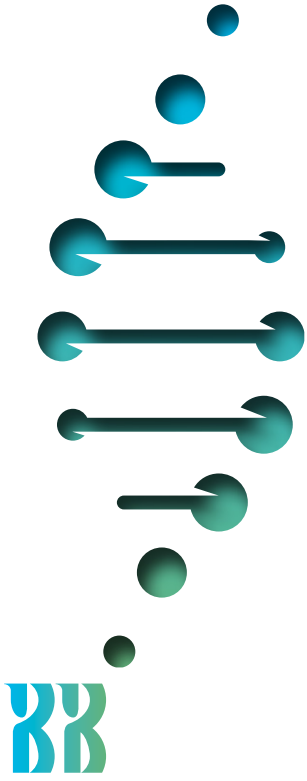
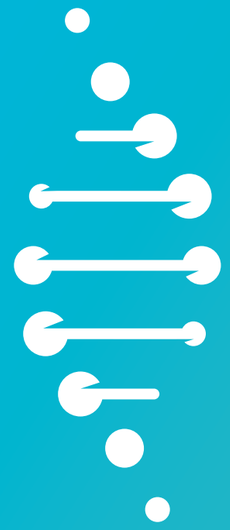
Korea
Research
Institute of
Bioscience and
Biotechnology



ANNUAL REPORT 2023

Technology for Life,
Our Future



KRIBB is paving the road to a sustainable future

INNOVATION CHALLENGE

Open innovation to bridge the gap and overxome the conventional life science research and development.

시험·연구용 LMO 안전관리
R&D LMO safety management

NATIONAL STRATEGIC TECI INOLOGY

A mission-oriented, world-class life science competitiveness.

CENTER OF KOREA S LIFE SCIENCE COMMUNITY

Academia-industry-institutional cooperation begins at KRIBB.

TECHNOLOGY FOR LIFE, OUR FUTURE

CONTENTS

PREFACE

New tools, technologies and approaches continue to revolutionize life science research, driving breakthrough discoveries in the complex and dynamic processes that govern our lives, and catalyzing innovations. In the coming years, rapid advances in life science discovery and innovation will be essential for driving the changes needed to maintain the health and well-being, and to protect and transform economy, environment and society.

As part of Korea's National Research Council of Science and Technology (NST), Korea Research Institute of Bioscience and Biotechnology (KRIBB) has been pivotal to the Korea's position at the forefront of the life science communities around the world since its foundation in 1985, driving innovation and impact by providing leadership, nurturing people, technologies and partnerships.

The role that the Korean life science community played in the global response to the COVID-19 pandemic, from rapid genome sequencing to track the emergence and spread of new variants, to the development of vaccines and therapeutics, illustrates the profound importance of life science research and innovation. The speed with which the life science community, alongside other disciplines, was able to mobilize highlights the importance of long-term investment in the fundamental research, skilled professionals and national infrastructure, facilities that are at the heart of KRIBB's strategic approach with Korean government's consistent financial support and policies.
KRIBB is not the only principal agent of Korea's life science; there are other significant public, private universities, hospitals, research institutions, along with partners in domestic and global, with whom we must work to ensure joined up and synergistic approaches. Furthermore, life science is inherently interdisciplinary; breakthrough discoveries often occur at the interfaces with other disciplines, and joint research and collaborations led by KRIBB frequently provides the foundations for more applied research.

The 2023 KRIBB Annual Report highlights our recent efforts, research programs derived from Korea's national strategic plans and initiatives and achievements. Collaboration continues to be central to our plans, and we look forward to working across Korea's life science communities with our many partners across the wider research and innovation system in delivering shared ambitions.

Jang-Seong Kim, Ph.D.
President
Korea Research Institute of Bioscience and Biotechnology

