobility, and fostering inclusive, long-term collaboration, Korea and Europe—together with IUBMB and FAOBMB—are helping to build a resilient, interconnected biomolecular research ecosystem.

**Keywords:** FEBS, KSBMB, IUBMB, FAOBMB





**S4-8 Global Horizons in Biochemistry and Molecular Biology: The IUBMB–FEBS  
Joint Spotlight**

# The importance of federalization at the national and supranational level for the development of life sciences from the Polish and former FEBS Congress Counsellor's perspective

Piotr LAIDLER

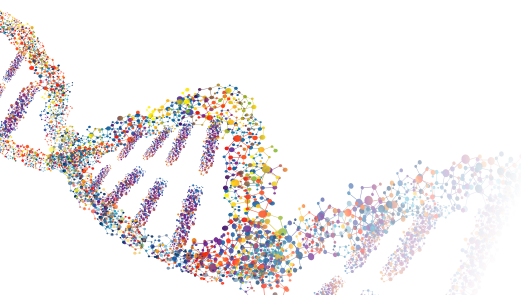
*Jagiellonian University // Medical College*

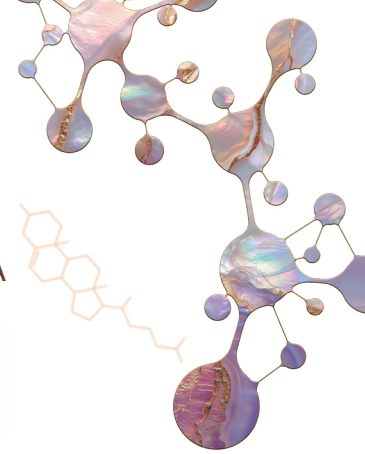
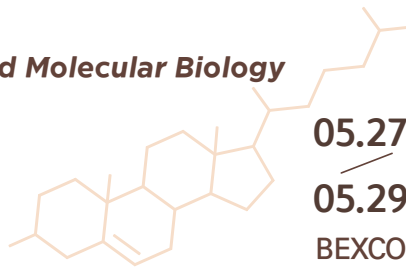
The vast majority of my professional life, aside from a few years at universities in the United States and Germany, was spent at the Jagiellonian University in Krakow, of which I am a graduate. In my opinion, the most powerful factor in allowing and accelerating development is broadly defined international scientific collaboration. Without a doubt, institutionalization and federalization, especially at the global level, are key to increasing its effectiveness.

For this reason, I was committed to creating conditions for collaboration and interaction between scientists, both in research and education, beyond the borders of my own country. Student exchanges, pre-graduate and postdoctoral training, and congresses are among the forms of direct contact between scientists. The strength of the largest scientific institutions stems from the fact that they employ talented people from around the world.

I first heard about S. Korea as a child in connection with the 1950-1953 war, which in Europe symbolized the fight for freedom against communism, which Poles also fought against! I learned about S. Korea for the second time in the 1960s as the land of the "Miracle on the Han River." This instilled in me a tremendous respect for people I had never met. Now, it's my third time. As FEBS Chair and Congress Counselor from 2021 to 2025, I experienced personal contact with Koreans and was struck. The participation of a significant number researchers from S. Korea in European FEBS Congresses can fill you with pride, and for us, it is a wonderful role model!

**Keywords:** federalization, internationalization, research, education





**S5-1 KRIBB Symposium: AI and Emerging Platforms for Molecular Bioscience**  
**(Korean Session)**

# Architecting the AI Co-Scientist for Molecular Bioscience: From Context Engineering to Quantum-Ready Virtual Labs

Seon-Kyu KIM

*AI-Bio Solution Team (ABSOLUT) at Korea Research Institute of Bioscience and Biotechnology (KRIBB)*

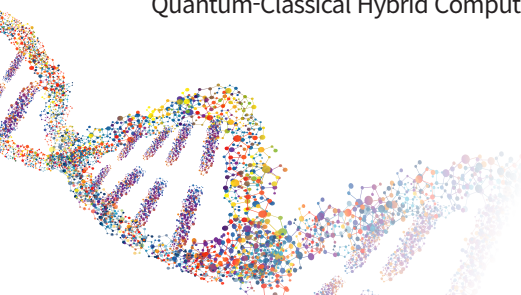
The emergence of large language models and agentic AI frameworks is fundamentally reshaping biological research. In this talk, I present a vision and hands-on implementation of the AI Co-Scientist — an autonomous, multi-agent virtual laboratory designed to accelerate discovery in biochemistry and molecular bioscience. Rather than treating AI as a passive query tool, we architect it as an active research collaborator capable of hypothesis generation, experimental design, literature synthesis, and cross-domain reasoning.

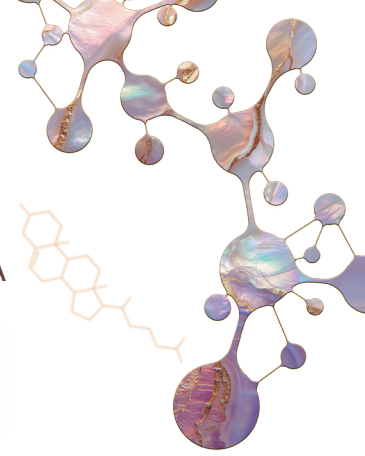
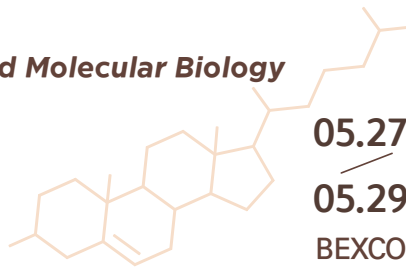
A central theme is Context Engineering and Harness Engineering — the disciplined craft of structuring prompts, memory, tool pipelines, and agent orchestration to reliably elicit expert-level scientific reasoning from foundation models. The quality of agentic AI output is not merely a function of model capability, but of how deliberately the surrounding harness is designed. Vibe coding with tools such as Claude Code and Gemini-CLI is not simply a productivity shortcut — it is the practical interface through which researchers define, iterate, and refine that harness in real time, closing the loop between scientific intuition, context design, and executable implementation.

Drawing from our laboratory's implementations — including the Cancer Foundation Model, Agentic Animal Atlas, AI Medical A2A consultation system, and the Quantum in Silico platform — we showcase how Agent-to-Agent (A2A) protocols and Model Context Protocol (MCP) enable specialized biological agents to collaborate across species, disease domains, and data modalities.

Finally, we present our ongoing work on Quantum-Ready AI, arguing that hybrid quantum-classical architectures will form the next computational substrate for virtual lab agents operating on high-dimensional multi-omics and molecular imaging data.

**Keywords:** AI Co-Scientist; Context and Harness Engineering; Multi-agent Systems; Molecular Foundation Models; Quantum-Classical Hybrid Computing





**S5-2 KRIBB Symposium: AI and Emerging Platforms for Molecular Bioscience**  
**(Korean Session)**

# Single-cell transcriptome based on physical tissue properties defines early aging process

Chuna KIM

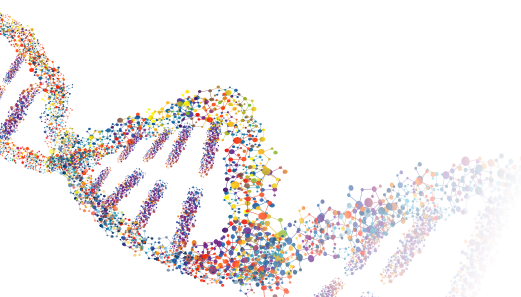
*Korea Research Institute of Bioscience and Biotechnology (KRIBB)*

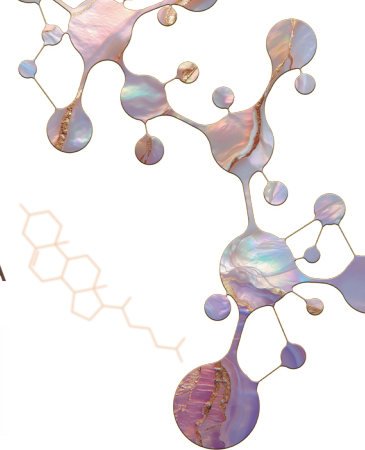
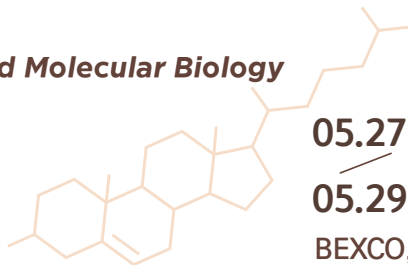
Aging manifests as a spatial mosaic within organs, yet the precise locations and mechanisms driving this heterogeneity remain poorly understood. Multi-omics studies consistently identify chronic inflammation and fibrosis as universal features of aged tissues, suggesting that unresolved tissue damage—"imperfect repair"—persists and remodels local microenvironments. However, tools to spatially isolate and molecularly characterize these pathological niches have been lacking. Here, we developed fibrotic niche enrichment sequencing (FiNi-seq), a method that physically isolates fibrotic microdomains based on tissue stiffness, and applied it to systematically define the cellular and molecular landscape of imperfect repair in the aged liver.

FiNi-seq revealed a periportal fibrotic niche in aged mouse liver densely populated by cell types resembling those found in human liver cirrhosis. This pathological microenvironment was orchestrated by three key populations absent in young liver: senescent-like endothelial cells, Smoc1 fibroblasts, and exhausted T cells. Single-cell and spatial transcriptomic analyses further demonstrated that these populations form a self-reinforcing microenvironment through reciprocal signaling among the senescent endothelium, pro-fibrotic stroma, and dysfunctional immune compartment. Importantly, the periportal localization of this niche aligns with emerging evidence that Zone 1 hepatocytes are preferentially vulnerable to age-related decline, linking vascular and metabolic zonation to the spatial patterning of organ aging.

Our findings establish that aging generates spatially confined, self-sustaining niches of imperfect repair with distinct cellular architecture, and provide FiNi-seq as a generalizable platform for mapping these niches across organs and aging contexts.

**Keywords:** Aging, Senescent cells, Single cell transcriptomics, Spatial transcriptomics





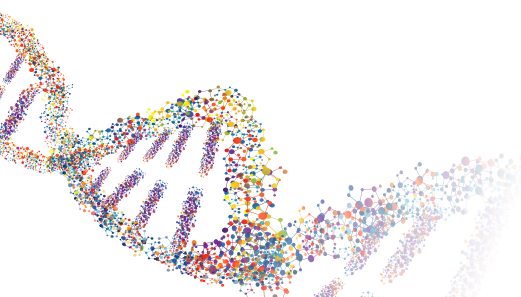
**S5-3 KRIBB Symposium: AI and Emerging Platforms for Molecular Bioscience**  
**(Korean Session)**

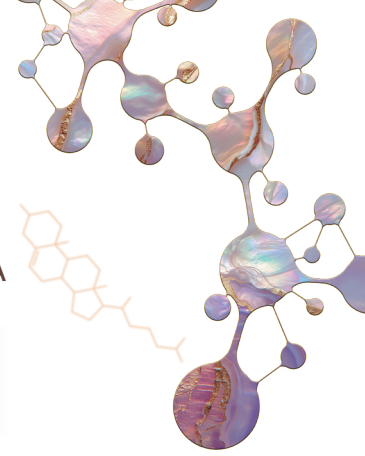
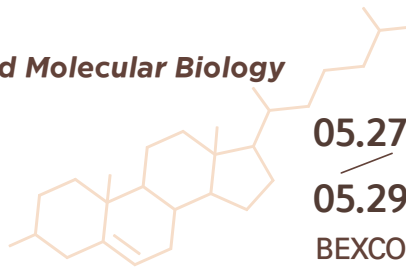
## **Advancing New Approach Methodologies (NAMs): Applications of Liver Organoid Platform**

Myung Jin SON

*Korea Research Institute of Bioscience and Biotechnology (KRIBB)*

The liver is the body's primary metabolic organ, responsible for processing a wide range of substances, including pharmaceuticals. Certain substances or their toxic metabolites can cause acute liver failure or contribute to chronic liver diseases. Despite extensive non-clinical and clinical studies, drug safety issues often emerge even after regulatory approval. However, existing model systems fall short of fully recapitulating the complex structure and cellular composition of the human liver, thereby limiting their utility for studying liver pathophysiology and assessing hepatotoxicity. To overcome these limitations, three-dimensional human liver models—particularly organoids—are being actively developed and proposed as an important new approach method. We have successfully established self-renewing and functionally mature human pluripotent stem cell-derived liver organoids that recapitulate both the cellular composition and structural organization of human liver tissue. Notably, these liver organoids have demonstrated the ability to detect the toxicity of drugs that were withdrawn from the market due to severe hepatotoxicity. Furthermore, they have been applied to screening platforms for the development of therapeutics targeting complex liver disorders, including metabolic, infectious, and genetic diseases. We are currently working to standardize both the endpoint quality assessment of human liver organoids under ISO/TC 276 and the development of organoid-based target organ toxicity testing methods under the OECD Test Guidelines Programme. Taken together, these organoid-based evaluation platforms address a critical gap in the field and provide a powerful tool for human-relevant disease modeling, toxicity assessment, and therapeutic development.





**S5-4 KRIBB Symposium: AI and Emerging Platforms for Molecular Bioscience  
(Korean Session)**

## Optimized mRNA and LNP platform for therapeutic and vaccine applications

Seyoung KIM<sup>1</sup>, Seok-Beom YONG<sup>1</sup>, Min-hyo KI<sup>2</sup>, Hyunji LEE<sup>3</sup>, Sungchan CHO<sup>1</sup>

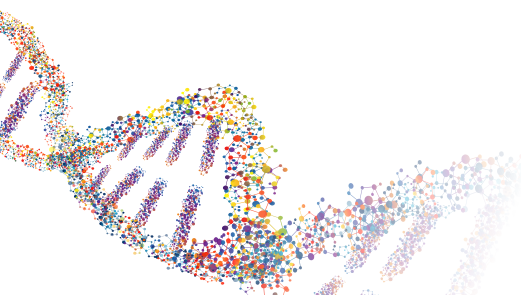
<sup>1</sup>Nucleic Acid Therapeutics Research Center, KRIBB, Korea

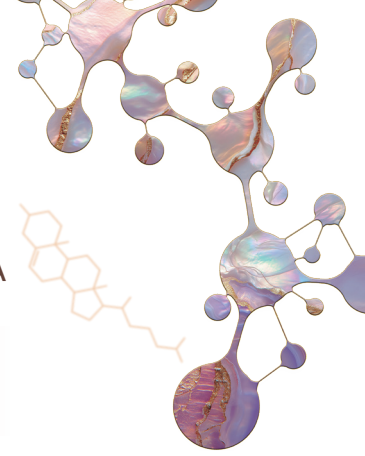
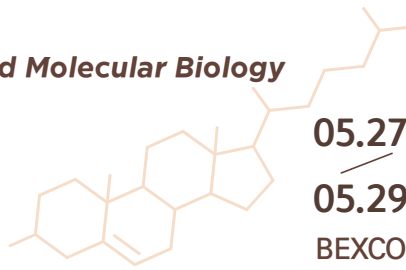
<sup>2</sup>MediciBIO, Korea

<sup>3</sup>BK21 Graduate Program, Department of Biomedical Sciences, Korea University College of Medicine, Korea

The COVID-19 pandemic, which caused an unprecedented global crisis, was effectively tackled through the development of innovative mRNA vaccines. The rapid development and flexible mass-scale manufacturing capabilities of mRNA-based vaccines played a crucial role in the global response to this health emergency. The success of COVID-19 mRNA vaccines and the advancements in associated technologies have paved the way for expanding mRNA applications into areas such as cancer and rare genetic diseases. However, challenges remain regarding the duration of expression, delivery efficiency, modulation of adaptive immune responses, and targeting specific tissues, all of which should be overcome to broaden the scope of mRNA therapeutics beyond COVID-19. In this presentation, I will discuss our group's recent progress in developing an advanced mRNA platform that enables significantly enhanced protein expression while maintaining minimal immunogenicity compared with conventional mRNA systems. In addition, I will introduce novel adjuvant-type lipid nanoparticle (LNP) platform designed to enhance adaptive immune responses, as well as a low-immunogenic ionizable lipid-based LNP system. Finally, I will present current applications of these platform technologies for the treatment of rare diseases, including Wilson's disease and Leber's Hereditary Optic Neuropathy (LHON).

**Keywords:** mRNA therapeutics, mRNA structure, Lipid nanoparticle (LNP), Rare diseases





**S6-1 Stem Cell I: Metabolism & Age-Associated Disease**

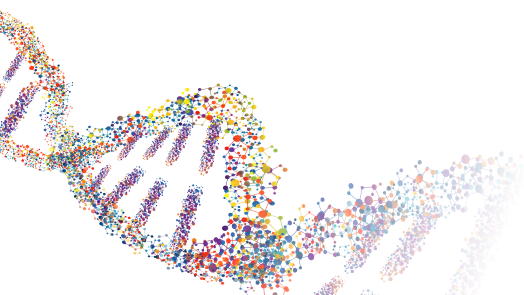
# Systemic Control of Tissue Regeneration and Immunosurveillance

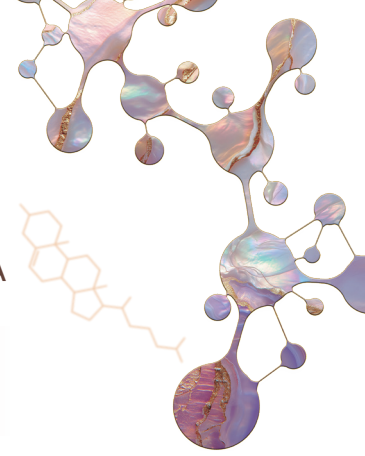
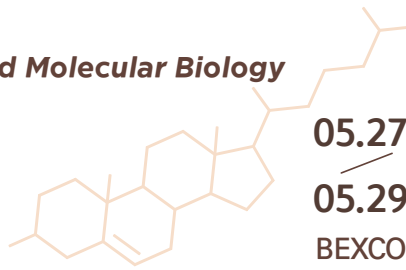
Bing ZHANG

*Westlake University*

The skin functions as both a regenerative organ and a crucial immune barrier, but the regulation of these critical functions by systemic physiological signals is not well understood. Our study demonstrates that systemic signals, such as dietary interventions and stress, significantly reshape the skin's regenerative and defensive capabilities. Specifically, we demonstrate that intermittent fasting, a common dietary regimen, can significantly impair hair follicle renewal through an interorgan communication between the HPA axis and hair follicle stem cell niche. Furthermore, we uncover a neuro-immune circuit that dynamically adjusts cutaneous immunosurveillance in response to stress. Together, these findings establish an integrated framework where systemic inputs—encompassing endocrine, metabolic, and neural pathways—precisely balance tissue regeneration and immune vigilance. This coordinated regulation optimizes resource allocation to meet environmental demands and has broad implications for how lifestyle factors affect tissue homeostasis, pathogen defense, and cancer surveillance.

**Keywords:** Adult stem cells, tissue regeneration, immunosurveillance, systemic physiological signal





**S6-2 Stem Cell I: Metabolism & Age-Associated Disease**

# A novel genetic mouse model for chronic stress uncovers the multifaceted mechanisms of stress-induced hair loss

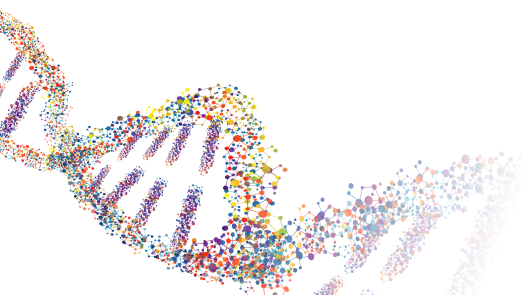
Seokmin YUN<sup>1</sup>, Sung Wook SHIM<sup>1</sup>, Hanseul YANG<sup>1\*</sup>

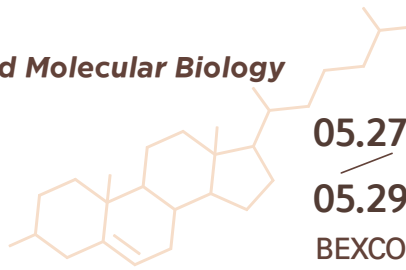
<sup>1</sup>Department of Biological Sciences, Korea Advanced Institute of Science and Technology (KAIST), DAEJEON 34141, Korea

Stressful circumstances trigger the secretion of stress hormones that modulate a wide range of physiological processes to help the body cope with threats. However, the long-term impacts of stress on tissue homeostasis, especially hair follicle maintenance and regeneration, remain poorly understood, and effective therapeutic strategies are still lacking. Here, we established a novel intrinsically stressed mouse model exhibiting mild elevations in both the fight-or-flight response and the hypothalamic-pituitary-adrenal axis response throughout the lifetime. This mouse model recapitulates physiological alterations similar to those observed in patients with stress-induced chronic depression or hypertension. Notably, the mouse model successfully reproduced stress-induced hair loss phenotypes, including shortened anagen phase, prolonged telogen phase, and progressive hair loss. We elucidated that telogen retention results from the disruption of micro-niche architecture composed of a tri-axial connection between hair follicle stem cells (HFSCs), arrector pili muscle (APM), and sympathetic nerves. Hypercontraction of the APM displaced sympathetic nerves away from the HFSCs, and pharmacological relaxation of the APM with minoxidil restored APM-HFSCs contact, reestablished sympathetic nerve-HFSCs association, and eventually promoted hair regeneration.

Collectively, our mouse model reveals how chronic stress impairs hair maintenance and regeneration, providing a foundational platform for the development of new therapeutic interventions.

**Keywords:** Hair regeneration, Chronic Stress, Microenvironment

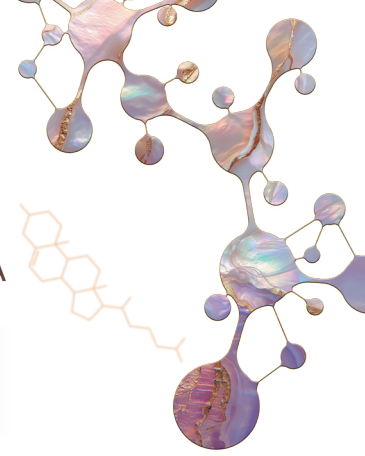




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BEXCO, BUSAN, KOREA



FROM MOLECULES TO MEGABYTES:  
AI AND BIG DATA TRANSFORMING LIFE SCIENCE

**S6-3 Stem Cell I: Metabolism & Age-Associated Disease**

# A physiological role for neutrophils in restraining adipocyte lipolysis during sympathetic activation

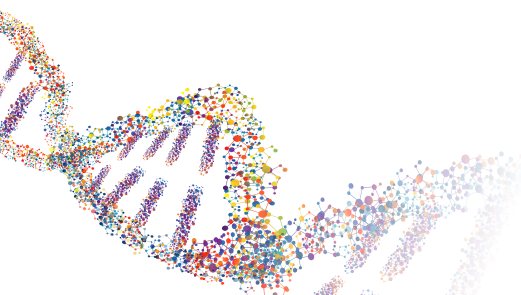
Seunghwan SON<sup>1</sup>, Cindy XU<sup>1</sup>, Haipeng FU<sup>1</sup>, Ronald EVANS<sup>2</sup>, Alan SALTIEL<sup>1\*</sup>

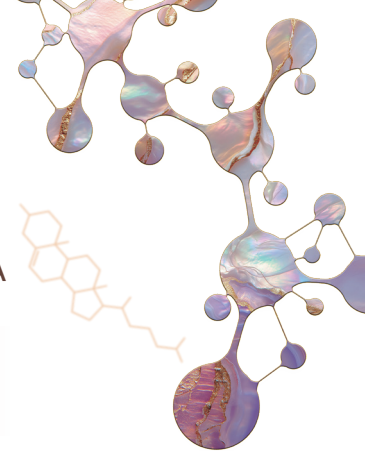
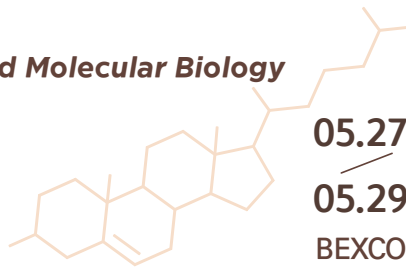
<sup>1</sup> Department of Medicine, UC San Diego, San Diego 92093, USA

<sup>2</sup> Molecular and Developmental Biology, Salk institute, San Diego 92093, USA

Adipose tissue maintains energy homeostasis by storing lipids during nutrient surplus and releasing them through lipolysis in times of energy demand. While lipolysis is essential for short-term metabolic adaptation, prolonged metabolic stress requires adaptive changes that preserve energy reserves. Here we report that  $\beta$ 3-adrenergic activation of adipocytes induces a transient and depot-specific infiltration of neutrophils into white adipose tissue (WAT), particularly in lipid-rich visceral WAT. Neutrophil recruitment requires the stimulation of both lipolysis and p38 MAPK in adipocytes, and is mediated by the secretion of leukotriene B4. Recruited neutrophils undergo activation in situ, and locally secrete IL-1 $\beta$ , which suppresses lipolysis and limits excessive energy loss. Neutrophil depletion or blockade of IL-1 $\beta$  production increases lipolysis, leading to reduced WAT mass after repeated  $\beta$ 3-adrenergic stimulation. Together, these findings reveal a role of neutrophil-derived IL-1 $\beta$  in preserving lipid stores during metabolic stress, highlighting a physiological function of innate immune cells in limiting lipid loss and maintaining energy homeostasis.

**Keywords:** Neutrophils, Adipose tissue, Inflammation





**S6-4 Stem Cell I: Metabolism & Age-Associated Disease**

# AHCYL1-IP3R axis links calcium signaling to thermogenesis in brown adipose tissue

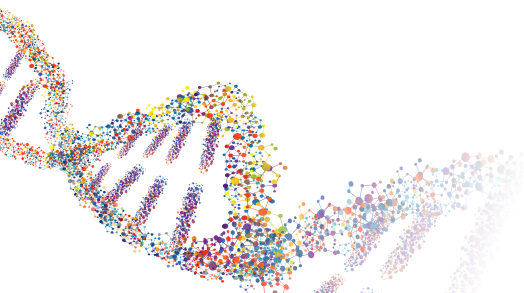
Soo Kyung KANG<sup>1,2</sup>, Sol Pin KIM<sup>1,2</sup>, Je Kyung SEONG<sup>1,2\*</sup>

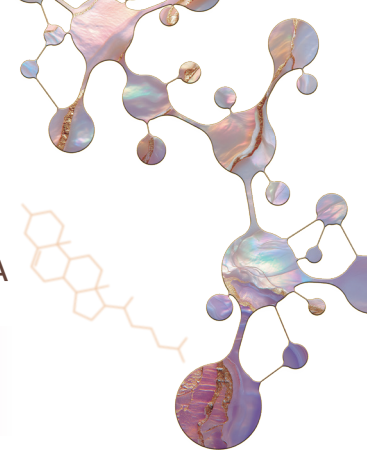
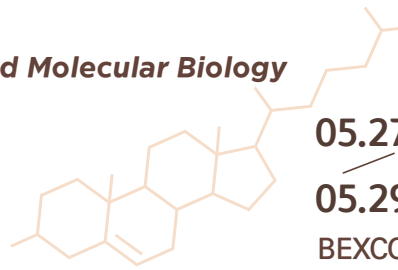
<sup>1</sup>College of Veterinary Medicine, Seoul National University, Seoul 08826, Korea

<sup>2</sup>Korea Model animal Priority Center, Seoul National University, Seoul 08826, Korea

Brown adipose tissue (BAT) plays a central role in adaptive thermogenesis, which is activated by norepinephrine (NE) in response to cold exposure. In addition to the canonical adrenergic pathway, intracellular calcium signaling contributes to thermogenic activation in brown adipocytes. However, the regulatory mechanisms governing the calcium-dependent processes remain unclear. Here, we investigated the role of AHCYL1, an inhibitory factor of inositol 1,4,5-trisphosphate receptors (IP3Rs), in calcium-dependent thermogenesis. Using brown adipocyte-specific *Ahcy1* knockout (cKO) mice, we found that *Ahcy1* deficiency enhanced thermogenic activation in BAT, supporting a suppressive role for AHCYL1 in this process. Furthermore, *Ahcy1* deficiency improved systemic metabolic phenotypes in mice with diet-induced obesity. Together, these findings identify the AHCYL1-IP3R axis as a regulatory node linking calcium signaling to thermogenesis in BAT and suggest that modulation of this pathway may serve as a potential therapeutic strategy for systemic metabolic disorders.

**Keywords:** Calcium, Thermogenesis, Ahcy1





**S6-5 Stem Cell I: Metabolism & Age-Associated Disease**

# CHIP ameliorates MASLD via promoting STX17 ubiquitination to facilitate autophagosome-lysosome fusion

Hyunjin RHO<sup>1,2</sup>, Jaewhan SONG<sup>1,2,3\*</sup>

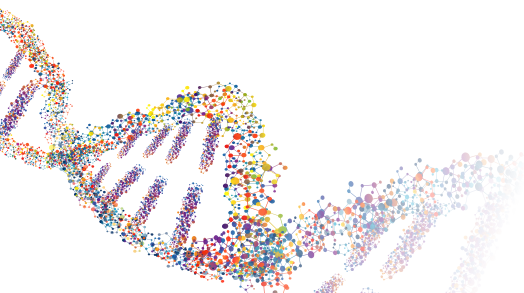
<sup>1</sup>Bio-Centennial Convergence Institute (NRL2.0), Yonsei University, Seoul 03722, Korea

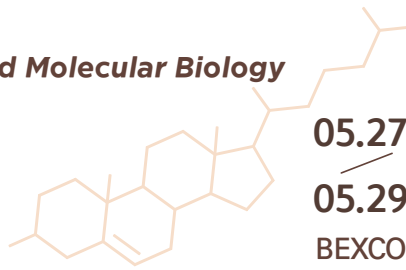
<sup>2</sup>Biochemistry, Yonsei University, Seoul 03722, Korea

<sup>3</sup>Underwood-Avison Institute of Science, Yonsei University, Seoul 03722, Korea

Aging is associated with an increased incidence of metabolic dysfunction-associated steatotic liver disease (MASLD) and is strongly linked to metabolic disorders such as obesity and type 2 diabetes. Although considerable efforts have been made to develop therapeutic strategies, resmetirom remains the only approved drug, showing only 25–30% improvement in fibrosis and MASH resolution. Therefore, identifying effective biomarkers and therapeutic targets for MASLD remains an urgent need. Here, we found that the expression of CHIP, an E3 ubiquitin ligase, was significantly decreased in MASH patients' liver samples compared to healthy controls. To investigate the role of CHIP in hepatic lipid metabolism, we generated hepatocyte-specific CHIP knockout (H-KO) mice. H-KO mice developed MASLD more rapidly under a high-fat diet or high-fat, high-fructose diet, accompanied by impaired autophagosome–lysosome fusion. Conversely, AAV8-mediated hepatic overexpression of CHIP attenuated diet-induced MASLD progression. Mechanistically, CHIP promoted K63- and K27-linked polyubiquitination of STX17 at K198, enhancing formation of the STX17–SNAP29–VAMP8 SNARE complex required for autophagosome–lysosome fusion. The STX17 K198R mutant failed to form this complex and could not suppress MASLD in vivo. Together, these findings suggest that CHIP protects against MASLD progression by promoting lipophagy.

**Keywords:** MASLD, Autophagy, Metabolism

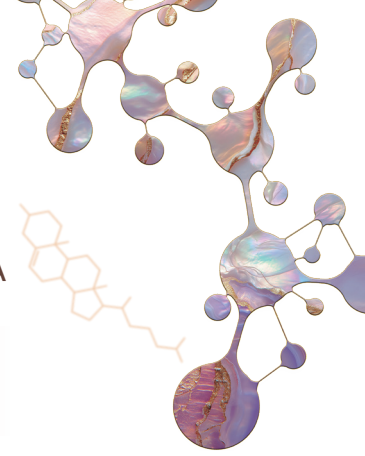




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FROM MOLECULES TO MEGABYTES:  
AI AND BIG DATA TRANSFORMING LIFE SCIENCE

**S7-1 KSBMB-JBS Joint Symposium: Living Droplet and  
Liquid-Liquid Phase Separation in Biological Systems**

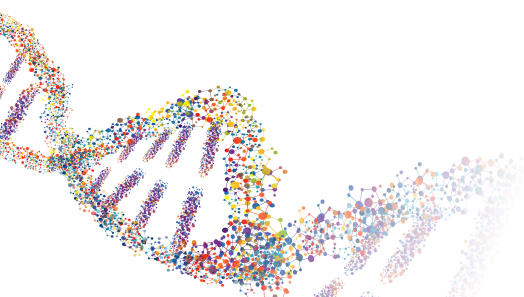
# A nucleolar route to nuclear protein aggregation in senescence

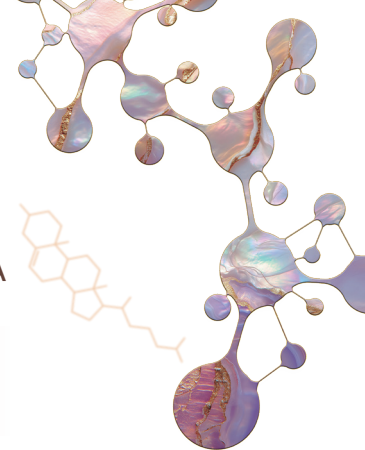
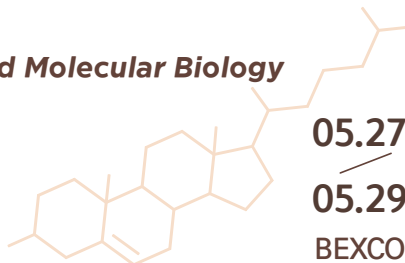
Youngdae GWON

*Sungkyunkwan University School of Medicine*

Cellular senescence is accompanied by profound alterations in nuclear organization, yet the origin of nuclear protein aggregation in senescent cells remains poorly understood. In this study, we investigated nucleolar remodeling during cellular senescence and identified a nucleolus-centered pathway leading to nuclear protein aggregation. We found that senescent cells exhibit marked structural changes in nucleoli, including altered size, morphology, and sub-nucleolar organization. Notably, the dense fibrillar component (DFC) displayed reduced dynamicity, increased mass density, and impaired coalescence behavior, suggesting a transition toward a more solid-like state. These changes were accompanied by the progressive accumulation of high-order protein assemblies, including oligomers and fibrillar aggregates, within nucleolar compartments. Furthermore, protein aggregation in senescent nucleoli differed from reversible stress-induced amyloid body formation, instead showing persistent and irreversible aggregation features. These findings suggest that nucleolar material transitions during senescence create a permissive environment for nuclear protein aggregation. Our results highlight the nucleolus as a key proteostasis node in aging cells and provide a mechanistic framework linking nucleolar dysfunction, condensate aging, and nuclear protein aggregation in cellular senescence.

**Keywords:** Nucleolus, Cellular senescence, Fibrillarin, RNA-Protein interaction, Protein aggregation





**S7-2 KSBMB-JBS Joint Symposium: Living Droplet and  
Liquid-Liquid Phase Separation in Biological Systems**

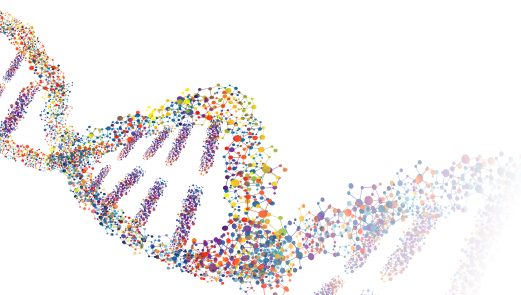
# Cellular sensing of osmotic environment via intracellular liquid-liquid phase separation

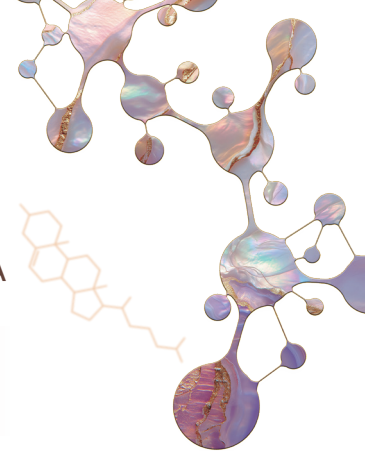
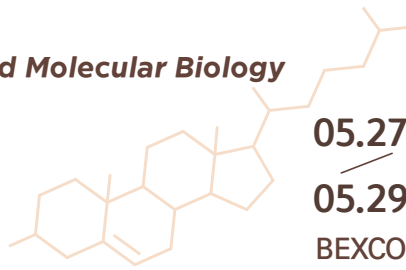
Isao NAGURO

*Faculty of Pharmacy, Juntendo University*

Osmotic homeostasis is crucial for physiological health. Recent technologies, such as  $^{23}\text{Na}$ -MRI, have uncovered distinct local osmotic environments within the body (e.g. lesions of tumor and infection). Although these environments are known to modulate the properties of cancer and immune cells, the molecular mechanisms underlying osmosensing remain elusive. Having identified ASK3 kinase as a key sensor that responds bidirectionally to osmotic fluctuations, our group has been investigating the mechanism and physiological roles of osmotic stress responses. We recently reported that under hyperosmotic stress, ASK3 undergoes liquid-liquid phase separation (LLPS) to form intracellular condensates. This phase transition is crucial for dephosphorylation and subsequent inactivation of ASK3. ASK3 condensates provide a reaction interface with the Protein Phosphatase 6 (PP6), facilitating efficient dephosphorylation. Simultaneously, the condensation sequesters ASK3 from its downstream substrates, WNK1 and SPAK/OSR1, efficiently silencing the signaling cascade. Critically, we discovered that the material properties, specifically the “fluidity”, of ASK3 condensates are essential for effective signal transduction. The fluidity is regulated by intracellular Poly (ADP-ribose) (PAR) and sodium ions; their depletion leads to “hardened” condensates that impair ASK3 dephosphorylation. Our findings demonstrate that cells utilize LLPS as a sophisticated mechanism to sense the osmotic environment. The modulation of condensate fluidity by intracellular molecules leads to a unique tuning mechanism of the signal transduction by physical state of the condensates. These insights provide a foundation for understanding the role of biomolecular condensates in environmental sensing and their implications in diseases associated with osmotic conditions, such as the tumor microenvironment.

**Keywords:** Osmotic stress, ASK3, Liquid-liquid phase separation, Fluidity, Sodium ion





**S7-3 KSBMB-JBS Joint Symposium: Living Droplet and  
Liquid-Liquid Phase Separation in Biological Systems**

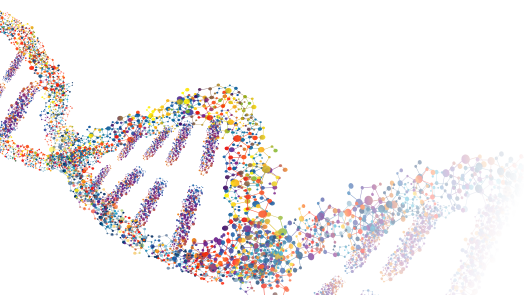
# The flow of genetic information and biomolecular condensation

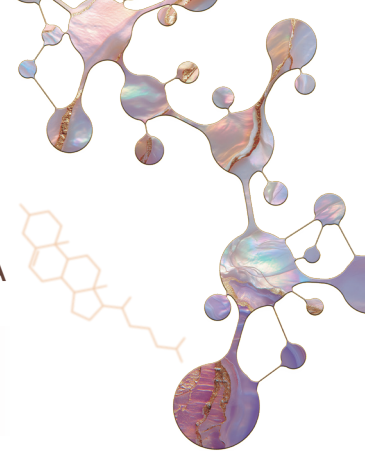
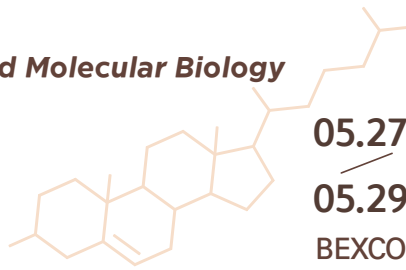
Yongdae SHIN

*Seoul National University*

Biomolecular condensates are ubiquitous along the flow of genetic information, from the birth of mRNA to protein degradation. However, the precise functions of these condensates and how these functions arise from the collective interactions of their components remain elusive. In this talk, I will discuss our efforts to address this question in the context of condensates involved in transcription. By controlling the nucleation of transcriptional condensates, we examine their functional impact on genome function and organization. Our approach sheds light on how the assembly of transcriptional condensates advances, along with associated epigenetic modifications and transcriptional activation.

**Keywords:** biomolecular condensate, phase separation, gene expression, promoter-enhancer interaction





**S7-4 KSBMB-JBS Joint Symposium: Living Droplet and  
Liquid-Liquid Phase Separation in Biological Systems**

## RNA Granule–Mediated Control of Local Translation and Memory Formation

Nobuyuki SHIINA

*National Institute for Basic Biology (NIBB), National Institutes of Natural Sciences (NINS)*

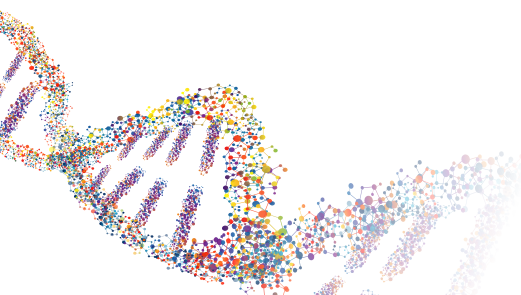
Neurons possess long cellular processes called dendrites and synthesize proteins locally in response to synaptic stimulation. Such spatially restricted translation, known as local translation, is essential for synaptic plasticity and long-term memory formation. This process is regulated by dynamic molecular assemblies called RNA granules, which consist of mRNAs, ribosomes, and RNA-binding proteins and are formed through liquid–liquid phase separation (LLPS).

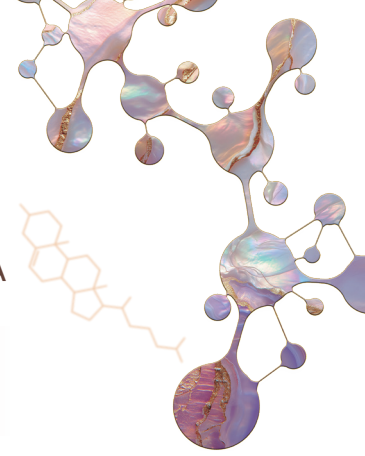
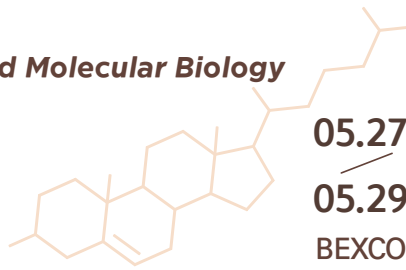
We have focused on the RNA granule protein RNG105 (Caprin1), which is highly expressed in neurons and serves as a key component of RNA granules. In RNG105 knockout mice, we observed defects in dendritic mRNA transport, impaired synapse formation, and deficits in long-term memory in spatial learning and fear-conditioning tasks, demonstrating that RNG105 is essential for memory formation.

Live-cell imaging further revealed that RNG105 exhibits high mobility within RNA granules and contributes to the formation of subcompartments with high translational activity. When neurodegeneration-associated proteins such as TDP-43 and FUS abnormally accumulate in RNA granules, RNG105 dissociates from the granules, leading to reduced local translation and impaired synapse formation.

In this session, I will discuss how changes in the physical properties of RNA granules—particularly their fluidity—affect translational regulation and ultimately influence higher-order neuronal functions such as memory formation. By integrating cellular and organismal analyses, I will present a perspective on how the dynamics of molecular assemblies regulate neuronal function and shape the molecular mechanisms of memory.

**Keywords:** RNA granules, Local translation, RNG105 (Caprin1), Synaptic plasticity, Memory formation





**S8-1 Systems Biology I: AI & Spatial Multi-Omics**

# Mapping genes to circuits by integrating connectomics and spatial transcriptomics

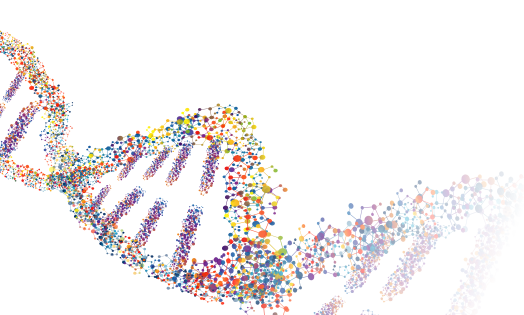
J. Alexander BAE<sup>1</sup>

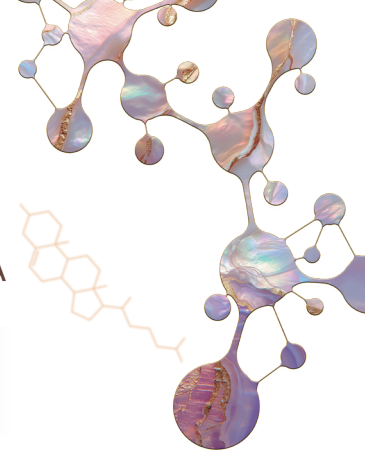
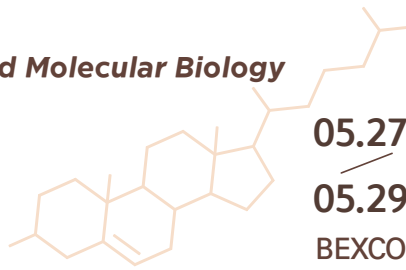
<sup>1</sup>Department of Biological Sciences, KAIST, Daejeon 34141, Korea

The neural circuits are constantly changing, and no two brains are shaped identically, yet they reliably perform the same computations accurately. My research aims to identify conserved circuit architectures that can predict consistent function using connectomics. I use large-scale 3D electron microscopy (EM) to reconstruct all neurons and their synaptic connectivity, enabling mapping of structure to function at cellular resolution. Over the past decade, we have achieved significant improvements in the image analysis pipeline using artificial intelligence (AI) for neural circuit reconstruction—ranging from image alignment to cell segmentation and synapse detection. This has resulted in dense mapping of petabyte-scale datasets containing hundreds of thousands of neurons, such as the whole *Drosophila* brain.

Recently, active efforts towards 3D spatial transcriptomics (3D ST) have become more prevalent; consequently, the comprehensive analysis of this large-scale data presents a new challenge. In this talk, I will discuss my plans to apply AI-driven approaches to analyze 3D ST data. Ultimately, this will lead to the integration of transcriptomics and connectomics, allowing us to map gene expression patterns directly onto cell connectivity graphs and identify the genetic factors governing specific circuit architectures underlying function.

**Keywords:** Connectomics, Spatial transcriptomics, AI





**S8-2 Systems Biology I: AI & Spatial Multi-Omics**

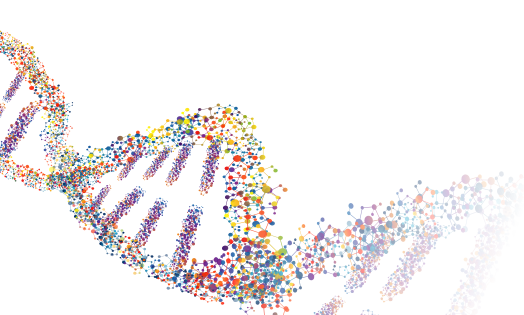
# Computational dissection of individual-dependent cis-regulatory elements across cellular contexts

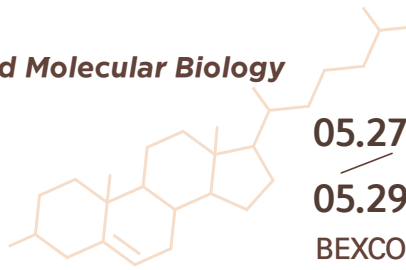
Seongkyu HAN<sup>1\*</sup>

<sup>1</sup>*Biological Sciences, Inha University, Incheon 22212, Korea*

Cis-regulatory elements (CREs) are functional DNA elements that control gene expression across diverse cellular contexts. While single-cell epigenomics has successfully catalogued cell-type-specific CREs, identifying individual-dependent variation in CRE activity remains a challenge due to data sparsity and technical batch effects. Here, I present computational frameworks to model context-specific CRE activity across both individuals and cell types. First, I introduce a pipeline that identifies individual-dependent CREs by leveraging sequence-based machine learning and multi-sample single-cell epigenomic data. Second, I integrate multi-modal single-cell datasets to map individual-level CRE-to-gene interactions within cell types, linking regulatory variants to phenotypic variation. Finally, by integrating individual-dependent epigenomic annotations with genome-wide association studies (GWAS), I refine the functional boundaries of CREs and prioritize regulatory variants previously overlooked flanking regions. Together, these approaches highlight the importance of individual-level epigenomics for resolving the genetic architecture of complex diseases.

**Keywords:** Cis-Regulatory elements, Individual epigenomics, Single-Cell multiomics

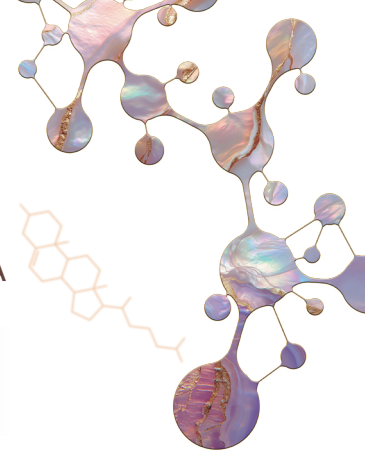




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FROM MOLECULES TO MEGABYTES:  
AI AND BIG DATA TRANSFORMING LIFE SCIENCE

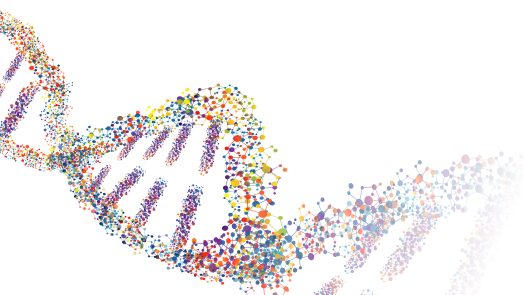
**S8-3 Systems Biology I: AI & Spatial Multi-Omics**

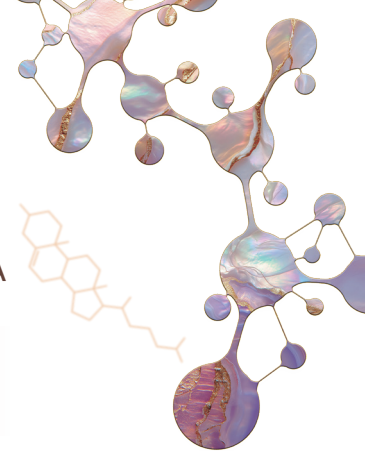
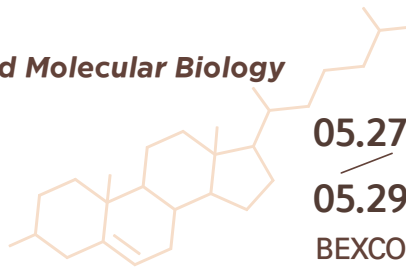
# Oncofetal Spatial Biology: A new framework for biomarker-driven oncology trials

Ankur SHARMA

*Garvan Institute of Medical Research*

Tumours co-opt fetal developmental programs to build permissive ecosystems that drive progression and therapy resistance. Using high-resolution spatial transcriptomics and proteomics, we resolve these oncofetal niches within the tumour microenvironment and uncover reproducible biomarkers of response. I will outline a framework for embedding oncofetal spatial signatures into biomarker-driven oncology trials to stratify patients and guide ecosystem-targeted therapies.





**S8-4 Systems Biology I: AI & Spatial Multi-Omics**

# Cutaneous vascular-immune crosstalk orchestrates type 17 immunity through CSF2-mediated priming of inflammatory monocytes

Hyunbeen JANG<sup>1#</sup>, Joohee LEE<sup>2#</sup>, Junhan KIM<sup>1#</sup>, Sung Hee KIM<sup>2#</sup>,  
Tae-Gyun KIM<sup>2\*</sup>, Seunghee HONG<sup>1\*</sup>

<sup>1</sup>Department of Biochemistry, College of Life Science and Biotechnology, Yonsei University, Seoul 03722, Korea

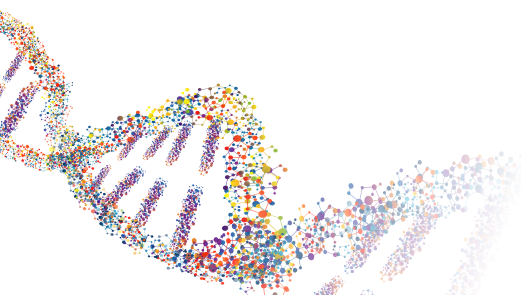
<sup>2</sup>Department of Dermatology, Severance Hospital, Cutaneous Biology Research Institute, Yonsei University College of Medicine, Seoul 03722, Korea

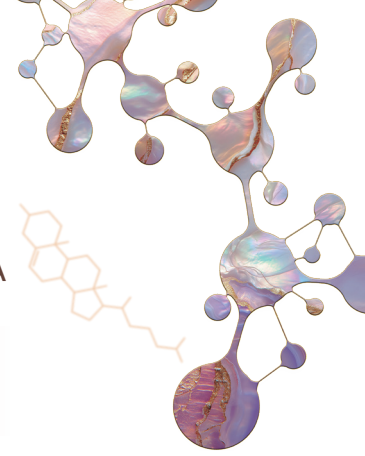
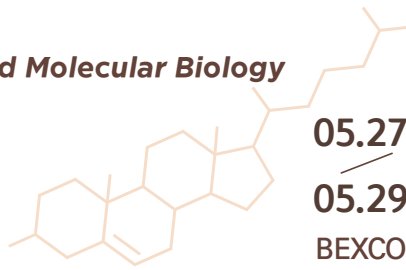
Type 17 immunity drives a broad spectrum of chronic immune-mediated inflammatory diseases, but the sub-tissular circuits that sustain pathogenic tissue inflammation are not fully defined. We identify a CSF2-centered vascular-immune niche that orchestrates cutaneous type 17 immunity by licensing proinflammatory monocytes (Inf-Mo).

To comprehensively delineate the intercellular communication underlying this circuit, we performed cell-cell interaction analysis. Although the widespread adoption of single-cell RNA sequencing has enabled researchers to decipher complex biological processes through intercellular signaling, current approaches often lose cell-level resolution due to bulk aggregation and rely on incomplete inference of surface signaling molecules owing to high dropout rates. To overcome these limitations, we constructed a cell-gene co-embedding space to infer ligand activity scores that predict regulation of target cells. Based on these scores, we performed high-resolution cell-cell interaction analysis to identify the signaling modules sustaining psoriatic inflammation.

Mechanistically, IL-17A derived from cutaneous resident T cells (TRM) induced CSF2 expression in vascular endothelial cells (VECs), establishing a pathogenic feed-forward loop linking IL23Ahi Inf-Mo, TRM17, and CSF2 VECs. Spatial transcriptomics further localized this tri-cellular network to discrete inflammatory microdomains and confirmed its contraction in psoriatic lesions pre and post IL-23 blockade therapy, validating the clinical relevance of this vascular-immune niche.

**Keywords:** Psoriasis Vulgaris, CCI Inference, Spatial Transcriptomics





**S8-5 Systems Biology I: AI & Spatial Multi-Omics**

# Clinical Implication of intratumoral CD8-T cells and their states in SCLC

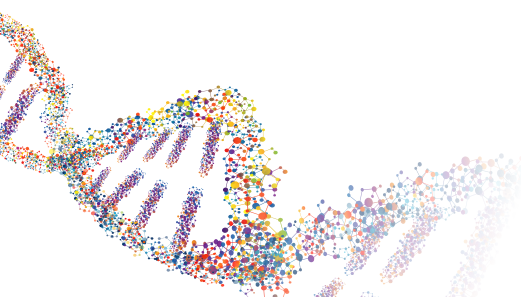
Yumin KIM<sup>1#</sup>, Stef ELINGS<sup>2#</sup>, Dwayne NAVES<sup>2#</sup>, Richard SCHOONHOVEN<sup>2</sup>,  
Teodora RADONIC<sup>2\*</sup>, Yongsoo KIM<sup>2\*</sup>

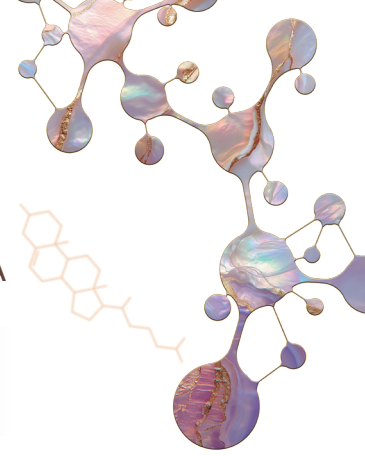
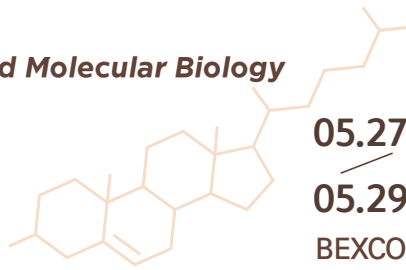
<sup>1</sup>Department of Biomedical Science and Engineering, Gwangju Institute of Science and Technology, Gwangju 61005, Korea

<sup>2</sup>Department of Pathology, Cancer Center Amsterdam (CCA), Amsterdam UMC, Amsterdam 1081 HV, Netherlands

Small cell lung cancer (SCLC) is characterized by profound immune evasion, but the spatial organization and functional states of tumor infiltrating T cells remain incompletely understood. We integrated clinicopathologic assessment with single cell spatial transcriptomic profiling to characterize intratumoral CD8<sup>+</sup> T cells in SCLC. A historical cohort of 170 patients treated with chemoradiation and 87 patients from the phase II STIMULI trial were analyzed for intratumoral CD8<sup>+</sup> T cell density by immunohistochemistry. To define the biological context of CD8<sup>+</sup> T cell infiltration, 15 tumors underwent Xenium single cell spatial transcriptomic profiling using a 380 gene immunooncology panel. Intratumoral CD8<sup>+</sup> T cell density was associated with improved survival in both limited stage and extensive stage SCLC. Spatial profiling showed that CD8<sup>+</sup> T cell infiltration positive tumors were enriched for immune niches marked by co-localization of CD8<sup>+</sup> T cells with CD4<sup>+</sup> T cells, regulatory T cells, and conventional dendritic cells. Patch level and proximity based transcriptomic analysis further revealed distinct clustering patterns and niche dependent T cell states. Notably, Treg-proximal CD8<sup>+</sup> T cells exhibited a progenitor exhausted (T<sub>pex</sub>)-like transcriptional program. These findings suggest that CD8<sup>+</sup> T cell infiltration in SCLC reflects spatially organized immune microenvironments with potential relevance to immunotherapy response.

**Keywords:** Small cell lung cancer, Xenium, Spatial transcriptome





**S8-6 Systems Biology I: AI & Spatial Multi-Omics**

# Chromatin Architecture Dynamics Modelling in Interpretable 3D Latent Space using Deep Generative Model

Kyukwang KIM<sup>1</sup>, Inkyung JUNG<sup>1\*</sup>

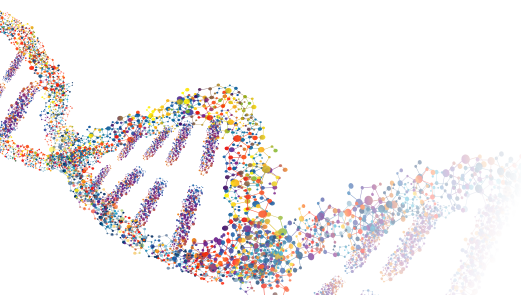
<sup>1</sup>Department of Biological Sciences, Korea Advanced Institute of Science and Technology, Daejeon 34141, Korea

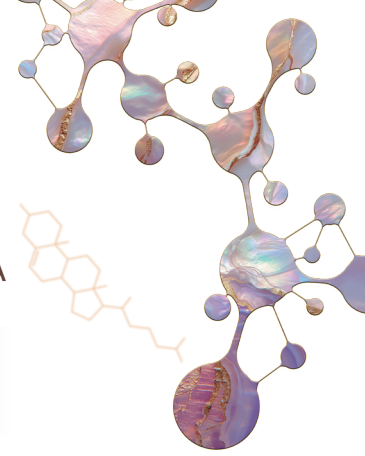
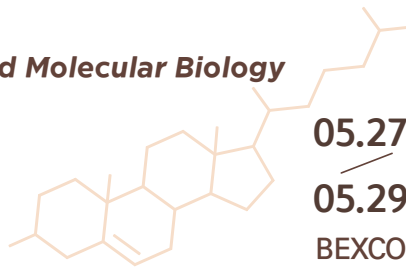
The 3D genome is known to undergo dynamic reorganization processes during cell differentiation to regulate gene expression. However, elucidating the causal relationship between the 3D genome and gene regulation remains challenging, as observable Hi-C patterns arise from the cumulative changes throughout the differentiation process.

Here, we present an interpretable deep generative model, which is capable of visualizing the 3D genome program that drives differences within the latent space. By applying the developed framework to human cardiomyocyte differentiation data, we identified 3D genomic features corresponding to a ‘main program’ that governs the overall differentiation trend, as well as ‘branch programs’ that operate before or after changes of gene expression level, which indicates the pre- or post- configuration of the 3D genome.

For validation, immature cardiomyocytes were generated by EZH1 knockout, a well-known regulator of late-stage cardiac differentiation. In EZH1 KO mutants, we observed an increase in 3D genome interactions, which corresponds to the early stage-related branch 3D genome program at the promoter of DPY19L4, a cardiac pathology-related gene. These results demonstrate that the developed framework offers a generalizable method to resolve the causal relationship between 3D genome dynamics and transcriptional regulation, providing new insights into how chromatin architecture governs cell fate.

**Keywords:** 3D genome, Gene regulation, Deep learning





**S8-7 Systems Biology I: AI & Spatial Multi-Omics**

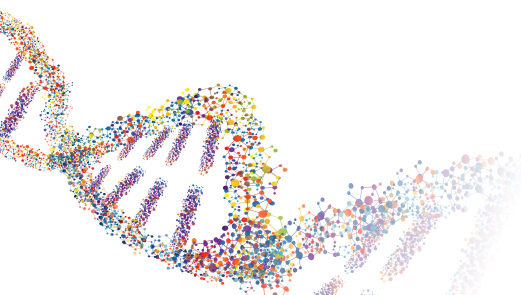
# Decoding Spatially Driven Transcriptomic Variability in Tumors via Transformer-Based Modeling

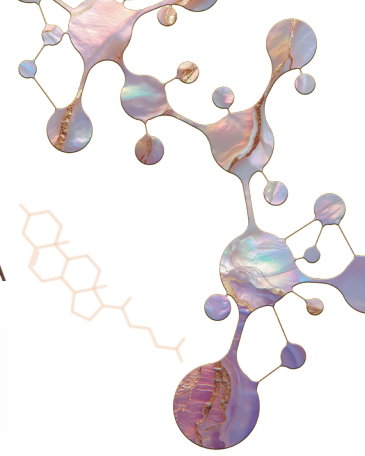
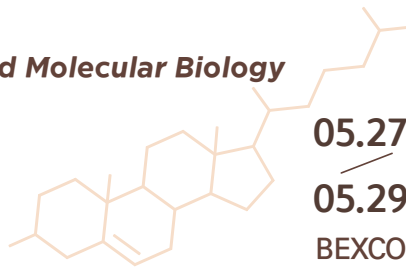
Jahanzeb SAQIB<sup>1</sup>, Gahyun KIM<sup>1</sup>, Junil KIM<sup>1\*</sup>

<sup>1</sup>Bioinformatics, Soongsil University, Seoul 06978, Korea

Spatial transcriptomics has emerged as a powerful technology for profiling gene expression within its native tissue context, facilitating the examination of cellular interactions and context-dependent effects of local tissue microenvironments on cellular states. However, existing foundation models primarily pretrained on single-cell RNA sequencing (scRNA-seq) data which limits the ability to capture spatial relationships and context-dependent variability inherent to tissue organization. Here, we present a transformer-based foundation model specifically designed for spatial transcriptomics to address these limitations. Leveraging high-resolution Xenium data across several cancer types, including lung, breast and pancreatic ductal adenocarcinoma and ovarian cancer, our model learns spatially informed representations directly from gene expression profiles. Unlike conventional approaches, it is trained to reconstruct spatial organization by predicting local neighborhood structure and spatial density, enabling the model to infer spatial context without explicit coordinate. By modeling spatial dependencies within the tumor microenvironment, our framework captures niche-driven transcriptional variability and facilitates the identification of niche-specific gene signatures associated with cell-cell communication. This approach provides a scalable and generalizable solution for decoding spatial transcriptomic landscapes and offers new opportunities to investigate the molecular mechanisms underlying tumor heterogeneity and microenvironmental regulation.

**Keywords:** Spatial transcriptomics, Large language model, Niche gene





**S8-8 Systems Biology I: AI & Spatial Multi-Omics**

# Decoding the Enteric Nervous System at Single-Cell and Spatial Resolution in Hirschsprung's Disease and Hypoganglionosis

Sung-Ryung CHOI<sup>1,2</sup>, Murim CHOI<sup>3\*</sup>

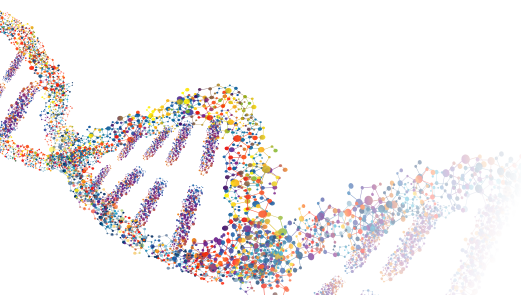
<sup>1</sup>Department of Translational Medicine, Seoul National University College of Medicine, Seoul 03080, Korea

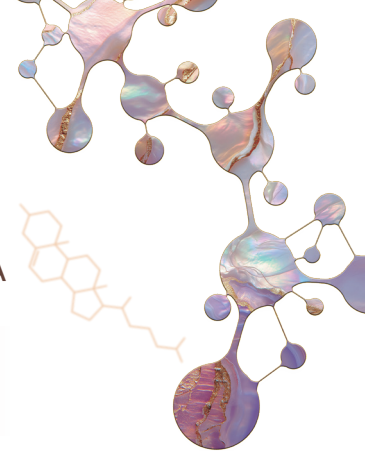
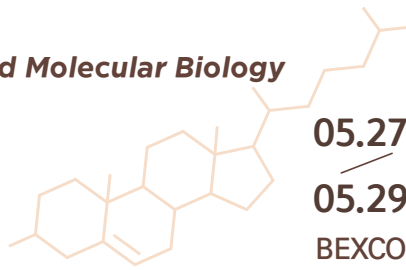
<sup>2</sup>Department of Surgery, Seoul National University Hospital, Seoul 03080, Korea

<sup>3</sup>Department of Biomedical Sciences, Seoul National University College of Medicine, Seoul 03080, Korea

The enteric nervous system (ENS) governs gastrointestinal motility through a complex network of neurons and glia, yet its cellular architecture remains poorly characterized due to inherent technical challenges in tissue accessibility and cell rarity. Disorders of ENS development, including Hirschsprung's disease (HSCR) and hypoganglionosis, cause severe intestinal dysmotility, but the transcriptional and spatial underpinnings of ENS pathology are largely undefined. Here we present an integrated single-cell and spatial transcriptomic framework to systematically dissect ENS composition across normal and diseased human intestinal tissue. Using FACS-enriched single-cell RNA sequencing and Xenium 5k spatial transcriptomics from tissue sections spanning normal, hypoganglionosis, and HSCR segments — including normoganglionic, transitional, and aganglionic zones — we construct a spatially resolved cellular atlas of the human ENS. Multi-model cell type annotation, combined with label transfer to spatial data, enables systematic mapping of ENS neuronal and glial subtypes in situ. This approach aims to reveal disease-specific transcriptional signatures and spatial remodeling of the ENS, providing a foundation for understanding the molecular basis of enteric neuropathies, with particular focus on identifying subtype-specific neuronal loss and altered glial states across disease segments.

**Keywords:** Enteric Nervous Systems, Hirschsprung's Disease, Intestinal Pseudo Obstruction





**S9-1 DNA Damage Repair & Genomic Instability**

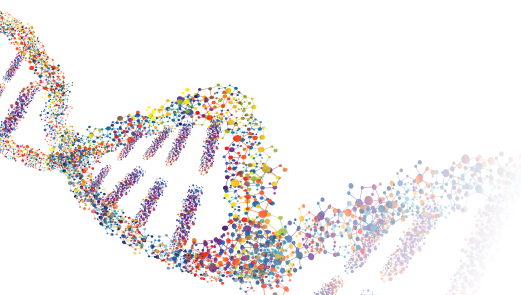
# SLFN11 as a Sensor of ssDNA Connecting Replication Stress and Innate Immunity

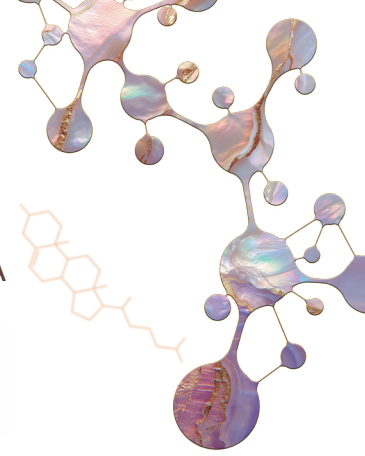
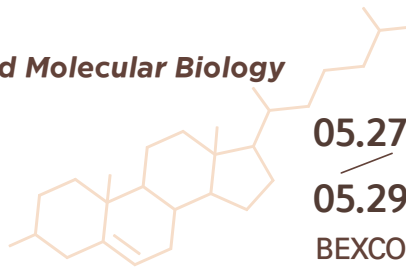
Junko MURAI

*Proteo-Science Center, Premier Institute for Advanced Studies, Ehime University*

DNA-damaging agents remain a cornerstone of cancer therapy, yet the molecular determinants that govern cellular responses to DNA damage remain incompletely understood. Schlafen 11 (SLFN11), a nuclear protein, has emerged as a critical determinant of sensitivity to DNA-damaging agents, including topoisomerase inhibitors and platinum compounds. Our previous work demonstrated that SLFN11 blocks DNA replication under replication stress by associating with chromatin—later revealed to be single-stranded DNA (ssDNA)—and enforcing irreversible replication arrest (Murai et al., *Mol Cell* 2018). More recently, an unexpected connection between SLFN11 activity and cellular stress signaling has emerged. SLFN11 triggers ribosomal stress through tRNA cleavage and ribosome stalling, leading to activation of stress-activated MAP kinase pathways, particularly JNK. This signaling cascade ultimately promotes rapid, p53-independent apoptosis in response to replication stress (Boon et al., *Science* 2024). In addition, we have found that SLFN11 suppresses rRNA synthesis and impairs ribosome biogenesis, resulting in global translation inhibition and apoptosis independently of p53 (Ogawa et al., *Mol Cell* 2025). Interestingly, SLFN11 can also be activated by transfection of ssDNA, which induces sterile innate immune-like responses characterized by JNK pathway activation (Zhang et al., *Science Immunology* 2024). These findings suggest that SLFN11 functions as a molecular sensor of ssDNA that converts replication stress into a broader cellular stress program resembling innate immune activation. In my presentation, I will discuss recent advances in our understanding of SLFN11 biology, focusing on how SLFN11 responds to ssDNA present in the genome versus ssDNA introduced into the cytosol. Understanding the similarities and differences in SLFN11 responses to ssDNA in these distinct contexts may help resolve the complexity of how SLFN11-positive cancers—present in approximately half of human tumors—respond to DNA-damaging anticancer therapies and may inform the development of new biomarkers and therapeutic strategies.

**Keywords:** Replication stress, innate immune response, DNA damage, SLFN11, DNA repair





**S9-2 DNA Damage Repair & Genomic Instability**

## Transcriptional Triage of DNA Repair

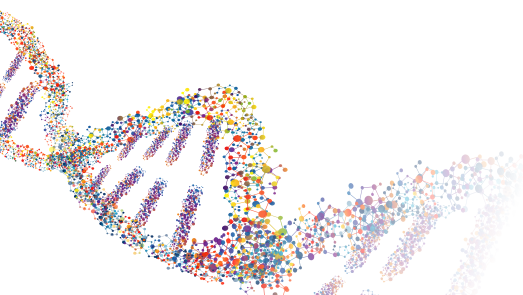
Gunhyoung LIM<sup>1</sup>, Dongwon JOO<sup>1</sup>, Changwon KANG<sup>2\*</sup>, Sungchul HOHNG<sup>1\*</sup>

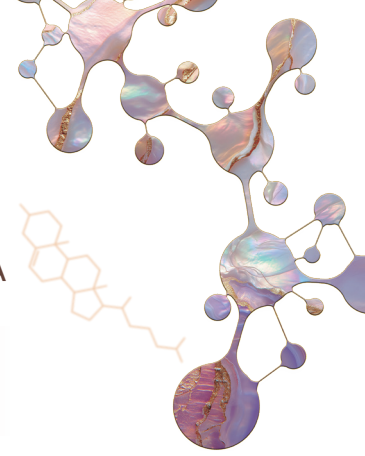
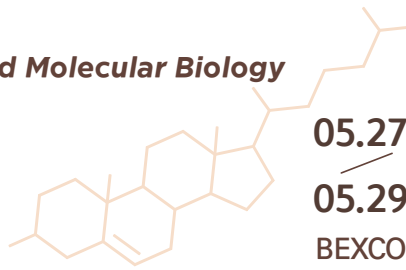
<sup>1</sup>Department of Physics and Astronomy, and Institute of Applied Physics, Seoul National University, Seoul 08826, Korea

<sup>2</sup>Department of Biological Sciences, and KAIST Stem Cell Center, Korea Advanced Institute of Science and Technology, Daejeon 34141, Korea

Genomic instability is caused by transcription, yet nascent transcripts are essential for directing DNA repair. How cells distinguish toxic from functional R-loops to recognize underlying lesions remains unknown. Using single-molecule fluorescence to monitor *Escherichia coli* transcription across 15 defined lesions, we demonstrate that translocating RNA polymerase is an autonomous mechanical sensor of lesion geometry. Cotranscriptional R-loop formation is facilitated by the topological freedom of the DNA template: while sterically constrained lesions (e.g., nicks, mismatches) are signaling-inert, flexible strand discontinuities (e.g., gaps, overhangs) achieve robust R-loop generation via an intramolecular template-switch we term the “transcriptional bridge.” Critically, break-end polarity governs transcript polarity within the R-loop to program repair trajectories. Specifically, single-stranded 5'-ends allow duplex-to-single-strand template switch to produce sense R-loops, scaffolding end-resection for repair. Conversely, single-stranded 3'-ends prompt sense-to-antisense strand switch to generate antisense R-loops, protecting resection-obviated ends to provide a shortcut to synapsis. This antisense signal is marked by a one-nucleotide transcript skip, reflecting the physical tension of intramolecular realignment. Thus, RNA polymerase is the primary sensor converting physical lesion geometry into biochemical signals of polarized R-loops, specifying repair paths before downstream recruitment. This capability, enabled by universally conserved transcription bubble architecture, represents an intrinsic mechanism for maintaining genomic stability.

**Keywords:** DNA repair, Antisense transcription, Single-Molecule fluorescence





**S9-3 DNA Damage Repair & Genomic Instability**

# PCNA Regulation and Repair Pathway Choice: From Biochemistry to AI-driven Discovery

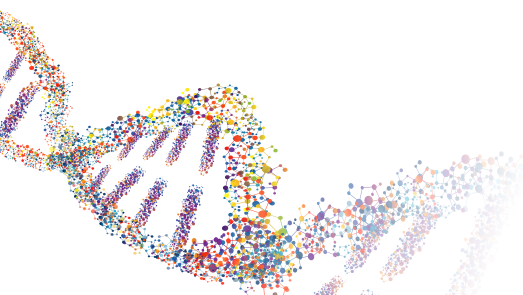
Eunjin RYU<sup>1</sup>

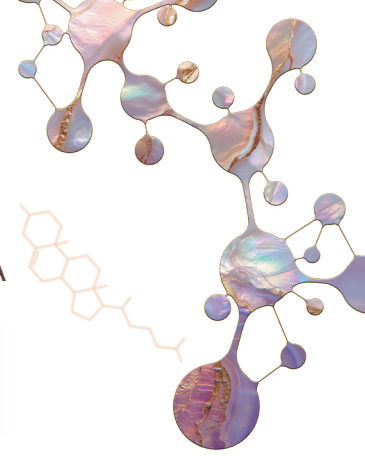
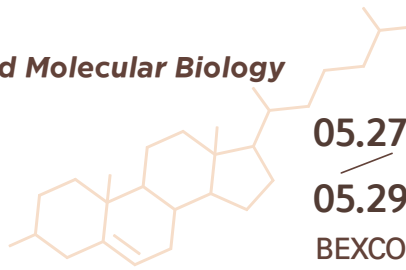
<sup>1</sup>Department of Biological education, Seoul National University, Seoul 08826, Korea

DNA replication preserves genomic integrity, yet replication forks frequently encounter DNA lesions that impede progression. Cells rely on DNA damage tolerance (DDT) pathways to complete replication under stress. Proliferating Cell Nuclear Antigen (PCNA) serves as a central coordinator of these responses by recruiting and releasing pathway-specific factors through regulated post-translational modifications. In our recent work, we identified the ATAD5–RFC-like complex (ATAD5-RLC) as a dedicated PCNA unloader that promotes PCNA turnover on chromatin. We further showed that ATAD5 facilitates deubiquitination of ubiquitinated PCNA via functional interaction with the USP1–UAF1 complex, linking clamp unloading to termination of damage-associated signaling. In a complementary human genetics study, we connected impaired clamp-loader function to a rare inherited disorder, providing mechanistic insight into how defective PCNA regulation contributes to disease.

Building on these findings, my future research will investigate how distinct PCNA modifications and interacting partners regulate activation of specific DDT pathways, including translesion synthesis, fork reversal, and repriming. By integrating AlphaFold-based structural prediction with a *Xenopus* egg extract replication system, I aim to define the molecular basis of pathway choice under replication stress.

**Keywords:** DNA replication, Damage tolerance, Damage repair





**S9-4 DNA Damage Repair & Genomic Instability**

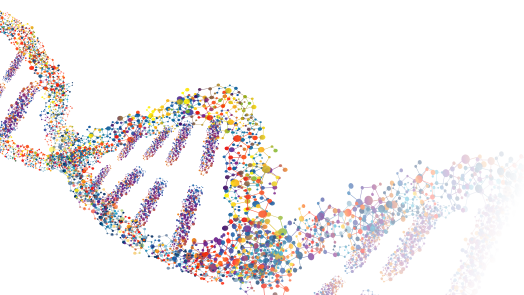
# Direct visualization of replication and R-loop collision using single-molecule imaging

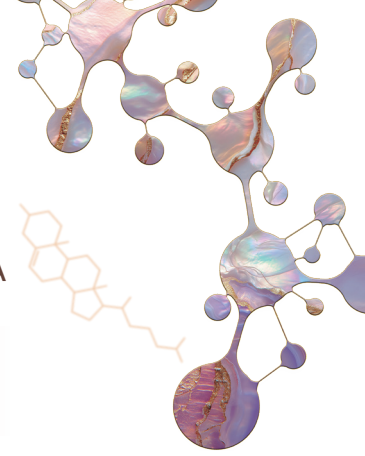
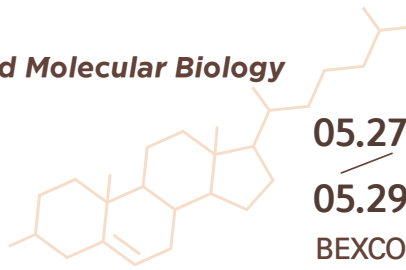
Subin KIM<sup>1</sup>, Ja Yil LEE<sup>1\*</sup>

<sup>1</sup>Department of Biological Sciences, Ulsan National Institute of Science and Technology, Ulsan 44919, Korea

R-loops, which are three-stranded nucleic acid structures consisting of a DNA-RNA hybrid and a displaced single-stranded DNA, are known to promote genomic instability by causing transcription-replication conflicts (TRCs). However, the detailed mechanism by which R-loops affect DNA replication remains elusive. Here we investigated the impact of R-loops on DNA replication using a novel single-molecule imaging technique DNA curtain. We use phi29 DNA polymerase (phi29 DNAP) which exhibits high processivity and high fidelity to observed the collision between replicating phi29 DNAP and a single R-loop. Phi29 DNAP could pass the R-loop having DNA-RNA hybrid on template strand during replication. However, more than 60% of phi29 DNAP was stalled when the phi29 DNAP encountered R-loop with DNA-RNA hybrid on non-template strand, and it was confirmed by observing the remaining RNA after replication. We also examined the collision with D-loop, and the results were similar to R-loop. It suggested that hybridized structure on non-template strand inhibited the progression of Phi29 DNAP replication. By testing various types of DNA secondary structures, we proposed that three-stranded structure affected the replication stalling. In addition, R-loop with G-quadruplex structure showed higher stalling portion, which suggests that G-quadruplex does stabilize R-loop structure.

**Keywords:** R-Loop, Transcription-Replication conflicts (TRC), Single-Molecule imaging technique





**S9-5 DNA Damage Repair & Genomic Instability**

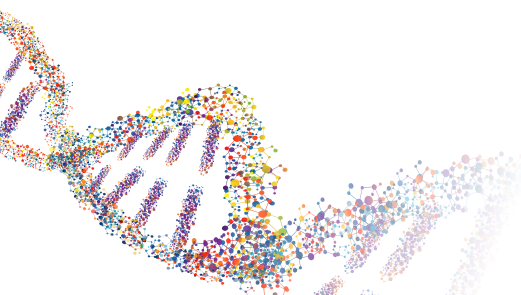
# The Role of PPM1G in the Replication Stress-Induced DNA Damage Response Pathway

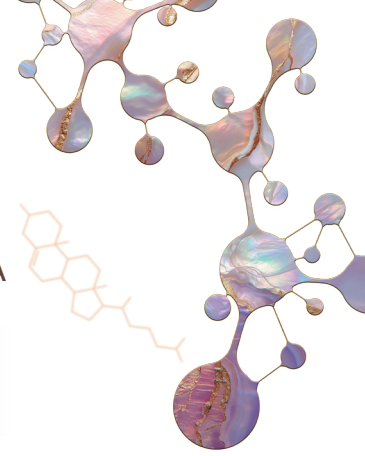
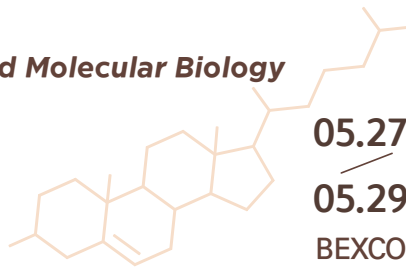
Renata KUSUMA<sup>1</sup>, Wootae KIM<sup>1\*</sup>

<sup>1</sup>Integrated Biomedical Science, Soonchunhyang Institute of Medi-bio-Science (SIMS), Cheonan 31151, Korea

Replication stress is one of the distinctive features of cancer, arising from oncogenic alterations and rapid proliferation, contributing to genomic instability and cancer progression. Cancer cells rely heavily on the ATR–CHK1 pathway, which is activated at stalled replication forks to maintain genome integrity and support cell survival under replication stress. Colorectal cancer (CRC), a highly proliferative tumor type, provides a relevant model to study replication stress responses. Given the role of ATR–CHK1 signaling in this process, its precise regulation is critical for an appropriate replication stress response. While kinase-mediated phosphorylation events driving ATR–CHK1 activation have been extensively characterized, the mechanisms that fine-tune this signaling through dephosphorylation remain incompletely understood. Here, we investigated whether the nuclear phosphatase PPM1G functions as a regulator of ATR–CHK1 signaling in CRC. PPM1G expression was elevated in tumor samples. PPM1G expression positively correlated with replication stress response and DDR gene signatures. Loss of PPM1G attenuated ATR–CHK1 signaling, as evidenced by reduced phosphorylation of replication stress markers. Consistently, PPM1G deficiency increased genomic instability, as indicated by elevated micronuclei formation. Together, these findings identify PPM1G as a nuclear phosphatase that fine-tunes ATR–CHK1 signaling and promotes replication stress tolerance in CRC.

**Keywords:** Replication stress, DNA damage response, ATR–CHK1 signaling





**S9-6 DNA Damage Repair & Genomic Instability**

# ATR Inhibition Remodels the Fibrotic Tumor Microenvironment and Restores Antitumor Immunity in Immunotherapy-Refractory Gastric Cancer

Minae AN<sup>1</sup>, Jeeyun LEE<sup>2\*</sup>

<sup>1</sup> Biointelligence Research Center, Samsung Medical Center, Gangnam-gu 06351, Korea

<sup>2</sup> Division of Hematology-Oncology, Samsung Medical Center, Gangnam-gu 06351, Korea

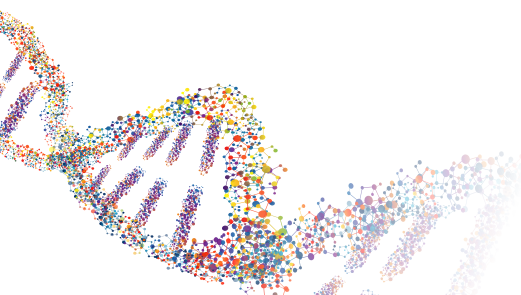
We investigated a phase II clinical trial evaluating the combination of an ATR inhibitor with anti-PD-L1 therapy in patients with immunotherapy-refractory advanced gastric cancer (n = 30). ATR inhibitors have been primarily developed to target the DNA damage response and replication stress in tumor cells; however, their effects on the tumor microenvironment (TME) remain poorly understood.

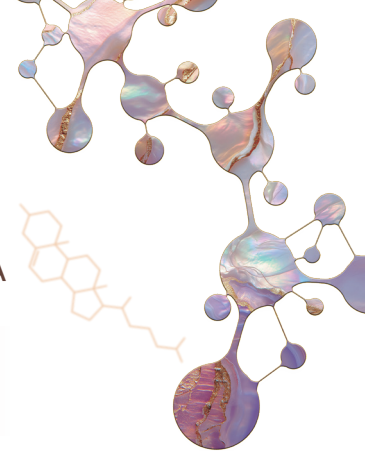
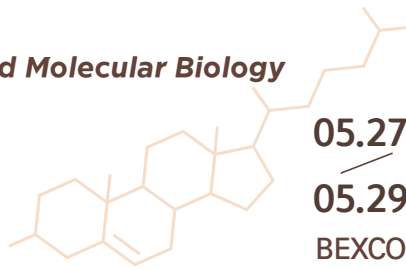
Using integrated single-cell RNA sequencing and spatial single-cell T cell receptor (TCR) sequencing, we characterized dynamic changes in tumor, cancer-associated fibroblast (CAF), and immune cell populations during treatment. ATR inhibition resulted not only in tumor cell depletion but also in a marked reduction of CAF subsets associated with extracellular matrix remodeling and immune exclusion, accompanied by increased immune cell infiltration.

Despite this increase, functional analyses revealed enhanced activation and expansion of tumor-reactive T cells. TCR profiling demonstrated increased clonal expansion and enrichment of tumor-specific T cell populations, alongside improved cytotoxic signatures and tumor-immune interactions.

Mechanistically, ATR inhibition disrupts stromal barriers while alleviating replication stress, thereby facilitating immune cell trafficking and restoring effective antitumor immunity. These findings provide a mechanistic rationale for combining ATR inhibition with immune checkpoint blockade and highlight stromal remodeling as a key determinant of therapeutic response.

**Keywords:** ATR inhibition, TME, Tumor reactive T cells





**S9-7 DNA Damage Repair & Genomic Instability**

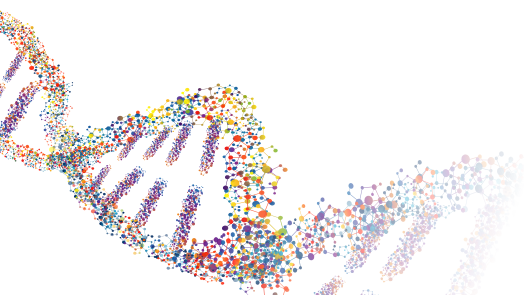
# RNF4 and USP7 Coordinate Spatial Regulation of SLX4 Stability within the PML Nuclear Bodies

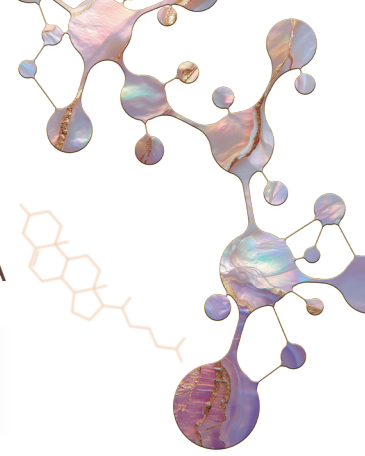
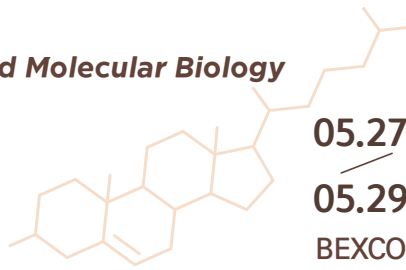
Eunyoung JUNG<sup>1</sup>, Yonghwan KIM<sup>1\*</sup>

<sup>1</sup>Department of Biological Sciences, Sookmyung Women's University, Seoul 04310, Korea

To protect the genome from the formation of DNA breaks by nucleases involved in DNA repair, cells have evolved multiple levels of regulatory strategies. One key regulator of nuclease activity is the scaffold protein SLX4, which plays important roles in repairing DNA damage induced by mitomycin C (MMC) and camptothecin (CPT) as well as in the resolution of stalled replication forks. Since SLX4 regulates the activity of nucleases such as SLX1, MUS81, and XPF, whose uncontrolled activity could jeopardize genome integrity, the protein level and localization of SLX4 must be tightly regulated. Here, we show that the ubiquitin E3 ligase RNF4 is associated with SLX4 and is responsible for the ubiquitin-dependent proteasomal degradation of excessive SLX4 under normal conditions. Conversely, PML Nuclear Bodies (NBs) promote SLX4 stability. In PML NBs, the stability of SLX4 is maintained by the deubiquitinase USP7, managing the amount of SLX4 necessary for a rapid response to DNA damage. These findings suggest that SLX4 and its associate nucleases are confined within PML NBs and that the optimal protein level of SLX4 is maintained by the coordinated activities of RNF4 and USP7. These findings reveal how cells spatially regulate potentially harmful factors under normal conditions.