01

ABOUT KRIBB

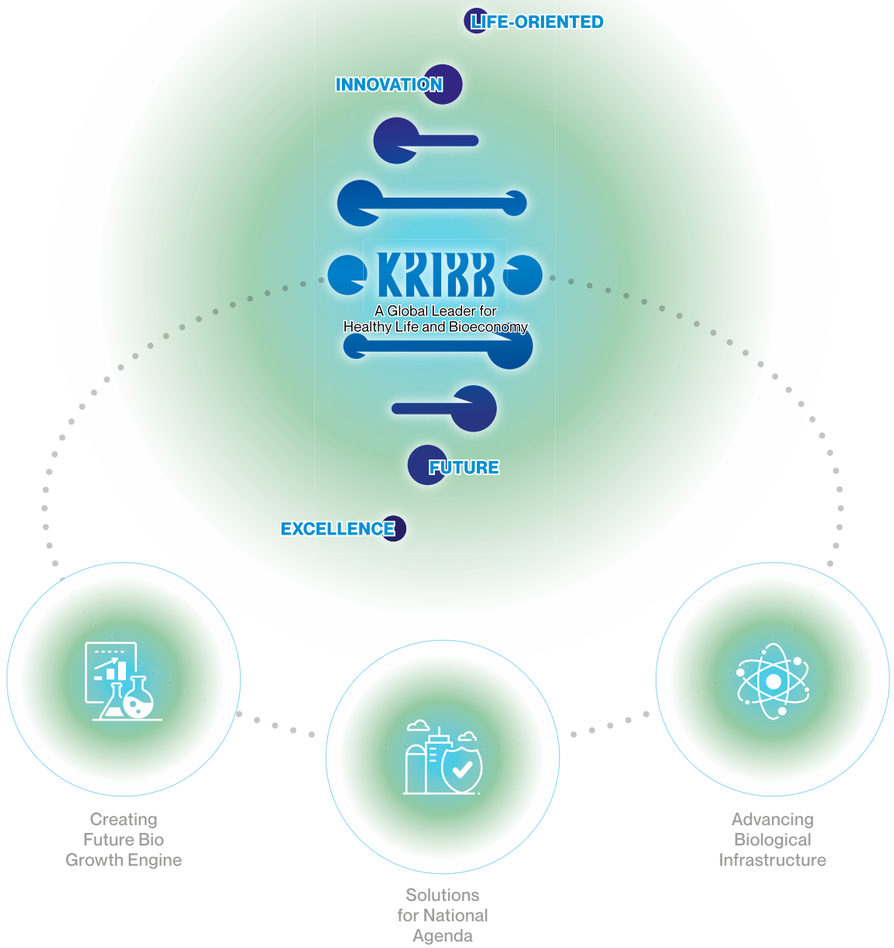
MISSION & VISION

MISSION

To carry out R&D activities and related projects in the field of bioscience and biotechnology in joint effort with other research institutes, academia, and industries at home and abroad.

To disseminate the results of scientific research and technological development.

VISION



FOUNDATION BASIS

Article 8, Act on the Establishment, Management and Promotion of Government-funded Research Institutes.

FOUNDATION BASIS

Develop and disseminate sophisticated core technology in bioengineering and bioeconomy

- Innovative bio convergence, creation of future growth engine, resolution of bio-based agenda Support public infrastructure for bioengineering R&D both at home and abroad
- Supporting establishment of public infrastructure, government-funded think tank, nurturing talented human resources, supporting commercialization of small/medium sized companies