**Keywords:** Genome Maintenance, DNA damage response, PML nuclear bodies





**S10-1** Cancer Immunology

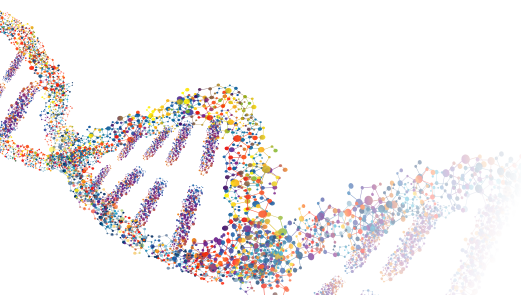
# **IgG1-mediated B cell immunity reshapes the tumor microenvironment to enhance anti-tumor responses**

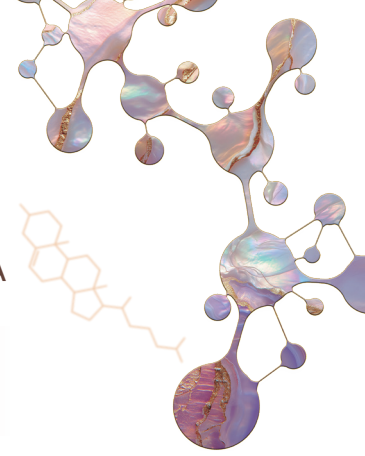
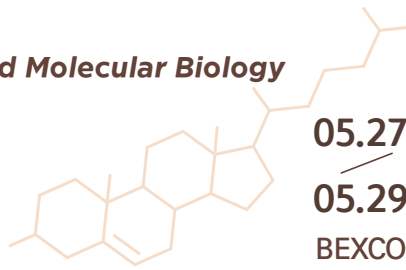
Wanli LIU

*Tsinghua University*

B cells in the tumor microenvironment (TME) play dual and complex roles in cancer progression, functioning both as drivers of anti-tumor immunity and, under certain conditions, as suppressors of immune responses. While their presence within tertiary lymphoid structures (TLSs) correlates with favorable prognosis in multiple cancers, the molecular mechanisms governing their protective functions remain incompletely understood. Here, we demonstrate that membrane-bound IgG1 on B cells plays a critical role in shaping effective anti-tumor immunity. Upon encountering tumor-associated antigens (TAAs), IgG1<sup>+</sup> B cells undergo enhanced differentiation into IgG1<sup>+</sup> plasma cells, leading to elevated production of TAA-specific antibodies. These antibodies drive antibody-dependent cellular phagocytosis and improve antigen presentation to T cells, fostering a TME enriched with CD8<sup>+</sup> T cells, CD103<sup>+</sup> dendritic cells, and mature TLSs. Comprehensive immune profiling of colorectal cancer (CRC) patients revealed that increased IgG1<sup>+</sup> plasma cell presence correlates with enhanced effector T cell infiltration and reduced T cell exhaustion, contributing to an anti-tumor microenvironment. In murine colon carcinoma models, adoptively transferred TAA-specific IgG1<sup>+</sup> memory B cells demonstrated therapeutic efficacy, significantly reducing tumor burden. Mechanistically, IgG1-mediated B cell receptor signaling potentiates plasma cell differentiation and amplifies TAA-specific antibody responses, which in turn mobilize broad immune effector functions within the TME. These findings reveal that harnessing IgG1<sup>+</sup> B cell responses can reshape the TME toward an anti-tumor phenotype, highlighting the therapeutic potential of targeting IgG1<sup>+</sup> B cells for next-generation cancer immunotherapies.

**Keywords:** B cells, IgG1, tumor microenvironment (TME), antibody-dependent phagocytosis, immunotherapy





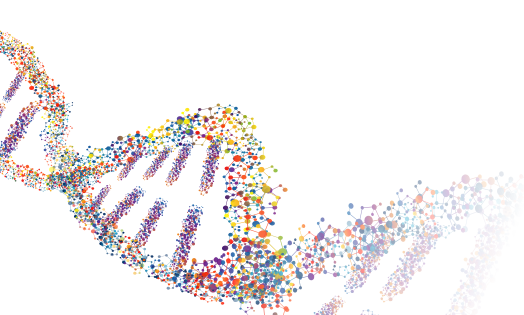
**S10-2 Cancer Immunology**

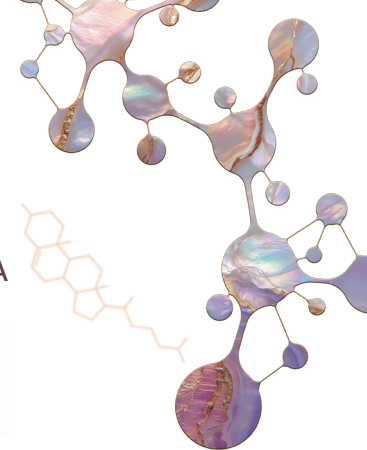
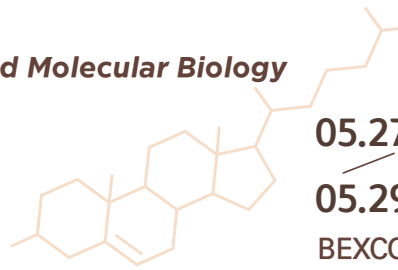
# IgM as a key determinant of anti-tumor responses

Karen HAAS

*Wake Forest University School of Medicine*

IgM is the first antibody isotype produced with a unique capacity to recognize repeating glycans expressed on cancer cells but lacking on healthy tissue, yet its role in cancer has been debated. Across complementary *in vivo* mucin-bearing adenocarcinoma models we show that secreted IgM functions in early control of tumor growth and promotes downstream adaptive responses. In particular, our focus on distinct solid and suspension tumors displaying high levels of the tumor-associated carbohydrate antigen, Tn antigen, has revealed a critical role for innate B cells and the production of IgM antibodies targeting this antigen which is expressed on a wide range of cancer types. Our work demonstrates the production of Tn-specific IgM can be increased by innate B cell-activating signals as well as by Tn-bearing mucin antigens. Further, we identify PD-1 as a critical regulator of these responses and the downstream anti-tumor adaptive responses that tumor-reactive IgM promotes. Together, our published studies and new, unpublished findings converge on a unifying model in which tumor-reactive IgM directs tumor cell killing and coordinates downstream anti-tumor responses across myeloid and lymphoid compartments. Enhancing the Tn-specific IgM response via PD-1 pathway modulation, innate B cell-directed adjuvants, and glycan-focused immunogens offers a tractable path to preventive and therapeutic strategies for metastatic, mucin-rich cancers.





**S10-3 Cancer Immunology**

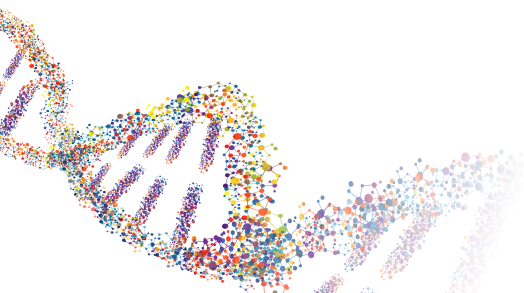
# SLAMF7 downregulation defines terminal CD8 T cell exhaustion

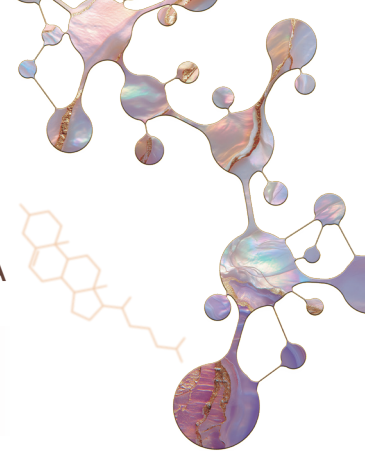
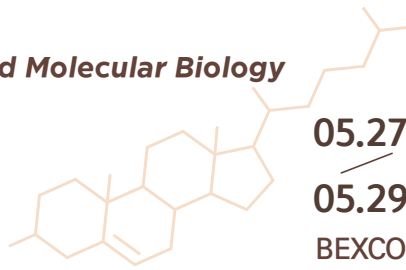
Se Jin IM

*Department of Immunology, Sungkyunkwan University School of Medicine, Korea*

T cell exhaustion is a dysfunctional state of T cells that arises under persistent antigenic stimulation, such as in chronic viral infections and tumors. Although immune checkpoint blockade can reinvigorate exhausted T cells, only a minority of patients respond, emphasizing the need for deeper understanding of T cell exhaustion. SLAMF7 is an immune-regulatory receptor, but its regulation and functional role during CD8 T cell exhaustion remain unclear. Here, we found that SLAMF7 was absent in naïve mouse and human CD8 T cells but rapidly induced upon *in vitro* activation. Following acute lymphocytic choriomeningitis virus (LCMV) infection, all effector and memory subsets expressed SLAMF7, with higher levels in more differentiated cytolytic populations. Under persistent antigenic stimulation, including chronic LCMV infection, murine tumors models, and human renal cell carcinoma (RCC), SLAMF7 was highly expressed in progenitor and transitory exhausted subsets but downregulated in PD-1hi terminally exhausted cells. This loss of SLAMF7 expression coincided with increased inhibitory receptor and TOX expression, attenuation of cytotoxic programs, and impaired polyfunctional cytokine production. Across models, SLAMF7 loss reflected prolonged antigen exposure rather than antigen burden. In RCC patients, SLAMF7-based stratification delineated distinct immunological states: SLAMF7-HI tumors retained progenitor-like CD8 T cells with preserved effector function, whereas SLAMF7-DN tumors were enriched for terminally exhausted cells and were more frequently associated with high nuclear grade. Collectively, these findings identify SLAMF7 downregulation as a conserved marker of terminal CD8 T cell exhaustion and suggest its potential as a biomarker of immune competence and disease severity in solid tumors.

**Keywords:** CD8 T cell exhaustion, SLAMF7, Tumor-infiltrating lymphocytes, Renal cell carcinoma





**S10-4 Cancer Immunology**

# CD25-mediated feedback control of B-cell receptor signaling and its oncogenic mimics

Jaewoong LEE

<sup>1</sup>Department of Integrated Biomedical and Life Science, Korea University, Seoul 02841, South Korea <sup>2</sup>Interdisciplinary Program in Precision Public Health, Korea University, Seoul 02841, South Korea

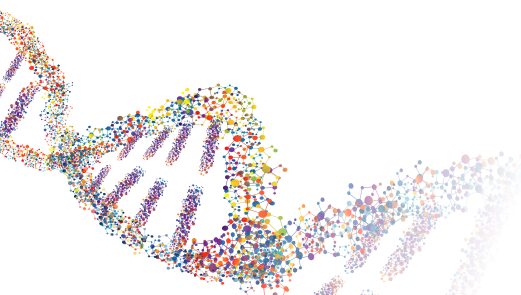
<sup>3</sup>School of Biosystems and Biomedical Sciences, College of Health Science, Korea University, Seoul 02841, South Korea

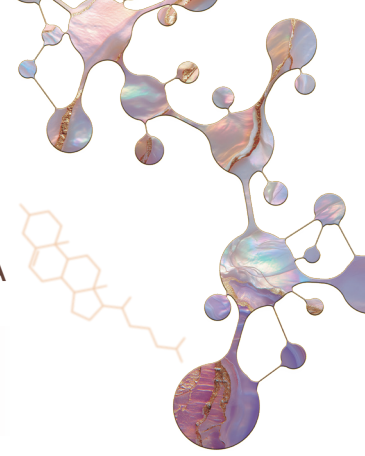
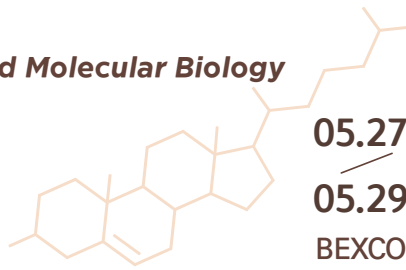
B-cell receptor (BCR) signaling is tightly regulated by the inhibitory phosphatase SHP1 to prevent autoimmunity and malignancy. While SHP1 activity increases 1,000-fold upon binding to immunoreceptor tyrosine-based inhibitory motifs (ITIM), its dephosphorylation range is limited to ~5 nm, leaving the mechanisms of site-specific BCR-proximal activation unclear.

This study identifies a novel mechanistic framework for dynamic BCR feedback control involving PKC-delta and CD25. Although CD25 is primarily known as an IL2-receptor component in T-cells, we found it is sharply upregulated during B-cell activation. Our genetic and interactome analyses reveal that BCR signaling triggers PKC-delta-mediated phosphorylation of CD25, leading to its recruitment to the BCR. Rather than transducing IL-2 signals, CD25 acts as a molecular scaffold that attracts ITIM-receptor nanoclusters. This proximity localizes and activates SHP1 within the necessary range to dephosphorylate BCR-signaling molecules, providing essential negative feedback.

The loss of CD25 or mutation of its PKC-delta-phosphorylation site disrupts SHP1 function, resulting in autonomous BCR signaling, pervasive autoantibody production, and lymphoproliferative B-cell expansion. Exploiting CD25 as a biomarker for oncogenic signaling, CD25-targeted antibody-drug conjugates (ADCs) demonstrated durable responses in preclinical B-cell lymphoma models. Furthermore, we restored defective BCR feedback in human CD25<sup>-/-</sup> germinal center B-cells using a novel bispecific antibody designed to recruit SHP1 to the BCR. These findings establish a previously unrecognized role for PKC-delta and CD25 in orchestrating inhibitory phosphatase assembly to suppress autoimmune and malignant transformation.

**Keywords:** CD25, IL2RA





**S11-1 Intercellular Communication in Diseases**

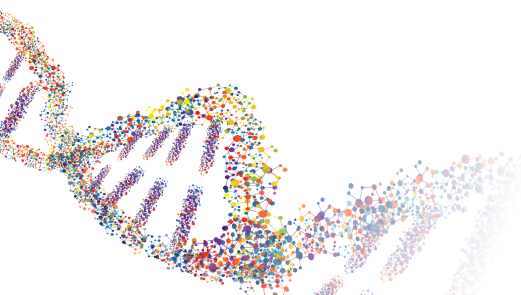
# Stroma-induced Senescence at the Invasive Front Drives Spatial Evolution of Invasive Programs in Colorectal Cancer

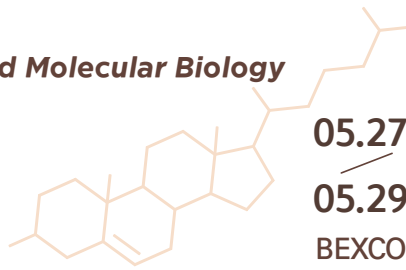
Soon Sang PARK, Hyung Rae LEE, Young Kyoung LEE, Young Won CHOI,  
Jang Hee KIM, Tae Jun PARK

*Ajou University School of Medicine*

Cellular senescence is a durable cell-cycle arrest state triggered by multiple forms of stress, yet the major determinants of senescence in advanced cancers are still not well defined. Through integrated IHC analysis and spatial transcriptomic profiling, we observed that senescent tumor cells are preferentially localized at the invasive front, where CD44 is reduced and p16INK4A is increased, with a strong inverse relationship consistently seen across multi-omics datasets. These findings support a model in which peri-tumoral stromal cells at the invasive margin induce a senescence program in neighboring cancer cells, in line with stromal cell-induced senescence observed in vivo. Extending our previous framework of spatial tumor evolution in colorectal cancer, we further propose that senescence at the invasive front is linked to a late-evolved, invasion-competent tumor-cell state characterized by LAMC2-MMP7 activation, consistent with tumor budding and a partial EMT-like phenotype at the leading edge. Because tumor cell senescence has been reported to be at least partly reversible, we additionally hypothesize that cancer cells may use a senescence-like state as an adaptive phenotype during dissemination, and subsequently exit this state in response to organ-specific cues to support metastatic outgrowth. To test this model, we will integrate multi-omics analyses with mouse models and patient-derived datasets to identify the stressors and microenvironmental signals that drive senescence at the invasive front, and to determine the functional role of senescent tumor cells in metastasis and reactivation.

**Keywords:** Senescent tumor cell, Colorectal cancer, CD44, Tumor invasion

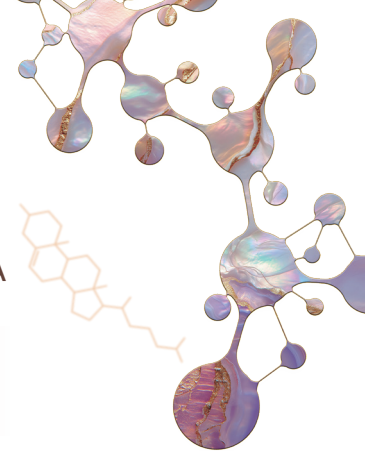




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BEXCO, BUSAN, KOREA



FROM MOLECULES TO MEGABYTES:  
AI AND BIG DATA TRANSFORMING LIFE SCIENCE

**S11-2 Intercellular Communication in Diseases**

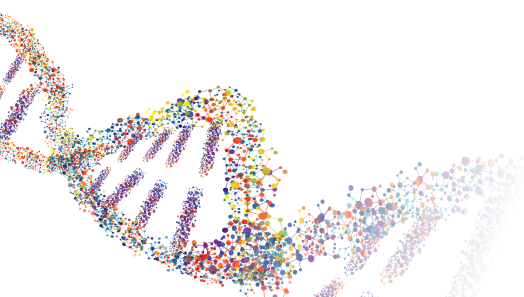
# How to solve a paradox of PD-L1 blockade: protecting muscle without losing tumor control

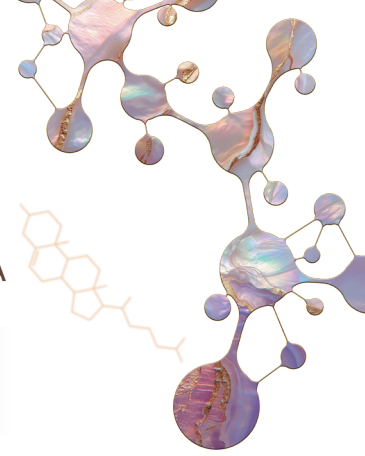
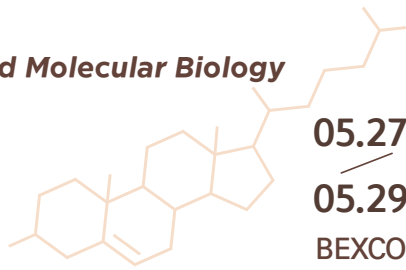
Na-Young SONG

*Yonsei University College of Dentistry*

Immune checkpoint inhibitors (ICIs) have revolutionized cancer therapy; however, their use is frequently associated with immune-related adverse events (irAEs). In this study, anti-PD-L1 therapy exacerbates muscle wasting in tumor-bearing male mice despite its anti-tumor efficacy, accompanied by an accumulation of CD8<sup>+</sup> T cells in muscle. Single-cell RNA sequencing identifies these cells as tissue-resident memory-like CD49a<sup>+</sup> CD8<sup>+</sup> T cells. While CD8<sup>+</sup> T cell depletion prevents muscle wasting, it compromises the anti-tumor efficacy of anti-PD-L1. To resolve this paradox, we identify cathepsin L (CTSL) as a dual-target capable of suppressing both tumor progression and CD8<sup>+</sup> T cell-mediated muscle wasting, through integrative transcriptomic analysis. Pharmacological inhibition of CTSL not only mitigates anti-PD-L1-induced muscle wasting but also further suppresses tumor growth, potentially via downregulation of BNIP3. Here, we show that CTSL is a dual-action target to uncouple anti-tumor efficacy from muscle-specific irAEs, offering a strategy to improve clinical outcomes of ICIs.

**Keywords:** Cancer Cachexia, Immune Checkpoint Inhibitors, Cytotoxic T Cells, Muscle Wasting, Cathepsin L





**S11-3 Intercellular Communication in Diseases**

# Hepatokine ORM2 Function in Metabolic Health and Disease

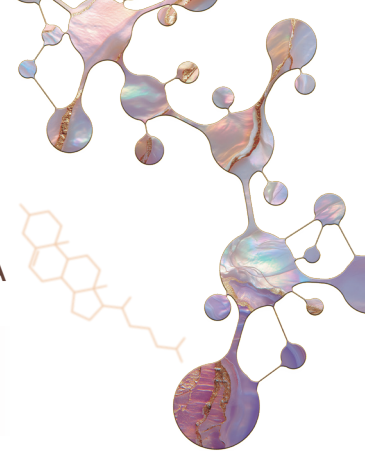
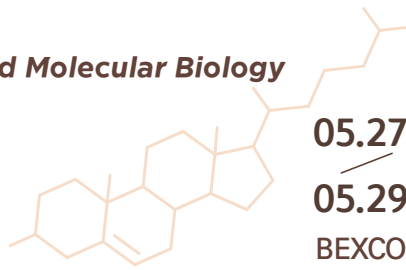
Kang Ho KIM

*The University of Texas Health Science Center at Houston*

Bile acids (BAs) are pleiotropic regulators of metabolism. Elevated levels of hepatic and circulating BAs improve energy metabolism in peripheral organs, but the precise mechanisms underlying the metabolic benefits and harm still need to be fully understood. In the current study, we identified orosomuroid 2 (ORM2) as a liver-secreted hormone (i.e., hepatokine) induced by BAs, which exerts protective metabolic functions. Under high BA stress, *Orm2* transcription can be regulated by two xenobiotic nuclear receptors, CAR and PXR. We further investigated its role in BA-induced metabolic improvements in mouse models of diet-induced obesity. When challenged with a high-fat diet (HFD) with cholic acid supplementation, *Orm2*-KO eliminated the anti-obesity effect of BAs, indicating that ORM2 governs BA-induced metabolic improvements. Hepatic ORM2 overexpression partially replicated BA effects by enhancing insulin sensitivity. Mechanistically, ORM2 suppressed interferon- $\gamma$ /STAT1 activities in inguinal white adipose tissue depots, forming the basis for anti-inflammatory effects of BAs and improving glucose homeostasis. In addition, we identified that ORM2 acts on hepatocytes to attenuate hepatic inflammation and liver injury in animal models of metabolic dysfunction-associated steatohepatitis (MASH). We will further discuss the underlying mechanisms of ORM2 functions in liver diseases. In conclusion, this talk provides new insights into the molecular mechanisms of BA-induced intercellular and interorgan crosstalk through ORM2 induction.

**Keywords:** Hepatokine, Orosomuroid, Obesity, Metabolic Dysfunction-Associated Steatohepatitis (MASH), Inflammation





**S11-4 Intercellular Communication in Diseases**

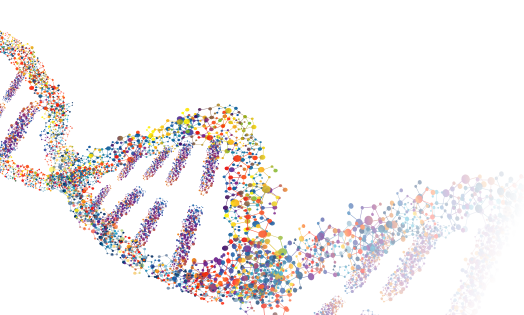
## Intercellular crosstalk in MASH-driven liver fibrosis

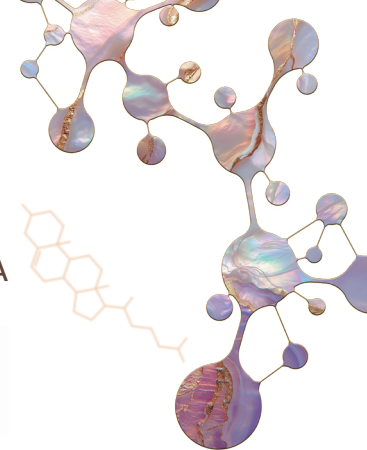
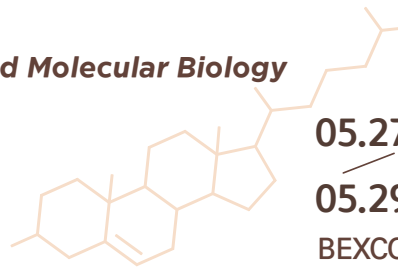
KyeongJin KIM

*Inha University*

Metabolic dysfunction-associated steatohepatitis (MASH) is a leading cause of chronic liver disease. Available therapies show inconsistent results on fibrosis, likely due to heterogeneity in disease trajectory or incomplete understanding of molecular determinants. Here, we identified increased *KCTD17* (potassium channel tetramerization domain-containing protein 17) levels in patients with MASH, and MASH diet-induced rodents, that showed an inverse correlation with expression of serine protease inhibitor a3k (*SERPINA3* or *Serpina3k* in mice). *KCTD17* depletion increased *SERPINA3* and reduced liver fibrosis in mice by inhibiting Par2 (protease-activated receptor 2)/TGF (transforming growth factor beta)-mediated activation of hepatic stellate cells (HSCs). Mechanistically, *Kctd17* regulates *Serpina3k* expression by facilitating ubiquitin-mediated degradation of *Zbtb7b* (zinc finger and BTB domain-containing protein 7b), which in turn diminishes *Serpina3k* secretion. As such, pharmacological inhibition of *Kctd17* effectively reverses MASH-induced liver fibrosis. In summary, these findings underscore the therapeutic potential of targeting *KCTD17* for the treatment of MASH-induced liver fibrosis and reveal a previously unrecognized *KCTD17*-*SERPINA3* axis in disease progression. Beyond liver fibrosis, we further discuss the emerging role of *SERPINA3* as a hepatokine regulated by obesity, which contributes to glucose homeostasis and may participate in adipose tissue remodeling during obesity.

**Keywords:** MASH; Liver fibrosis; Hepatokine





**S12-1 Computational Precision Medicine**

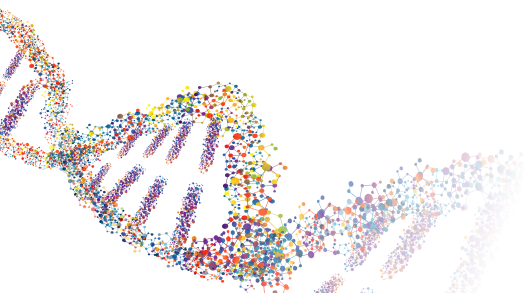
# Recurrent intra-tumour heterogeneity is a hallmark of metastatic prostate cancer

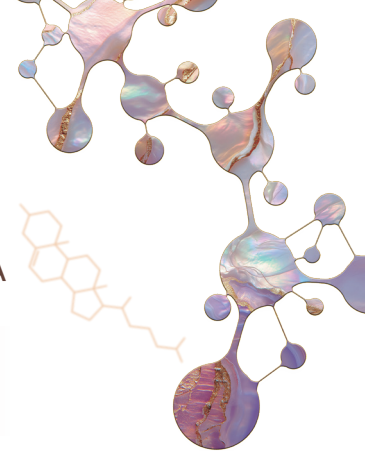
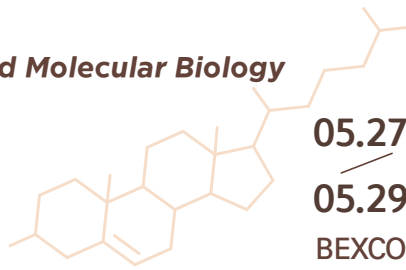
Anna S TRIGOS

*Peter MacCallum Cancer Centre, The University of Melbourne, Monash University,  
St Vincent's Institute of Medical Research*

The evolution from low grade to metastatic tumour is a major determinant of cancer mortality. Cancer evolution involves a complex interplay between intrinsic genetics and transcriptional alterations and the microenvironment. To define mechanisms underpinning metastatic development, we focused on metastatic castration-resistant prostate cancer (mCRPC) and employed single-cell multi-omics and whole-genome sequencing to deeply profile 34 metastatic lesions from 9 patients by rapid autopsy. We found that intra-tumour heterogeneity is an indicator of key evolutionary processes, characterised by recurrent tumour populations acting as critical functional components of the tumour ecosystem, irrespective of clonal and microenvironmental backgrounds. Unexpectedly, microenvironments only played a limited role while clonal evolution primarily promoted transcriptional noise. Intra-patient functional convergence of tumour ecosystems was observed across metastases, showing system-level selection pressures that drive the heterogeneity landscape of mCRPC. Our findings reveal functional evolutionary convergence of metastatic disease into units of intra-tumour heterogeneity, identifying critical determinants for therapeutic targeting.

**Keywords:** Cancer, evolution, single-cell, metastasis, microenvironment





**S12-2 Computational Precision Medicine**

# Pathway-Centric AI for Interpretable and Integrative Omics Analysis

Sangsoo LIM

*Dongguk University*

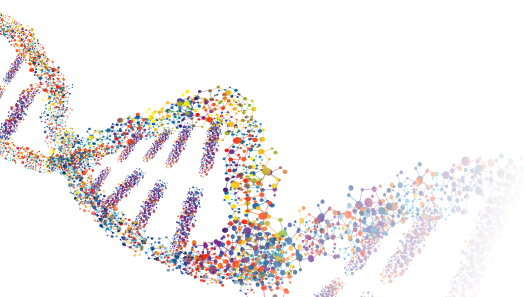
Advances in bulk RNA sequencing, single-cell transcriptomics, and spatial transcriptomics have transformed our ability to investigate cellular states and tissue architecture. Yet, the analytical challenge remains substantial: gene-level features are high dimensional, noisy, and often difficult to interpret mechanistically. From a bioinformatics perspective, a key question is how to structure AI models so that they remain predictive while aligning with established biological knowledge.

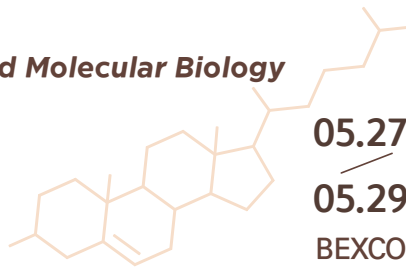
In this talk, I will present a pathway-centric AI framework in which curated signaling and metabolic pathways serve as the central representation layer for omics data analysis. Rather than operating directly on thousands of genes, transcriptomic profiles are encoded into pathway-level embeddings that capture coordinated molecular programs. This structured representation provides a biologically meaningful space for integrating heterogeneous data.

First, I will show how pathway embeddings enable bulk-to-single-cell co-embedding, allowing drug response knowledge learned from large bulk datasets to be transferred to single-cell data under substantial domain shift. Second, I will introduce a differential substructure-pathway attention model that links chemical substructures with cellular pathway states, improving drug response prediction while offering mechanistic interpretation. Third, I will describe a pathway-augmented contrastive learning framework for spatial transcriptomics that integrates gene expression and histopathology to identify spatial domains and region-specific signaling activities.

Together, these studies demonstrate that positioning pathways at the center of AI architectures provides a robust and interpretable foundation for multi-scale omics analysis.

**Keywords:** Pathway-based modeling; Spatial transcriptomics; Drug response prediction; Bulk-to-single-cell transfer; Biology-informed AI

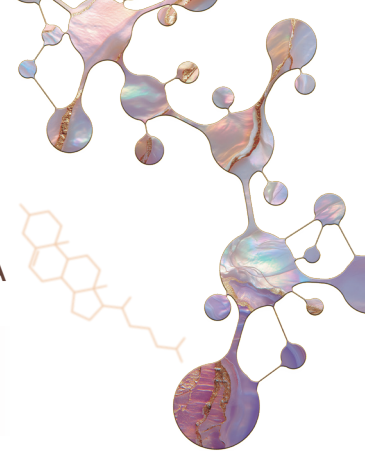




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BEXCO, BUSAN, KOREA



FROM MOLECULES TO MEGABYTES:  
AI AND BIG DATA TRANSFORMING LIFE SCIENCE

**S12-3 Computational Precision Medicine**

# Resolving disease mechanisms through rare mutation discovery: complex disease genetics and somatic mosaicism

Yoo-Jin Jiny HA

*Department of Life Science, Hanyang Univeristy*

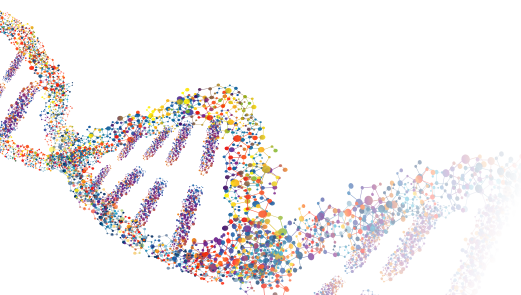
Disease mechanisms are often encoded in mutations that are difficult to detect or interpret, either because the genetic architecture is complex or because causal variants exist as ultra-rare somatic mosaicism. We addressed both challenges using complementary study designs and sequencing technologies.

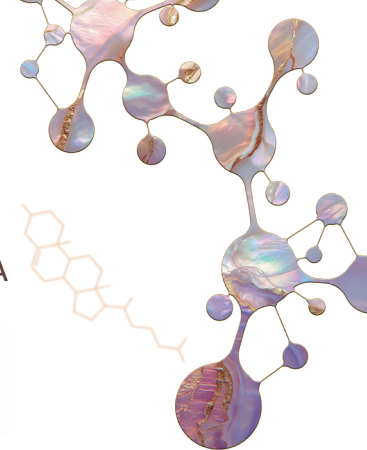
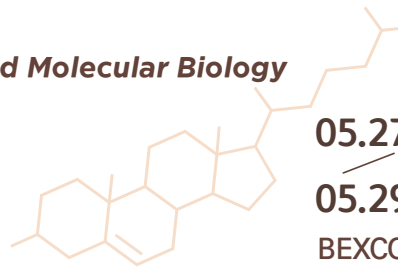
To study a complex developmental disorder, meningomyelocele (spina bifida), we analyzed 851 affected trios and 732 control trios and found likely gene-disruptive or damaging missense de novo mutations in ~22% of cases, with ~28% of these variants estimated to contribute to disease risk. Network propagation projected dispersed rare variants onto the interactome and revealed previously unrecognized disease-relevant functional modules, supported by functional perturbation assays consistent with defective neural tube closure.

In parallel, we developed a roadmap for genome-wide detection of ultra-rare mosaic mutations. Using the COLO829BLT50 cell-line mixture, we benchmarked Illumina short-read whole-genome sequencing for VAF <2% and found that accuracy is strongly shaped by genomic context, with difficult-to-map regions contributing disproportionately to errors and motivating depth-aware, region-stratified best practices. We then evaluated mosaicism directly in primary human tissues using ultra-deep (~200×), depth-matched Illumina, PacBio, and Nanopore whole-genome sequencing and found that callsets remain highly method dependent, reflecting algorithm-specific strengths and distinct artifact signatures that intensify in low-mappability sequence. Long-read haplotype-aware analysis and phasing provided orthogonal validation and extended discovery into repetitive and structurally complex regions.

Together, these studies show how integrating rare-variant genetics, network-based interpretation, and multi-platform genomics can uncover disease-relevant mechanisms from mutations that are otherwise hard to measure.

**Keywords:** Somatic mosaicism, De novo mutation, Complex disease genetics, Network propagation, Multi-platform whole genome sequencing





**S12-4 Computational Precision Medicine**

# Computational Multi-Omics Dissection of Environment and Metabolism-Driven Immune Reprogramming

Dae Yeol YANG, Song-I YANG, Seok June HONG, Seheum PARK,  
Soo-Jong HONG, Sung Eun KIM, Kwoneel KIM

*Kyung Hee University*

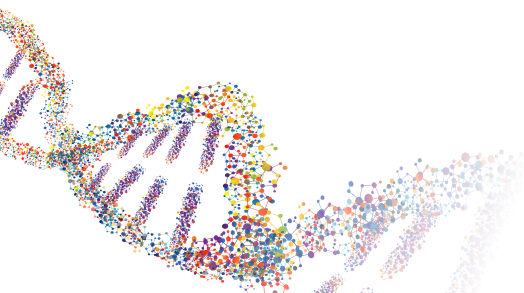
Computational precision medicine enables the integration of multi-layered omics data to uncover context-specific immune regulatory programs across developmental and disease states. Here, we applied integrative epidemiologic, epigenomic, transcriptomic, spatial, and single-cell analyses to define immune-modulatory axes operating in atopic dermatitis (AD) and colorectal cancer (CRC).

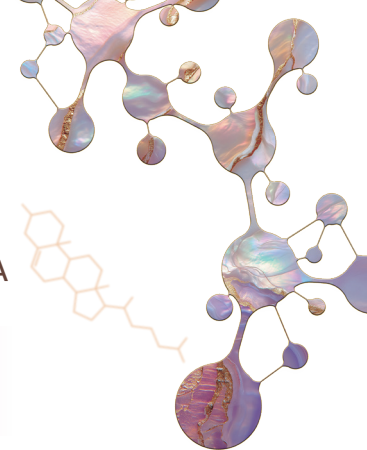
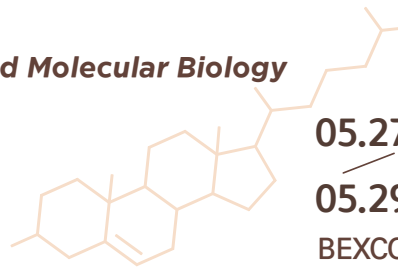
In a population-based birth cohort of 986 children, first-trimester PM2.5 exposure was associated with increased AD risk at age three. Multiomics profiling of placentae identified PM2.5-associated hypomethylation and overexpression of FCER1G in fetal macrophages. Cross-tissue single-cell analyses spanning placental, fetal, and adult skin datasets revealed enrichment of FCER1G-high macrophages and reactivation of a shared M2-like program. Network modeling and functional assays delineated an FCER1G-centered axis linked to NADPH oxidase signaling and Th2-associated inflammatory circuits.

In CRC, integrative multiomics of 258 tumors defined an SLC39-enriched subtype characterized by zinc influx and immune exclusion. Mechanistically, SLC39-mediated zinc signaling activated CDX2-dependent transcription of CD24 in malignant epithelial cells. Single-cell and spatial analyses identified CD24 interactions with SIGLEC10-positive myeloid cells, establishing localized immune-suppressive niches. A seven-gene SLC39-CDX2-CD24-SIGLEC10 signature predicted response to immune checkpoint blockade across independent cohorts.

Together, these findings demonstrate how computational integration of multiomics data resolves environmentally and metabolically driven immune programs, advancing precision strategies for immune-mediated and oncologic diseases.

**Keywords:** Multiomics integration, Single-cell and spatial transcriptomics, Macrophage reprogramming, Environmental and metabolic signaling, Tumor-immune crosstalk





**S13-1 Stem Cell II: Regenerative Medicine & Organoid Technology**

# Spatial organization and pathological remodeling of epidermal stem cells: principles from tail skin to human biology

Aiko SADA

*Medical Institute of Bioregulation, Kyushu University*

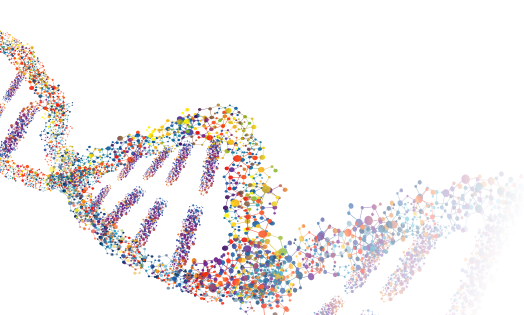
Spatial compartmentalization of heterogeneous cell populations is a fundamental principle in epithelial tissues. Using mouse tail skin as a model of spatially patterned epithelium, we identified slow-cycling (Dlx1) and fast-cycling (Slc1a3) epidermal stem cell populations that exhibit regionally biased localization and lineage contribution.

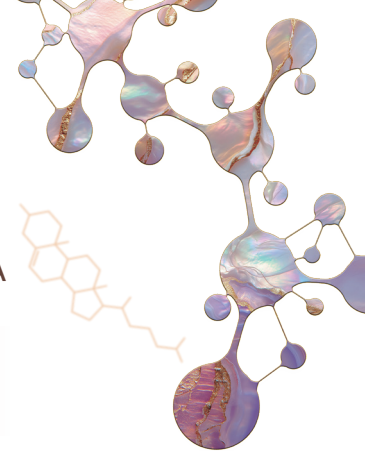
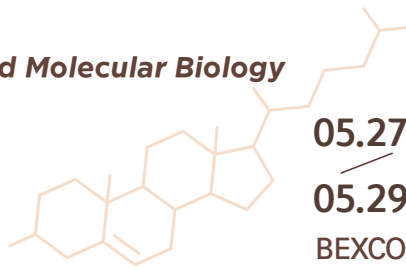
Chronic aging and acute inflammation remodel this stem cell compartment in different ways. Aging progressively depletes fast-cycling clones while maintaining slow-cycling populations, resulting in a long-term shift in population balance. In contrast, acute inflammatory stress induces rapid and largely reversible reorganization. Mechanistically, IL-1 signaling suppresses canonical Wnt signaling in fast-cycling stem cells, contributing to their lineage alteration toward a slow-cycling state and the reorganization of stem cell compartments. These results suggest that inflammatory signals modulate homeostatic signaling inputs, altering the stem cell population balance under inflammatory stress.

Importantly, analogous spatial organization extends beyond the tail skin. In human skin and oral mucosa, the undulating epidermal-dermal junction creates topographical niches associated with epithelial heterogeneity. Using micropatterned scaffolds in a 3D human skin model, we observed partial induction of spatial bias in epidermal proliferation and YAP activation.

Together, our findings suggest that epidermal stem cell heterogeneity is shaped by coordinated biochemical and mechanical cues. Disruption of this regulatory framework may contribute to pathological tissue remodeling in epithelial tissues.

**Keywords:** Epidermal stem cells, Stem cell heterogeneity, Aging, Inflammation, 3D culture





**S13-2 Stem Cell II: Regenerative Medicine & Organoid Technology**

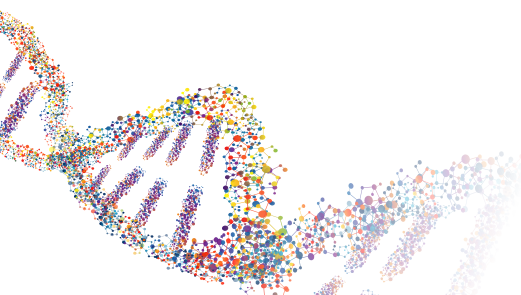
# Stem cell plasticity and niche remodeling in tissue regeneration and early tumor development

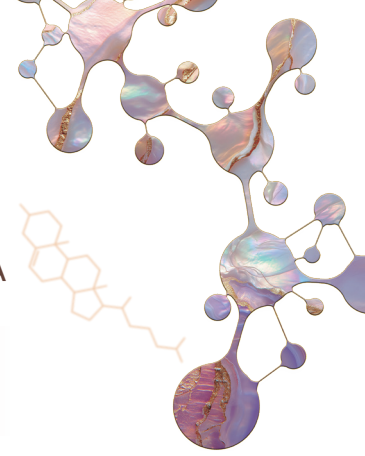
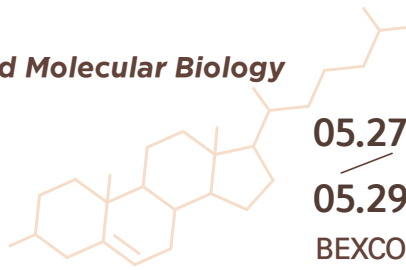
Jinwook CHOI<sup>1\*</sup>

<sup>1</sup>Department of Life Sciences, Gwangju Institute of Science and Technology, Gwangju 61005, Korea

Pathologic transformation represents a pivotal yet poorly defined window during which early alterations in epithelial stem cells remodel their surrounding niche to prime tumour initiation. Here, we integrate single-cell, spatial, and functional analyses to map the dynamics of this early multicellular reorganisation. We show that KrasG12D-mutant alveolar type II cells undergo an early reprogramming transition that transforms them into signalling hubs, with the Amphiregulin (Areg)-EGFR axis emerging as a central driver of cross-compartmental cooperation. Mutant epithelial cells secrete Areg to activate EGFR in adjacent fibroblasts, eliciting a regenerative-like fibrotic programme. These reprogrammed fibroblasts, in turn, reshape the immune landscape by expanding and reprogramming alveolar macrophages, amplifying inflammatory signalling, immune recruitment, and epithelial plasticity. Together, these interactions establish a self-reinforcing multicellular circuit that generates and maintains a tumour permissive niche. Disrupting that circuit through genetic and pharmacological perturbation of the Areg-EGFR axis prevents both early niche cell reprogramming and tumour formation. Findings from KRASG12D-inducible human alveolar organoids and early-stage lung adenocarcinoma tissues confirm conservation of these interactions, identifying early mutant epithelial-stromal crosstalk as a targetable step in pathologic transformation with potential to avert establishment of treatment-resistant disease.

**Keywords:** Lung Regeneration, Stem cell plasticity, Early tumor development





**S13-3 Stem Cell II: Regenerative Medicine & Organoid Technology**

## Epithelial stem cell-derived IGFBP2 supports a pre-injury regenerative state

Dong-oh KIM<sup>1</sup>, Yun Ha HUR<sup>1\*</sup>

<sup>1</sup>Department of Life Sciences, POSTECH, Pohang 37666, Korea

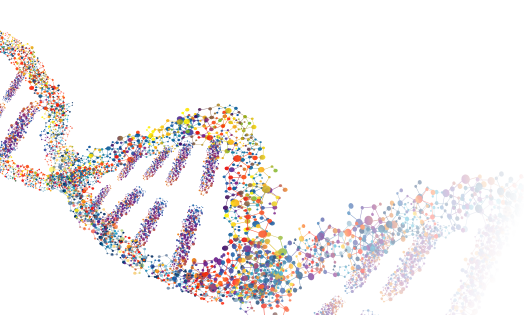
Epithelial stem cells are essential for wound repair. Traditionally, their role has been viewed primarily as responders that proliferate and migrate to restore epithelial integrity after injury. However, emerging evidence suggests that epithelial stem cells can also function as signaling hubs that coordinate repair by influencing neighboring cells within the microenvironment.

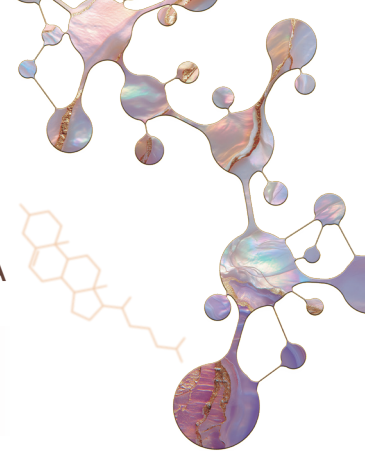
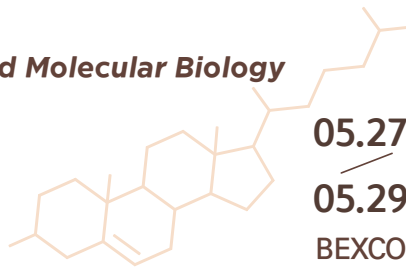
Adult skin heals slowly with scarring, whereas oral tissues such as the hard palate regenerate rapidly with minimal fibrosis. Expression analysis of candidate gene sets revealed that palate epithelium exhibits a pre-injury primed state characterized by elevated regenerative gene expression. Notably, IGFBP2 was highly enriched in basal epithelial stem cells of the palate and rapidly decreased following injury, while showing minimal expression in skin.