HISTORY

FACILITIES

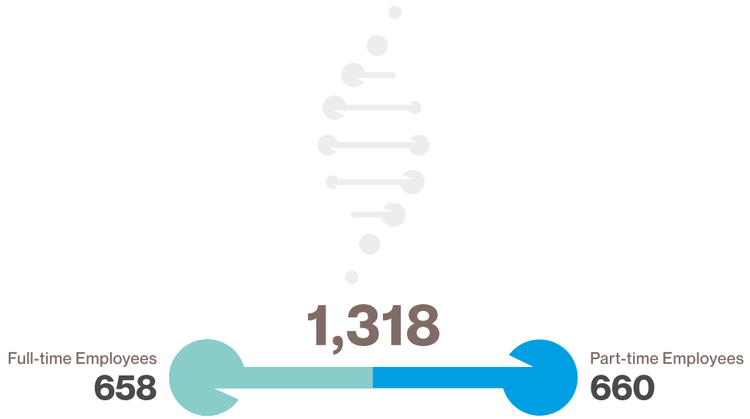
Headquarter
103,684m^2

Ochang Branch Institute
212,258m^2

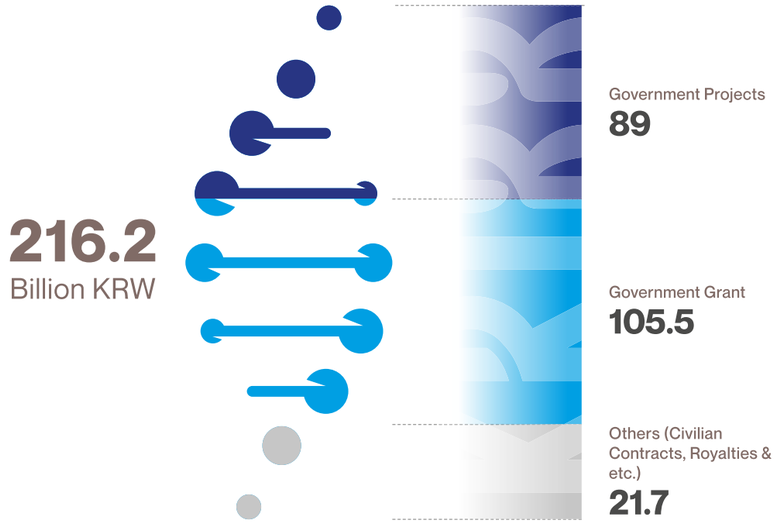
Jeonbuk Branch Institute
160,709m^2

CURRENT STATUS

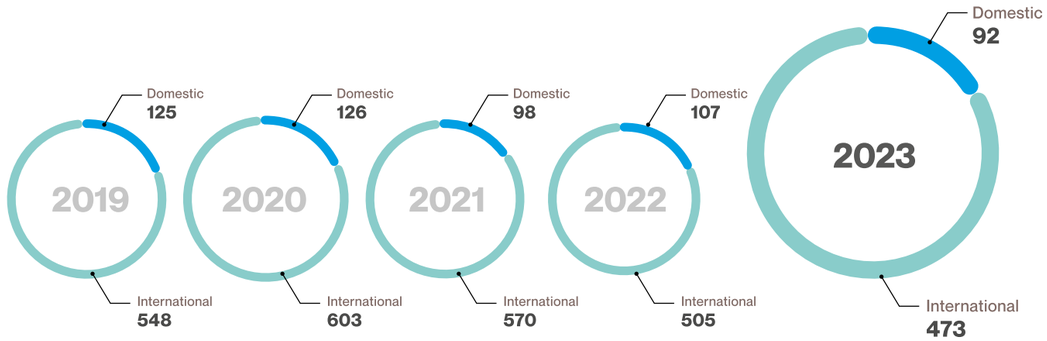
PERSONNEL



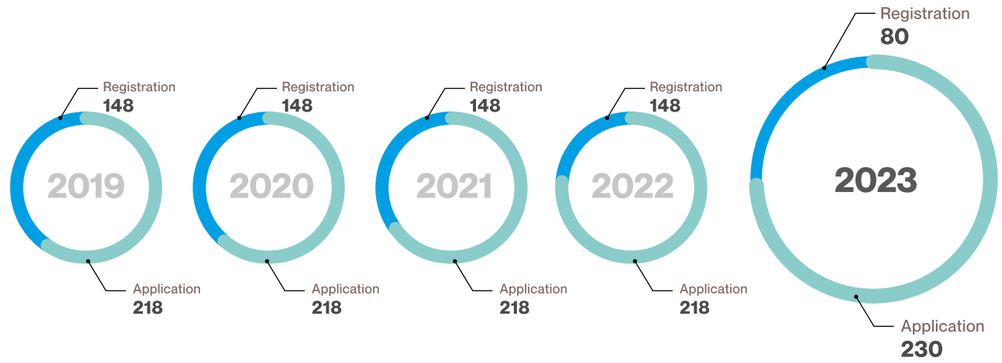
2023 BUDGET



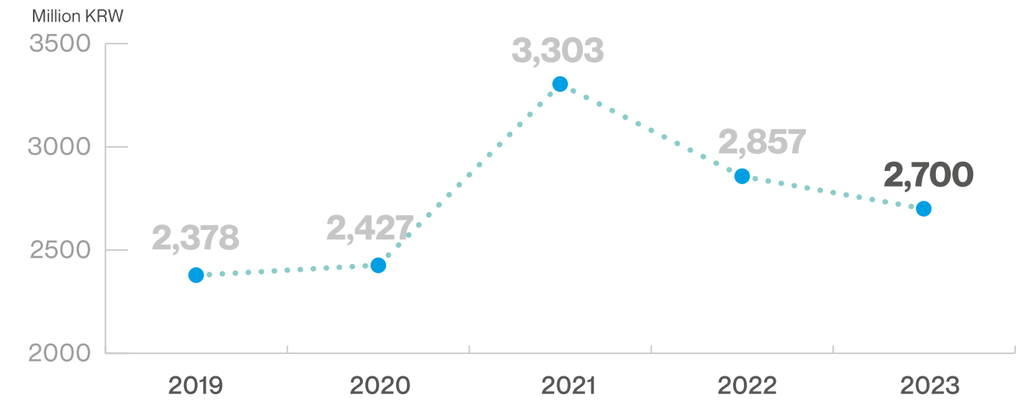
PUBLICATIONS