To model this oral primed state, IGFBP2 was injected intradermally into skin prior to wounding, which accelerated re-epithelialization. In vitro, keratinocytes and fibroblasts were pre-exposed to IGFBP2 and then subjected to IGFBP2 withdrawal. Under these conditions, keratinocytes exhibited increased proliferation, whereas fibroblasts showed shifts in collagen-associated gene expression.

Together, these findings support a model in which epithelial stem cell-derived IGFBP2 maintains a pre-injury regenerative state and modulates repair responses, highlighting epithelial stem cells as organizers of tissue-specific wound healing.

**Keywords:** Regeneration, Epithelial stem cell, Wound healing





**S13-4 Stem Cell II: Regenerative Medicine & Organoid Technology**

# Gasdermin D pore formation promotes airway epithelial repair through epigenetic regulation of reparative genes in alveolar macrophages

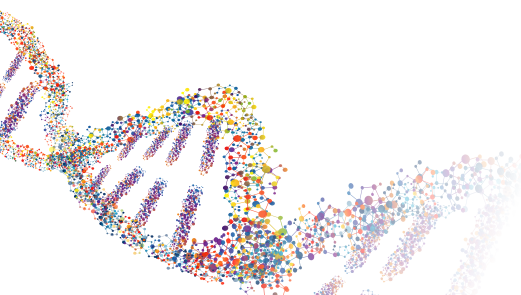
Bokeum CHOI<sup>1,2</sup>, Byeong Jun CHAE<sup>1,2</sup>, In-hwa HWANG<sup>1,2</sup>, Je-Wook YU<sup>1,2\*</sup>

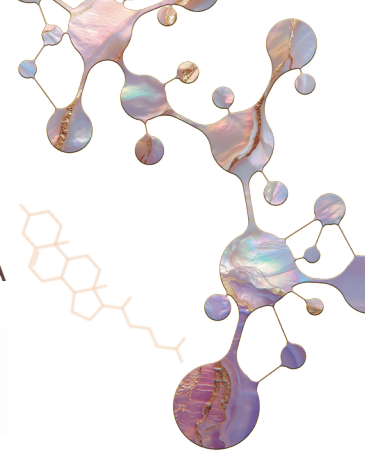
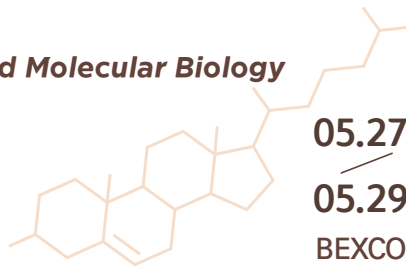
<sup>1</sup>Department of Microbiology and Immunology, Institute for Immunology and Immunological Diseases, Yonsei University College of Medicine, Seoul 03722, Korea

<sup>2</sup>Department of Microbiology and Immunology, Graduate School of Medical Science, Brain Korea 21 Project, Yonsei University College of Medicine, Seoul 03722, Korea

As a barrier organ, the lung epithelium is frequently subjected to tissue-damaging injury, creating a DAMP-rich environment. Failure to properly repair damaged tissue can lead to various pulmonary pathologies. Gasdermin D (GSDMD) is an inflammasome-activated protein that forms transmembrane pores to trigger pyroptosis and IL-1 $\beta$  secretion. While macrophages play essential role in tissue repair, how GSDMD activation within DAMP-activated macrophages orchestrate regenerative process remains poorly understood. Using a naphthalene-induced club cell depletion model, we show that GSDMD-deficient mice exhibit impaired epithelial repair accompanied by reduced club cell proliferation. Notably, IL-1 $\beta$  signaling was dispensable for epithelial repair. Instead, adoptive transfer and myeloid-specific deletion showed that GSDMD in alveolar macrophages (AMs) is essential for inducing regenerative genes, such as *Wnt7a*, following injury. scRNA-seq analysis revealed that Polycomb Repressive Complex 2 (PRC2) component was significantly downregulated in GSDMD-deficient AMs. Consistently, damaged lung tissue accumulated H3 lysine 27 tri-methylation (H3K27me3) marks, whereas these marks were lost in the absence of GSDMD. Mechanistically, we found that GSDMD pore formation enhanced PRC2-mediated H3K27me3 deposition, indirectly promoting *Wnt7a* expression. Together, these findings newly identify a non-canonical role of GSDMD pores as upstream activators of epigenetic regulator, thereby enabling the induction of reparative genes during airway regeneration.

**Keywords:** Tissue repair, Gasdermin D, Macrophage





**S13-5 Stem Cell II: Regenerative Medicine & Organoid Technology**

# Sustained Release of Retinoic Acid via Porous Silicon Microparticle for Enhanced Microenvironmental Regulation of Motor Neuron Differentiation derived from Human Induced Pluripotent Stem Cells (hiPSCs)

Juyoung SEONG<sup>1#</sup>, Changho CHUN<sup>1,2#</sup>, Alec SMITH<sup>2</sup>, David MACK<sup>2\*</sup>, Jinmyoung JOO<sup>1\*</sup>

<sup>1</sup>Biomedical Engineering, Ulsan National Institute of Science and Technology (UNIST), Ulsan 44919, Korea

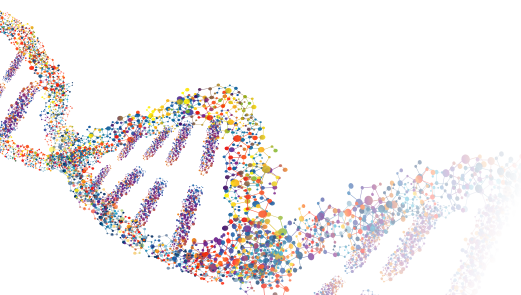
<sup>2</sup>Neurobiology & Biophysics, University of Washington, Seattle 98109, USA

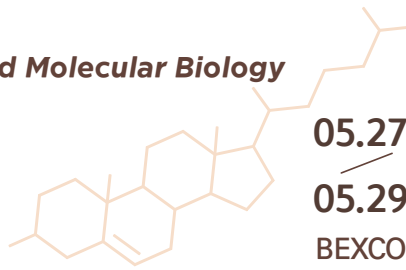
The generation of functional motor neurons (MNs) from human induced pluripotent stem cells (hiPSCs) represents a crucial approach for both modeling neurodegenerative diseases and developing regenerative therapies. Nevertheless, traditional morphogen delivery methods frequently fail to achieve the functional maturity observed *in vivo*, primarily because they do not replicate the sustained signaling gradients.<sup>1</sup> To overcome this limitation, we present a platform designed for sustained retinoic acid (RA) supplementation, using porous silicon microparticles to create a biomimetic gap for hiPSC-derived MN differentiation. Sustained RA supplementation demonstrably increased the expression of MN markers (HB9, ISL1) at the transcriptional level. Furthermore, electrophysiological analysis indicated substantial functional maturation, as evidenced by enhanced neural networks and more frequent repetitive firing patterns. Comparative transcriptomic analysis revealed that MNs derived via sustained RA supplementation exhibit a closer resemblance to human embryonic MNs compared to traditional models, especially concerning pathways associated with synapse formation, RA signaling, and acetylcholine metabolism. These observations suggest that the sustained RA supplementation successfully alters the neurogenic microenvironment via continuous release, thereby guiding high-fidelity MN differentiation. This approach presents a more effective method for promoting functional regeneration.

**Keywords:** Motor neuron differentiation, Human induced pluripotent stem cell (hiPSC), Sustained release of Retinoic acid

**References:**

1. Ho, R. et al. Nature neuroscience 19, 1256-1267 (2016)

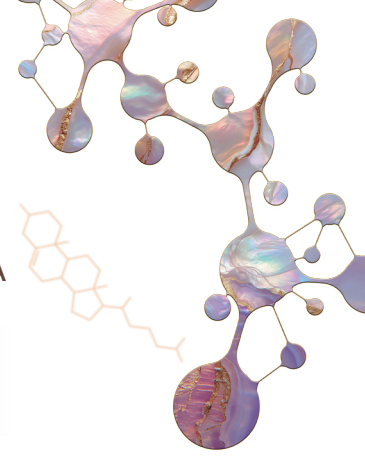




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FROM MOLECULES TO MEGABYTES:  
AI AND BIG DATA TRANSFORMING LIFE SCIENCE

**S14-1 Genome Engineering II: Therapeutic Application of Genome Engineering**

# In vivo mitochondrial base editing restores genotype and visual function in a mouse model of LHON

Hyunji LEE

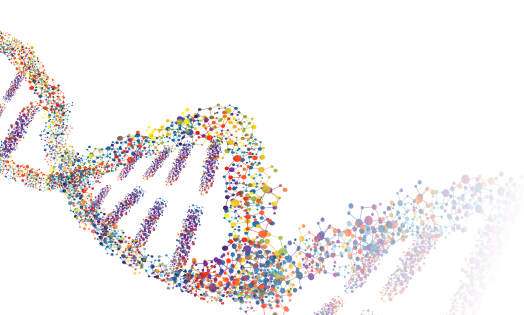
*Korea University College of Medicine, Korea*

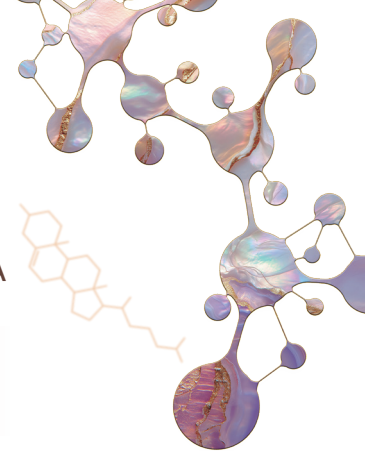
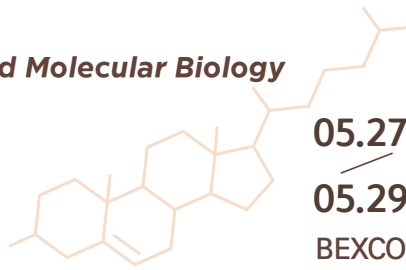
Leber hereditary optic neuropathy (LHON) is a maternally inherited mitochondrial disorder caused by point mutations in mitochondrial DNA (mtDNA), most commonly affecting the MT-ND4 gene. To date, no animal model carrying authentic LHON mutations has been available, limiting therapeutic development.

In attempting to generate such models using mitochondrial base editors, we found that activity-enhanced DddA11-based cytosine base editors (DdCBEs) induce off-target mtDNA mutations and cause developmental arrest in embryos. By contrast, using a high-fidelity DdCBE (HiFi-DdCBE), we successfully generated mice harboring the pathogenic MT-ND4 G11778A mutation, the most prevalent LHON variant. These mice exhibited hallmark phenotypes, including retinal ganglion cell loss and impaired visual function.

Finally, intravitreal delivery of an adeno-associated virus encoding TALE-linked deaminases (TALEDs) restored both genotype and phenotype in these mice, highlighting the potential of mitochondrial base editing as a therapeutic strategy for mtDNA-associated diseases.

**Keywords:** LHON, mitochondria, mitochondria disease, genome editing, TALED





**S14-2 Genome Engineering II: Therapeutic Application of Genome Engineering**

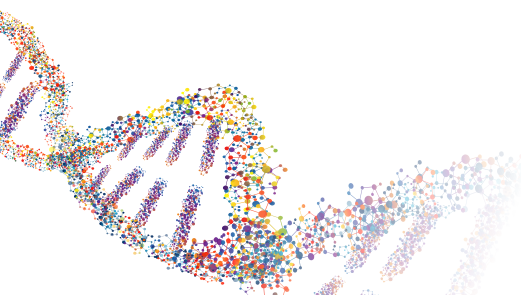
# Development of highly efficient delivery vehicles for CRISPR effectors for gene- and cell-therapy

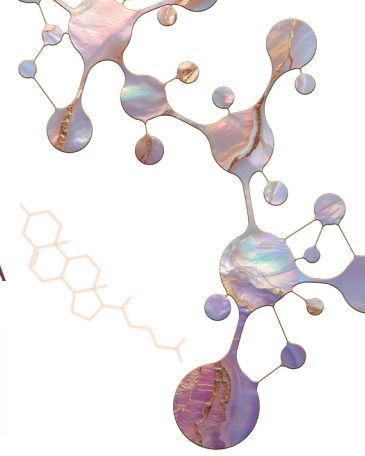
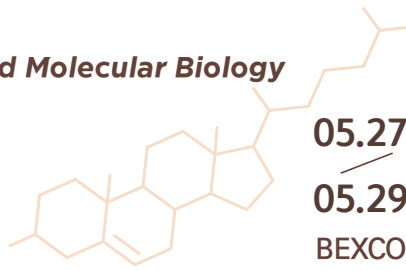
Dong-Jiunn Jeffery TRUONG

*Helmholtz Munich, Technical University of Munich*

Despite the recent development of advanced CRISPR gene-editing tools, such as base editors and prime editors, clinical applications are fundamentally limited by the lack of clinically applicable delivery systems that combine high-efficiency delivery with the transient activity of genome-editing enzymes. Approaches harnessing viral vectors such as adeno-associated virus (AAVs) enable robust gene transfer useful for gene therapies that deliver long-lasting functional copies of deficient genes but are less suited for the delivery of gene editors, where prolonged editor expression increases the risk of off-target and unintended bystander editing, as well as anti-editor immune responses. Thus, there is a need for a transient but highly efficient delivery modality for gene-editing ribonucleoprotein (RNP) complexes as a safe alternative. Recent advances in engineered virus-like particle (VLP) technologies have emerged to bridge this gap by enabling the packaging and transfer of genome editing proteins and guide RNAs as preassembled RNPs. Through systematic engineering of particle assembly, cargo recruitment, and membrane fusion mechanisms, we have developed a highly efficient and modular VLP platform, ENVLPE, that enables efficient delivery of diverse CRISPR effectors, including nucleases, base editors (BEs), and prime editors (PEs). We demonstrated that ENVLPE enabled highly efficient nuclease-, base-, and prime-editing across multiple cell types and showed PE-mediated gene correction in two mouse models of a genetically inherited retinal disease in vivo, indicating that cell-derived virus-like particles are a promising therapeutic delivery vehicle for CRISPR gene editors.

**Keywords:** Gene Therapy, Cell Therapy, Prime Editing, Base Editing, Gene Delivery





**S14-3 Genome Engineering II: Therapeutic Application of Genome Engineering**

## Strategic selection of AAV capsids for human liver gene therapy

Jaejun KIM

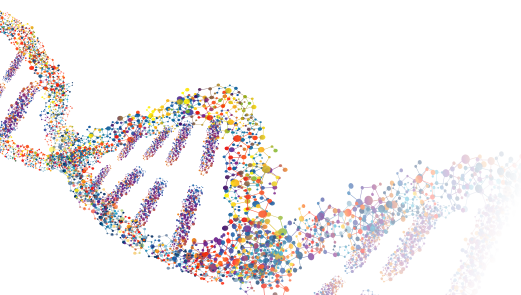
*School of Medicine, Sungkyunkwan University, Korea*

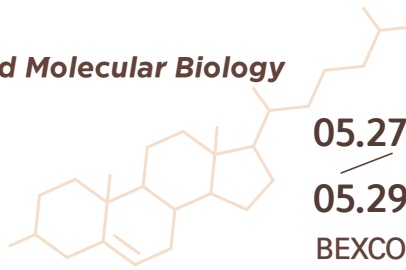
For the development of liver-directed AAV gene therapies, selecting AAV capsids that effectively transduce hepatocytes or other therapeutically relevant cell types in the human liver is essential. In our first study, we systematically evaluated AAV capsid performance at single-cell resolution in human livers maintained under near-clinical conditions using normothermic perfusion machine, including livers with alcohol-induced steatosis. This platform enabled direct assessment of capsid tropism in a disease-relevant human setting, revealing how fatty liver disease alters zonation, cellular susceptibility and episomal forms of AAV vectors. Importantly, we found substantial variability in capsid performance between normal and diseased human livers, highlighting the limitation of extrapolating from animal liver models. These findings provide a rational framework for capsid selection tailored to diseased human livers, beyond simple transduction efficiency.

In our second study, we screened a peptide-display AAV capsid library in mouse liver and identified AAV-BEC, a capsid that efficiently transduces biliary epithelial cells (BECs). To assess its translational potential, we evaluated AAV-BEC in a humanized BEC mouse model and further tested its therapeutic applicability in models of bile duct injury and cholangiocarcinoma. By combining AAV-BEC with CRISPR/Cas9-based genome editing and immune-modulatory strategies, we aim to develop a clinically viable gene therapy for biliary diseases.

Altogether, these studies lay the groundwork for precision AAV vector design, demonstrating that capsid selection must incorporate disease context and human-specific tropism to enable effective gene therapies for currently incurable liver diseases.

**Keywords:** Adeno-associated virus (AAV), AAV capsid selection, Normothermic machine perfusion, Fatty liver disease, Bile duct injury

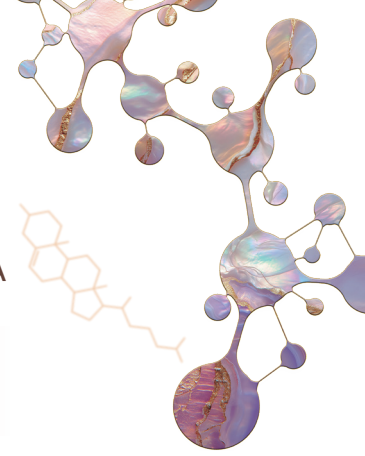




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FROM MOLECULES TO MEGABYTES:  
AI AND BIG DATA TRANSFORMING LIFE SCIENCE

**S14-4 Genome Engineering II: Therapeutic Application of Genome Engineering**

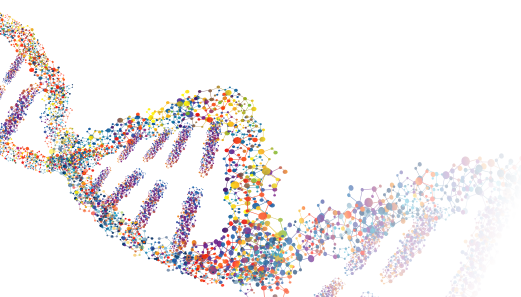
# Genome Engineering to Enhance the Therapeutic Potency of Immune and Stromal Cell Therapies

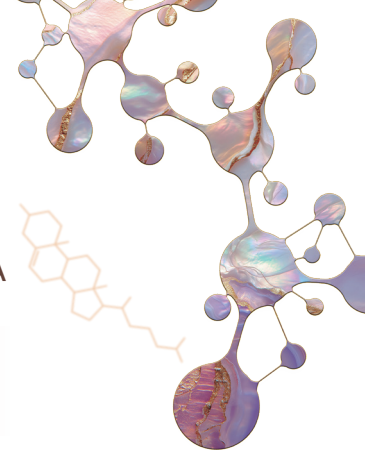
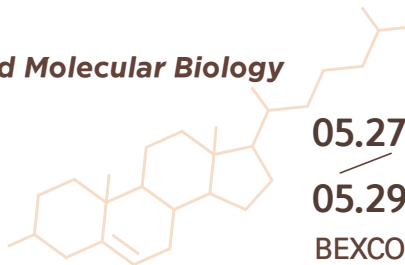
Jae young LEE

*Department of Health Science and Technology, Samsung Advanced Institute of Health Sciences and Technology (SAIHST), Sungkyunkwan University, Seoul  
Cell and Gene Therapy Institute (CGTI), Research Institute for Future Medicine, Samsung Medical Center, Seoul 06351, Republic of Korea.  
I 06351, Republic of Korea*

Genome engineering has emerged as a transformative tool for developing “next-generation” cell therapies capable of overcoming hostile microenvironments associated with solid tumors and ischemic diseases. This study demonstrates the versatile application of CRISPR/Cas9 technology to improve the therapeutic functionality of CAR-T cells, iPSC-derived CAR-NK cells, and mesenchymal stem cells (MSCs). To address the challenges of solid cancers, we utilized gene editing to modulate inhibitory signaling in CAR-T and iPSC-CAR-NK cells, thereby enhancing their persistence and cytotoxic activity within immunosuppressive environments. In parallel, we tackled the limitations of MSC therapy for chronic limb-threatening ischemia (CLTI), where reactive oxygen species (ROS) typically compromise cell survival and paracrine function. Collectively, our findings highlight that targeted genome editing—whether applied to enhance immune cell potency against solid cancers or to augment MSC resistance in oxidative ischemic environments to maximize the clinical potential of diverse cell-based regenerative and immunotherapeutic platforms.

**Keywords:** CRISPR/Cas9, Cell Therapy, Genome Engineering, Immune cells, MSCs





**S15-1 Beyond Protein Structure Prediction and Design**

# Structural Virology at Hokkaido University: Current Achievements and Future Perspectives of the Cryo-EM Facility

Shunsuke KITA, Hideo FUKUHARA, Katsumi MAENAKA

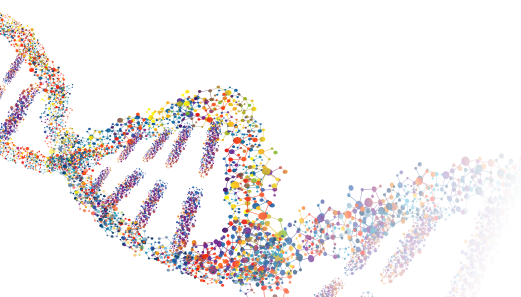
*Hokkaido University*

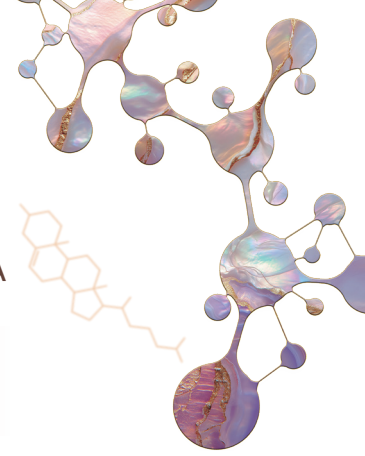
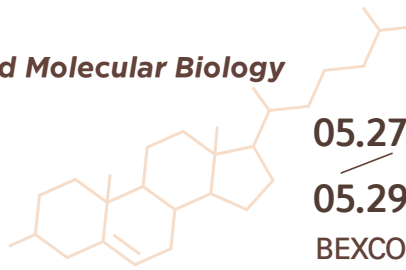
Hokkaido University installed a cryo-electron microscope in 2019 and has since advanced structural virology research, primarily through single-particle analysis. One of our representative achievements has been the structural analysis of the SARS-CoV-2 spike protein. We have determined not only the structure of the spike protein in complex with its host receptor, ACE2, but also numerous structures in complex with neutralizing antibodies and inhibitors. These studies have provided important structural insights that form a basis for antiviral drug discovery and therapeutic development.

In 2021, we further expanded our cryo-EM platform by introducing a cryo-electron microscope into a BSL-3 facility. Using this system, we were among the first to report direct observations of native virus particles under high-biosafety conditions. Building on these advances, we are now extending our research toward in situ structural biology of virus-infected cells through the use of cryo-FIB-SEM. This approach allows us to examine viral infection processes in a cellular context and to bridge structural information across multiple biological scales.

Through the integration of these cryo-electron microscopy-based methodologies, we aim to promote structural virology research from the molecular level of viral proteins to the levels of intact virus particles and infected cells. Ultimately, our goal is to contribute both to a deeper understanding of viral life processes and to the development of novel antiviral strategies.

**Keywords:** SARS-CoV-2, spike protein, neutralizing antibodies, cryo-EM,





**S15-2 Beyond Protein Structure Prediction and Design**

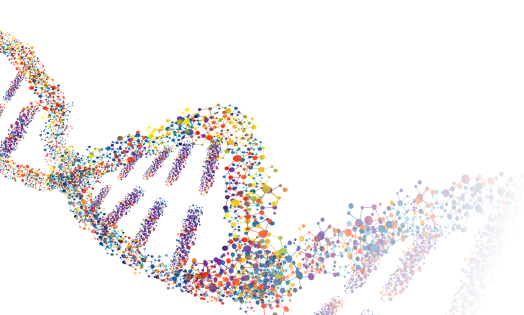
# Molecular anatomy of the N-recognin, Ubr1

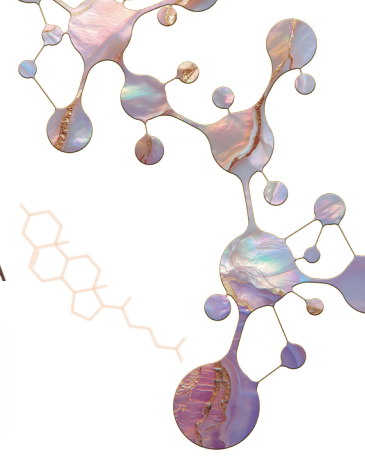
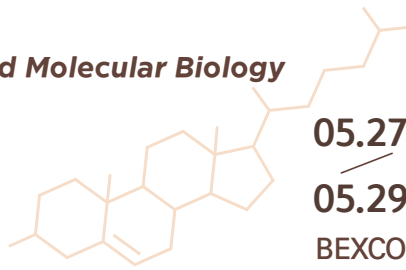
Hyun Kyu SONG

*Division of Life Sciences & National Research Laboratory for Convergence Degradation Biology, Korea University, Korea*

The N-degron pathway is a regulated proteolytic system that targets proteins bearing destabilizing N-terminal residues for ubiquitination and subsequent proteasomal degradation. In the Arg/N-degron pathway, N-terminal positively charged type-1 (Arg, Lys, and His) and bulky hydrophobic type-2 residues (Leu, Ile, Phe, Tyr, and Trp) are recognized by the E3 ligase Ubr1. It consists of multiple modular domains, including the UBR box, ClpS-homology, winged-helix, U2BR, RING, CHD, and UBLC. Recognition of type-1 N-degron substrates by Ubr1 has been elucidated by our previous crystal structures of the UBR box in complex with various N-degron peptides, as well as by the cryo-EM structure of full-length Ubr1 bound to a type-1 N-degron substrate. In contrast, the molecular basis for recognition of type-2 N-degron by ClpS-homology domain has remained unclear. To determine the cryo-EM structure of Ubr1 in complex with type-2 substrates, we employed native chemical ligation to assemble a quaternary complex consisting of Ubr1, Ub, Ubc2, and a type-2 N-degron substrate. In addition to N-terminal degrons, Ubr1 also recognizes internal degrons, such as those in Cup9, which has long been a longstanding enigma in the study of N-recognins. Notably, degradation of Cup9 is markedly enhanced by the addition of dipeptides (Arg-Ala and Leu-Ala). To elucidate the structural basis of this activation, we used native chemical ligation to generate a modified Cup9 internal degron and determined the structure of the Ubr1-Cup9-Ub-Ubc2 complex in the presence of dipeptides. These results provide the molecular basis for the versatile recognition modes of the first characterized E3 ligase Ubr1.

**Keywords:** Cryo-EM, E3 ligase, N-degron, Ubiquitin, Ubr1





**S15-3 Beyond Protein Structure Prediction and Design**

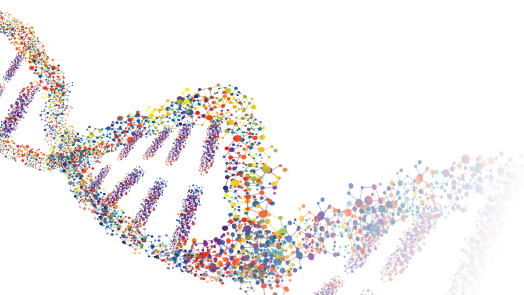
# De novo design of functional protein complexes using deep generative models

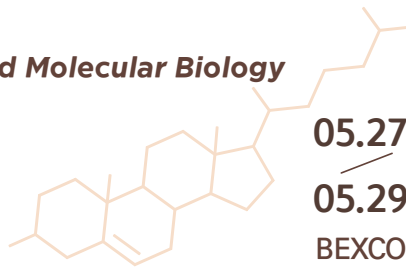
Sangmin LEE

*Pohang University of Science and Technology (POSTECH)*

Protein complexes such as protein oligomers, cages, bundle, and patterned layers are often found in nature or by design and involved in diverse biological functions including delivering genetic materials, activating immune systems, and causing diseases. Hence, there is considerable interest in designing artificial protein nanostructures capable of controlling such biological phenomena. For past decades, computational protein design approach has been focused on physics-based methods, for instance, calculating scoring functions defined by theoretical chemistry and physics, but recent development of AI-based approaches, such as folding prediction, sequence design and protein generative model, have dramatically expanded our capable range of protein structure design. In this talk, I will introduce an overview of computational design for de novo protein nanostructures using AI-based software and show several examples of designed nanostructures including virus-like nanocages. Experimentally, the designed proteins were expressed in *E. Coli.*, and the designed nanostructures were validated by electron microscope.

**Keywords:** Protein design, AI, nanocage, self-assembly

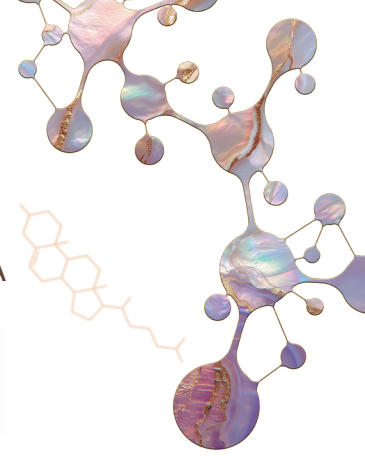




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FROM MOLECULES TO MEGABYTES:  
AI AND BIG DATA TRANSFORMING LIFE SCIENCE

**S15-4 Beyond Protein Structure Prediction and Design**

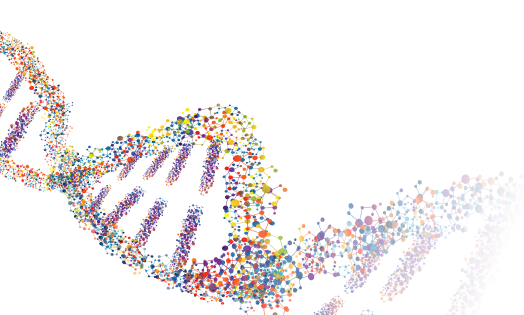
# Structural dissection of $\alpha\beta$ -tubulin heterodimer assembly and disassembly by human tubulin-specific chaperones

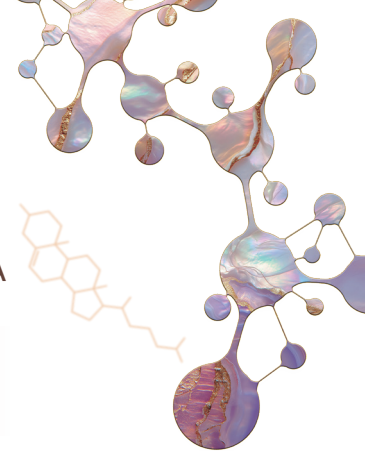
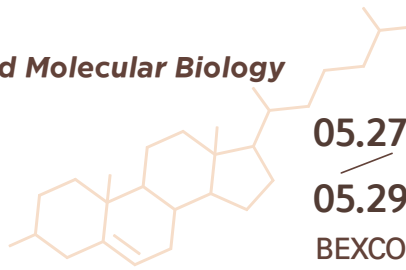
Yeonjae SEONG, Hyunmin KIM, Kyumi BYUN, Yeon-Woo PARK, Soung-Hun ROH

*School of Biological Sciences, Seoul National University, Seoul, Republic of Korea*  
*Institute of Molecular Biology and Genetics, Seoul National University, Seoul, Republic of Korea*

Microtubule assembly requires tubulin-binding cofactors (TBCs) that regulate  $\alpha\beta$ -tubulin heterodimer formation. Here, we used cryo-electron microscopy to visualize how human TBCs and the small GTPase Arl2 coordinate tubulin assembly and disassembly. We captured multiple conformational states, revealing how TBCs orchestrate tubulin heterodimer biogenesis through a series of regulated intermediates. Our analysis shows that TBCs stabilize tubulin subunits, guide their association, and couple GTPase activity to a quality control mechanism that ensures the formation of functional heterodimers. These findings establish a structural framework for tubulin biogenesis and recycling.

**Keywords:** Chaperone, Cryo-electron microscopy, protein homeostasis





**S16-1** Next-Generation Epigenome Regulation and Editing Technologies

# Epigenomic aberrations accumulated by environments at precancerous stages and gastric tumorigenesis

Atsushi KANEDA

*Department of Molecular Oncology, Graduate School of Medicine, Chiba University*

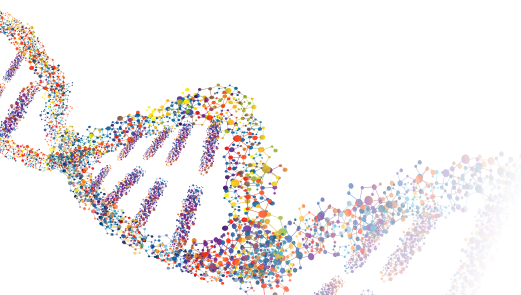
Cells alter epigenomic state during adapting various environments at precancerous stages; infection of *Helicobacter pylori* (HP) and Epstein-Barr virus (EBV), for example, causes epigenetic aberrations to develop gastric cancer (GC).

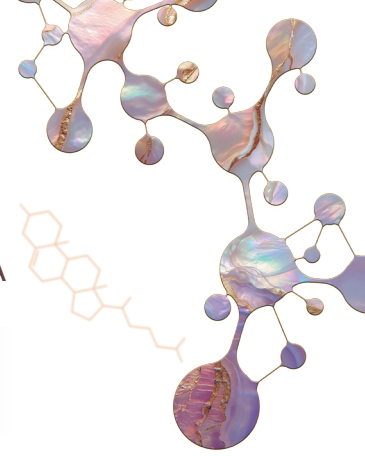
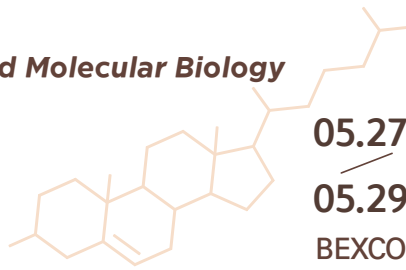
EBV is an epi-mutagen causing severe DNA methylation in >3,000 promoter CpG islands to inactivate tumor suppressor genes. In addition, integrated interactome and epigenome analyses by Hi-C, 4C-seq, and ChIP-seq revealed that episomal EBV DNA bound to heterochromatin of the host genome, and induced dynamic B-to-A compartment shift in EBV-interacting regions with aberrant activation of enhancers and near-by proto-oncogenes. This is because of cross-species interaction between viral and human chromatins inducing aberrant rewiring of H3K9me3(+) heterochromatin to H3K4me1(+)/H3K27ac(+) euchromatin, observed not only in gastric cancer, but also other EBV-related tumors including nasopharyngeal cancer and hematopoietic malignancies.

As for environments other than EBV, we analyzed two large prospective longitudinal cohorts of healthy people who underwent gastric endoscopy and mucosal biopsy. GC incidence during observation period significantly correlated with *H. pylori* status as well as age, drinking, smoking, and GC family history. Accumulation of DNA hypermethylation of gene promoter regions in biopsied gastric mucosa, observed several years before GC development, was predictive of higher GC risk and shorter duration to GC development. Pro-carcinogenic epigenetic aberrations initiated by *H. pylori* exposure are found to be amplified by unfavorable but modifiable lifestyle choices, e.g. heavy drinking and smoking.

These indicate critical roles of environmental factors in inducing epigenomic aberrations and gastric tumorigenesis.

**Keywords:** Gastric cancer, epigenome, Epstein-Barr virus, *Helicobacter pylori*, environmental factors





**S16-2** Next-Generation Epigenome Regulation and Editing Technologies

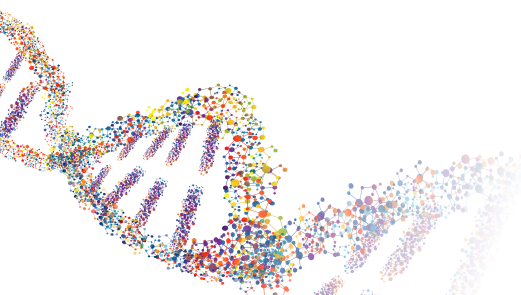
# Trans-histone crosstalk establishes distinct H3K79 methylation zones with differential transcriptional functions

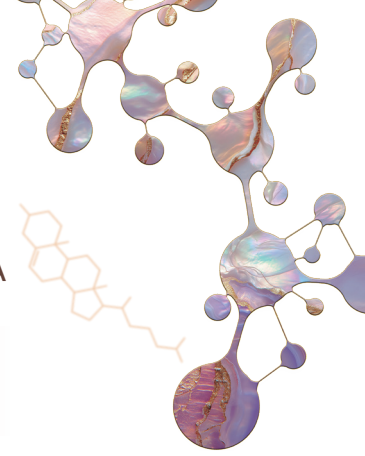
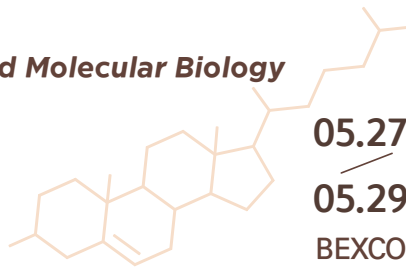
TaeSoo KIM

*Department of Life Sciences and Multitasking Macrophage Research Center,  
Ewha Womans University, Seoul 03760, Republic of Korea*

H3K79 methylation by Dot1 (disruptor of telomeric silencing-1) plays critical roles in multiple cellular processes potentially by modulating chromatin structure and gene expression. However, the genome-wide distribution patterns of H3K79me1, H3K79me2, and H3K79me3 and the mechanisms specifying these patterns remain unclear. Here, we mapped H3K79 methylation patterns across the yeast genome using ChIPseq and identified three distinct gene groups, termed state-specific methylation zones, each predominantly marked by one methylation state. These zones remain largely stable during transcriptional reprogramming. They may be established and/or maintained via H2B ubiquitination by the Rad6–Bre1 complex: loss of Rad6 leads to the complete loss of the H3K79me3 zone, converting it into an H3K79me1-enriched region while simultaneously diminishing the H3K79me1 zone. Loss of H4K16 acetylation also similarly disrupted the H3K79me1 zone, albeit weakly. Interestingly, Dot1 occupancy does not always correlate with the H3K79me3 level, as translation-related genes exhibit high Dot1 occupancy but are depleted of H3K79me3. Functionally, H3K79me3 and H3K79me1 appear to play differential roles in transcriptional regulation: Dot1-activated genes are enriched for H3K79me3, whereas a majority of Dot1-repressed genes are associated with H3K79me1. We therefore propose that H3K79 methylation states define specific chromatin zones that contribute to differential transcriptional outputs and whose establishment and maintenance depend on trans-histone crosstalk.

**Keywords:** Dot1, H3K79 methylation, H2B ubiquitination, H4K16 acetylation, transcription regulation





**S16-3** Next-Generation Epigenome Regulation and Editing Technologies

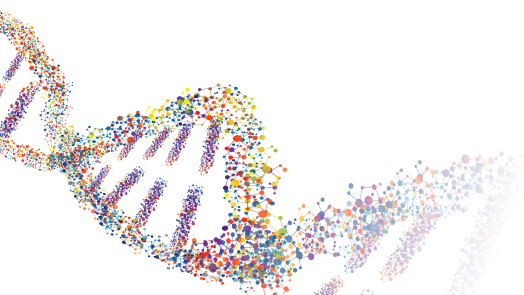
## 4D Nucleome in Health and Diseases

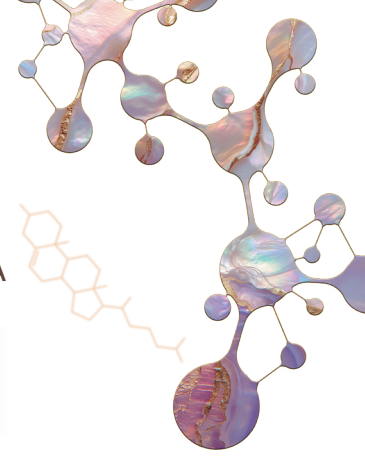
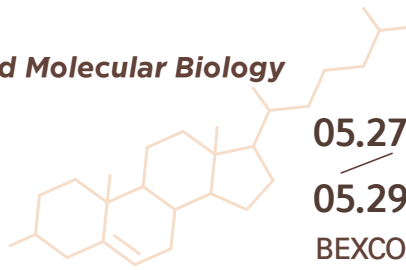
Hyung-Pyo KIM

*Department of Tropical Medicine, Yonsei University College of Medicine, Korea*

The chromatin architecture of mammalian genomes exhibits a complex, multilayered three-dimensional structure. The spatial folding of chromosomes and their organization in the nucleus have profound effects on gene expression and cellular function, and changes in nuclear organization affect both normal development and various diseases. Investigating the three-dimensional organization of DNA within the nucleus, along with its temporal dynamics, constitutes a primary focus of research in the 4D Nucleome Project. Recent technological advances in investigating the 3D organization of DNA in the nucleus and the functional implications of the 4D Nucleome in physiology and human disease will be discussed.

**Keywords:** Chromatin; enhancer; transcription; epigenome; 3D genome





**S16-4** Next-Generation Epigenome Regulation and Editing Technologies

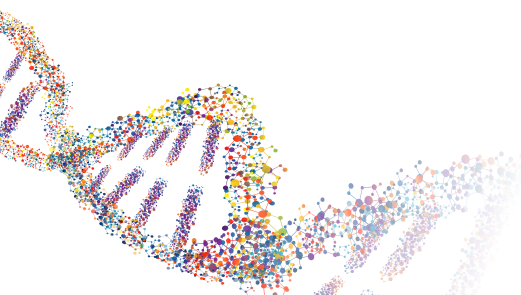
# Transient VLP-Mediated CRISPR Delivery Enables Efficient Genome and Epigenome Editing for Precision Cancer Therapy

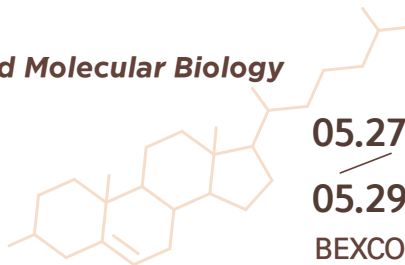
Kyoungmi KIM

*Seoul National University*

CRISPR-based genome and epigenome editing offer powerful strategies for precision cancer therapy, but their clinical application is hindered by delivery limitations. Here, we develop a transient, DNA-free virus-like particle (VLP) platform for efficient delivery of CRISPR ribonucleoproteins (RNPs). VLP-mediated delivery enabled robust genome editing across multiple cancer types and supported mutation-selective targeting of oncogenic alleles with high specificity and minimal effects on normal cells. Importantly, delivery of the epigenome editor CRISPRoff induced sustained gene silencing and suppressed cancer cell growth, with effects maintained for over 120 days. Compared to DNA-based approaches, the VLP system provided transient exposure, reduced off-target activity, and improved safety. In vivo analyses further demonstrated rapid signal decline without detectable toxicity. Together, these results establish transient VLP-mediated CRISPR delivery as a versatile and safe platform for efficient genome and durable epigenome editing in precision cancer therapy.

**Keywords:** CRISPR RNP Delivery, Virus-Like Particles (VLP), Epigenome Editing, CRISPRoff, Precision Cancer Therapy

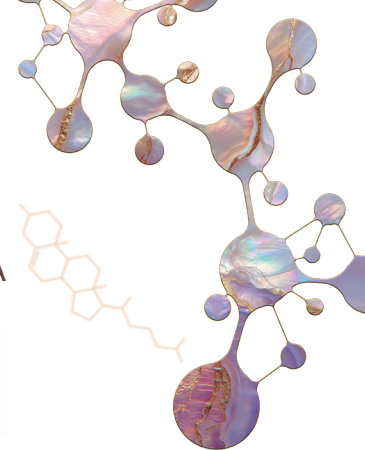




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FROM MOLECULES TO MEGABYTES:  
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**S17-1 Organ-to-Organ Communication**

# Rewiring the Brain to Drive Metabolic Adaptation and Performance

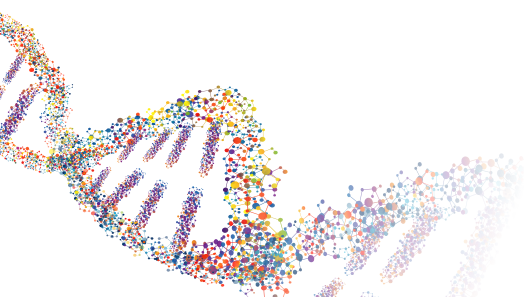
Kevin W. WILLIAMS

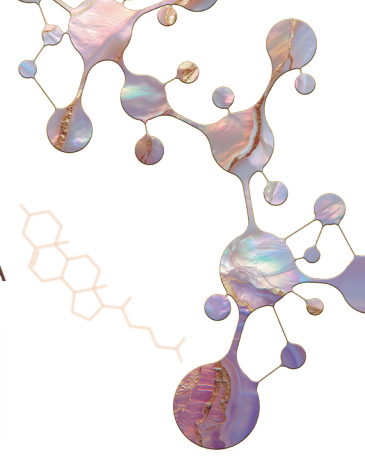
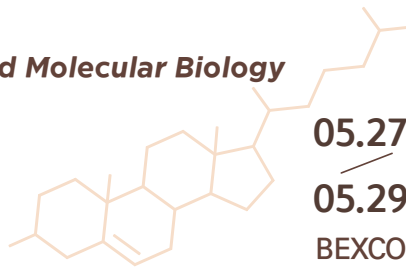
*Center for Hypothalamic Research, Department of Internal Medicine, Peter O'Donnell Jr. Brain Institute,  
The University of Texas Southwestern Medical Center*

Regular physical activity has profound effects on brain function, influencing cognition, mood, energy balance, and glucose metabolism. Recent studies highlight that exercise induces structural and functional changes in key metabolic circuits. These dynamic neural adaptations are associated with enhanced insulin sensitivity, appetite regulation, and improved systemic metabolism. While the precise mechanisms linking physical activity to brain-mediated metabolic benefits remain under investigation, emerging evidence suggests that key brain regions, including the hypothalamus, play a critical role in these adaptations. Understanding how exercise modulates neural activity and plasticity will provide insights into its therapeutic potential for metabolic and neurological disorders.