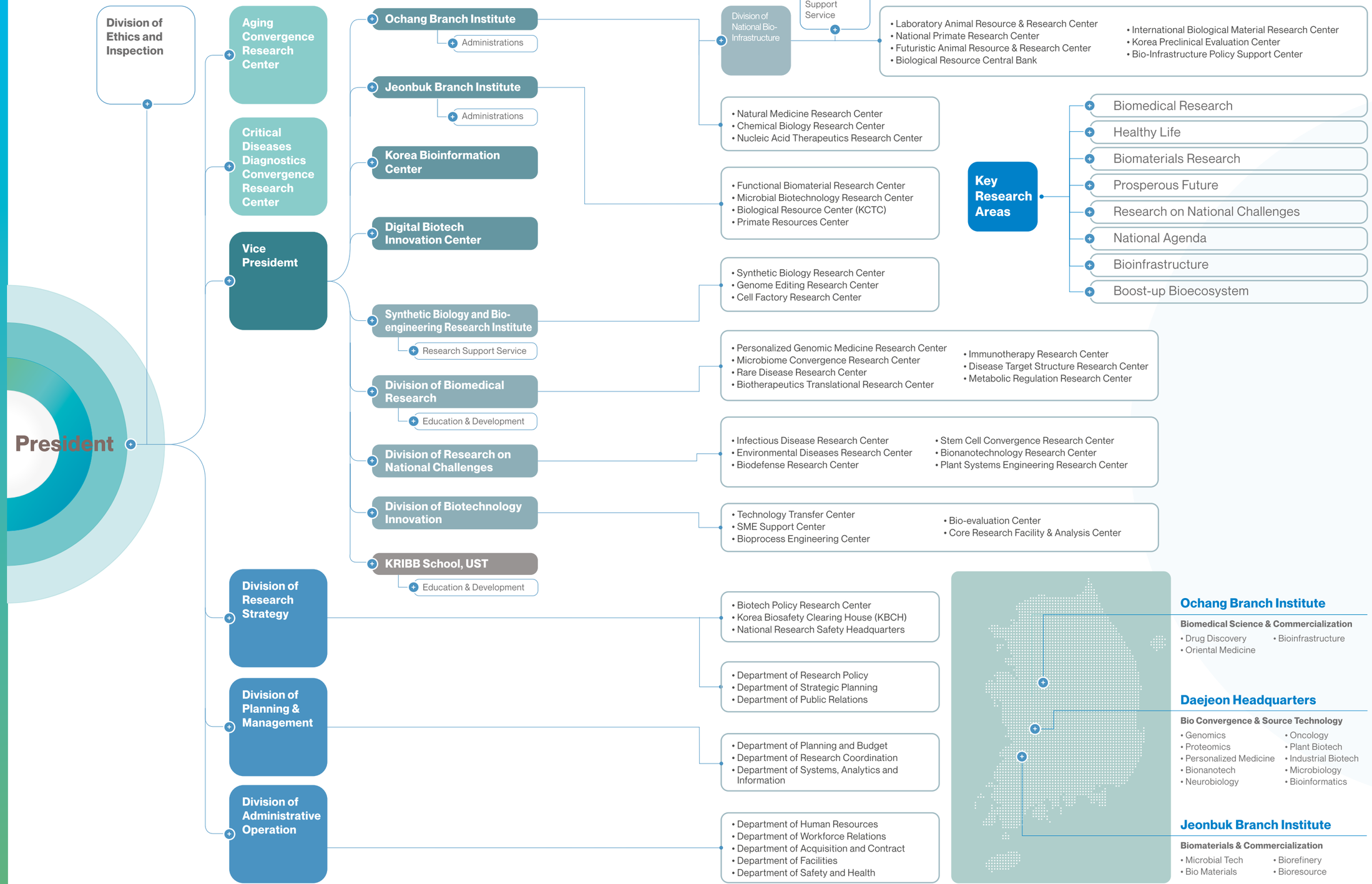
PATENTS



ROYALTIES



ORGANIZATION



Ochang Branch Institute

Biomedical Science & Commercialization

- Drug Discovery
- Oriental Medicine
- Bioinfrastructure

Daejeon Headquarters

Bio Convergence & Source Technology

- Genomics
- Proteomics
- Personalized Medicine
- Bionanotech
- Neurobiology
- Oncology
- Plant Biotech
- Industrial Biotech
- Microbiology
- Bioinformatics