In this presentation, I will discuss recent advances in our understanding of exercise-induced neuroplasticity, with a particular focus on hypothalamic circuits that regulate energy balance and glucose metabolism. I will highlight how exercise engages metabolically relevant neuron populations and explore how these changes contribute to improvements in metabolic health.

**Keywords:** Exercise, Neuroplasticity, Melanocortin, Obesity, Diabetes





**S17-2 Organ-to-Organ Communication**

# Beyond the Diseased Organ: Endothelial Cells as Gatekeepers in Systemic Inflammatory Disease

Hongryeol PARK

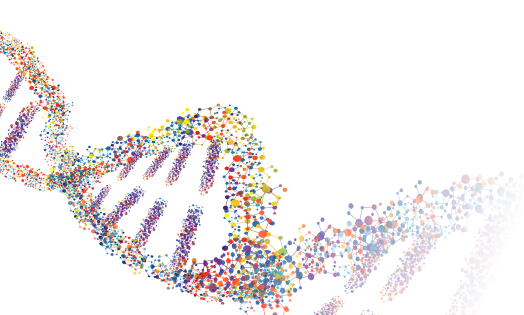
*Max Planck Institute for Molecular Biomedicine, Münster, Germany*

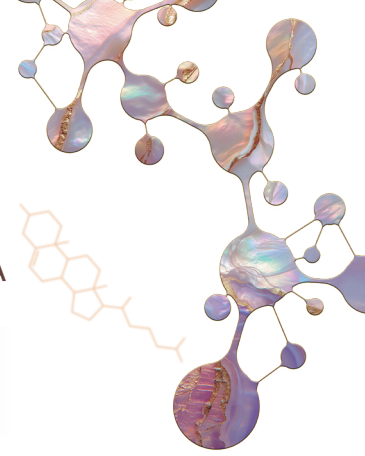
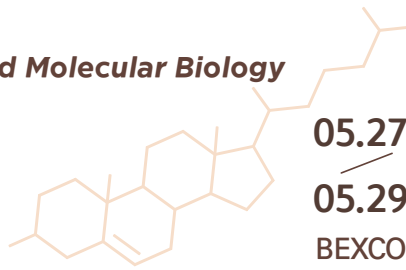
Systemic inflammatory diseases are traditionally defined by pathology in a single affected organ. However, immune activation and redistribution begin across multiple tissues before clinical symptoms arise. This suggests that critical regulatory events occur outside the visibly diseased site, challenging the prevailing organ-centered view of inflammation. To address this, we propose the concept of Immunomodulatory Latent Organs (ILOs)—clinically silent tissues that actively shape systemic immune dynamics through organ-specific endothelial programs. In this framework, endothelial cells are not passive barriers but gatekeepers that integrate inflammatory signals and regulate immune cell trafficking, positioning, and redistribution across the body.

As a proof of principle, we identified a lung–brain axis in autoimmune neuroinflammation in which immune organization within the lung precedes central nervous system pathology. Modulating endothelial signaling in this asymptomatic organ reshaped systemic immune dynamics and altered disease progression without directly targeting immune cells. These findings demonstrate that upstream vascular niches can govern inflammatory trajectories before damage becomes evident in the primary target organ.

By repositioning ILOs as active regulators of immune mobilization, this framework expands the landscape of therapeutic intervention. Organs previously considered secondary or uninvolved may represent novel entry points for early disease modulation, opening opportunities to intercept systemic inflammation before irreversible tissue damage occurs.

**Keywords:** Inter-organ Communication, Lung-Brain Axis, Systemic Inflammation, Endothelial Cells, Immunomodulatory Latent Organs (ILOs)





**S17-3 Organ-to-Organ Communication**

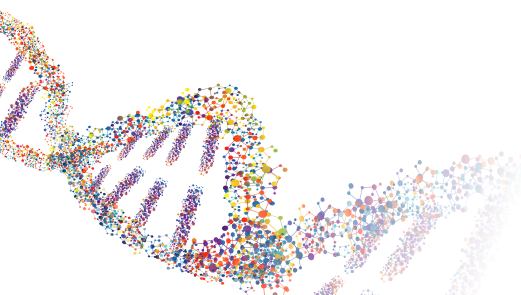
# Potential role of astrocytic MAO-B in the hypothalamus in age-related sarcopenia

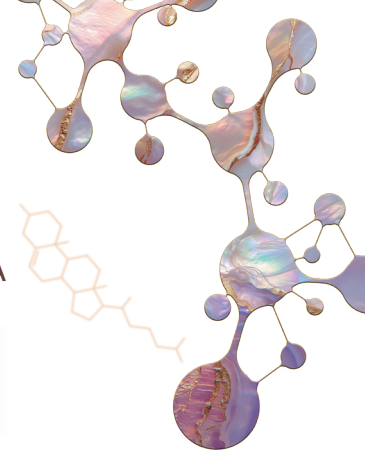
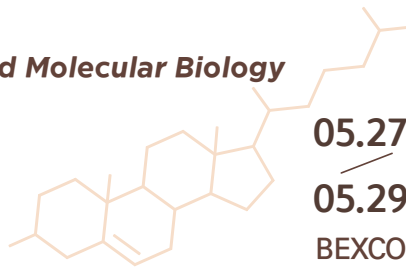
Min Soo KIM

*Korea Institute of Science & Technology (KIST)*

Sarcopenia, the progressive loss of muscle mass and strength with aging, is increasingly recognized as a systemic disorder involving not only peripheral tissues but also central regulatory mechanisms in the brain. Recent evidence suggests that the hypothalamus plays a pivotal role in controlling whole-body aging processes, including muscle function. Monoamine oxidase B (MAO-B), an enzyme that is upregulated in the hypothalamus during aging, has emerged as a critical mediator of neuroinflammation, oxidative stress, and impaired neurogenic signaling. These processes can indirectly disrupt hypothalamic control of endocrine and metabolic pathways, thereby accelerating skeletal muscle decline. In this presentation, we will discuss emerging data linking hypothalamic MAO-B overexpression to sarcopenia, with a focus on its mechanistic roles in neuromodulation, systemic inflammation, and anabolic signaling. Furthermore, we will highlight the therapeutic potential of targeting MAO-B activity in the hypothalamus as a novel strategy to prevent or attenuate age-related muscle wasting, thus opening new avenues for interventions to extend health span.

**Keywords:** MAO-B, hypothalamus, aging, sarcopenia, astrocyte





**S17-4 Organ-to-Organ Communication**

# Multi-Organ Actions of an Obesity Gene in the Regulation of Energy Homeostasis

Joe Eun SON

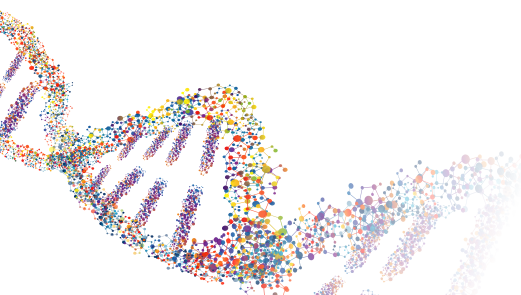
*Kyungpook National University*

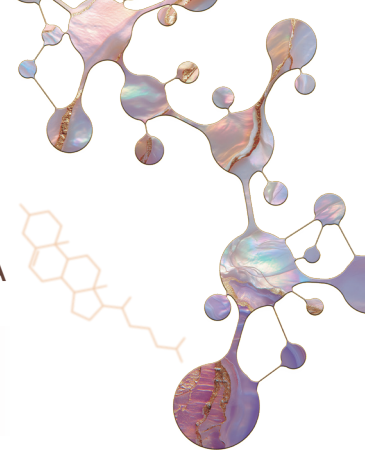
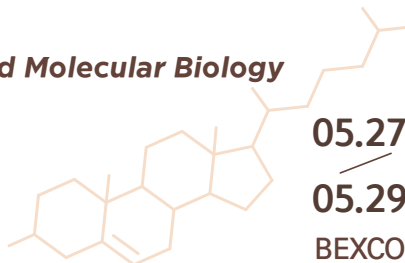
Obesity arises from a chronic imbalance in energy homeostasis and is driven by dysfunction across multiple metabolic organs. Among these, the hypothalamus and adipose tissue play central roles in the regulation of whole-body energy balance. Here, our research identifies the multi-organ actions of the Iroquois (IRX) homeobox genes, IRX3 and IRX5, genetic determinants of human obesity, in the regulation of energy homeostasis through their distinct actions in the hypothalamus and adipose tissue.

Specifically, by combining multi-omics with mouse genetics approaches, we found that *Irx3* and *Irx5* exhibit abnormal expression in the hypothalamic and adipose tissues of obese individuals, and that their expression levels are implicated in the leptin-mediated hypothalamic satiety response and in thermogenic regulation through the control of adipocyte beiging. In the hypothalamus, *Irx3/5* are expressed in postnatal hypothalamic neural stem cells, and *Ins2-Cre*-mediated deletion of IRX3/5 in this lineage enhances postnatal hypothalamic neural stem cell activity and promotes postnatal remodeling of neuronal circuits involved in leptin responsiveness and feeding control. In adipose tissue, *Irx3/5* are expressed in adipose tissue macrophages, and *LysM-Cre*-mediated deletion of IRX3/5 in macrophages suppresses adipose inflammation, promotes thermogenic remodeling, increases energy expenditure, and protects against obesity.

Together, these findings reveal that IRX3/5 act in a tissue-specific yet convergent manner in the hypothalamus and adipose tissue to govern whole-body energy balance. This work provides a conceptual framework for understanding how a human obesity gene exerts multi-organ control over metabolic homeostasis.

**Keywords:** Obesity, Energy Homeostasis, Hypothalamus, Adipose, IRX3/5





**S17-5 Organ-to-Organ Communication**

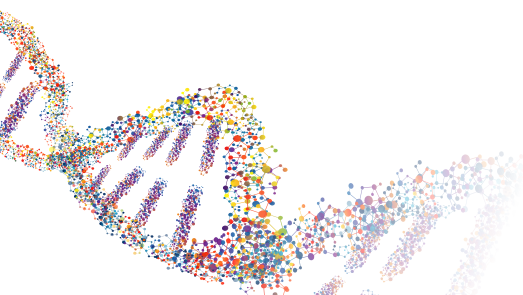
# Statin-induced hepatic senescence disrupts liver-to-muscle endocrine axis and impairs skeletal muscle homeostasis

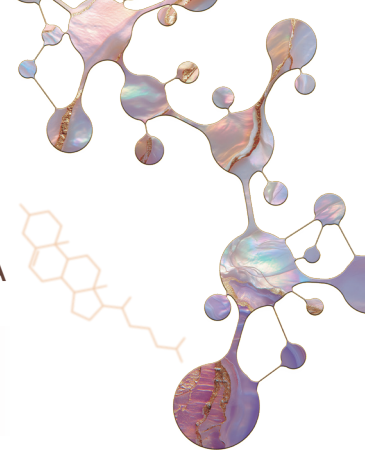
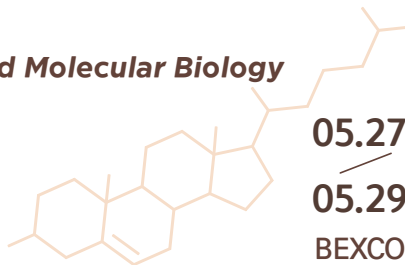
Wonkyung KIM<sup>1,2</sup>, Young-Kyo SEO<sup>1,2\*</sup>

<sup>1</sup>*Aging Convergence Research Center,  
Korea Research Institute of Bioscience and Biotechnology (KRIBB), Daejeon 34141, Korea*  
<sup>2</sup>*Biomolecular Science, KRIBB School of Bioscience,  
Korea University of Science and Technology (UST), Daejeon 34141, Korea*

Statins lower circulating cholesterol by inhibiting hepatic 3-hydroxy-3-methylglutaryl-CoA reductase (HMGCR), their use can be limited by muscle-related side effects whose mechanisms remain unclear. In this study we investigate statins induce hepatic senescence and that reduced hepatokine signaling impairs skeletal muscle homeostasis via inter-organ crosstalk. We demonstrate that lovastatin induces hepatic senescence and reduces systemic IGF-1 levels, leading to impaired myogenesis, increased protein degradation, and decreased muscle synthesis. These findings support a liver-to-muscle endocrine axis in which hepatic senescence suppresses IGF-1 and contributes to muscle atrophy. Targeting hepatic senescence or restoring IGF-1-AKT/mTOR signaling may represent a therapeutic strategy for statin-associated myopathy.

**Keywords:** Hepatic Senescence, Muscle atrophy, IGF-1





**S17-6 Organ-to-Organ Communication**

## Advanced human FcRn knock-in mice for pharmacokinetic profiling of therapeutic antibodies

SuBin LEE<sup>1,5#</sup>, Munsu KYUNG<sup>2,3,4#</sup>, Miyeon PARK<sup>5</sup>, Sunha PARK<sup>5</sup>, JaeHoon LEE<sup>1,5</sup>,  
Suyeon KIM<sup>2,3,4</sup>, Seunghyeon LEE<sup>4,6</sup>, Migyeong JO<sup>4</sup>,  
Sang Taek JUNG<sup>4,6,7\*</sup>, Han-Woong LEE<sup>1,5\*</sup>

<sup>1</sup>Department of Biochemistry, College of Life Science and Biotechnology, Yonsei University, Seoul 03722, Korea

<sup>2</sup>Department of Biomedical Sciences, BK21 Graduate Program, College of Medicine, Korea University, Seoul 02841, Korea

<sup>3</sup>Department of Biomedical Sciences, Graduate School, Korea University, Seoul 02841, Korea

<sup>4</sup>Institute of Chemical Processes, Seoul National University, Seoul 08826, Korea

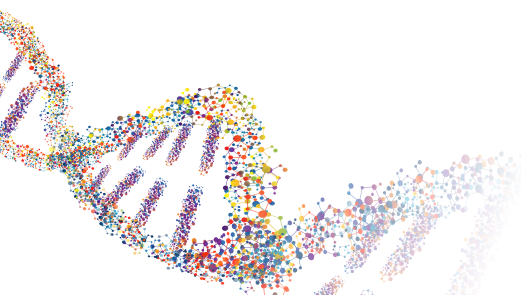
<sup>5</sup>R&D center, Gemcro, Seoul 03722, Korea

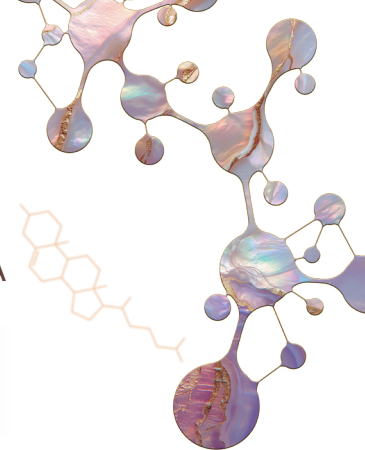
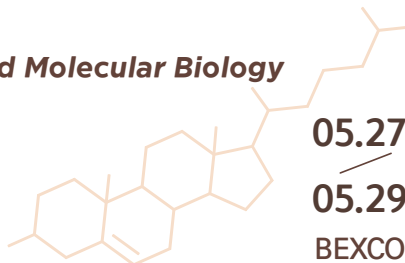
<sup>6</sup>School of Chemical and Biological Engineering, College of Engineering, Seoul National University, Seoul, 08826, Korea

<sup>7</sup>Interdisciplinary Program for Bioengineering, Seoul National University, Seoul, 08826, Korea

IgG-based therapeutic antibodies are increasingly adopted for diverse human diseases, such as cancer and autoimmune disorders displaying remarkable therapeutic performance. A key factor in their success lies in the extended half-life of IgG molecules, which is regulated by the pH-dependent interaction between IgG and neonatal Fc receptor (FcRn). This interaction prevents lysosomal degradation of IgG. Despite the frequent use of humanized rodent models expressing human FcRn (hFcRn) in preclinical studies, these models often fail to accurately replicate human antibody pharmacokinetics (PK) due to the use of non-native promoters that influence FcRn expression. To overcome this limitation, we developed an innovative humanized FcRn knock-in (hiFcRn) mouse model using CRISPR/Cas9 technology. This model integrates hFcRn cDNA into the endogenous locus of the mouse Fcgrt gene, completely replacing native mouse FcRn (mFcRn) expression. The hiFcRn mouse model offers a more human-relevant platform for the preclinical evaluation of therapeutic antibodies and Fc-fusion proteins.

**Keywords:** FcRn, Pharmacokinetics, Therapeutic IgG





**S18-1** Frontiers in Chemical Biology:  
Emerging Concepts and Innovative Technologies

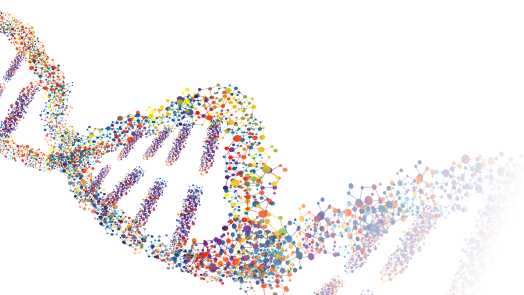
## Decoding and manipulating tumor-immune interaction with proximity labeling

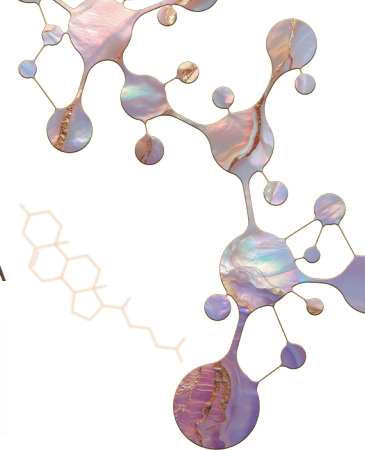
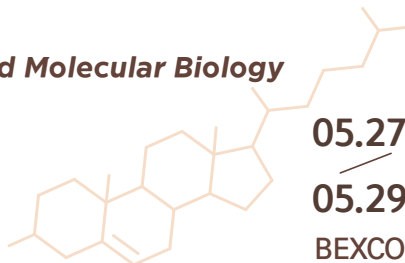
Shuo HAN

*Shanghai Institute of Biochemistry and Cell Biology, Chinese Academy of Sciences*

The application of proximity labeling, a chemical biology strategy that uses enzyme-catalyzed, promiscuously-reactive intermediates for nanometer scale biotinylation of neighboring proteins, as a discovery tool has yielded tremendous insights into molecular and cellular interactions over the past decade. However, in theory, proximity labeling is by no means restricted to biotin-containing substrates for detection purposes and whether the chemical features of proximity labeling reactions can be harnessed for other applications has thus far not been explored. In this talk, I will present our recent work on using proximity labeling both as a research tool for decoding molecular and cellular interaction at the tumor-immune interface, and, more importantly, as an antigen engineering approach for manipulating cellular interaction, which we hope would lay the groundwork for future therapeutic application of this unique and diverse class of chemistry.

**Keywords:** Proximity labeling, proteomics, transcriptomics, cancer, immunotherapy





**S18-2** **Frontiers in Chemical Biology:**  
**Emerging Concepts and Innovative Technologies**

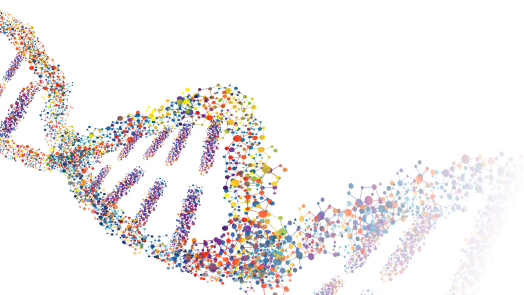
## Development of a principle guided virtual screening AI

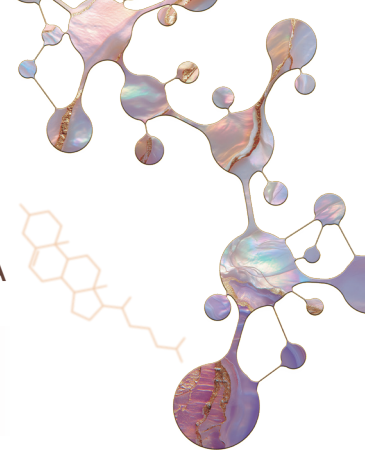
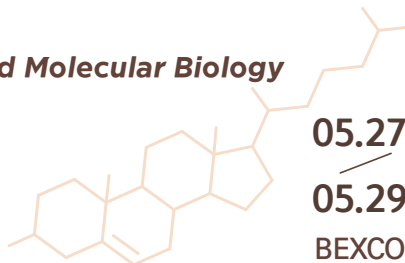
Hahnbeom PARK

*Korea Institute of Science and Technology*

While artificial intelligence (AI) has brought breakthroughs to many research areas, an important question remains on how such a revolution can be transferred to the computational drug discovery field. Despite the technical advances, recent AIs are still highly overfit to existing data, lacking transferability to new data or having issues with chemical feasibility, suggesting needs for alternative approaches. I will share our ongoing work to mitigate these issues by introducing physicochemical knowledge into chemical compound virtual screening. Benchmark and experimental validation results show principle-guided networks are broadly generalizable to unseen data while keeping performance on par with or better than the best existing tools.

**Keywords:** Virtual Screening, AI, structure-based drug design





**S18-3** **Frontiers in Chemical Biology:**  
**Emerging Concepts and Innovative Technologies**

# **RaPID Platform for the Construction and Screening of Natural Product-Inspired Macrocyclic Peptide Libraries**

Kang Ju LEE

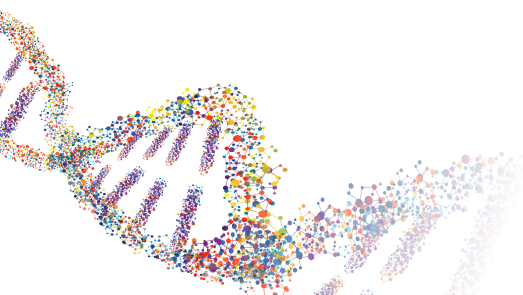
*Korea Research Institute of Chemical Technology (KRICT)*

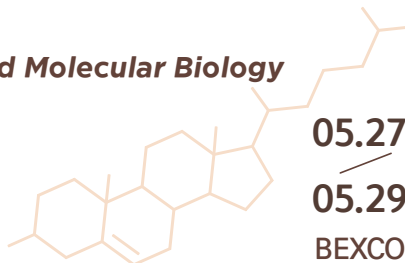
Macrocyclic peptides are an emerging class of therapeutic modalities that occupy a unique pharmaceutical space between traditional small molecules and antibodies. Their intermediate size enables effective engagement with challenging targets such as protein-protein interactions. Compared with antibodies, macrocyclic peptides often exhibit improved tissue penetration, reduced immunogenicity, and greater accessibility to intracellular targets. Recent clinical advances and FDA approvals of macrocyclic peptide drugs further highlight the growing potential of this modality.

The RaPID system (Random non-standard Peptides Integrated Discovery) represents a powerful screening technology for the discovery of macrocyclic peptide ligands. By integrating mRNA display with genetic code reprogramming, this platform enables the construction and screening of ultra-large (>10<sup>12</sup>) macrocyclic peptide libraries while allowing the site-specific incorporation of diverse non-proteogenic amino acids (npAAs). This capability provides substantial flexibility in library design, facilitating the construction of structurally diverse peptide scaffolds.

In this presentation, I will describe our application of the RaPID system to the design and screening of natural product-inspired macrocyclic peptide libraries. By incorporating diverse npAAs, we constructed macrocyclic peptide libraries that adopt natural product-derived architectures. Screening of these libraries against therapeutically relevant targets, including the SARS-CoV-2 main protease and interleukin-4 receptor  $\alpha$ , led to the identification of potent macrocyclic peptide ligands with improved drug-like properties.

**Keywords:** Macrocyclic peptides, mRNA display, RaPID system, Peptide drug discovery

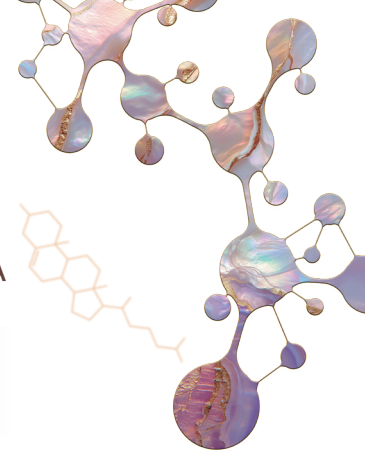




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BEXCO, BUSAN, KOREA



FROM MOLECULES TO MEGABYTES:  
AI AND BIG DATA TRANSFORMING LIFE SCIENCE

**S18-4** **Frontiers in Chemical Biology:**  
**Emerging Concepts and Innovative Technologies**

# Harnessing Damaged DNA to Regulate mRNA Translation in Cells

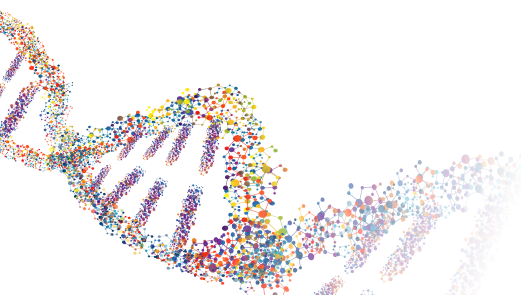
Yong Woong JUN

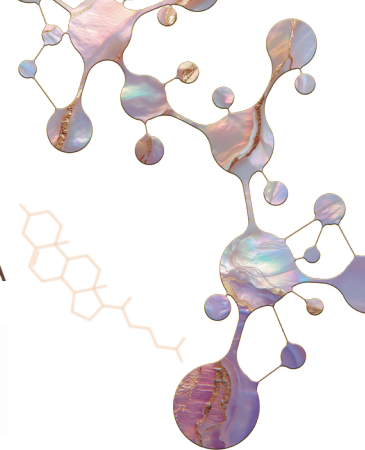
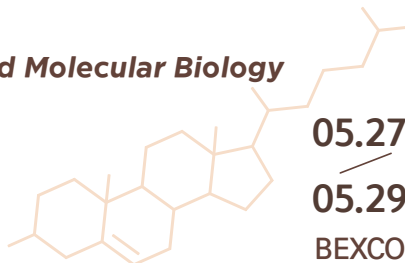
*Korea Advanced Institute of Science and Technology (KAIST)*

Messenger RNA (mRNA) drugs deliver genetic instructions to direct the *in vivo* synthesis of therapeutic proteins. Despite their immense potential, broader clinical application is hindered by a fundamental challenge: precise dose control. The instant surge in translation following mRNA delivery often causes localized protein overexpression, triggering local inflammation, and other adverse effects in susceptible individuals. Consequently, regulating the kinetics of *in vivo* protein expression is critical for the safe deployment of mRNA drugs.

Here, we introduce a simple biochemical approach that repurposes “damaged DNA” as a natural modulator of mRNA translation kinetics. When hybridized to mRNA, these DNA strands transiently suppress translation initiation. Their displacement through endogenous base excision repair (BER) gradually restores translation, allowing tunable and sequential protein expression without any chemical modification of the mRNA itself. The resulting DNA fragments are 100% recyclable in cells, providing a biocompatible, low-cost, and easily programmable strategy for translation control.

**Keywords:** mRNA therapeutics, DNA repair, Base excision repair, mRNA translation





**S19-1** Translational Drug Discovery

# Viral RNA Methyltransferases as Emerging Targets for Antiviral Drug Development

Radim NENCKA

*IOCB Prague*

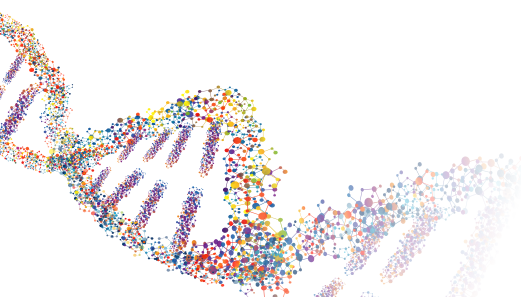
Viral RNA methyltransferases (MTases) are essential enzymes conserved across diverse virus families, including coronaviruses, flaviviruses, and poxviruses, where they catalyze key steps in RNA cap formation required for efficient translation and immune evasion. In our work, we have systematically investigated MTases from these distinct viral systems, including coronaviral nsp14/nsp16, flaviviral NS5, and poxviral VP39, providing a unified structural and mechanistic framework for their inhibition.

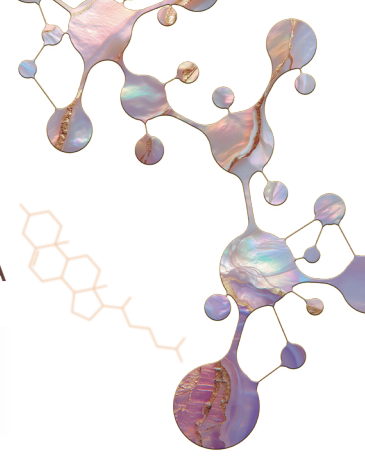
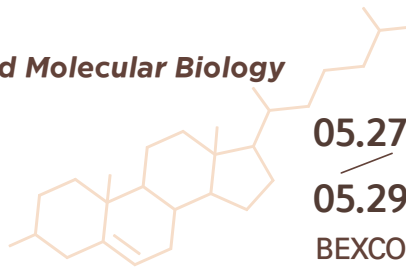
The presentation will focus on structure-based drug discovery approaches targeting viral MTases. Using high-resolution structural data, we identify conserved cofactor-binding sites and RNA interaction interfaces that serve as key hotspots for inhibitor design. Structure-guided strategies, including the development of SAM-competitive ligands and rational optimization of binding interactions, enable the design of novel compounds with improved potency and selectivity. Comparative structural analyses across virus families further allow the identification of shared pharmacophores as well as exploitable differences for selective targeting.

Special emphasis will be placed on the design and characterization of new MTase inhibitors, including recent advances in targeting flaviviral NS5 and poxviral VP39 enzymes. These efforts illustrate how structural biology, combined with medicinal chemistry, drives the discovery of antiviral compounds capable of disrupting RNA capping and viral replication.

**Acknowledgement:** This research was funded by the project New Technologies for Translational Research in Pharmaceutical Sciences/NETPHARM, project ID CZ.02.01.01/00/22\_008/0004607, which is co-funded by the European Union.

**Keywords:** Viral RNA methyltransferases; Structure-based drug design; Antiviral inhibitors; RNA capping machinery; Flavivirus, coronavirus, and poxvirus MTases





**S19-2 Translational Drug Discovery**

## Gene therapy for genetic hearing loss

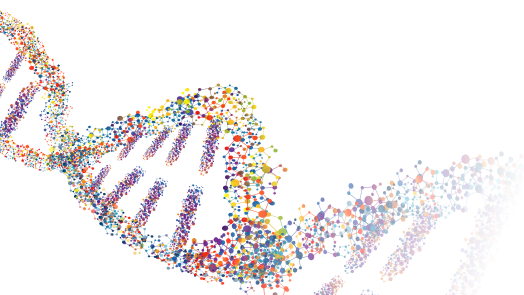
Heon Yung GEE<sup>1\*</sup>

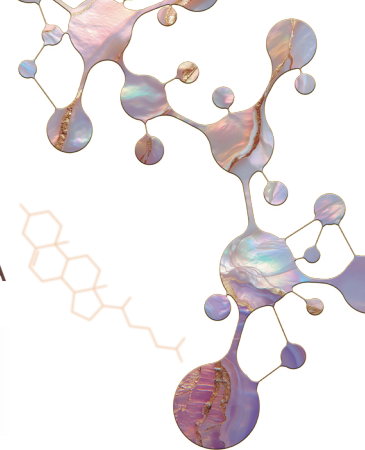
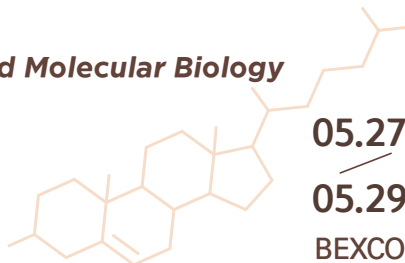
<sup>1</sup>Pharmacology, Yonsei University College of Medicine, Seoul 03720, Korea

Hereditary hearing loss is a genetically heterogeneous condition that affects millions of people worldwide and currently has limited curative treatment options. Recent advances in gene therapy have opened promising opportunities for correcting the underlying genetic defects in the inner ear. This review highlights the latest progress in vector platforms, delivery strategies, target genes, preclinical models, and clinical trials related to both gene supplementation and gene editing approaches, as well as future perspectives. Among these, adeno-associated virus (AAV) vectors have emerged as the leading platform for inner ear gene transfer due to their favorable safety and efficacy profiles. Clinical programs, such as those targeting OTOF mutations, are already underway and supported by robust preclinical data.

As a representative example, our recent work on MPZL2-associated autosomal recessive hearing loss (DFNB111) demonstrated the feasibility of AAV-mediated gene supplementation in a knock-in mouse model, underscoring both the therapeutic potential and the critical importance of precise promoter selection in achieving safe and durable auditory restoration. Collectively, these advances provide a strong foundation for the clinical translation of gene therapy into effective treatments for hereditary hearing loss.

**Keywords:** Hearing loss, MPZL2, AAV





**S19-3 Translational Drug Discovery**

# Targeting PRX-dependent redox regulation of RTK signaling and related diseases with PRX mimetics

Sang Won KANG<sup>1\*</sup>

<sup>1</sup>Life Science, Ewha womans University, Seoul 03760, Korea

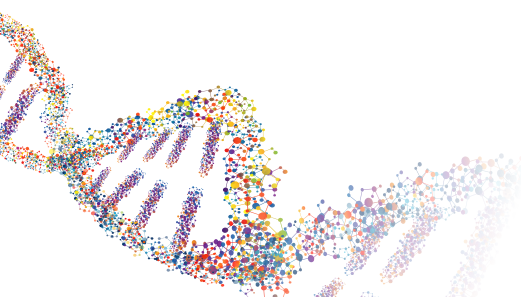
Receptor tyrosine kinase (RTK) signaling plays a central role in diverse physiological and pathological processes, with dysregulated redox signaling emerging as a critical determinant of aberrant RTK activation. Peroxiredoxins (PRXs) are key antioxidant enzymes that tightly regulate intracellular hydrogen peroxide levels, thereby modulating redox-dependent signaling pathways. However, PRX function can be compromised through hyperoxidation or epigenetic suppression, leading to sustained oxidative stress and uncontrolled RTK signaling.

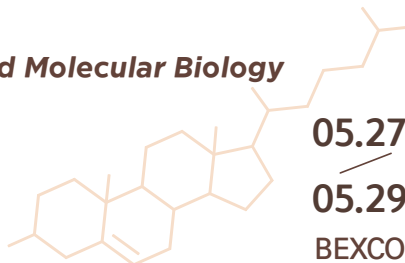
Accumulating evidence links PRX dysfunction to a spectrum of diseases, including atherosclerosis, Alzheimer's disease, and multiple cancers such as melanoma and triple-negative breast cancer (TNBC). In these contexts, loss of PRX activity enhances oxidative modification of signaling components, resulting in persistent activation or inactivation of RTKs and downstream pathways.

To address this unmet need, we propose a novel therapeutic modality based on small-molecule PRX mimetics (Chemzymes) that complement the PRX deficiency and selectively modulate RTK signaling. These PRX mimetics functionally substitute endogenous PRX activity, either eliminating excess hydrogen peroxide and preventing aberrant oxidation of key signaling proteins or sensing primarily hydrogen peroxide and transmitting redox equivalent to client signaling proteins.

In this presentation, I will show the efficacy of this approach across multiple disease-relevant models.

**Keywords:** Peroxiredoxin, Receptor Tyr Kinase, Chemzyme

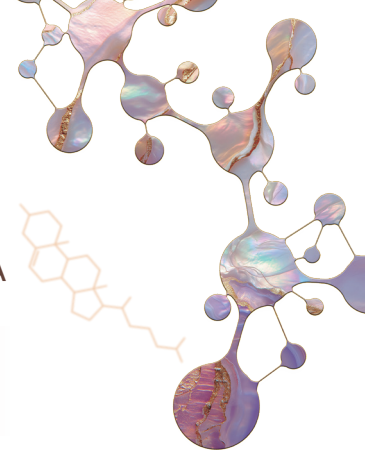




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FROM MOLECULES TO MEGABYTES:  
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**S19-4 Translational Drug Discovery**

## Recent Progress on the K-DEL screening platform at K-MEDI hub

Minsoo SONG<sup>1\*</sup>

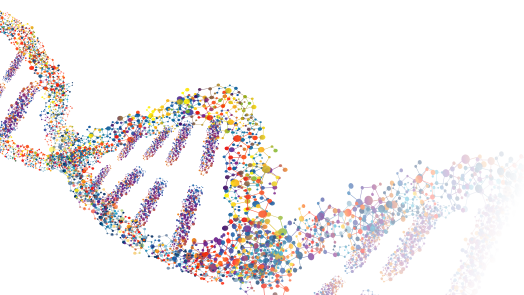
<sup>1</sup>New Drug Development Center, K-MEDI hub, Daegu 41061, Korea

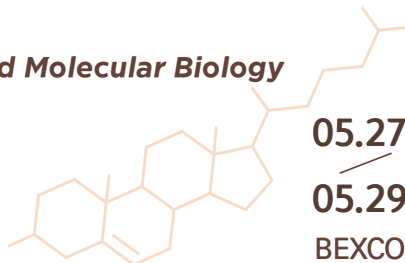
DNA-encoded library technology (DEL) has been recognized as a highly useful tool for the hit-finding process in small molecule drug discovery research for over 30 years. A DNA-encoded library (DEL) is a collection of small molecules individually coupled to unique DNA tags. Each DNA tag serves as an identification code for the individual building blocks used in DEL construction. Library synthesis proceeds through a split-and-pool strategy in three to four synthetic cycles, generating a library of approximately 10<sup>6</sup> to 10<sup>7</sup> compounds. Through solid-phase affinity-based DEL selection, molecules that bind to a target protein can be easily separated. The chemical structures of these target-binding molecules can then be decoded using next-generation sequencing (NGS) analysis.

The most prominent advantage of DELT is the ability to obtain target-binding molecules from a single affinity-based selection assay using an ultra-large compound library. This approach offers very nice benefits in early-stage drug discovery research in terms of cost, time, and productivity.

Through our presentation at the 2026 Spring Meeting of KSBMB, we aim to share updates on our DELT research progress and discuss future perspectives to better serve our drug discovery community.

**Keywords:** Drug discovery platform, DNA-Encoded library, DEL screening

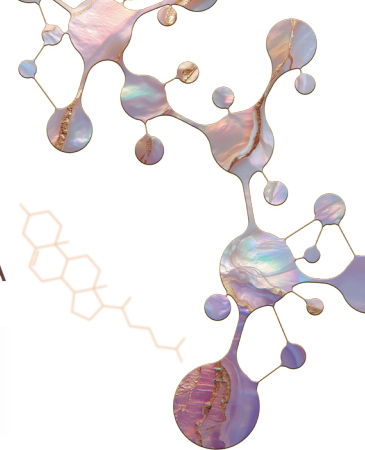




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FROM MOLECULES TO MEGABYTES:  
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**S19-5 Translational Drug Discovery**

## Targeting noncanonical TEAD to overcome DNA repair-driven chemoresistance

Dong Hyeon KIM<sup>1#</sup>, Jongwan KIM<sup>2#</sup>, Hwa-Ryeon KIM<sup>1</sup>, Sangwoo KANG<sup>3</sup>, Donghyuk SHIN<sup>3</sup>,  
Jae-Seok ROE<sup>1</sup>, Kyoung Tai NO<sup>2\*</sup>, Hyun Woo PARK<sup>1\*</sup>

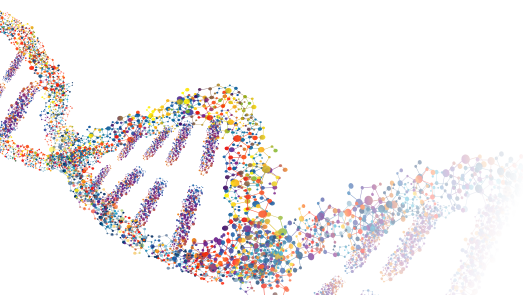
<sup>1</sup>Biochemistry, Yonsei University, Seoul 03722, Korea

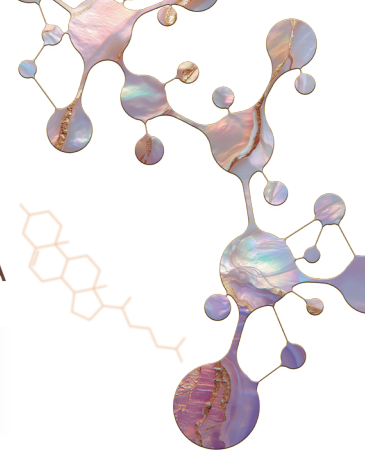
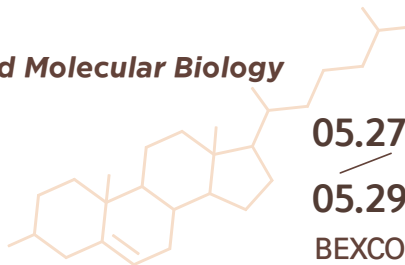
<sup>2</sup>Biotechnology, Yonsei University, Seoul 03722, Korea

<sup>3</sup>Systems Biology, Yonsei University, Seoul 03722, Korea

How transcription factors contribute to DNA damage repair (DDR) independent of canonical gene regulation remains poorly understood. Here, we show that DNA double-strand break (DSB) triggers a functional state transition in TEAD, disengaging it from YAP-dependent transcription and translocating it to DNA lesions as a chromatin-associated DDR component. Upon genotoxic stress, TEAD is rapidly recruited to damaged chromatin through a biphasic mechanism involving early poly(ADP-ribose)-dependent recruitment followed by ATM-driven  $\gamma$ H2AX-mediated retention. At DNA lesions, TEAD constrains chromatin over-relaxation, suppresses excessive end resection, and promotes non-homologous end joining (NHEJ) independent of its canonical function. Conserved residues within the TEA domain mediate this noncanonical chromatin engagement of TEAD and define a druggable N-terminal interface. Pharmacological targeting of this interface impaired TEAD-dependent DSB repair and sensitized tumors to chemotherapy. Together, these findings establish noncanonical TEAD as a physiologically important regulator of DNA repair and a clinically actionable driver of chemoresistance, while providing a conceptual framework for understanding how broader families of transcription factors may be repurposed as targetable DNA damage regulators in cancer.

**Keywords:** TEAD, Chemoresistance, Drug development





**S19-6 Translational Drug Discovery**

## Transglutaminase 2 exacerbates ovarian cancer survival by directly inactivating GSK3 $\beta$

Joon Hee KANG<sup>1,2#</sup>, Ho LEE<sup>1,2#</sup>, Hyun Jung KIM<sup>3#</sup>, Kyun HEO<sup>4</sup>, Mi Kyung PARK<sup>5</sup>,  
Jeong Hwan PARK<sup>1</sup>, Byung Il LEE<sup>6</sup>, Jong In YOON<sup>7</sup>, Soo-Youl KIM<sup>1\*</sup>

<sup>1</sup>Division of Cancer Biology, National Cancer Center, Goyang 10408, Korea

<sup>2</sup>Graduate School of Cancer Science and Policy, National Cancer Center, Goyang 10408, Korea

<sup>3</sup>Department of Medicine, University of Ulsan College of Medicine, Seoul 05505, Korea

<sup>4</sup>Biopharmaceutical Chemistry Major, Kookmin University, Seoul 02707, Korea

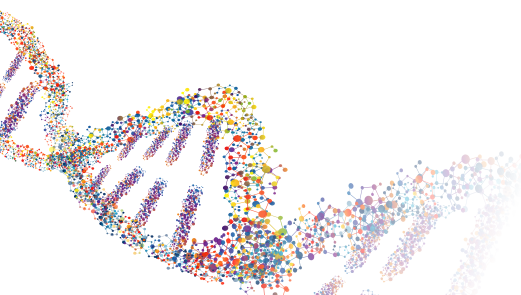
<sup>5</sup>Department of Biomedical Science, Hwasung Medi-Science University, Hwasung 18274, Korea

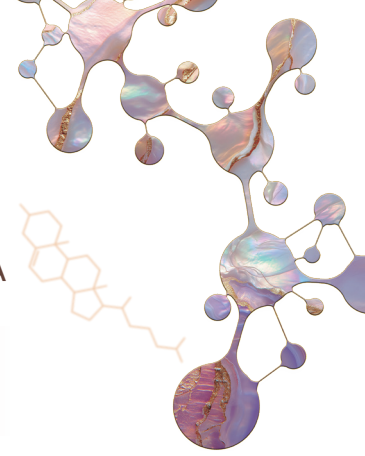
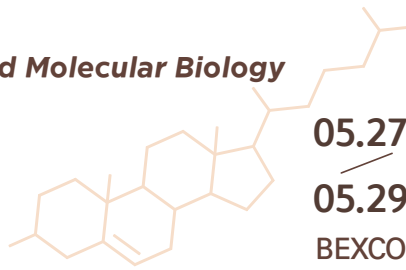
<sup>6</sup>Division of Technology Convergence, National Cancer Center, Goyang, 10408, Korea

<sup>7</sup>Department of Oral Pathology, Oral Cancer Research Institute, College of Dentistry, Yonsei University, Seoul, 03722, Korea

Elevated expression of transglutaminase 2 (TGase 2, EC 2.3.2.13, protein-glutamine  $\gamma$ -glutamyltransferase, gene name TGM2) is known as one of the most upregulated genes during epithelial-mesenchymal transition (EMT) in ovarian cancer. Despite initial complete responses to conventional chemotherapy, ovarian cancer often recurs with metastasis, presenting a significant clinical challenge. Drug-resistant ovarian cancer cells exhibit markedly higher levels of TGase 2 compared to normal ovarian epithelium, which is associated with EMT activation, enabling them to evade chemotherapy effects. Intracellular TGase 2 is recognized as a key factor in maintaining the mesenchymal phenotype. Therefore, while EMT expression can be effectively reversed by inhibiting TGase 2, the underlying mechanism of this effect remains unclear. We found that TGase 2 promotes EMT by directly binding to glycogen synthase kinase-3 $\beta$  (GSK3 $\beta$ ), promoting the stabilization of  $\beta$ -catenin. Domain mapping revealed that the N-terminus of TGase 2 interacts with the mid-region of GSK3 $\beta$ , leading to the autophagic degradation of GSK3 $\beta$ . Pharmacological disruption of this N-terminal interaction by streptonigrin, in combination with standard chemotherapy, extended overall survival in a xenograft model of ovarian cancer. This study identified TGase 2 as a pivotal regulator of EMT-driven metastasis and drug resistance.