Jeonbuk Branch Institute

Biomaterials & Commercialization

- Microbial Tech
- Bio Materials
- Biorefinery
- Bioresource

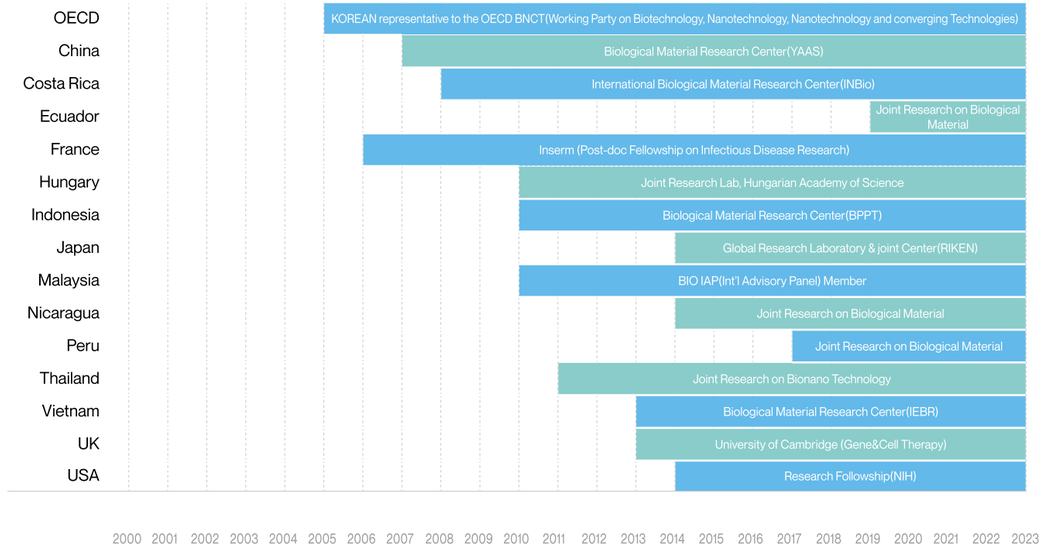
INTERNATIONAL NETWORK

TO STRENGTHEN GLOBAL COOPERATION IN MUTUALLY BENEFICIAL RELATIONSHIPS

R&D globalization by the Ministry of Science and ICT

Research collaboration with World's renowned research institutes

Establishment of network for the preservation and utilization of biological materials with China, Vietnam, Costa Rica and Indonesia



RESEARCH INFRASTRUCTURE

LIFE-CYCLE INFRASTRUCTURE SERVICE FROM BASIC RESEARCH TO COMMERCIALIZATION

1980

1985
Biological Resource Center

2005
National Primate Research Center

2000

2006
Bio Evaluation Center

2010

2010
Korea Bioinformation Center

2012
Futuristic Animal Resource Center

2013
Biotechnology Process Engineering Center

2013
Eco-friendly Bio Material R&D Center

2018
Primate Resource Support Center

2020

2022
- Bio-resource Central Bank
- Animal Model Natural Product Microorganism
- Korea Preclinical Evaluation Center

KRIBB 2023

02

RESEARCH HIGHLIGHTS

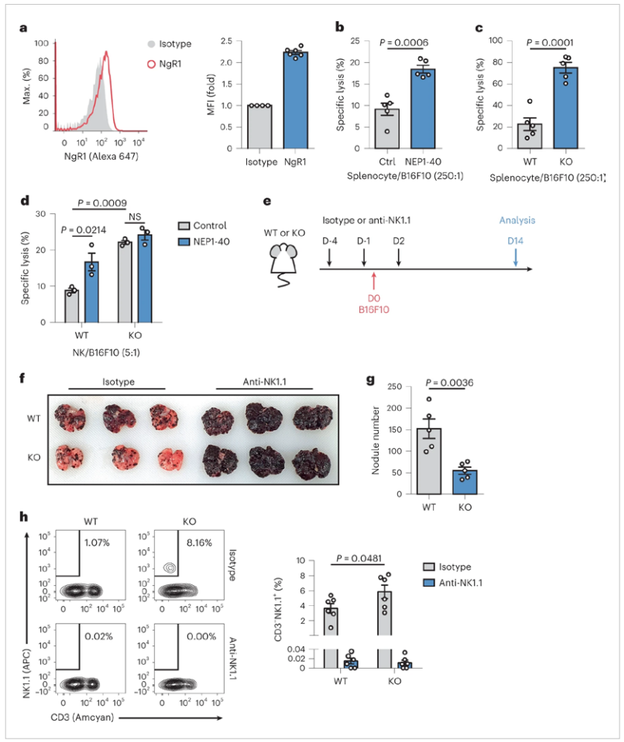
2023 KRIBBIAN OF THE MONTH AWARDEES

Dr. Tae-Don Kim

Immunotherapy
Research Center

NgR1 is an NK cell inhibitory receptor that destabilizes the immunological synapse

The formation of an immunological synapse (IS) is essential for natural killer (NK) cells to eliminate target cells. Despite an advanced understanding of the characteristics of the IS and its formation processes, the mechanisms that regulate its stability via the cytoskeleton are unclear. Here, we show that Nogo receptor 1 (NgR1) has an important function in modulating NK cell-mediated killing by destabilization of IS formation. NgR1 deficiency or blockade resulted in improved tumor control of NK cells by enhancing NK-to-target cell contact stability and regulating F-actin dynamics during IS formation. Patients with tumors expressing abundant NgR1 ligand had poor prognosis despite high levels of NK cell infiltration. Thus, our study identifies NgR1 as an immune checkpoint in IS formation and indicates a potential approach to improve the cytolytic function of NK cells in cancer immunotherapy.