**Keywords:** Transglutaminase 2, GSK3-Beta, Ovarian cancer





**S20-1 KSBMB-KPS Joint Session: Neurobiology of Addiction**

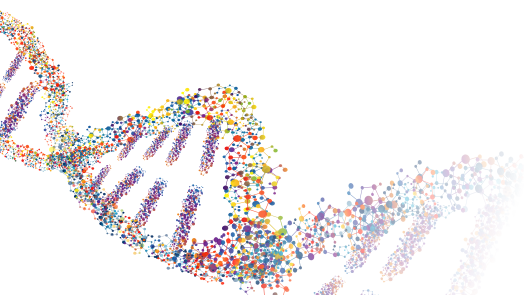
# From molecules to behavior: examining the neuronal basis of addiction

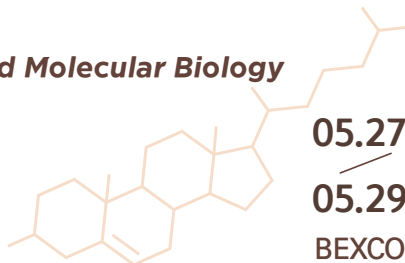
David DIETZ

*University of Kansas*

Substance use disorder is manifested by maladaptive behavioral plasticity, often enduring for long-periods following drug abstinence. The exact cellular mediators leading to these long term-changes has remained elusive, stymying the development of effective treatments to prevent relapse. Our current work examines the diverse cellular functions and signaling cascades, that bridge more acute cellular responses with the more sustained transcriptional changes following exposure to commonly misused substances (e.g., cocaine, heroin). This work demonstrates an essential role of cellular plasticity in mediating addiction-like behaviors and identifying these signaling cascades as being ideal targets for novel and efficacious pharmacological therapeutics.

**Keywords:** plasticity, addiction, TGF-beta, transcription, sn-RNAseq

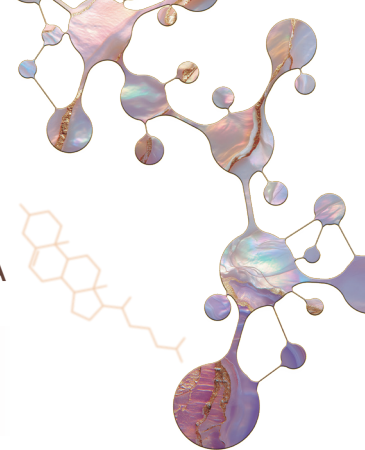




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FROM MOLECULES TO MEGABYTES:  
AI AND BIG DATA TRANSFORMING LIFE SCIENCE

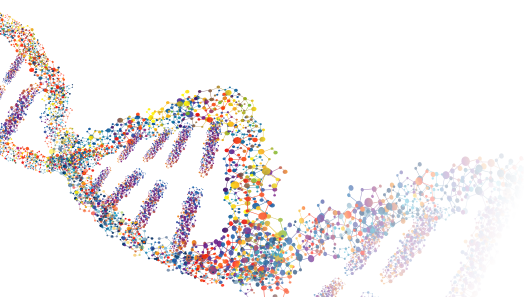
**S20-2 KSBMB-KPS Joint Session: Neurobiology of Addiction**

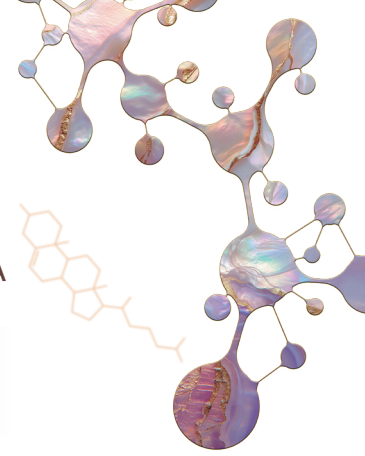
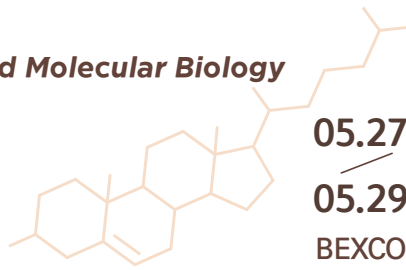
## Neuroimmune signals directly regulates nicotine reward

Zuxin CHEN

*Shenzhen Institutes of Advanced Technology (SIAT), Chinese Academy of Sciences (CAS)*

Neuroimmune signals can regulate neuronal function and affect behavior through mechanisms that are not yet fully understood. Here we investigated the action of interleukin 13 (IL-13), a cytokine that can be produced in the brain by both microglia and neurons. We show that dopamine-containing neurons in the ventral tegmental area (VTA) predominantly express the IL-13 receptor alpha 1 (IL-13R $\alpha$ 1) and exhibit presynaptic vesicular localization of neuronal IL-13. Exogenous application of IL-13, or its endogenous mobilization by optogenetics, reduced the activity of VTA dopaminergic neurons and opposed the stimulatory effects of nicotine on these neurons in rodents. These actions required IL-13R $\alpha$ 1, activation of the PI3K/AKT pathway, and functional HCN channels. Consistently, local infusion of IL-13 into the VTA markedly reduced nicotine self-administration in rodents. Collectively, these findings demonstrate that IL-13 acts in a neuromodulator-like fashion on mesolimbic dopamine neurons expressing IL-13R $\alpha$ 1. Our data also indicate that IL-13R $\alpha$ 1 signaling regulates the stimulatory actions of nicotine, suggesting a potential role for this neuronal immune signaling in reward processing and the addictive properties of nicotine.





**S20-3 KSBMB-KPS Joint Session: Neurobiology of Addiction**

# Leveraging Enhancer RNAs to Understand Brain Organization and Function

Tae-Kyung KIM

*Dept. of Life Sciences, POSTECH*

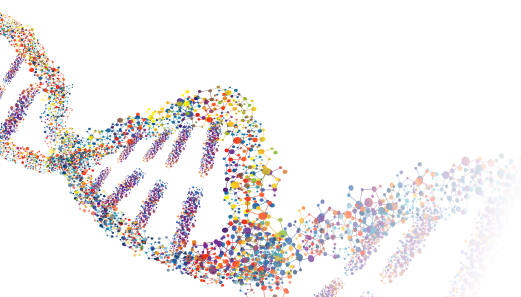
Enhancer RNAs (eRNAs) are dynamically transcribed from active enhancers and provide temporally precise readouts of regulatory activity. Unlike stable transcripts, eRNAs are rapidly and transiently induced in response to external stimuli and are tightly controlled at the transcriptional level. Epigenomic studies across diverse cell types have established eRNAs as robust hallmarks of active enhancers, yet their functional potential as tools for interrogating gene regulation and cellular states remains underexplored.

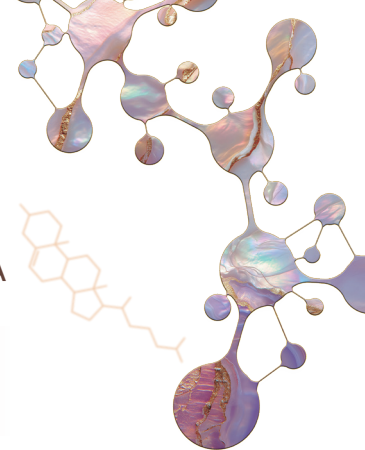
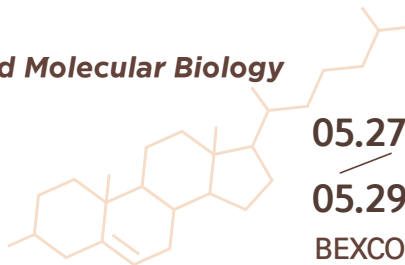
Here, we leverage stimulus-evoked eRNA signatures to develop ENSNARE (Enhancer-based Stimulus-specific Neuronal Activity Reporter), a molecular framework for labeling and manipulating neuronal ensembles defined by specific stimuli or signaling pathways. By systematically profiling eRNA dynamics, we identify enhancers with high spatiotemporal specificity and use them to construct selective reporters that overcome the broad and heterogeneous responses of conventional activity-dependent systems.

Using cocaine exposure as a proof-of-concept, we show that an ENSNARE reporter selectively labels dorsal striatal neurons engaged by BDNF-TrkB-dependent signaling from defined upstream inputs. This population is molecularly and functionally distinct from ensembles identified by canonical immediate-early gene reporters, revealing previously inaccessible neural subtypes.

More broadly, eRNA-guided design establishes a generalizable strategy for decoding and targeting regulatory states across cell types. In the long term, this approach enables systematic mapping and manipulation of functionally defined cell populations, linking enhancer activity to cellular identity, circuit function, and disease mechanisms.

**Keywords:** Enhancer, Enhancer RNAs, Drug Addiction, Activity Reporter, Epigenome





**S20-4 KSBMB-KPS Joint Session: Neurobiology of Addiction**

# Aversive Stress, Corticosterone and Dopamine Dysfunction: Neural Mechanisms Connecting Negative Emotions and Drug Relapse

Suchan CHANG

*Department of Acupuncture, Moxibustion, & Acupoint, College of Korean Medicine, Daegu Haany University*

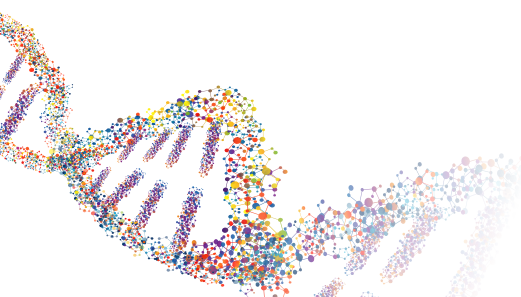
Stress is a major trigger of negative emotional states and relapse in substance use disorders, yet the neural mechanisms linking stress hormones, emotional processing, and reward circuitry remain unclear. Here, we investigated how aversive stress and acute glucocorticoid signaling influence mesolimbic dopamine function and addiction-related behaviors.

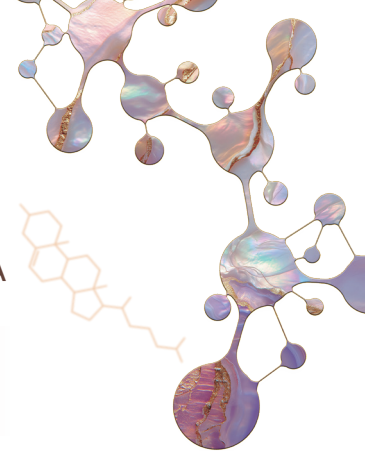
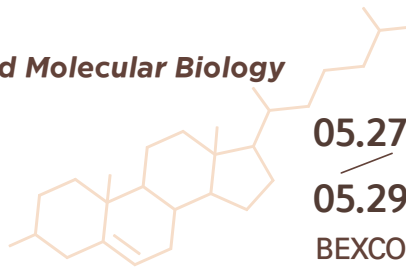
Using a rodent model of aversive auditory stress, rats were exposed to artificial low-frequency ultrasound (22–38 kHz), which induces strong aversive responses. This stimulation produced anxiety-like behaviors, increased 22-kHz ultrasonic vocalizations, and activation of neurons in the central amygdala. During aversive sound exposure, dopamine release in the nucleus accumbens was significantly reduced. Importantly, in rats previously trained to self-administer cocaine, aversive sound stimulation reinstated cocaine-seeking behavior after extinction.

To examine the role of stress hormones, we also tested the effects of acute corticosterone exposure in mice. A single corticosterone administration induced robust depression-like behaviors in the forced swim and tail suspension tests. Immunohistochemical analyses revealed increased activation of GABAergic neurons in the ventral tegmental area and reduced neuronal activity in the nucleus accumbens, suggesting suppression of mesolimbic dopaminergic signaling.

Together, these findings indicate that aversive stress and acute glucocorticoid signaling converge on mesolimbic dopamine circuits, promoting negative emotional states and increasing vulnerability to drug relapse.

**Keywords:** Stress; Corticosterone; Mesolimbic Dopamine; Negative Emotion; Drug Relapse





**TIS1-1 From Understanding to Programming Life:  
Emerging Technologies for Reconstructing Biological Systems**

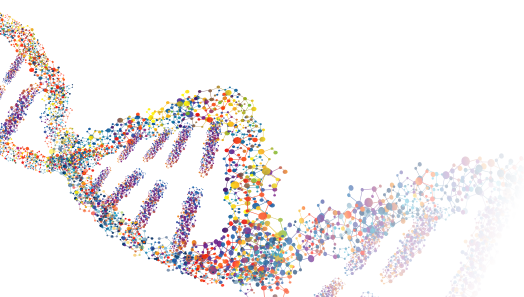
# From CRISPR to Beyond: The Evolution and Future of Genome Editing

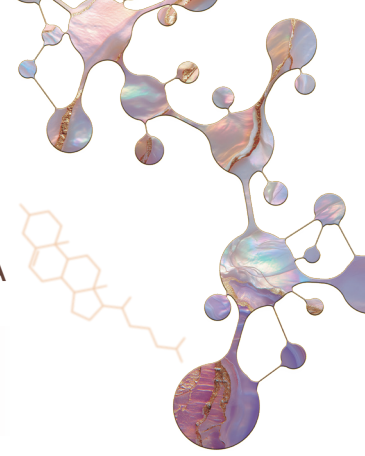
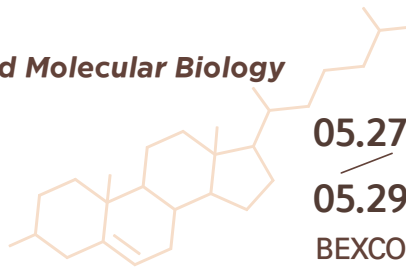
Sung-Ik CHO

*Department of Brain and Cognitive Sciences, Korea Advanced Institute of Science and Technology (KAIST),  
291 Daehak-ro, Daejeon 34141, South Korea*

Genome editing within nuclear, mitochondrial, and chloroplast DNA holds significant promise across the fields of biomedical research, medicine, and biotechnology. Current genome editing technologies are rapidly advancing with CRISPR which was awarded the Nobel Prize in Chemistry in 2022 and is now widely utilized in laboratories around the world. This presentation will provide an overview of the history of genome editing, outlining key developments and breakthroughs that have shaped the field. Particular attention will be given to the recent advancements in mitochondrial genome editing, a novel approach that has expanded the scope of genetic research and therapeutic potential. Finally, the future of Genome editing will be discussed, highlighting emerging technologies and their anticipated applications in medicine, biotechnology, and beyond.

**Keywords:** Genome Editing, CRISPR, Organelle, Mitochondria, Gene Therapy





**TIS1-2 From Understanding to Programming Life:  
Emerging Technologies for Reconstructing Biological Systems**

# Engineering Living Systems: From Bottom-Up Design to Translational Biological Systems

Keel Yong LEE

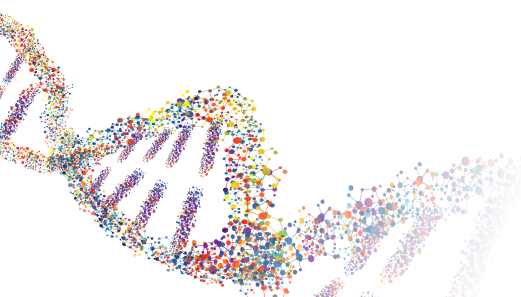
*Department of Integrative Bioscience and Biotechnology, Sejong University, Seoul, Republic of Korea*

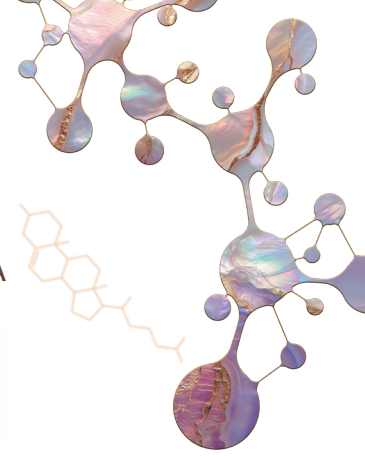
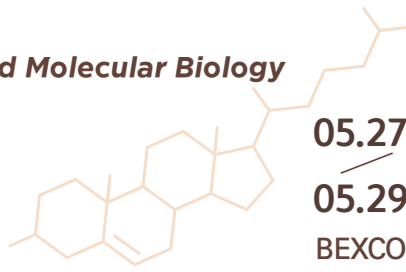
Biological function emerges from precisely organized architectures spanning molecular, cellular, and tissue scales. Our research investigates how nature encodes function through structure and translates these design principles into engineered living systems with programmable and translational capabilities. By integrating synthetic biology, stem cell engineering, and tissue biofabrication, we build biological systems across multiple scales to uncover and harness fundamental organizational rules.

At the molecular scale, bottom-up synthetic cellular platforms reconstruct life-like metabolic functions through artificial organelles and protocellular systems. By embedding photosynthetic protein machinery within lipid membrane compartments, these platforms achieve spatially organized ATP generation and regulation, emulating key metabolic behaviors of living cells. At the tissue scale, stem cell-derived cardiac microphysiological systems capture disease-relevant structural and electrophysiological features of the human heart. iPSC-derived cardiomyocytes integrated into biomimetic organ-on-a-chip platforms provide a mechanistic window into how altered structure–function coupling drives inherited arrhythmogenic disorders.

At the systems scale, biohybrid living machines combine engineered biological tissues with synthetic structural frameworks to convert intrinsic biological actuation into autonomous motion. Through biomimetic geometrical design and cardiac mechano-electrical feedback, these systems reveal governing principles for self-sustaining biological actuation. By connecting nature's form–function relationships across biological scales, this work provides a foundation for disease modeling, regenerative medicine, and adaptive biomedical technologies

**Keywords:** Structure–Function Relationships, Synthetic Biology, Microphysiological Systems, Biohybrid Systems, Living Systems Engineering





**TIS1-3 From Understanding to Programming Life:  
Emerging Technologies for Reconstructing Biological Systems**

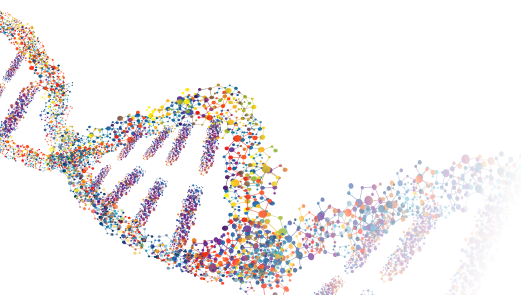
# **Tubular Hepatobiliary Tissue Construct Enabling Bile Acid Drainage for Treating Pediatric Hepatobiliary Diseases**

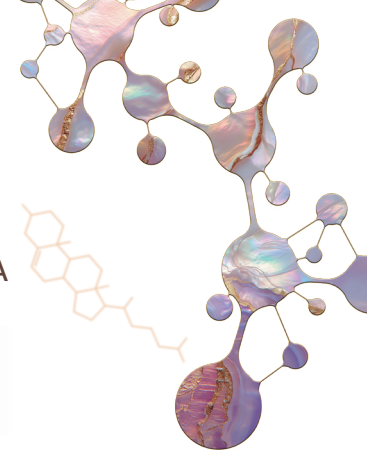
Seon-Jin KIM

*Pohang University of Science and Technology (POSTECH)*

Bile acid drainage (BAD) failure characterizes severe pediatric hepatobiliary disorders like biliary atresia and Alagille syndrome, ultimately requiring transplantation. While organoids replicate aspects of liver function, they fail to recapitulate BAD due to lacking a macroscopic tubular bile duct (BD). To address this, we developed a tubular hepatobiliary tissue construct (THTC) enabling hierarchical bile acid (BA) transport and drainage. Using a liver-specific bioink and in-bath co-axial bioprinting, we engineered a THPTC that features a multi-scale intrahepatic BD at the native scale. Within this THPTC, bile canaliculi formation reached levels comparable to native pediatric liver tissue. To validate functional BA transport from hepatocytes to the BD, we confirmed BD morphogenesis and structural integrity via immunofluorescence. Crucially, forskolin-induced BD lumen swelling confirmed the BD's active secretory function, and its physiological reactivity to acetylcholine verified the capacity for active BA uptake and drainage. Evaluating various THPTC configurations, we established that active BA transport and drainage exclusively occurs when cholangiocytes form a macroscopic tube. This proved that a 3D tubular geometry cue is essential to overcome the BAD limitations of closed-geometry organoids. Ultimately, our THPTC demonstrates profound potential as a transplantable tissue construct, representing a substantial step toward organ replacements for pediatric hepatobiliary disorders.

**Keywords:** Bioprinting, Tubular, Hepatobiliary, Tissue Construct, Bile acid drainage





**TIS1-4 From Understanding to Programming Life:  
Emerging Technologies for Reconstructing Biological Systems**

**Cross-species intestinal organoids for comparative vertebrate stem cell Intestinal organoid zoo of 26 species reveals conserved and divergent programs of biology**

Sujin PARK<sup>1,#</sup>, Youngchul OH<sup>1,2,#</sup>, Sangmin LEE<sup>1,3,#</sup>, Thomas M. KLOMPSTRA<sup>1,4,#</sup>, Jeongmin HA<sup>1</sup>, Young-Woong KIM<sup>1</sup>, Hyo-Yeong OH<sup>1</sup>, Se-Mi KIM<sup>5</sup>, Eun-Ha KIM<sup>6</sup>, Isaac CHOI<sup>5</sup>, Seo-Young HEO<sup>5,7</sup>, Jae-Woo AHN<sup>5</sup>, Seung-Gyu JANG<sup>6,8</sup>, Young-Il KIM<sup>9</sup>, Tim SCHMÄCHE<sup>9,10</sup>, Tae-Keun JEONG<sup>4</sup>, Jun KIM<sup>11,12</sup>, Yeongjun KIM<sup>1,3</sup>, Ohbin KWON<sup>1,13</sup>, Dae-Sik LIM<sup>4,13</sup>, Daeryeok KO<sup>4,13</sup>, Hanseul YANG<sup>4,13</sup>, YongKeun PARK<sup>14,15,16,17</sup>, Dong-Hyeok KWON<sup>18</sup>, Goo JANG<sup>18</sup>, Jeong Hun KIM<sup>19,20</sup>, Bo-Young JEON<sup>21</sup>, Tae Il KIM<sup>22</sup>, Hyunki KIM<sup>23</sup>, Ji-Su KIM<sup>24</sup>, Kyoung-Sun LEE<sup>25</sup>, Thomas J. PARK<sup>26</sup>, Daniel E. STANGE<sup>9,10</sup>, Ki-Jun YOON<sup>4,13,27</sup>, Ho-Seok LEE<sup>1,3</sup>, Jong Kyoung KIM<sup>2</sup>, Ji-Hyun LEE<sup>1</sup>, Hyunjoon KIM<sup>5,\*</sup>, Young Ki CHOI<sup>15,6,7,8,\*</sup>, Bon-Kyoung KOO<sup>1,2,13,\*</sup>, and Heetak LEE<sup>1,\*</sup>

<sup>1</sup>Center for Genome Engineering, Institute for Basic Science, Expo-ro 55, Yuseong-gu, Daejeon 34126, Republic of Korea.

<sup>2</sup>Department of Life Sciences, Pohang University of Science and Technology (POSTECH), Pohang 37673, Republic of Korea.

<sup>3</sup>Department of Biology, College of Sciences, Kyung Hee University, Seoul 02447, Republic of Korea.

<sup>4</sup>Department of Biological Sciences, Korea Advanced Institute of Science and Technology (KAIST), Daejeon, Republic of Korea

<sup>5</sup>Center for Study of Emerging and Re-emerging Viruses, Korea Virus Research Institute, Institute for Basic Science, Daejeon 34126, Republic of Korea.

<sup>6</sup>Virus Research Resource Center, Korea Virus Research Institute, Institute for Basic Science, Daejeon 34126, Republic of Korea.

<sup>7</sup>Department of Metabiohealth, Sungkyunkwan University, Suwon 16419, Republic of Korea.

<sup>8</sup>College of Medicine and Medical Research Institute, Chungbuk National University, 1 Chungdae-ro, Seowon-gu, Cheongju 28644, Republic of Korea.

<sup>9</sup>Department of Visceral, Thoracic and Vascular Surgery, Medical Faculty and University Hospital Carl Gustav Carus, Technische Universität Dresden, Fetscherstraße 74, Dresden, 01307, Germany

<sup>10</sup>National Center for Tumor Diseases Dresden (NCT/UCC), a partnership between DKFZ, Faculty of Medicine and University Hospital Carl Gustav Carus, TUD Dresden University of Technology, and Helmholtz-Zentrum Dresden - Rossendorf (HZDR), Dresden, Germany

<sup>11</sup>Department of Convergent Bioscience and Informatics, College of Bioscience and Biotechnology, Chungnam National University, 99, Daehak-ro, Yuseong-gu, Daejeon 34134, Republic of Korea.

<sup>12</sup>Graduate School of Life Sciences, College of Bioscience and Biotechnology, Chungnam National University, 99, Daehak-ro, Yuseong-gu, Daejeon 34134, Republic of Korea.

<sup>13</sup>Graduate School of Stem Cell and Regenerative Biology, KAIST, Daejeon, Republic of Korea.

<sup>14</sup>Graduate School of Medical Science and Engineering, Korea Advanced Institute of Science and Technology (KAIST), Daejeon 34141, Republic of Korea

<sup>15</sup>KAIST Institute for Health Science and Technology, Daejeon 34141, Republic of Korea

<sup>16</sup>Tomocube Inc., Daejeon, Republic of Korea

<sup>17</sup>Department of Physics, KAIST, Daejeon 34141, Republic of Korea

<sup>18</sup>Laboratory of Theriogenology and Biotechnology, Department of Veterinary Clinical Sciences, College of Veterinary Medicine, Seoul National University, Seoul, Republic of Korea.

<sup>19</sup>Fight against Angiogenesis-Related Blindness (FARB) Laboratory, Biomedical Research Institute, Seoul National University Hospital, Seoul 03080, Republic of Korea.

<sup>20</sup>Department of Ophthalmology, Seoul National University College of Medicine, Seoul 03080, Republic of Korea.

<sup>21</sup>Department of Biomedical Laboratory Science, College of Software and Digital Healthcare Convergence, Yonsei University, Wonju 26493, Republic of Korea.

<sup>22</sup>Department of Internal Medicine and Institute of Gastroenterology, Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea.

<sup>23</sup>Department of Pathology, Yonsei University College of Medicine, Seoul, Republic of Korea.

<sup>24</sup>Primate Resources Center, Korea Research Institute of Bioscience and Biotechnology (KRIBB), Jeongeup-si, Jeonbuk 56216, Republic of Korea.

<sup>25</sup>Non-Clinical Evaluation Center, Osong Medical Innovation Foundation, Cheongju, Republic of Korea.

<sup>26</sup>Laboratory of Integrative Neuroscience, Department of Biological Sciences, University of Illinois Chicago, Chicago, IL 60607, USA.

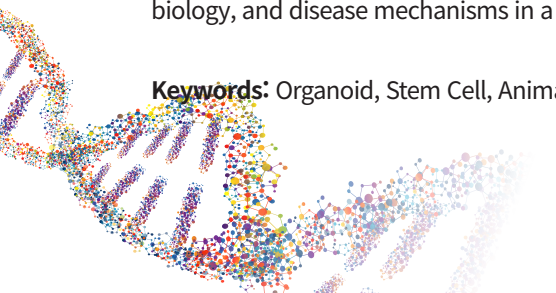
<sup>27</sup>KAIST-Wonjin Cell Therapy Center, KAIST, Daejeon, Republic of Korea.

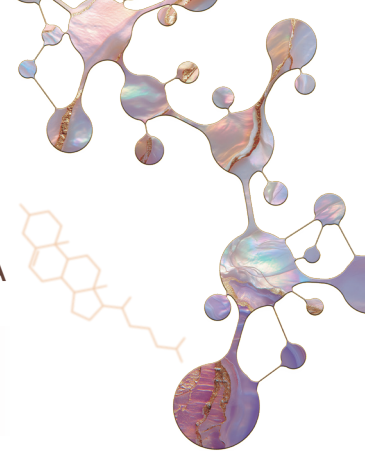
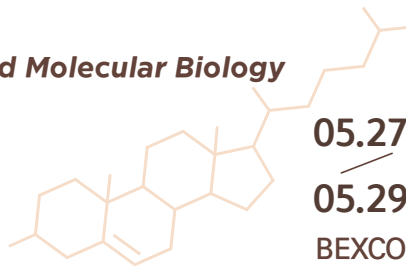
\*These authors contributed equally to this work.

Comparative genomics has revealed extensive diversity across species, but functional studies of vertebrate biology have been limited by the lack of a unified experimental platform. To address this, we established an “organoid zoo” consisting of small intestinal organoids derived from a wide range of vertebrate species and maintained under standardized culture conditions. This adult stem cell-based platform enables direct cross-species comparisons of stem cell features, regenerative potential, viral susceptibility, and drug responses.

Using this system, we identified conserved intestinal stem cell markers across distant species and demonstrated that organoid-based comparative analysis can uncover both shared and species-specific biological traits. The platform also allowed us to investigate differences in regeneration, host-virus interactions, and pharmacological responses across animals. Overall, the organoid zoo provides a scalable and versatile framework for studying biodiversity, stem cell biology, and disease mechanisms in a controlled environment.

**Keywords:** Organoid, Stem Cell, Animal Science, Comparative biology





**TIS1-5 From Understanding to Programming Life:  
Emerging Technologies for Reconstructing Biological Systems**

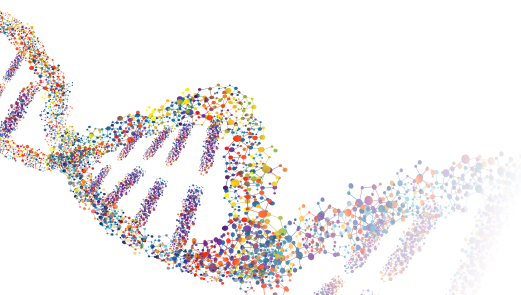
# Remodeling tissue-wide networks to promote repair through mosaic and transient in vivo reprogramming

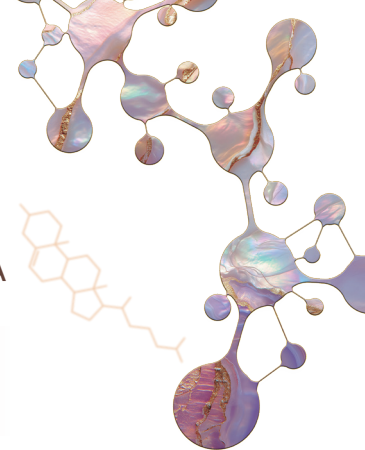
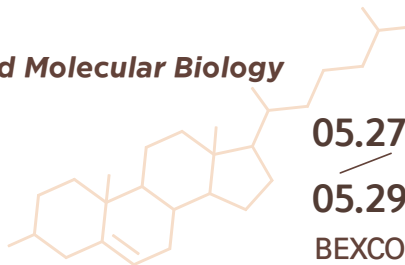
Minjun KWAK

*Department of Life Sciences, Pohang University of Science and Technology (POSTECH), Pohang, Republic of Korea*

Cellular reprogramming is the process of converting a differentiated cell into another cell type by altering its gene expression and identity. It was first achieved through the introduction of the Yamanaka factors (Oct4, Sox2, Klf4, and c-Myc), which reprogram somatic cells into induced pluripotent stem cells. More recently, in vivo partial reprogramming—established by transiently introducing Yamanaka factors into living tissues to induce moderate cellular plasticity—has emerged as a promising approach to reshape cellular states and fates within intact biological systems. This approach has demonstrated reproducible functional improvements across multiple tissues, including the restoration of aging-associated phenotypes, enhanced regeneration, and improved tissue function. In this talk, we introduce recent findings showing that the effects of in vivo partial reprogramming are not limited to the reprogrammed cells themselves, but can extend to neighboring cells and the surrounding microenvironment. This was accomplished through mosaic partial epidermal reprogramming, in which transient expression of Yamanaka factors was induced in a subset of epidermal cells. This induced injury-responsive-like healing properties not only in the reprogrammed cells themselves, but also in neighboring epithelial cells and the skin immune niche, even in the absence of actual injury. Upon actual wounding, this led to accelerated re-epithelialization, along with altered angiogenic patterns and reduced scar formation. Furthermore, the beneficial effects were also observed in a hyperglycemic disease model, where an improvement in wound healing kinetics was evident. Together, these findings highlight in vivo partial reprogramming as a promising strategy to systemically modulate tissue-wide networks and improve regenerative outcomes.

**Keywords:** Partial reprogramming, Yamanaka factors, wound healing, epidermal stem cells





**TIS2-1** Toward Predictive Metabolism: Multimodal AI, Wearable Sensors, and Lifelog Data for Disease Prediction

# From Data to Foresight: Generative Multimodal AI for Early Disease Prediction and Precision Medicine

Hwiyoung KIM

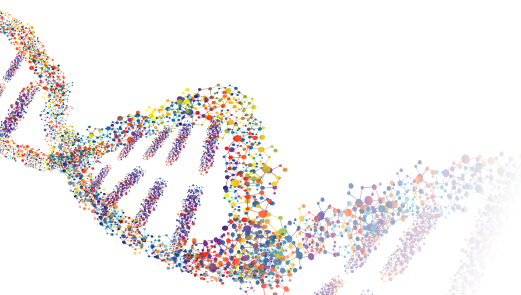
*Hallym University Medical Center*

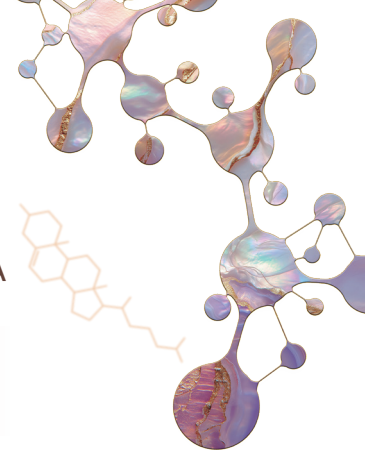
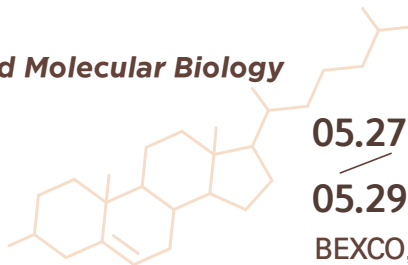
Recent advances in generative artificial intelligence (AI) are transforming healthcare from reactive diagnosis to proactive and predictive medicine. This talk introduces a unified framework for multimodal AI that integrates wearable sensor data, lifelog records, and clinical information to enable early disease prediction and personalized intervention.

Building on these data streams, multimodal AI models—including transformer-based architectures and large language multimodal models—can fuse heterogeneous inputs such as electronic health records, laboratory results, and biosignals to predict disease onset and progression. Recent studies demonstrate the feasibility of early prediction of conditions like insulin resistance using multimodal learning frameworks. Furthermore, lifelog-based activity modeling enables continuous health state estimation, offering new opportunities for digital biomarker discovery and real-time risk stratification.

This lecture emphasizes how generative AI extends beyond prediction to interpretation and clinical reasoning by translating complex multimodal data into actionable insights. By bridging real-world data and mechanistic biological understanding, these approaches accelerate translational medicine and support the development of clinically deployable, personalized AI systems. Practical use cases—including early disease detection, treatment response prediction, and AI-assisted clinical decision-making—will be discussed, along with challenges in reliability, interpretability, and integration into healthcare systems.

**Keywords:** Generative AI, multi-modal, disease prediction, precision medicine





**TIS2-2** Toward Predictive Metabolism: Multimodal AI, Wearable Sensors, and Lifelog Data for Disease Prediction

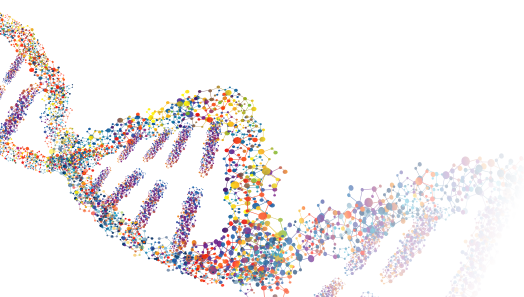
# Generative AI-Driven Analysis of Lifelog Multimodal Data for Health Prediction

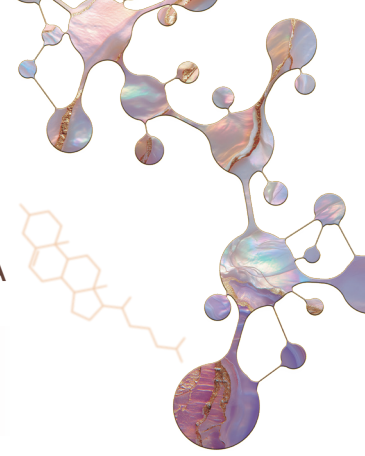
Soo Youn LEE

*Division of Healthcare Artificial Intelligence Research, National Institute of Health*

Recent advances in generative AI and multimodal data analysis are rapidly expanding lifelog-based digital healthcare research. This lecture introduces recent research trends in applying artificial intelligence to lifelog multimodal data for the analysis and prediction of sleep, stress, emotion, and cardiovascular health status. Particular attention is given to data collected from wearable devices, including photoplethysmography (PPG), heart rate variability (HRV), physical activity, sleep, and behavioral patterns, which are increasingly used to capture dynamic changes in individual health. Recent studies using CNN, BiLSTM, and Transformer-based models have shown promising performance in sleep stage classification, stress detection, emotion recognition, autonomic nervous system assessment, and early identification of cardiovascular risk signals. In addition, the integration of large language models (LLMs) and generative AI has broadened the possibility of contextual interpretation and personalized inference from lifelog data. This lecture aims to highlight how AI-driven lifelog analytics can support the next generation of digital healthcare and precision health management.

**Keywords:** LLM, Lifelog, AI, Generative AI





**TIS2-3** Toward Predictive Metabolism: Multimodal AI, Wearable Sensors, and Lifelog Data for Disease Prediction

# Host Metabolic Rewiring as a Therapeutic Target: A Genome-Scale Metabolic Model for Rapid Antiviral Discovery

Yong-ki LEE<sup>A,b,c,\*</sup>, Seongmo KANG<sup>B,\*</sup>, JinA LIM<sup>B,\*</sup>, Kanghee KIM<sup>A,d</sup>, Se-Mi KIM<sup>A</sup>,  
Mark Anthony B. CASEL<sup>A</sup>, Issac CHOI<sup>A</sup>, Young Ki CHOI<sup>A,d,#</sup>, Hyun Uk KIM<sup>B,e,f,#</sup>,  
Yoosik KIM<sup>B,c,e,g,#</sup> (\*co-first, #corresponding)

<sup>a</sup>Center for Study of Emerging and Re-emerging Viruses, Korea Virus Research Institute, IBS, Daejeon, Republic of Korea

<sup>b</sup>Department of Chemical and Biomolecular Engineering, KAIST, Daejeon, Republic of Korea

<sup>c</sup>KAIST Institute for Health Science and Technology, KAIST, Daejeon 34141, Republic of Korea

<sup>d</sup>College of Medicine and Medical Research Institute, Chungbuk National University, Cheongju 28644, Republic of Korea

<sup>e</sup>Graduate School of Engineering Biology, KAIST, Daejeon 34141, Republic of Korea

<sup>f</sup>BioProcess Engineering Research Center and Bioinformatics Research Center, KAIST, Daejeon 34141, Republic of Korea

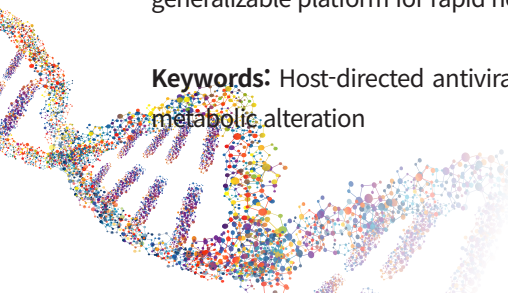
<sup>g</sup>KAIST Institute for BioCentury, KAIST, Daejeon 34141, Republic of Korea

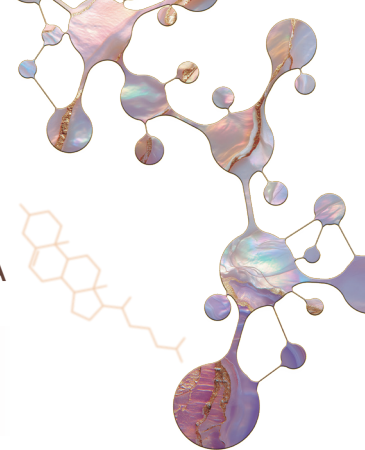
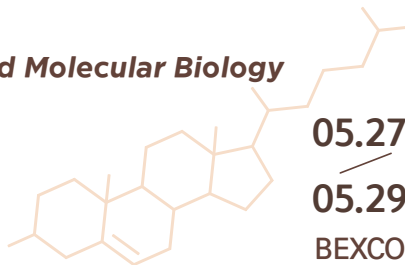
Emerging viral threats demand antiviral strategies faster than conventional drug screening or virus-specific characterization can provide. Here, we present a transcriptome-based computational framework combining genome-scale metabolic models (GEMs) with Uniform Manifold Approximation and Projection (UMAP)-based dimensionality reduction to systematically identify host metabolic vulnerabilities exploited during viral infection. The framework builds infection-specific GEMs from RNA-seq data, performs single-gene knockout simulations, and pinpoints genes whose perturbation restores the infected metabolic flux profile toward an uninfected state.

Applying this framework across multiple human coronavirus-infected models revealed distinct and conserved host metabolic targets. In HCoV-229E-infected MRC-5 cells, porphyrin metabolism emerged as a key target, and knockdown of ALAD and SLC25A38 reduced viral replication. In HCoV-OC43-infected A549-ACE2 cells, oxidative phosphorylation complex IV was identified, and its inhibition with ADDA 5 effectively suppressed viral replication. In HCoV-OC43-infected HBE organoids, complex I was highlighted instead, and treatment with IACS-010759 reduced viral replication. In both SARS-CoV-2- and MERS-CoV-infected HBE organoids, pyrimidine catabolism consistently emerged as a conserved target, and inhibition of its rate-limiting enzyme DPYD with Eniluracil significantly suppressed replication of both viruses.

Notably, none of these targets were detectable by conventional differential gene expression or pathway enrichment analyses, underscoring the unique advantage of our metabolic flux-based approach. These results establish a generalizable platform for rapid host-directed antiviral discovery without prior viral characterization.

**Keywords:** Host-directed antiviral discovery; Genome-scale metabolic model; Dimensionality reduction; Virus-induced metabolic alteration





**TIS2-4** Toward Predictive Metabolism: Multimodal AI, Wearable Sensors, and Lifelog Data for Disease Prediction

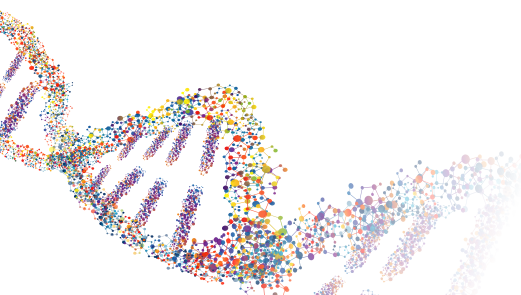
## Wearable Microfluidic Platform for Label-Free Metabolite Profiling in Sweat

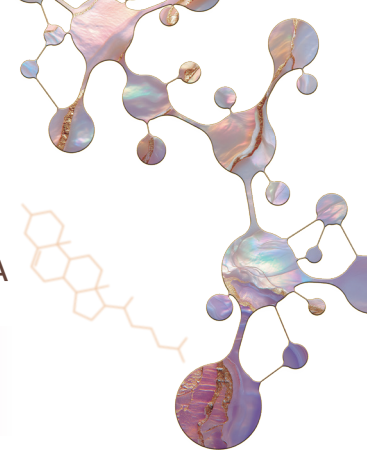
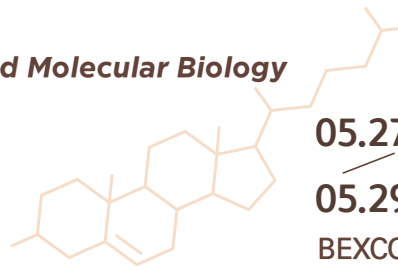
Jaehun JEON

KAIST

Metabolic profiling offers significant insights into individual physiological states, enhancing the scope of digital phenotyping and advancing personalized healthcare. Recent biosensing wearables monitor the metabolic kinetics in biological fluids such as tear fluid, saliva, or sweat. Sweat, unlike others, exhibits chemical abundance and simple sample collection with less contamination, thus allowing in-situ profiling of metabolite alteration in proactive healthcare. Furthermore, sweat is readily collected by epidermal interfaces with simple absorbents, or microfluidic patches, exhibiting high compatibility with assorted wearable sensors. Such epidermal sweat sensors often utilize electrochemical or colorimetric methods. However, molecular recognition elements such as antibodies or enzymes on active sensing sites still constrain multiplexed and unbiased biomarker detection, hindering full insight into individual physiology. This presentation reports an all-flexible chronoepifluidic surface-enhanced Raman spectroscopy (SERS) patch for label-free and chronometric profiling of sweat metabolites. The nanoplasmonic structures are interfaced with the functional microfluidic network for chronometric sweat collection and analysis. The wearable patch adheres conformally to skin, collects sequential sweat samples, and supports label-free and multiplexed SERS detection of assorted metabolites. Machine learning-assisted quantification of lactate, uric acid, and tyrosine yields robust metabolic profiles in distinct physical activity states. Such unique integration of nanoplasmonics, microfluidics, and machine learning also allows biomarker candidate narrowing for diverse physiological conditions. This wearable optofluidic sensor platform advances molecular sweat sensing and offers a new paradigm for individualized phenotyping toward proactive, data-driven healthcare.

**Keywords:** Sweat, Metabolite profiling, Wearable sensors, Label-free, Microfluidics





**TIS2-5** Toward Predictive Metabolism: Multimodal AI, Wearable Sensors, and Lifelog Data for Disease Prediction

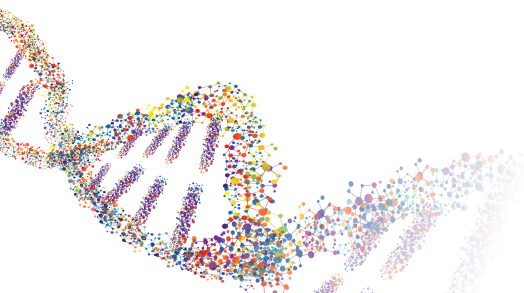
# Predicting Metabolic and Cardiovascular Diseases from Lifestyle Questionnaires: Quantifying the Incremental Value of Clinical Measurement

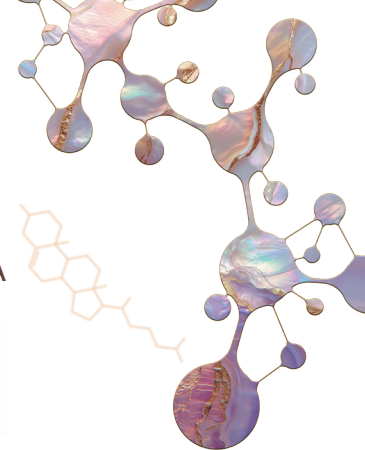
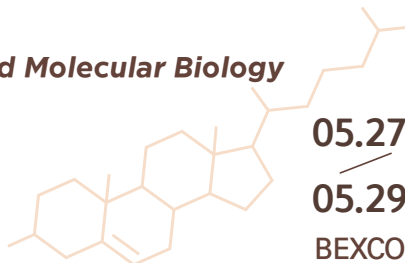
Minkyung CHOI, Younghee LEE

*Lab. of Veterinary Informatics and Bioinformatics, College of Veterinary Medicine, Seoul National University*

Modifiable lifestyle factors such as diet, physical activity, sleep, and alcohol consumption are well-established contributors to metabolic and cardiovascular disease risk. While these factors can be captured through self-administered questionnaires without clinical measurement, their standalone predictive capacity has rarely been evaluated across multiple chronic diseases within a unified analytical framework. In this study, we analyzed 2,811 adults (mean age 46.2 years; 54.3% male) from the Korea 4K cohort to predict nine chronic diseases using regularized logistic regression on self-administered lifestyle questionnaires covering 16 domains. Four predictor configurations were compared: questionnaire alone, health checkup measurements alone, both combined, and a hierarchical design that quantifies the incremental value of clinical data on top of questionnaire predictors. Questionnaire-only models achieved  $AUC \geq 0.70$  for five of nine diseases and approached this threshold for two others, demonstrating that lifestyle patterns carry substantial predictive information for most metabolic and cardiovascular conditions without any clinical measurement. Adding health checkup data significantly improved prediction for most diseases, but the magnitude of gain varied markedly — large for conditions defined by direct physical measurements, modest where lifestyle patterns already captured much of the disease risk. This disease-specific pattern provides an empirical basis for determining which conditions can be effectively screened through lifestyle assessment alone and which require clinical measurement. Building on these findings, future work will integrate continuous lifelog and wearable sensor data to construct cross-disease comorbidity maps, moving from single-disease prediction toward simultaneous multi-disease risk profiling for personalized early intervention.

**Keywords:** lifestyle questionnaire, chronic disease prediction, metabolic disease, hierarchical modeling, comorbidity mapping





**TIS3-1 Genome State Rewiring in Cancer: Hidden Drivers of Tumor Evolution and Therapy Resistance**

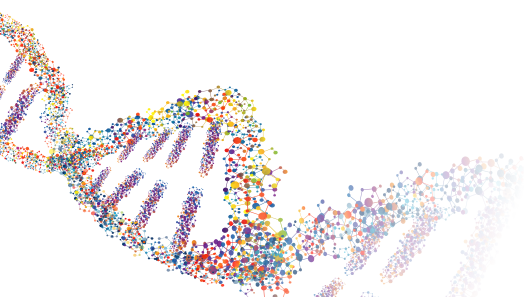
# Investigating and translating for potential clinical application of molecular mechanisms of genomic integrity

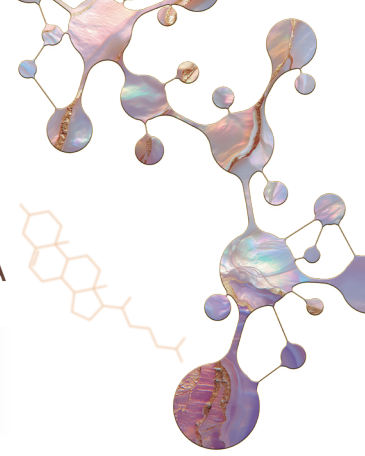
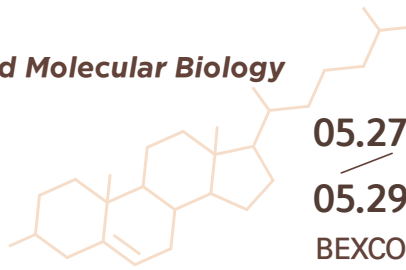
Kyungjae MYUNG

*IBS, UNIST*

Homologous recombination (HR) is crucial for maintaining genomic integrity and is tightly regulated, yet the role of ubiquitin-dependent degradation in HR proteins remains poorly understood. Through high-throughput screening for compounds that modulate the DNA replication stress response, we identified ML367 and its derivative, UNI418. Kinase profiling and detail molecular analyses revealed that UNI418 inhibits PIKfyve and PIP5K1C, reducing inositol hexaphosphate (IP6) levels and triggering Cul4A-dependent degradation of RAD51, CtIP, and CHK1. Further analysis identified WDR5 as a DCAF protein that facilitates Cul4A-mediated proteolysis of RAD51 and CHK1. Functionally, UNI418 suppresses HR, enhances tumor sensitivity to PARP inhibitors (PARPis), and re-sensitizes PARPi-resistant tumor cells in both in vitro and in vivo xenograft models. These findings reveal a previously unrecognized Cul4A-WDR5-dependent proteolysis pathway regulating HR protein stability via phosphatidyl inositol signaling. This mechanism offers a promising therapeutic strategy for overcoming PARPi resistance and improving combinatorial cancer treatment strategies.

**Keywords:** Cancer, PARP inhibitor, homologous recombination, proteolysis, drug resistance





**TIS3-2 Genome State Rewiring in Cancer: Hidden Drivers of Tumor Evolution and Therapy Resistance**

# Radiotherapy-induced senescent cells orchestrate a pro-metastatic niche and drive radio-resistance in head and neck cancer

Yuseong LEE<sup>1</sup>, Seok June HONG<sup>1</sup>, MinJeong KIM<sup>2,3</sup>, Young Chan LEE<sup>2,3</sup>, Kwoneel KIM<sup>1,4</sup>

<sup>1</sup>Department of Biomedical and Pharmaceutical Sciences, Kyung Hee University, Seoul, Republic of Korea

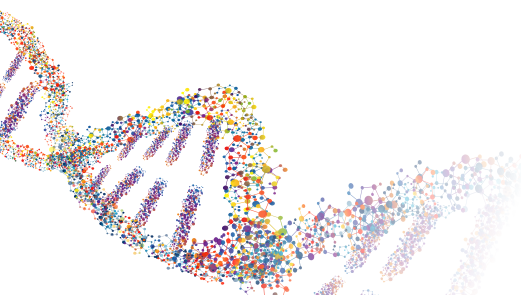
<sup>2</sup>Department of Medicine (AgeTech-Service Convergence Major) College of Medicine, Kyung Hee University, Seoul, Republic of Korea

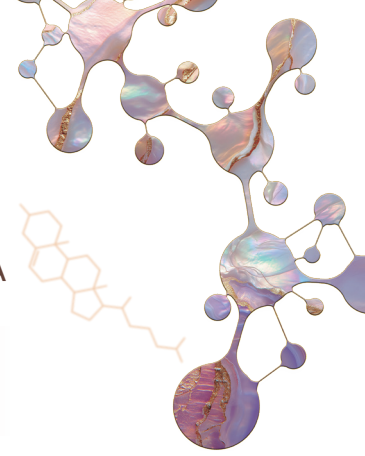
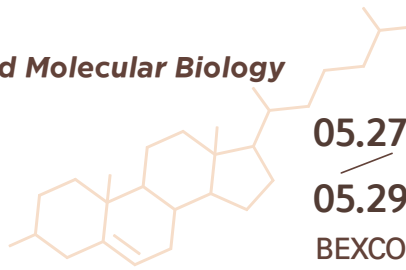
<sup>3</sup>Department of Otolaryngology-Head and Neck Surgery, Kyung Hee University School of Medicine, Kyung Hee University Hospital at Gangdong, Seoul, Republic of Korea

<sup>4</sup>Department of Biology, Kyung Hee University, Seoul, Republic of Korea

Radiotherapy is a cornerstone treatment for head and neck squamous cell carcinoma (HNSCC), yet therapeutic efficacy is frequently limited by tumor recurrence driven by radio-resistance. Emerging evidence implicates therapy-induced senescence (TIS) as a critical contributor to this process; however, the molecular identity of TIS cells and their functional roles within the tumor microenvironment (TME) remain insufficiently defined. Here, we integrate bulk RNA sequencing, single-cell transcriptomics, and spatial transcriptomics to systematically characterize radiotherapy-induced senescent cells in HNSCC. We delineate their transcriptional programs, identify key regulatory networks, and trace their clonal dynamics, revealing distinct molecular signatures that distinguish TIS cells from other tumor populations. Spatial and ligand-receptor interaction analyses further demonstrate that TIS cells actively remodel the TME by establishing a pro-metastatic niche. Specifically, senescence-associated secretory phenotypes (SASPs) derived from TIS cells promote endothelial permeability and drive invasive phenotypic transitions in adjacent malignant cells. Collectively, these findings define the molecular and functional landscape of TIS cells in HNSCC and uncover their central role in tumor relapse, highlighting TIS-associated signaling as a potential therapeutic target to overcome radio-resistance.

**Keywords:** Radio-resistance, Radiotherapy-induced senescence, Tumor microenvironment remodeling, SASPs





**TIS3-3 Genome State Rewiring in Cancer: Hidden Drivers of Tumor Evolution and Therapy Resistance**

# Transcriptomic Dissection of the Tumor Microenvironment to Guide Target Discovery and Response Prediction

Hee Jin CHO

<sup>1</sup>Department of Biomedical Convergence Science and Technology, Advanced Institute of Science and Technology, Kyungpook National University, Daegu 41566, Republic of Korea

<sup>2</sup>Department of Advanced Bioconvergence, Kyungpook National University, Daegu 41944, Republic of Korea

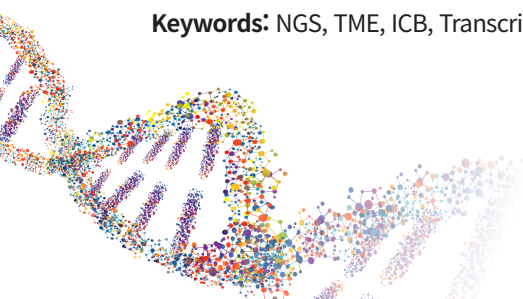
The advent of next-generation sequencing (NGS) has transformed cancer treatment, with transcriptomic data emerging as a cornerstone in precision oncology. Beyond identifying therapeutic targets, transcriptomics now plays a pivotal role in predicting patient responses to treatment, particularly in the context of immunotherapy. Despite the success of immune checkpoint blockade (ICB), only a subset of patients experience durable clinical benefits, highlighting the urgent need to better understand the tumor microenvironment (TME) and identify predictive biomarkers.

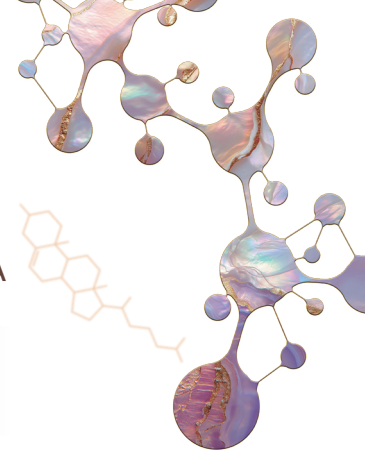
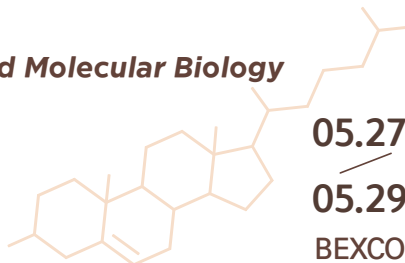
To address this, we performed integrative transcriptomic analyses in a phase II clinical trial evaluating the anti-VEGF receptor tyrosine kinase inhibitor pazopanib in combination with the anti-PD-L1 antibody durvalumab in patients with metastatic or recurrent soft tissue sarcoma (STS). The combination therapy demonstrated promising clinical activity with an overall response rate of 30.4% and a median progression-free survival of 7.7 months.

Transcriptome-guided immune profiling revealed that a B-lineage transcriptional signature was significantly associated with therapeutic response. Consistent with these findings, *in situ* analyses demonstrated that tumors with high CD20 B-cell infiltration and increased vessel density exhibited significantly longer progression-free survival and higher response rates than tumors with low B-cell infiltration. Multivariate analysis further identified CD20 B-cell infiltration as the only independent predictor of progression-free survival.

These findings underscore the potential of transcriptome-based TME profiling to identify predictive biomarkers and guide rational combination strategies integrating immune checkpoint blockade with anti-angiogenic therapy. Such transcriptomic frameworks may facilitate the development of more effective immunotherapy combinations across diverse cancer types.

**Keywords:** NGS, TME, ICB, Transcriptome, Cancer





**TIS3-4 Genome State Rewiring in Cancer: Hidden Drivers of Tumor Evolution and Therapy Resistance**

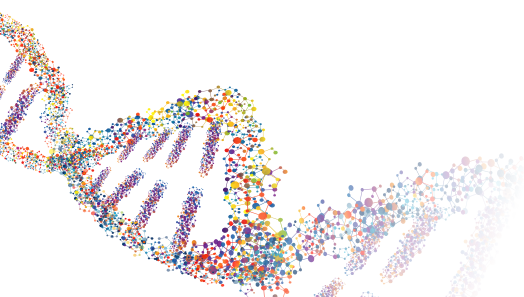
## Toward Anti-Cancer Anti-Resistance Therapy

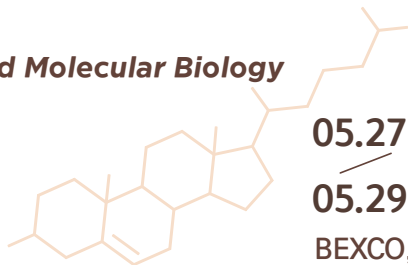
Taeyoung YOON

*Oscotec Inc.*

Drug resistance remains one of the most formidable obstacles in modern cancer therapy. Emerging evidence suggests that, in response to the genotoxic stress of anti-cancer treatment, cancer cells undergo transient whole-genome duplication. While this polyploid state provides a survival advantage at the expense of proliferation (thereby cancer dormancy), cells may subsequently undergo meiosis-like depolyploidization, generating stem-like progeny that re-enter the cell cycle and give rise to proliferative offsprings that acclimate to the hostile environment, hence acquired resistance. Therefore, targeting the ploidy cycle may offer a novel “anti-resistance” strategy. Thus, blockade of such an escape mechanism simultaneously with the standard-of-care anti-cancer drug treatment is anticipated to dramatically enhance the durability of the latter. Supporting evidence from selected literature, putative clinical observations, and our internal data along this line will be presented.

**Keywords:** drug resistance; drug tolerant persisters, polyploidy, combination

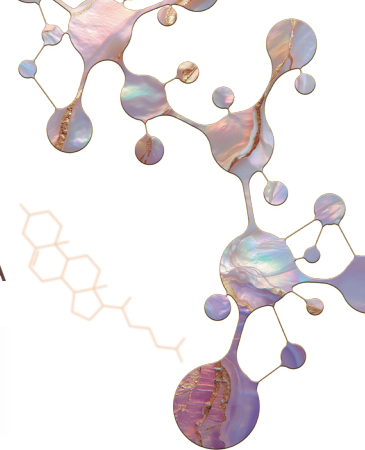




05.27<sup>(WED)</sup>

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BEXCO, BUSAN, KOREA



FROM MOLECULES TO MEGABYTES:  
AI AND BIG DATA TRANSFORMING LIFE SCIENCE

**TIS4-1** The Big Question: What is the Destiny of the ‘Wet Lab’ in the AI Era?

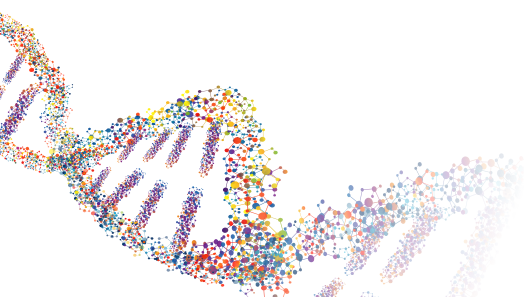
## Human learning vs. machine learning in AI-driven bio-discovery

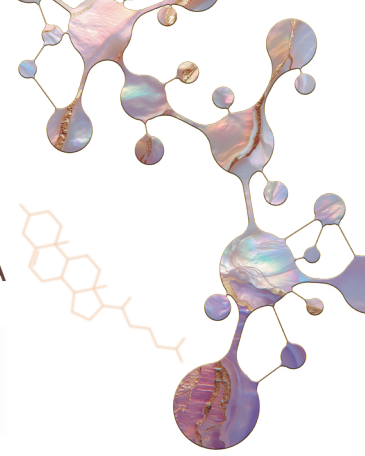
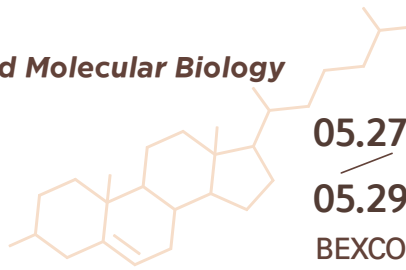
Sanguk KIM

*Pohang University of Science and Technology*

What is the role of a biologist in the age of AI? If AI continues to advance, what will biologists do? Artificial intelligence learns from data and performs well on familiar tasks and challenges. Then, who will step up to find solutions to the unknown and lesser-known questions? If AI-powered robots take over the task of producing data, what will humans do? The importance of asking good questions to drive good science becomes even more critical. Asking good questions requires an integrated knowledge of chemistry, physics, mathematics, and biology. Ultimately, the life sciences and biology are convergent disciplines. If artificial intelligence divides black and white, the gray area persists. Human intelligence becomes important in areas where problems are difficult to distinguish, and new hypotheses are required. Through this presentation, I intend to demonstrate several machine learning tasks that require various AI methods. However, the important thing is not the machine learning tasks themselves, but rather which question to focus on, what hypotheses can be formulated, and what the basis for those hypotheses is.

**Keywords:** Artificial intelligence, Bioinformatics, Drug discovery, Precision medicine, Machine learning





**TIS4-2 The Big Question: What is the Destiny of the 'Wet Lab' in the AI Era?**

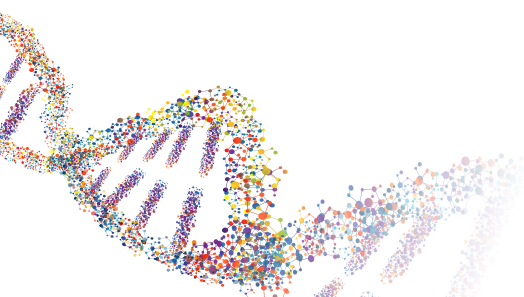
# Beyond Algorithms: The Essential Role of Wet Lab Biology in Adipose Tissue Research

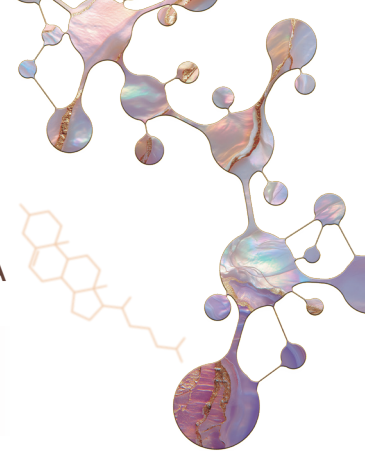
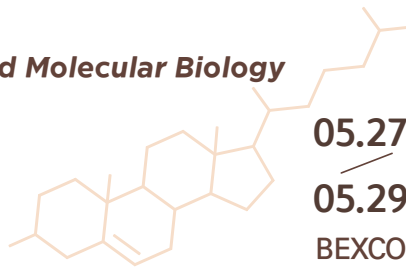
Jae Bum Kim

*Center for Adipocyte Structure and Function, Institute of Molecular Biology and Genetics,  
School of Biological Sciences, Seoul National University*

Adipose tissue plays a central role in maintaining whole-body energy homeostasis through its diverse metabolic, endocrine, and thermogenic functions. It serves as a dynamic reservoir for energy storage and mobilization, secretes a range of bioactive hormones, contributes to thermoregulation and insulation, and exerts significant influence on immune modulation. Broadly categorized into white adipose tissue (WAT) and brown adipose tissue (BAT), each depot exhibits distinct physiological roles: WAT primarily stores lipids, while BAT dissipates energy as heat. At the cellular level, adipocytes—classified as white, brown, or beige—carry out specialized functions aligned with these tissue-specific roles. Moreover, adipocytes engage in active crosstalk with various non-adipocyte populations, including immune cells, which shape the adipose tissue microenvironment and influence metabolic outcomes. In this presentation, I will provide an overview of the current understanding of adipose tissue biology, with a particular focus on the functional characteristics of adipocytes and their interactions with neighboring cells. Recent advances and emerging concepts in adipocyte research will also be discussed.

**Keywords:** Adipose tissue, WAT, BAT, thermogenesis





**TIS4-3 The Big Question: What is the Destiny of the ‘Wet Lab’ in the AI Era?**

## **BENEIN: Development and validation of a single-cell Boolean network pipeline for identifying master regulators of colorectal cancer reversion**

Jeong-Ryeol GONG\*, ChunKyung LEE\*, Hoon-Min KIM\*, Juhee KIM\*, Jaeog JEON, Geunyoung PARK, Jae Hyuk CHOI, Seoyoon JEONG, Hyemin LEE, Kwang-Hyun CHO

*Korea Advanced Institute of Science and Technology (KAIST), Daejeon, Republic of Korea*

Current anticancer therapies rely predominantly on cytotoxic strategies, yet remain limited by resistance and recurrence. Cancer reversion has emerged as an alternative paradigm that drives malignant cells toward a normal-like differentiated state. However, a systematic computational methodology for identifying master regulators governing entire differentiation trajectories has long been lacking.

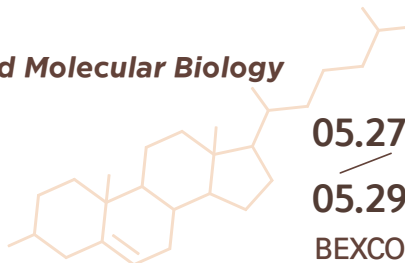
To address this, we developed BENEIN (single-cell Boolean network inference and control), a pipeline that reconstructs Boolean gene regulatory networks (GRNs) from single-cell transcriptomes and derives control targets. Using exonic and intronic reads, BENEIN partitions each cell into pre- and post-transition states, infers Boolean regulatory logic, and identifies master regulators through attractor analysis grounded in control theory.

Applying BENEIN to human colonic enterocyte differentiation, we identified MYB, HDAC2, and FOXA2 as master regulators. In three colorectal cancer cell lines (HCT-116, CACO-2, HT-29), their simultaneous knockdown suppressed proliferation and significantly reduced xenograft tumor growth. Transcriptomes of the reverted cells converged toward those of TCGA adjacent normal tissues, with inactivation of MYC and WNT pathways.

Unlike data-driven AI prediction, BENEIN is an interpretable, mechanistic framework built on Boolean logic and control theory that reconstructs cellular state-transition dynamics. Yet a network trained on normal differentiation is not guaranteed to hold in mutation-laden cancer cells, and partial simulation-experiment discrepancies were observed in this study. Selecting three regulators from five feedback vertex set candidates and validating them across three cell lines and xenograft models underscores that interpreting computational outputs in biological context and establishing causality ultimately depend on the biologist’s judgment and wet lab validation.

**Keywords:** Cancer reversion, Boolean gene regulatory network, Master regulator identification, Colorectal cancer, Single-cell transcriptomics

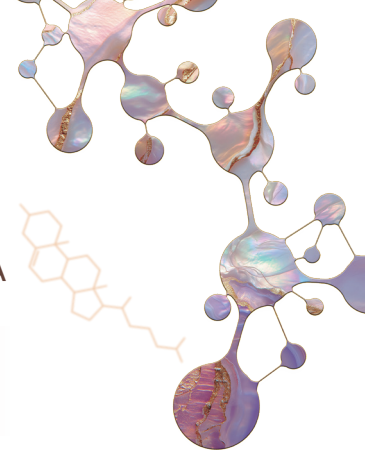




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FROM MOLECULES TO MEGABYTES:  
AI AND BIG DATA TRANSFORMING LIFE SCIENCE

**TIS4-4** The Big Question: What is the Destiny of the ‘Wet Lab’ in the AI Era?

## AI Needs Biology: Structure-Based Deep Learning for Mechanistic Modeling of Allostery in Ligand-Induced GPCR Activity

Hyojin SON\* and Gwan-Su YI

*Department of Bio and Brain Engineering, Korea Advanced Institute of Science and Technology (KAIST), Daejeon, Republic of Korea*

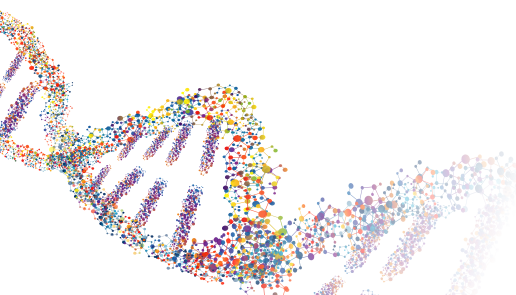
G protein-coupled receptors (GPCRs) are targeted by approximately 34% of approved drugs, yet predicting ligand-induced functional outcomes—agonism versus antagonism—remains a fundamental challenge. The difficulty is mechanistic: receptor activation is driven by cascading allosteric communication linking orthosteric binding to distal G-protein engagement. Prevailing sequence-based AI models are structurally disconnected from this biophysical process and systematically fail on allosterically complex receptors.

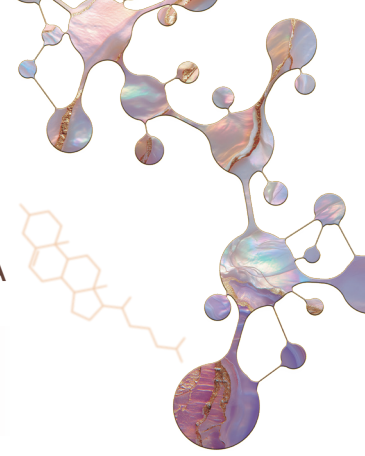
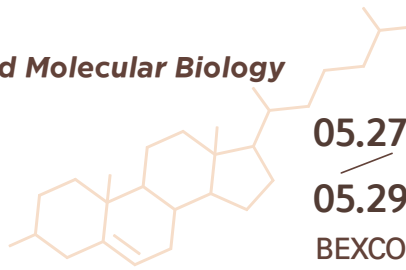
To address this, we developed GPCRact, a hierarchical E(n)-equivariant graph neural network (EGNN) that explicitly models the full activation cascade. Built upon atomistic 3D structural graphs of binding and allosteric sites, GPCRact employs a dual-attention architecture: cross-attention captures initial ligand-receptor interactions, while self-attention propagates allosteric signals toward distal G-protein coupling domains.

Validated on GPCRactDB, our large-scale database of curated GPCR-ligand interactions, GPCRact achieves state-of-the-art performance with particularly robust accuracy on allosterically complex receptors. Critically, learned attention weights independently recover validated allosteric pathways and conserved activation motifs (DRY, NPxxY), resolving the black-box limitation of prior methods.

Extending these mechanistic principles toward clinical translation, we demonstrate that AI-predicted functional profiles can systematically address coverage gaps in hierarchical in vitro assay chains, substantially improving the prediction of clinical approval outcomes. This finding crystallizes a central thesis: AI achieves its full predictive power only when grounded in mechanistic biological knowledge. The wet lab is not displaced—it is the compass that orients the model. The biologist’s role evolves accordingly: from bench operator to data architect, hypothesis generator, and interpreter of AI-driven discovery.

**Keywords:** GPCR; allosteric communication; equivariant graph neural network; drug discovery; wet lab-AI synergy





**ST1-1 AI-Driven Genomics: From Data Generation to Insights**  
(powered by Illumina)

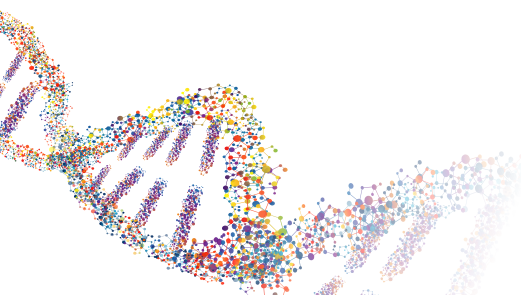
# **BIG LIFE: A Multi-Omics Digital Twin Cohort for Healthy Longevity and Future-Ready Prevention**

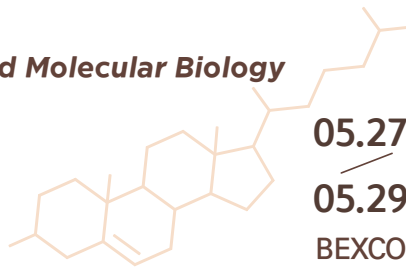
Jungmin CHOI

*Korea University, Korea*

The BIG LIFE Digital Twin Cohort is a 7-year, prospective, population-based study in Gimhae, South Korea, designed to shift healthcare from reactive treatment to predictive, preventive, personalized, participatory, and precision prevention. The cohort will enroll 10,000 adults aged 19–69 years and establish an integrated longitudinal platform combining clinical phenotypes, laboratory measures, lifestyle and dietary assessments, wearable signals, and multi-omics profiles spanning the genome, epigenome, transcriptome, proteome, metabolome, and microbiome. Using AI-powered multimodal analytics—including deep learning, network modeling, and causal inference—BIG LIFE will construct digital twins: dynamically updated virtual health profiles capable of modeling disease trajectories, simulating intervention scenarios, and identifying individualized windows for early prevention. The primary translational focus is early risk stratification and targeted intervention for cardiovascular disease, diabetes, obesity, and related cardiometabolic disorders. At the same time, the platform is designed to support satellite cohorts tailored to occupational and regional health priorities, including aerospace and marine workers, thereby enabling scalable and interoperable expansion beyond the initial cohort. Led by Inje University under the Glocal University 30 initiative, BIG LIFE brings together academic medicine, public health institutions, university-affiliated hospitals, local innovation infrastructure, and a bio-foundry platform to create a regionally grounded yet globally extensible research ecosystem. Beyond data integration and algorithm development, BIG LIFE is founded on public trust, participant partnership, and reciprocal value creation. It is therefore conceived not only as a cohort study, but as a civic-scientific compact through which citizens, clinicians, scientists, and cities co-design a learning health system for healthy longevity and future-ready prevention.

**Keywords:** Multi-omics. AI, Digital twin, Cohort, Future-ready prevention

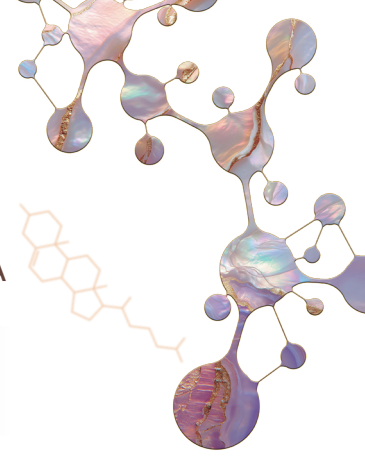




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BEXCO, BUSAN, KOREA



FROM MOLECULES TO MEGABYTES:  
AI AND BIG DATA TRANSFORMING LIFE SCIENCE

**ST1-2 AI-Driven Genomics: From Data Generation to Insights**  
(powered by Illumina)

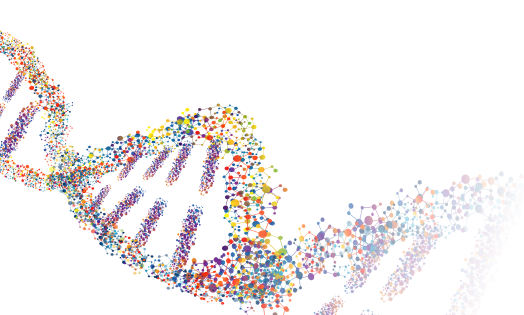
# The genome and beyond - unlocking deeper biology through multiomic and multimodal analysis

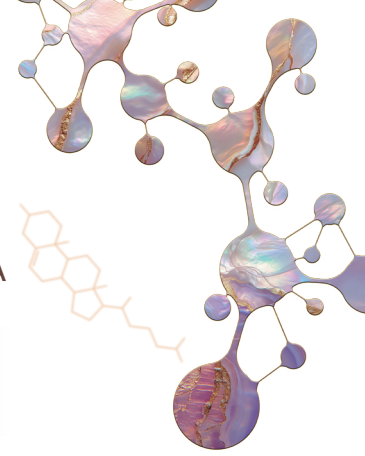
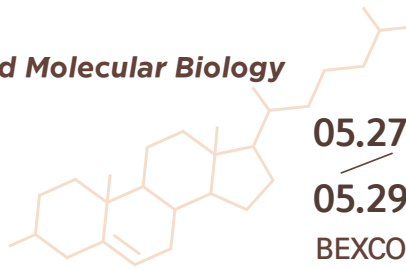
Joel FELLIS

*Illumina, Inc.*

Biological discovery is increasingly constrained by fragmented, costly, and narrowly focused analytical tools that limit scale and impact. This presentation highlights Illumina's emerging multiomic and multimodal portfolio and roadmap, and its strategy to deliver a unified, scalable platform that transforms how biological insight is generated. By advancing integrated solutions across genomics, epigenomics, transcriptomics, proteomics, single cell, and emerging spatial modalities, Illumina eliminates traditional tradeoffs between depth, breadth, and throughput. Coupled with streamlined workflows and AI enabled data integration, this platform empowers researchers to rapidly interrogate complex genotype-phenotype relationships, stratify populations, and identify actionable biomarkers—accelerating translational discovery and enabling systems level understanding of biology and disease at scale.

**Keywords:** Multiomics, genome, proteomics, spatial, transcriptome





**ST1-3 AI-Driven Genomics: From Data Generation to Insights**  
(powered by Illumina)

# From Sequencers to Insights – How Illumina Informatics are transforming genomic discovery

JP CHAIB

*Illumina BioInsight*

The rapid advancement of next-generation sequencing (NGS) has transformed basic research by enabling deeper exploration of genomic and transcriptomic landscapes. However, the growing scale and complexity of sequencing data present challenges in data processing, analytical accuracy, and cross-study integration.

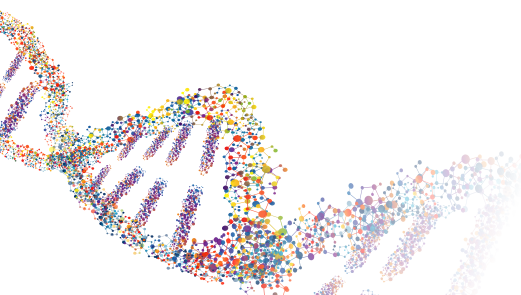
In this presentation, we introduce Illumina Software as a unified informatics ecosystem designed to support scalable and reliable genomic analysis. It provides an end-to-end environment connecting data generation, secondary analysis, data management, and interpretation, allowing researchers to efficiently handle large and complex datasets while maintaining consistency and reproducibility.

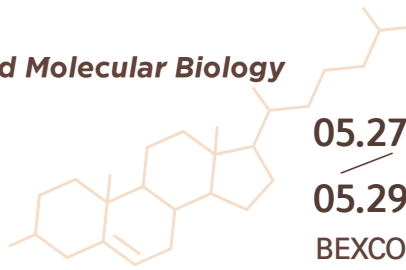
At the core of this ecosystem is DRAGEN (Dynamic Read Analysis for GENomics), Illumina's high-performance secondary analysis platform. We highlight how DRAGEN enables accurate and comprehensive analysis across applications including whole-genome and whole-exome sequencing, RNA sequencing, and somatic and germline variant detection. Through optimized algorithms and hardware acceleration, DRAGEN delivers high sensitivity and fast turnaround times.

Beyond single-omics, Illumina Software also supports integrative research by enabling multiomics data integration. We further discuss how AI-driven analytics enhances interpretation and supports deeper biological insights into complex systems.

Together, Illumina Software enables researchers to move from high-quality data to meaningful, integrated multiomics discovery.

**Keywords:** Illumina Software, Dragen, AI, Data integration, E2E

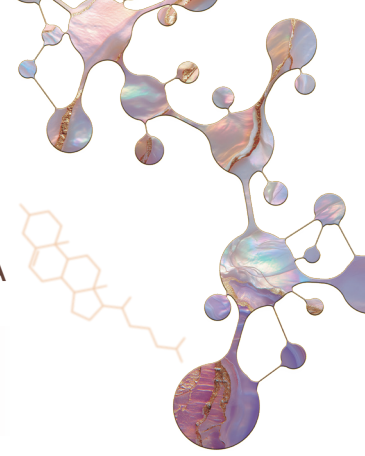




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BEXCO, BUSAN, KOREA



FROM MOLECULES TO MEGABYTES:  
AI AND BIG DATA TRANSFORMING LIFE SCIENCE

**ST1-4 AI-Driven Genomics: From Data Generation to Insights**  
(powered by Illumina)

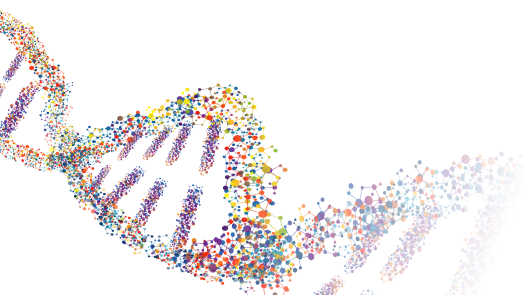
## National and Population Genomic Health Initiatives: Building multiomic data assets for research and precision medicine

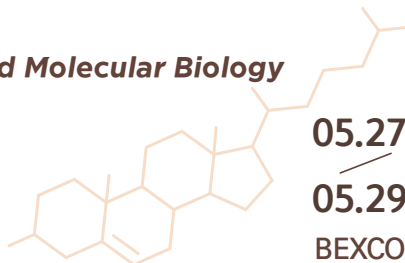
Helen SPEIRS

*Illumina, Inc.*

National and population scale genomics initiatives are rapidly reshaping healthcare, biomedical research, and national innovation ecosystems. This presentation explores the current state and future trajectory of large scale genomic programmes, highlighting their role in accelerating precision medicine and improving population health outcomes. It also outlines how Illumina partners with governments and health systems to design, implement, and scale population level genomics programmes. Drawing on global exemplars, it demonstrates Illumina's role from sequencing and bioinformatics to data platforms and ecosystem development to translating large scale genomic data into clinical and research impact.

**Keywords:** population genomics, precision medicine, multiomics, genome

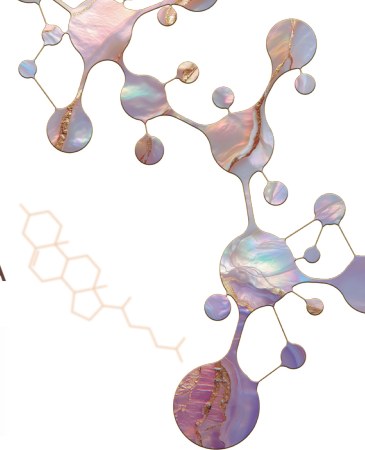




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FROM MOLECULES TO MEGABYTES:  
AI AND BIG DATA TRANSFORMING LIFE SCIENCE

**ST2-1** Yonsei NRL2.0 BCCI-SPARK Symposium on Biomedical Innovation and Translation (Supported by Yonsei NRL2.0 Bio-Centennial Convergence Institute)

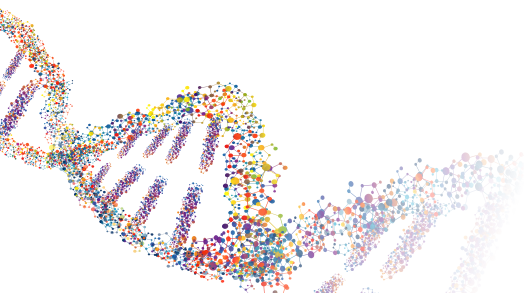
## Transforming Academic Innovations into Solutions for Patients

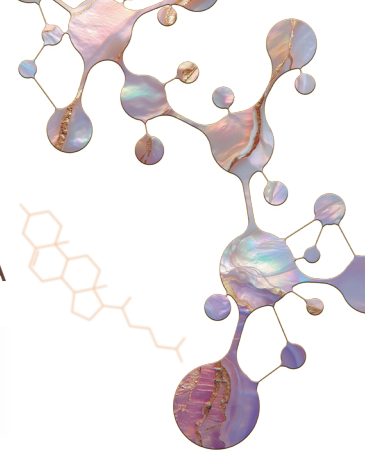
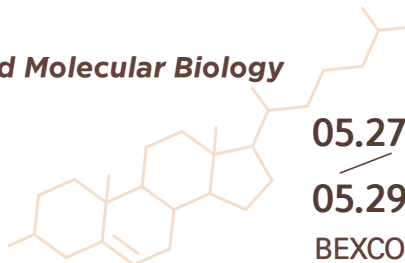
Daria MOCHLY-ROSEN

*Stanford University School of Medicine*

I founded the SPARK program at Stanford in 2006 and co-direct the Program with Dr. Kevin Grimes since 2008. The establishment of the program is a result of my experience in my first startup, KAI Pharmaceuticals. During my time in industry, I realized that most academics are not familiar with the science of drug development. Thus, SPARK's goal was to close that knowledge gap and to advance academic biomedical discoveries into real-world impact. Through its network of faculty, fellows, project managers, and over 100 industry expert advisors, SPARK achieved 53% success rate at advancing projects to licensing by existing or new companies and/or entering clinical trials. The on-going collaboration between several dozen industry experts and dozens of driven academics is unique and may be the reason for SPARK's success. In the past 20 years, the program has educated 600 faculty and fellows in the sciences of drug development and our efforts led to establishing 62 startups, licensing of SPARK-supported projects to 30 existing biopharma companies and to conducting 25 clinical trials. The SPARK model has been successfully scaled and adopted in over 70 academic institutes in over 30 countries. I serve as the Founder President of SPARK GLOBAL and through our global outreach and by adopting our models to local culture and needs, the programs advance academic discoveries to the benefit of patients around the world.