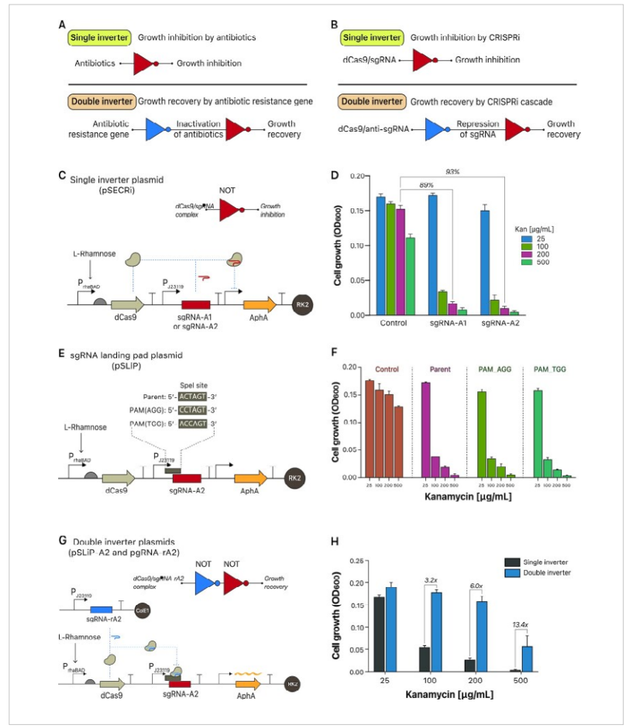


Dr. Seong Keun Kim

Synthetic Biology
Research Center

CRISPRi-based programmable logic inverter cascade for antibiotic-free selection and maintenance of multiple plasmids

Antibiotics have been widely used for plasmid-mediated cell engineering. However, continued use of antibiotics increases the metabolic burden, horizontal gene transfer risks, and biomanufacturing costs. There are limited approaches to maintaining multiple plasmids without antibiotics. Herein, we developed an inverter cascade using CRISPRi by building a plasmid containing a single guide RNA (sgRNA) landing pad (pSLiP); this inhibited host cell growth by repressing an essential cellular gene. Anti-sgRNAs on separate plasmids restored cell growth by blocking the expression of growth-inhibitory sgRNAs in pSLiP. We maintained three plasmids in Escherichia coli with a single antibiotic selective marker. To completely avoid antibiotic use and maintain the CRISPRi-based logic inverter cascade, we created a novel d-glutamate auxotrophic E. coli. This enabled the stable maintenance of the plasmid without antibiotics, enhanced the production of the terpenoid, (-)-α-bisabolol, and generation of an antibiotic-resistance gene-free plasmid. CRISPRi is therefore widely applicable in genetic circuits and may allow for antibiotic-free biomanufacturing.

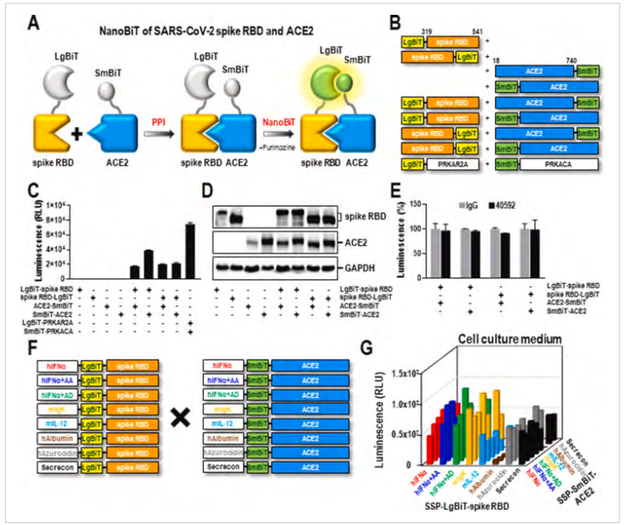


Dr. Sungchan Cho

Nucleic Acid Therapeutics
Research Center

The SpACE-CCM: A facile and versatile cell culture medium-based biosensor for detection of SARS-CoV-2 spike-ACE2 interaction

The COVID-19 pandemic is an ongoing global public health threat. COVID-19 is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, and binding of the SARS-CoV-2 spike to its receptor, angiotensin-converting enzyme 2 (ACE2), on host cells is critical for viral infection. Here, we developed a luminescent biosensor that readily detects interactions of the spike receptor-binding domain (RBD) and ACE2 in cell culture medium ('SpACE-CCM'), which was based on bimolecular complementation of the split nanoluciferase-fused spike RBD and ectodomain of ACE2 and further engineered to be efficiently secreted from cells by adding a heterologous secretory signal peptide (SSP). Screening of various SSPs identified 'interferon-α+alanine-aspartate' as the SSP that induced the highest activity. The SpACE-CCM biosensor was validated by observing a marked reduction of the activity caused by interaction-defective mutations or in the presence of neutralizing antibodies, recombinant decoy proteins, or peptides. Importantly, the SpACE-CCM biosensor responded well in assay-validating conditions compared with conventional cell lysate-based NanoLuc Binary Technology, indicating its advantage. We further demonstrated the biosensor's versatility by quantitatively detecting neutralizing activity in blood samples from COVID-19 patients and vaccinated individuals, discovering a small molecule interfering with the spike RBD-ACE2 interaction through high-throughput screening, and assessing the cross-reactivity of neutralizing antibodies against SARS-CoV-2 variants. Because the SpACE-CCM is a facile and rapid one-step reaction biosensor that aptly recapitulates the native spike-ACE2 interaction, it would be advantageous in many experimental and clinical applications associated with this interaction.