**Keywords:** SPARK, drug development, academic, discoveries, collaboration





**ST2-2** Yonsei NRL2.0 BCCI-SPARK Symposium on Biomedical Innovation and Translation (Supported by Yonsei NRL2.0 Bio-Centennial Convergence Institute)

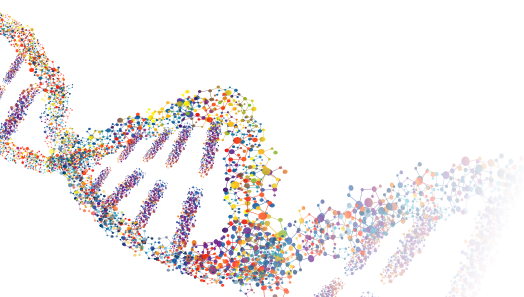
## Acoustophoretic Bioassembly Technique for Therapeutic Tissue Fabrication

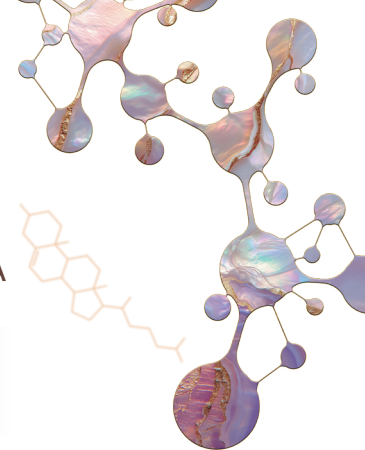
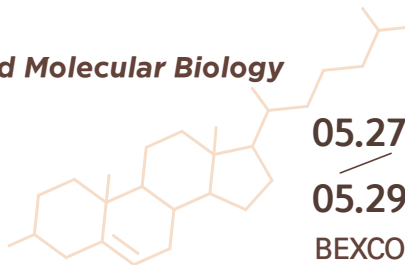
Hyungsuk LEE

*Yonsei University*

Preparation of in vitro tissues is critical for biomedical applications, including drug development and regenerative medicine. Here, we present an acoustophoretic bioassembly technique capable of replicating tissue architecture by precisely controlling the spatial organization of cells. Using this approach, we fabricate vascular tissues with a three-dimensional and collateral vessel network. The engineered tissues exhibit enhanced cell-cell interactions, upregulated gene expression, and increased secretion of angiogenic and anti-inflammatory paracrine factors. Their mechanical functionality is quantitatively evaluated through permeability and perfusability assays. We further demonstrate tunable control over vessel diameter, density, and spacing. The therapeutic potential of these constructs is validated in an ischemic mouse model. Owing to its versatility, the acoustophoretic bioassembly technique can be extended to varied tissue types. As an additional application, we demonstrate fabrication of neuromuscular tissue constructs exhibiting an enhanced contraction dynamics, electrophysiological performance, and therapeutic efficacy. The acoustophoretic bioassembly technique provides an alternative or complementary tool for engineering functional tissues that recapitulate both structural and physiological properties with implications for drug screening and disease modeling.

**Keywords:** Acoustophoretic, Bioassembly, Tissue Fabrication, Vessel, Neuromuscular





**ST2-3 Yonsei NRL2.0 BCCI-SPARK Symposium on Biomedical Innovation and Translation (Supported by Yonsei NRL2.0 Bio-Centennial Convergence Institute)**

## Exploring Targeted Protein Degraders

Taebo SIM

*Yonsei University College of Medicine*

Targeted protein degradation (TPD) technology such as proteolysis-targeting chimera (PROTAC) is an emerging and promising therapeutic modality from an innovative drug discovery point of view as TPD could address previously inaccessible drug targets and non-catalytic functions.

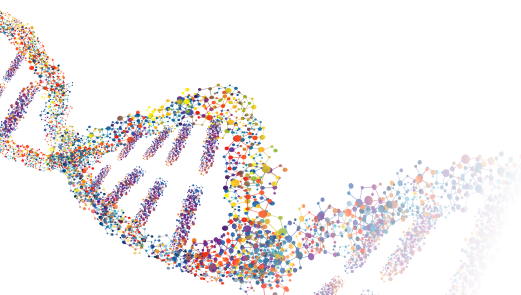
In order to provide useful degrader chemical probes and clinically relevant leads across the kinome, we synthesized a variety of different kinds PROTACs of which warheads are different chemo-types of small molecule kinase inhibitors. We use chemo-proteomics to annotate the degradable kinome. Our expansive dataset provides chemical leads for degrading over 200 kinases.

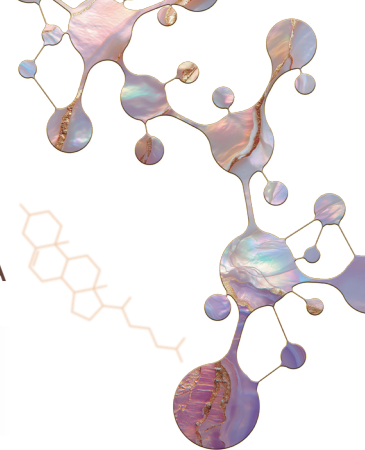
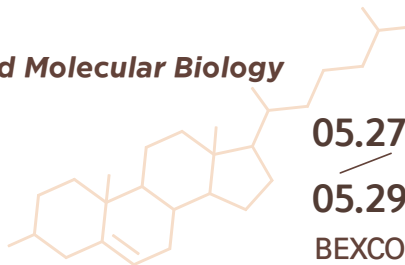
KRASG12D is the most prevalent KRAS mutant in various cancers. We have identified a selective KRASG12D degrader, YUH91138 capable of degrading selectively KRASG12D over other KRAS mutants as well as KRASWT.

Accumulating evidence reveals the oncogenic role of methyltransferase-like 3 (METTL3) in a variety of cancer types, either dependent or independent of its m<sup>6</sup>A methyl transferase activity. We have designed proteolysis-targeting chimeras (PROTACs) targeting METTL3 and identified KH12 as a potent METTL3 degrader. KH12 significantly suppresses the growth of various gastric cancer (GC) cells, where the m<sup>6</sup>A-independent activity of METTL3 plays a crucial role in tumorigenesis. This study highlights the therapeutic potential of targeted degradation of epitranscriptomic writer METTL3 as an anti-cancer strategy.

We have reported the first example of TPDs that use Kelch-Like Homology Domain Containing protein 2 (KLHDC2) as an ubiquitin E3 ligase for targeted endogenous protein degradation and recently identified CDK6 selective KLHDC2 degrader as a potential therapeutic strategy for AML.

**Keywords:** TPD, PROTAC, KLHDC2, AUTAC





**ST2-4 Yonsei NRL2.0 BCCI-SPARK Symposium on Biomedical Innovation and Translation (Supported by Yonsei NRL2.0 Bio-Centennial Convergence Institute)**

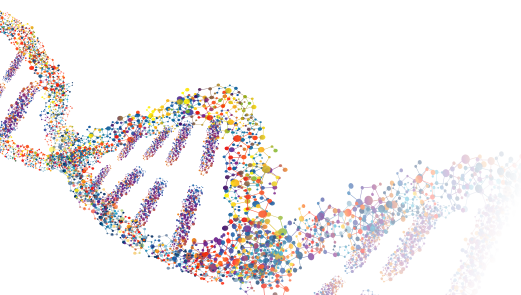
## Gene Editing for Therapy and Precision Medicine

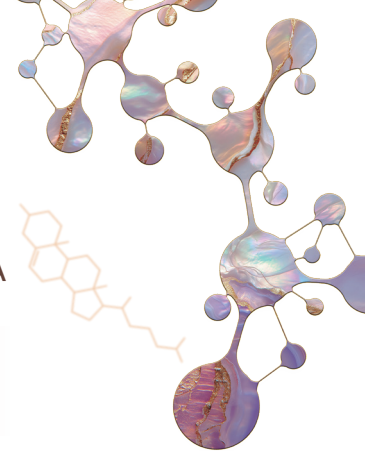
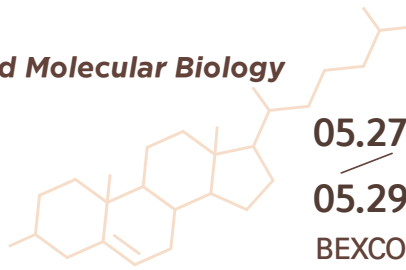
Hyongbum Henry KIM

*Department of Pharmacology, Yonsei University College of Medicine*

In this presentation, I will provide an overview of gene-editing technologies, focusing on the fundamentals of CRISPR-Cas9, base editors, and prime editors. I will explore the underlying mechanisms of each tool, highlighting their unique capabilities and advancements. CRISPR-Cas9, widely recognized for its ability to introduce precise double-strand breaks, revolutionized genetic manipulation. Building on this, base editors enable single-nucleotide changes without double-strand breaks, offering a more refined approach for correcting point mutations. The latest innovation, prime editing, combines CRISPR-Cas9 and reverse transcriptase, allowing precise editing of targeted DNA sequences with minimal off-target effects. I will also discuss the therapeutic applications of these tools, including their potential in developing treatments for genetic disorders. Particular attention will be given to prime editing, which shows promise in addressing previously intractable mutations. Furthermore, I will delve into the use of prime editors for functional evaluation of variants of uncertain significance (VUS). This method provides crucial insights into the pathogenicity of VUS, contributing to more accurate genetic diagnoses and personalized medicine. By bridging the gap between cutting-edge gene editing and clinical application, this talk aims to shed light on the future of genomic medicine

**Keywords:** CRISPR-Cas9, Prime Editing, Precision Medicine, Genetic Disorders, Variants of Uncertain Significance





**ST3-1 Decoding Bi-Wi Imbalance in Korean Medicine:  
Evidence-based Molecular and Multi-omics Insights**

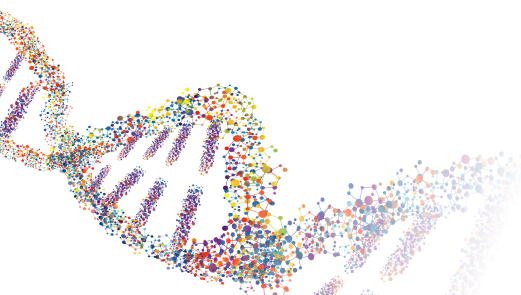
# Integrating GWAS and Targeted Cohort Validation to Define the Genomic Architecture of Cold-Heat Patterns

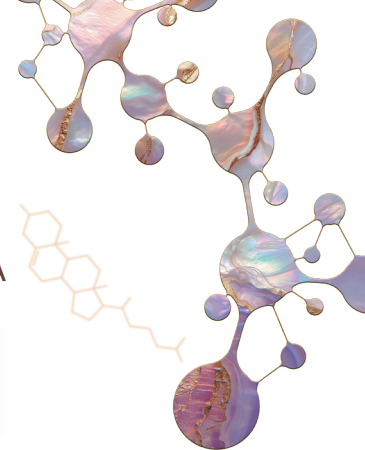
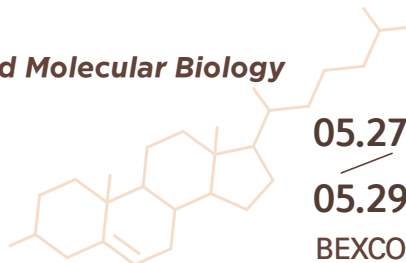
Seogyun JEONG, Sanghun LEE\*

*Department of Bioconvergence and Engineering, Graduate School, Dankook University,  
Yongin-Si 16890, Gyeonggi-Do, Republic of Korea.*

This study bridges the gap between Traditional Korean Medicine and modern genomics by identifying the molecular markers underlying Cold-Heat Patterns (C-HPs), a diagnostic framework for physiological thermal sensitivity. By integrating results from existing Genome-Wide Association Studies (GWAS) on thermogenesis and thyroid hormones with a validation cohort of 90 Korean individuals, we identified 39 high-priority single-nucleotide polymorphisms (SNPs) associated with these constitutional types. Our findings reveal that the 20 SNPs associated with “Heat” patterns, such as those in the *CAPZB* and *CDKN2C* genes, are predominantly linked to vascular development and circulatory regulation. In contrast, the 19 “Cold” pattern SNPs, including markers in *PDE4B* and *GOLPH3L*, are significantly enriched in mitochondrial organization and metabolic heat production. Furthermore, Principal Component Analysis demonstrates that these markers exhibit distinct ethnic clustering across East Asian and African populations, suggesting an evolutionary basis for these patterns. By mapping traditional phenotypes to specific genetic variations in vascular and mitochondrial pathways, this research provides a plausible scientific basis for C-HP diagnosis. These 39 SNPs offer a promising foundation for integrating traditional constitutional theory into precision medicine, enabling more personalized approaches to managing individual thermal sensitivity and metabolic health.

**Keywords:** East Asian medicine; SNPs; cold pattern; genetics; heat pattern; integrative research.





**ST3-2 Decoding Bi-Wi Imbalance in Korean Medicine:  
Evidence-based Molecular and Multi-omics Insights**

# Melittin modulates Akt/GSK-3 $\beta$ / $\beta$ -catenin and androgen receptor signaling in benign prostatic hyperplasia: A multi-level molecular analysis

Hyo-Jin An

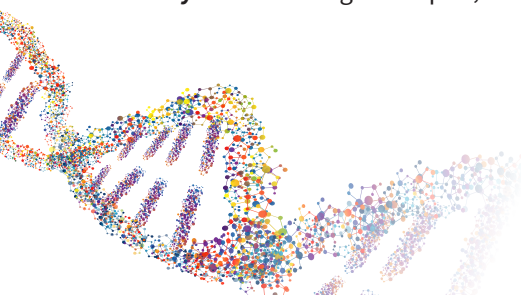
*College of Pharmacy and Institute of Integrated Pharmaceutical Sciences, Kyung Hee University, 26 Kyungheedaero, Dongdaemun-gu, Seoul 02447, Republic of Korea*

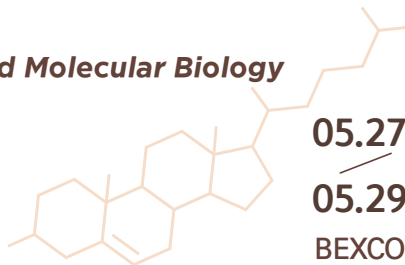
Benign prostatic hyperplasia (BPH) is associated with dysregulated interactions among metabolic, inflammatory, and endocrine pathways. In Korean medicine, such systemic dysregulation is conceptualized as Bi-Wi imbalance, reflecting disrupted digestive-metabolic and immune homeostasis. Bee venom therapy has traditionally been used to modulate inflammatory conditions, and melittin (Mel), its principal bioactive component, is a key mediator of these effects. However, its molecular mechanisms in BPH and relevance to systemic imbalance remain unclear.

This study aimed to elucidate the multi-level molecular actions of Mel in BPH by integrating network pharmacology, transcriptomic analysis, and experimental validation. Network analysis identified key hub genes, including AKT1, TNF, IL1B, and GSK3B, with enrichment in PI3K-Akt, MAPK, and TNF signaling pathways, suggesting involvement of metabolic and inflammatory pathways. Experimental validation demonstrated that Mel modulates Akt signaling through interaction with the substrate-recognition domain, leading to reduced GSK-3 $\beta$  phosphorylation, enhanced  $\beta$ -catenin degradation, and suppression of androgen receptor (AR) signaling. These effects were observed in dihydrotestosterone-stimulated prostate cells and a testosterone-induced BPH rat model, where Mel attenuated prostate enlargement and histological hyperplasia. Transcriptomic analysis identified EMX2 as a consistently downregulated gene in human, cellular, and animal BPH models, with partial restoration following Mel treatment, suggesting a role in tissue homeostasis.

Collectively, these findings demonstrate that Mel regulates the Akt/GSK-3 $\beta$ / $\beta$ -catenin/AR signaling axis while attenuating oxidative stress-associated inflammatory responses at cellular and organismal levels. These results suggest a potential association with systemic regulatory alterations in Bi-Wi imbalance and provide a molecular and systems-level basis for interpreting this concept in Korean medicine.

**Keywords:** Androgen receptor, Benign prostatic hyperplasia, Melittin, Network pharmacology, Transcriptomic analysis

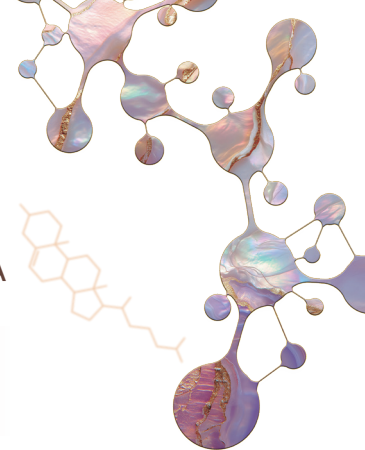




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**ST3-3 Decoding Bi-Wi Imbalance in Korean Medicine:  
Evidence-based Molecular and Multi-omics Insights**

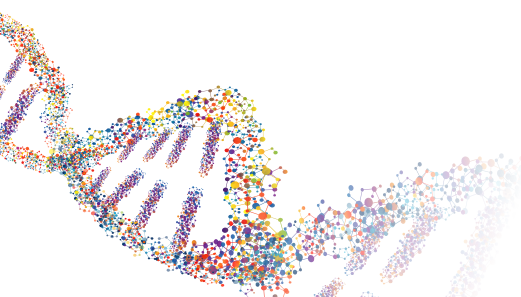
# Reinterpreting Microbiome–Host Interactions through Biomimetic Chemistry: Molecular Insights Bridging Traditional Korean Medicine and Microbiome Science

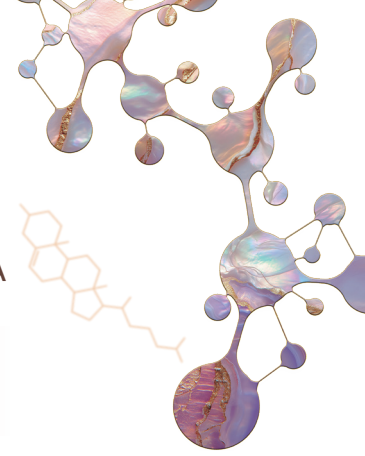
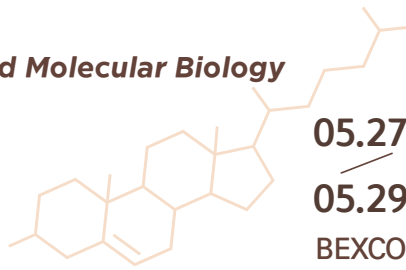
Hwang In HYUN

*Department of Pharmacy, Woosuk University*

The human microbiome is widely recognized as a key contributor to host health; however, the molecular mechanisms underlying diverse systemic effects thereof remain incompletely understood. Traditional Korean medicine has long emphasized the importance of systemic homeostasis and host–environment interactions, offering a conceptual framework that can be reinterpreted in the context of microbiome–host interactions. In this study, we sought to identify bioactive small molecules derived from the human microbiome by mimicking physiologically relevant conditions *in vitro*. Our recent efforts revealed non-enzymatic transformations of microbe-derived metabolites under conditions relevant to the human body. These reactions occur at physiological temperature in the presence of reactive microbial metabolites, including monoamine-containing neurotransmitters, short-chain fatty acids, and digested natural products. In addition, by modulating culture parameters associated with host states, we further observed dynamic changes in microbial chemical profiles and identified candidate molecular messengers. Our findings provide molecular-level evidence that microbiome-derived small molecules may act as key mediators of host–microbe interactions. These results suggest that traditional Korean medicine concepts can be interpreted through a molecular perspective, potentially bridging multi-omics and chemical biology approaches.

**Keywords:** Human microbiome, Microbiome-host interactions, Microbial metabolites





**ST3-4 Decoding Bi-Wi Imbalance in Korean Medicine:  
Evidence-based Molecular and Multi-omics Insights**

## Gut Microbiota-Derived Metabolites and Healthy Aging

Dongryeol RYU

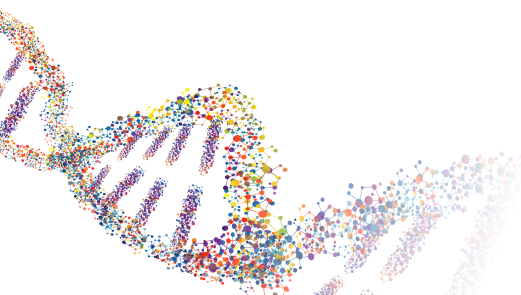
*GIST*

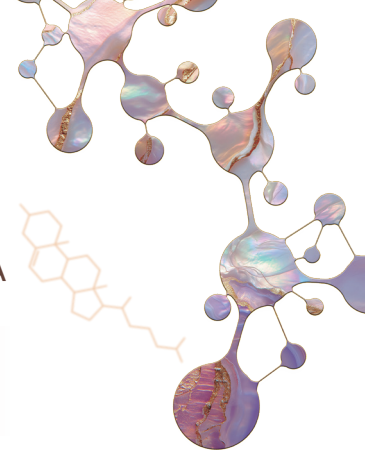
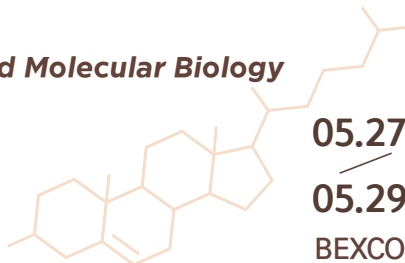
Gut microbiota-derived metabolites are increasingly recognized as critical mediators of communication between the gut and peripheral organs, potentially serving as key mechanistic links underlying Bi-Wi imbalance. These metabolites function as systemic signaling molecules that influence metabolic homeostasis, inflammation, and aging processes across tissues.

Among these, urolithin A (UA), a metabolite derived from dietary ellagitannins by gut microbiota, has gained significant attention for its role in mitochondrial quality control. Preclinical studies demonstrated that UA induces mitophagy, enhances mitochondrial function, and improves muscle health, leading to extended lifespan in *Caenorhabditis elegans* and improved physical performance in rodent models.

Importantly, these findings have been translated into humans. Clinical trials have shown that UA supplementation is safe and suggests improvements in muscle strength and mitochondrial function in both elderly and middle-aged adults. Furthermore, emerging evidence indicates that UA may exert beneficial effects on immunosenescence, highlighting its broader role in systemic aging regulation.

Mechanistically, UA promotes mitochondrial turnover and preserves cellular homeostasis, addressing a central hallmark of aging. These findings position UA as a prototype for microbiome-derived interventions targeting systemic aging and provide a conceptual framework linking gut-derived metabolites to multi-organ regulation and Bi-Wi imbalance. In this presentation, urolithin A will be introduced as a representative example illustrating the continuum from basic discovery to translational and clinical research.





**ST4-1** Powering Breakthroughs from Research to Results: Agentic AI and Foundation Models for Life Sciences Innovation (Korean Session)

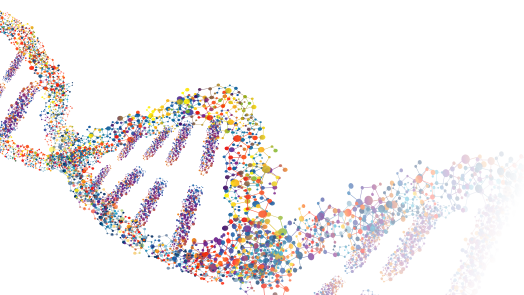
## Building the Foundation: AWS Cloud Infrastructure for Life Sciences Research

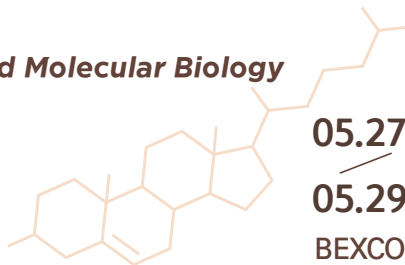
Yoohoon WON

*AWS Korea, Korea*

Life sciences research often faces practical challenges around managing diverse data formats, fragmented workflows, and the computational demands of large-scale omics analysis. This talk provides a practical introduction to how AWS cloud services can help address these challenges. We start with a brief overview of common bottlenecks in research computing environments, and then walk through the core AWS infrastructure stack relevant to life sciences—including Amazon EC2, AWS ParallelCluster, AWS PCS, and AWS HealthOmics. For each service, we discuss what problems it solves and how it fits into a broader research architecture. The goal is not to cover everything, but to give attendees a clear and actionable starting point for thinking about cloud adoption in their own research or organizational context.

**Keywords:** Cloud Infrastructure, HPC, AWS HealthOmics, Genomics Pipeline, Parallel Computing

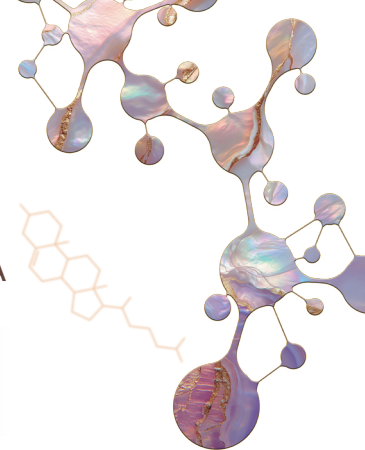




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FROM MOLECULES TO MEGABYTES:  
AI AND BIG DATA TRANSFORMING LIFE SCIENCE

**ST4-2 Powering Breakthroughs from Research to Results: Agentic AI and Foundation Models for Life Sciences Innovation (Korean Session)**

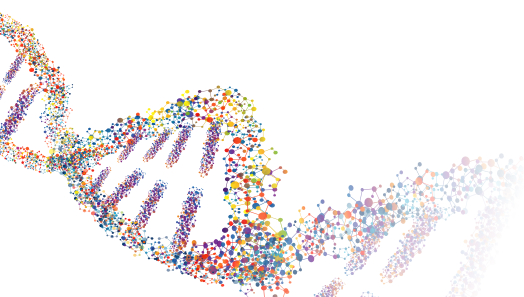
# Powering Breakthroughs from Research to Results: Agentic AI and Foundation Models for Life Sciences Innovation

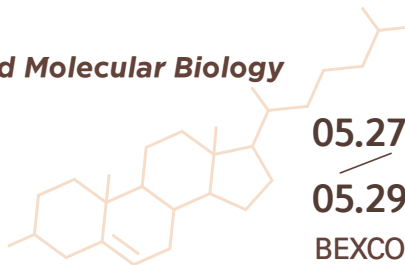
Yoocheon Won, Hyunmin Kim, Jongho Kim

*Amazon Web Services (AWS) Korea*

Life sciences research faces critical bottlenecks: fragmented pipelines, heterogeneous multi-omics data, and computational limits that stretch discovery timelines to decades. This talk presents how scalable cloud infrastructure (AWS HPC, HealthOmics, Research Innovation Cloud) combined with agentic AI and biological foundation models (BioFMs) fundamentally accelerates this process. Amazon Bio Discovery exemplifies this convergence—AI agents orchestrate specialized BioFMs to generate and rank antibody candidates, then seamlessly route top performers to integrated lab partners for synthesis and testing, creating a lab-in-the-loop cycle that continuously refines models with real wet-lab outcomes. Using a live multi-agent demo on NSCLC radiogenomics data via Amazon Bedrock AgentCore and Model Context Protocol (MCP), we show how this paradigm transforms a single natural language query into multimodal research insights, bridging bench to clinic.

**Keywords:** Agentic AI, Biological Foundation Models, Multi-agent Systems, Cloud-based Research Infrastructure, Lab-in-the-Loop

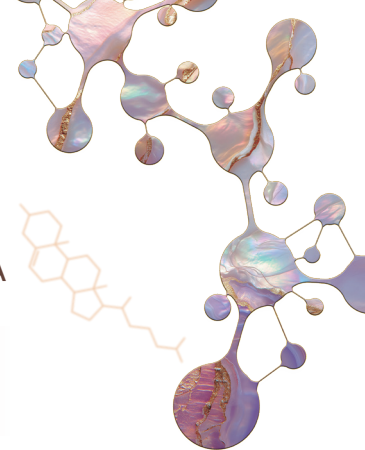




05.27<sup>(WED)</sup>

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BEXCO, BUSAN, KOREA



FROM MOLECULES TO MEGABYTES:  
AI AND BIG DATA TRANSFORMING LIFE SCIENCE

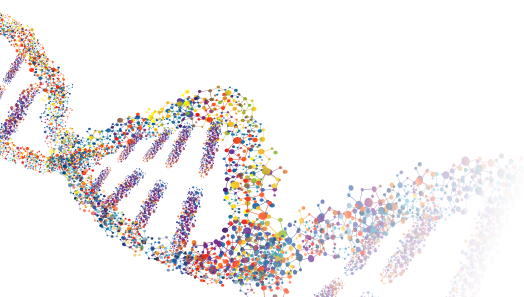
**ST4-3** Powering Breakthroughs from Research to Results: Agentic AI and Foundation Models for Life Sciences Innovation (Korean Session)

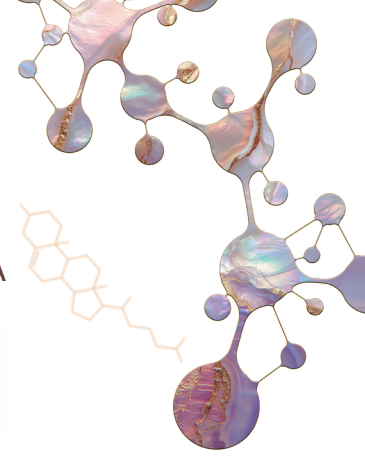
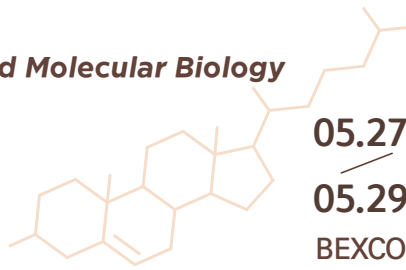
## Real-World AWS Life Sciences Implementations: Lessons and Offerings from ETECH SYSTEM

ChanYoung MOON

*ETECH SYSTEM, Korea*

Moving from a cloud pilot to a working production environment is often harder than it looks. This talk shares ETECH SYSTEM's experience working with life sciences organizations on AWS-based implementations, including genomics data processing, multi-omics integration, and research workflow automation. We walk through project examples to illustrate common challenges encountered in real engagements and how they were addressed. We also briefly introduce ETECH SYSTEM—our engineering background, areas of focus, and the types of support we offer as an AWS Advanced Partner. The aim is to give attendees a grounded view of what these projects actually involve, and what to consider when planning a similar initiative.





**ST5-1 Meet the Editors**

## **Bridging the gap: The future of cancer research and clinical oncology in *Cancer Cell***

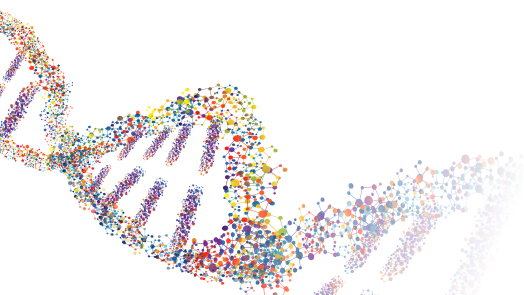
Steve MAO

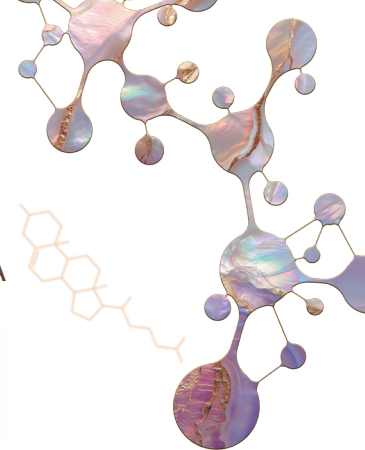
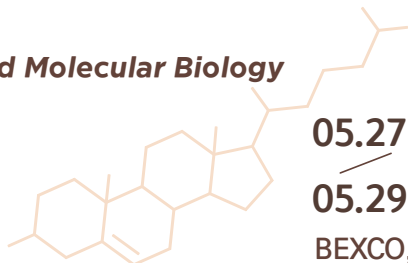
*Cancer Cell*

This presentation outlines the evolving role of *Cancer Cell* as a leading platform connecting foundational cancer biology with clinical oncology. It highlights the journal's growth, editorial philosophy, and recent strategic changes, including a broader scope that embraces the complexity of cancer as a systemic disease and a stronger emphasis on translational and clinically relevant research.

Central to the vision is addressing the persistent gap between basic discoveries and clinical application. *Cancer Cell* aims to accelerate this translation by fostering interdisciplinary research, implementing a rigorous and constructive peer review process, and prioritizing studies with clear clinical impact or potential. The journal is positioned as a hub for integrating emerging technologies, diverse biological insights, and clinical advances.

Ultimately, the presentation emphasizes *Cancer Cell's* commitment to serving both scientists and clinicians, enhancing its global influence, and driving meaningful progress from bench to bedside and back, with the goal of improving patient outcomes.





**ST5-2 Meet the Editors**

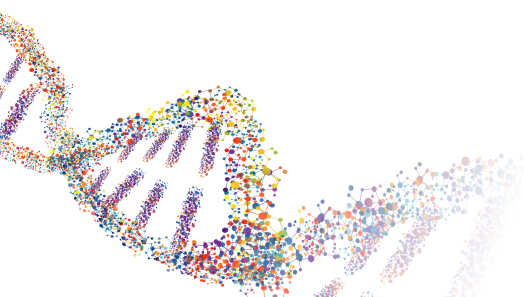
## Navigating the publication process: Tips from a Scientific Editor

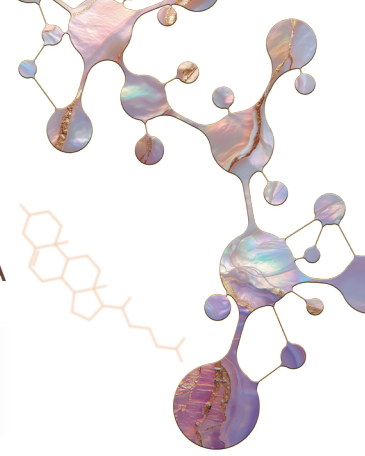
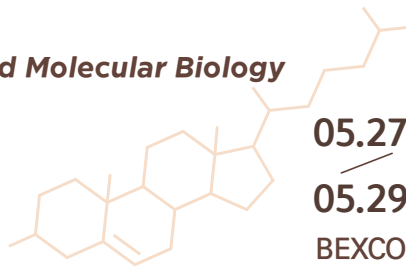
Weiyan HUANG

*Cell Press, Elsevier*

Publishing in high quality journals requires more than strong data; it demands clear storytelling, rigorous methods, and precise communication with editors. This talk provides a practical, editor centered tour of the manuscript lifecycle—from submission through desk review, peer review, revision, and final acceptance—offering concrete strategies to streamline the process. I will outline what editors look for: novelty, methodological rigor, clarity of figures and data, and alignment with a journal's scope and readership. The talk then focuses on two practical tools that often determine a manuscript's trajectory: the cover letter and the author rebuttal. For the cover letter, I will discuss how to articulate the work's core advance, justify the journal choice, and tailor language to engage editors without overclaiming. For rebuttals, I will propose a disciplined, point by point structure, tips for constructive, professional dialogue with reviewers, and how to present updated analyses or experiments while preserving manuscript coherence. Attendees will leave with a practical checklist and ready to use language to apply in their next submission, increasing efficiency and the likelihood of a favorable editorial decision.

**Keywords:** Cover letter, Rebuttal, novelty





**ST6-1 Multi-omics in RNA Biology**

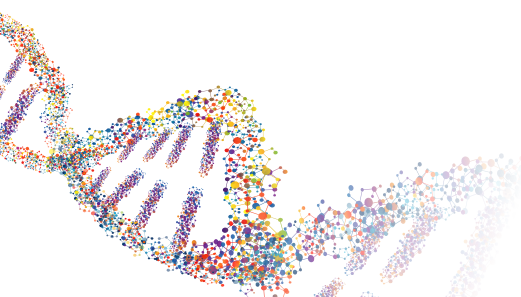
# Synthetic RNA Technologies for Programmable Gene Expression and Cell Fate Control

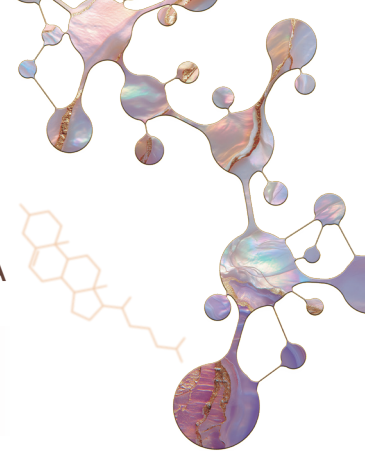
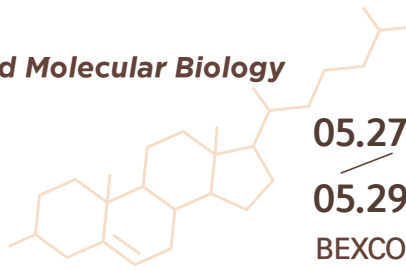
Hirohide SAITO

<sup>1</sup>Institute for Quantitative Biosciences, The University of Tokyo, Tokyo, Japan;  
<sup>2</sup>Center for iPS Cell Research and Application (CiRA), Kyoto University, Kyoto, Japan

Synthetic RNAs provide programmable platforms for controlling gene expression, cell identity, and therapeutic functions without permanent genome modification. We have developed microRNA (miRNA)-responsive mRNA switches that sense endogenous miRNA signatures and regulate translation in a cell-type-specific manner. A miRNA-responsive OFF switch suppresses translation in unwanted cells, whereas a miRNA-responsive ON switch activates translation in target cells through an engineered sequence placed downstream of the poly(A) tail. Combining ON and OFF switches enables efficient purification of desired cells and elimination of unwanted cells using only mRNA delivery, without cell sorters. More recently, we developed Split RNA switches, which integrate multiple RNA-switch outputs through protein splicing to greatly improve the ON/OFF ratio and enable precise cell-type-specific gene expression and genome editing. We are also extending synthetic RNA technologies toward therapeutic cell programming. In addition, I will present our recent progress in next-generation RNA expression platforms, including self-amplifying RNA and AI-assisted RNA design, as emerging strategies to achieve durable, controllable, and programmable regulation of cell fate. Together with AI-assisted functional RNA design such as RfamGen and ongoing RNA-based cellular reprogramming studies, these advances establish a foundation for next-generation RNA technologies to read, write, and execute cell fate programs.

**Keywords:** synthetic RNA; mRNA switch; split RNA switch; self-amplifying RNA; cell fate control





**ST6-2 Multi-omics in RNA Biology**

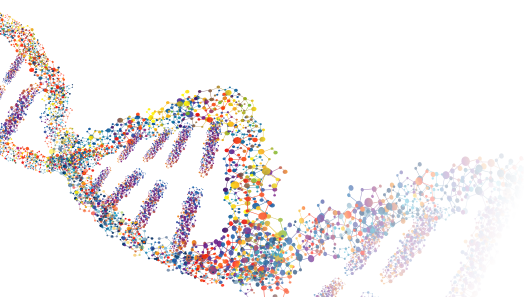
# Spatio-temporal regulation of Treg differentiation in the tumor microenvironment

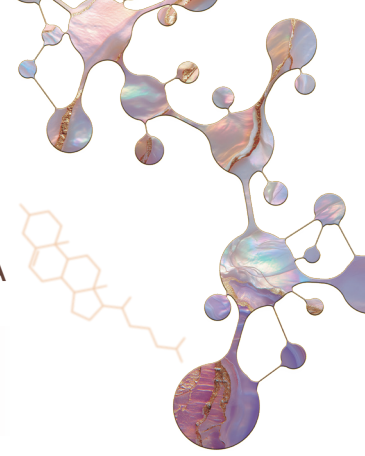
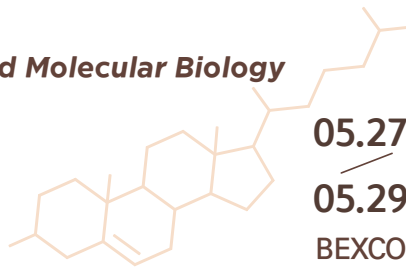
Sang-Jun HA

*Department of Biochemistry, College of Life Science and Biotechnology, Yonsei University*

Tumor-infiltrating regulatory T cells (Tregs) represent a major barrier to effective anti-tumor immunity and immune checkpoint blockade therapy. However, the differentiation pathways and functional heterogeneity of Tregs within the tumor microenvironment (TME) remain poorly understood. In this study, we investigated the accumulation, differentiation, and spatial organization of tumor-infiltrating Tregs during tumor progression using mouse syngeneic tumor models. We observed progressive enrichment of Tregs in tumor tissues, strongly correlating with tumor growth. Single-cell RNA sequencing identified five distinct Treg subsets—naïve, proliferating, intermediate, effector, and terminally differentiated states—forming a linear developmental trajectory. These subsets were further validated by flow cytometry using CCR7, CD69, PD-1, and CCRL2 as key markers. Differentiation was accompanied by gradual upregulation of suppressive and activation-associated molecules, including CCR8, CD39, and PD-1. Functional assays demonstrated that effector Tregs exhibited maximal suppressive activity, whereas terminal Tregs displayed apoptotic features and reduced function. Spatial imaging revealed that effector and terminal Tregs occupy distinct tumor niches, with effector Tregs enriched in fibroblast- and M2 macrophage-associated suppressive regions, while terminal Tregs localized to immune-inflamed areas dominated by M1 macrophages. Importantly, analogous Treg subsets were also detected in human lung cancer single-cell datasets, supporting clinical relevance. Together, these findings provide a framework for selectively targeting tumor-specific Treg subsets to improve cancer immunotherapy outcomes.

**Keywords:** Regulatory T cell, Differentiation, Tumor microenvironment, Cancer Immunotherapy





**ST6-3 Multi-omics in RNA Biology**

# LncRNA Wee1-AS coordinates oxidative fatty acid metabolism through the activation of mitochondrial CDK1/CYCLIN B1

Hyeon-Ji KIM<sup>1,2#</sup>, Cheolhee JEONG<sup>1#</sup>, Sang-Heon LEE<sup>1</sup>, Seungchan AN<sup>1,2</sup>,  
Gyu Hwan HYUN<sup>1,2</sup>, Ga Young LIM<sup>1</sup>, Ju-Yeon KIM<sup>1</sup>, Junhyeong LEE<sup>3,4</sup>, Min-Jung PARK<sup>3</sup>,  
Sung Won KWON<sup>1,2</sup>, Won KIM<sup>5</sup>, Minsoo NOH<sup>1,2</sup>, Yong-Hyun HAN<sup>6</sup>, Mi-Ock LEE<sup>1,7,8\*</sup>

<sup>1</sup>College of Pharmacy, Seoul National University, Seoul 08826, Korea

<sup>2</sup>Research Institute of Pharmaceutical Sciences, Seoul National University, Seoul 08826, Korea

<sup>3</sup>Department of Veterinary Physiology, Chonnam National University, Gwangju 61186, Korea

<sup>4</sup>College of Veterinary Medicine and BK21 FOUR Program, Chonnam National University, Gwangju 61186, Korea

<sup>5</sup>Department of Internal Medicine, Seoul Metropolitan Government Boramae Medical Center, Seoul 07061, Korea

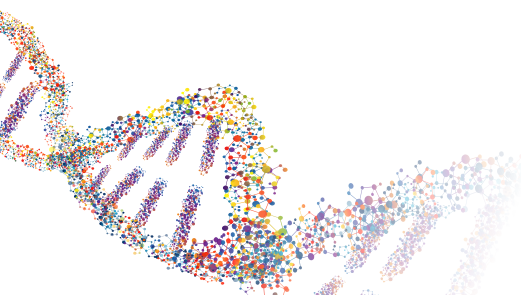
<sup>6</sup>Laboratory of Pathology and Physiology, Kangwon National University, Chuncheon, 24341, Korea

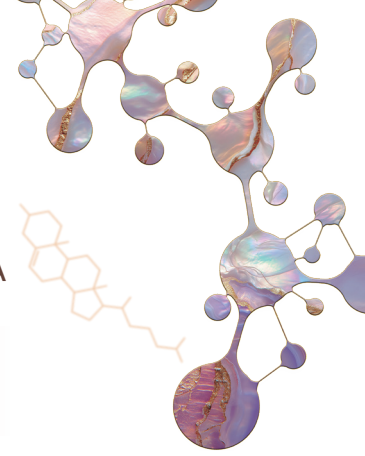
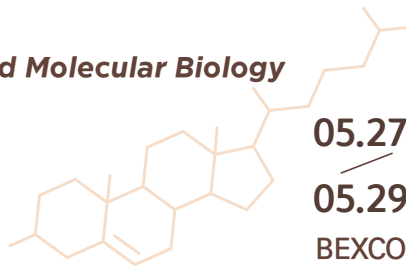
<sup>7</sup>Bio-MAX Institute, Seoul National University, Seoul, 08826, Korea

<sup>8</sup>Natural Product Research Institute, Seoul National University, Seoul, 08826, Korea

This study identifies Wee1-AS, a novel long noncoding RNA (lncRNA) transcribed from the antisense strand of the *Wee1* gene, as a critical regulator of Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD). Primarily expressed in pericentral hepatocytes, Wee1-AS expression is significantly induced by a high-fat diet. Mechanistically, Wee1-AS functions as a potent suppressor of MASLD by enhancing mitochondrial fatty acid oxidation through the activation of the CDK1/CYCLIN B1 complex. This occurs via two distinct pathways: first, by hindering transcriptional machinery access to the *Wee1* locus to suppress its transcription; and second, by binding and stabilizing the CYCLIN B1 protein against ubiquitin/proteasome-mediated degradation. Experimental data show that adeno-associated virus-mediated overexpression of Wee1-AS markedly alleviates MASLD symptoms in mice. Furthermore, pharmacological inhibition of WEE1 using adavosertib mirrored these protective effects, reversing lipid accumulation and mitochondrial dysfunction caused by Wee1-AS knockdown. Notably, the identification of a human homolog, LNC106435.1, which similarly improves mitochondrial function, highlights the Wee1-AS/WEE1 axis as a promising therapeutic target for managing MASLD in humans.

**Keywords:** MASLD, LncRNA Wee1-AS, Mitochondria





**ST6-4 Multi-omics in RNA Biology**

# Advancing Cancer Discovery with the Latest Multi-omics Technologies

Mingshan LIU

*Novogene*

The convergence of advanced multi-omics technologies is reshaping our understanding of cancer biology. By integrating genomics, transcriptomics, proteomics, metabolomics, and single-cell omics, researchers can now uncover deeper molecular insights that drive cancer initiation, progression, and therapeutic response. This presentation will explore how recent innovations in high-throughput sequencing, long-read and spatial omics, and AI-driven data analytics are accelerating translational discoveries. Drawing on Novogene's global expertise and large-scale project experience, we highlight how comprehensive multi-omics approaches are empowering scientists to move from data generation to discovery and clinical impact more efficiently than ever. Together, these advancements are not only enhancing cancer research precision but also paving the way for a new era of personalized medicine.

**Keywords:** Multi-omics, Sequencing, Mass spectrometry