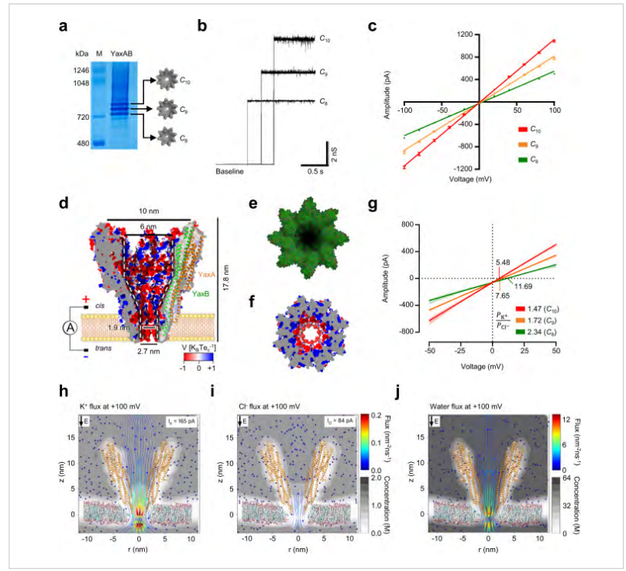


Dr. Ki Baek Jeong

Critical Diseases
Diagnostics Convergence
Research Center

Single-molecule fingerprinting of protein-drug interaction using a funneled biological nanopore

In drug discovery, efficient screening of protein-drug interactions (PDIs) is hampered by the limitations of current biophysical approaches. Here, we develop a biological nanopore sensor for single-molecule detection of proteins and PDIs using the pore-forming toxin YaxAB. Using this YaxAB nanopore, we demonstrate label-free, single-molecule detection of interactions between the anticancer Bcl-xL protein and small-molecule drugs as well as the Bak-BH3 peptide. The long funnel-shaped structure and nanofluidic characteristics of the YaxAB nanopore enable the electro-osmotic trapping of diverse folded proteins and high-resolution monitoring of PDIs. Distinctive nanopore event distributions observed in the two-dimensional (ΔI/Io-versus-IN) plot illustrate the ability of the YaxAB nanopore to discriminate individual small-molecule drugs bound to Bcl-xL from non-binders. Taken together, our results present the YaxAB nanopore as a robust platform for label-free, ultrasensitive, single-molecule detection of PDIs, opening up a possibility for low-cost, highly efficient drug discovery against diverse drug targets.



Dr. Kyoung-Jin Oh

Metabolic Regulation
Research Center

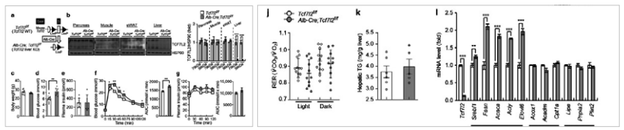
Tcf7l2 in hepatocytes regulates de novo lipogenesis in diet-induced non-alcoholic fatty liver disease in mice

Aims/hypothesis: Non-alcoholic fatty liver disease (NAFLD) associated with type 2 diabetes may more easily progress towards severe forms of non-alcoholic steatohepatitis (NASH) and cirrhosis. Although the Wnt effector transcription factor 7-like 2 (TCF7L2) is closely associated with type 2 diabetes risk, the role of TCF7L2 in NAFLD development remains unclear. Here, we investigated how changes in TCF7L2 expression in the liver affects hepatic lipid metabolism based on the major risk factors of NAFLD development.

Methods: Tcf7l2 was selectively ablated in the liver of C57BL/6N mice by inducing the albumin (Alb) promoter to recombine Tcf7l2 alleles floxed at exon 5 (liver-specific Tcf7l2-knockout [KO] mice: Alb-Cre;Tcf7l2f/f). Alb-Cre;Tcf7l2f/f and their wild-type (Tcf7l2f/f) littermates were fed a high-fat diet (HFD) or a high-carbohydrate diet (HCD) for 22 weeks to reproduce NAFLD/NASH. Mice were refed a standard chow diet or an HCD to stimulate de novo lipogenesis (DNL) or fed an HFD to provide exogenous fatty acids. We analysed glucose and insulin sensitivity, metabolic respiration, mRNA expression profiles, hepatic triglyceride (TG), hepatic DNL, selected hepatic metabolites, selected plasma metabolites and liver histology.

Results: Alb-Cre;Tcf7l2f/f essentially exhibited increased lipogenic genes, but there were no changes in hepatic lipid content in mice fed a normal chow diet. However, following 22 weeks of diet-induced NAFLD/NASH conditions, liver steatosis was exacerbated owing to preferential metabolism of carbohydrate over fat. Indeed, hepatic Tcf7l2 deficiency enhanced liver lipid content in a manner that was dependent on the duration and amount of exposure to carbohydrates, owing to cell-autonomous increases in hepatic DNL. Mechanistically, TCF7L2 regulated the transcriptional activity of Mlxipl (also known as ChREBP) by modulating O-GlcNAcylation and protein content of carbohydrate response element binding protein (ChREBP), and targeted Srebf1 (also called SREBP1) via miRNA (miR)-33-5p in hepatocytes. Eventually, restoring TCF7L2 expression at the physiological level in the liver of Alb-Cre;Tcf7l2f/f mice alleviated liver steatosis without altering body composition under both acute and chronic HCD conditions.

Conclusions/interpretation: In mice, loss of hepatic Tcf7l2 contributes to liver steatosis by inducing preferential metabolism of carbohydrates via DNL activation. Therefore, TCF7L2 could be a promising regulator of the NAFLD associated with high-carbohydrate diets and diabetes since TCF7L2 deficiency may lead to development of NAFLD by promoting utilisation of excess glucose pools through activating DNL.

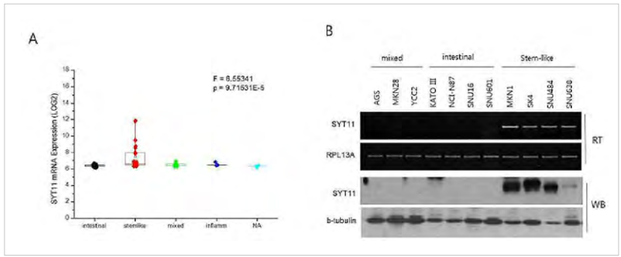


Dr. Misun Won

Personalized Genomic
Medicine Research Center

A composition for treating stomach cancer comprising an inhibitor of SYT11

The present invention relates to a composition comprising a synaptotagmin-11 (SYT11) inhibitor as an effective component for treating stomach cancer, and a method of detecting stem-like stomach cancer, comprising measuring the expression of SYT11. According to the present invention, the composition comprising an SYT11 inhibitor inhibits the migration and infiltration of stomach cancer cells, inhibits the same from attaching to extracellular matrix, and also inhibits the secretion of various cytokines associated with cancer metastasis, and inhibits the proliferation of stomach cancer cells, thereby exhibiting excellent effects as a composition for suppressing stomach cancer metastasis, or for preventing or treating stomach cancer. In addition, the present invention has confirmed a correlation between the expression of SYT11 and stem-like stomach cancer, and thus, provides excellent effects in detecting stem-like stomach cancer by measuring the expression level of SYT11.

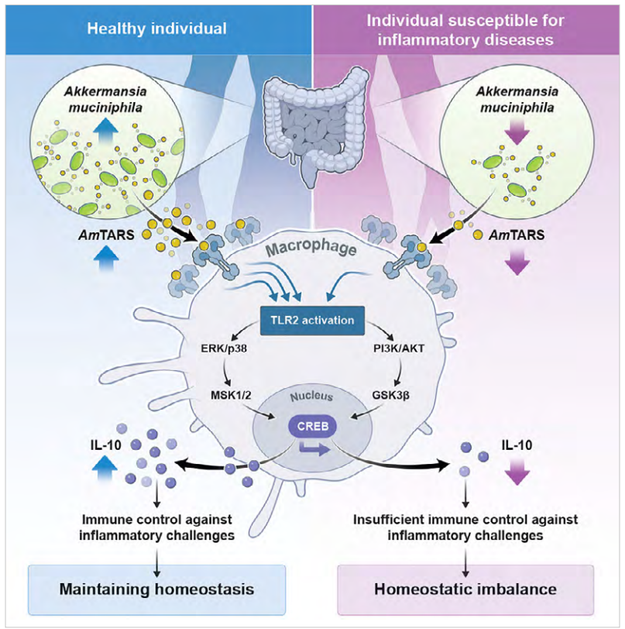


Dr. Myung Hee Kim

Microbiome Convergence
Research Center

Secreted Akkermansia muciniphila threonyl-tRNA synthetase functions to monitor and modulate immune homeostasis

Commensal bacteria are critically involved in the establishment of tolerance against inflammatory challenges, the molecular mechanisms of which are just being uncovered. All kingdoms of life produce aminoacyl-tRNA synthetases (ARSs). Thus far, the non-translational roles of ARSs have largely been reported in eukaryotes. Here, we report that the threonyl-tRNA synthetase (AmTARS) of the gut-associated bacterium Akkermansia muciniphila is secreted and functions to monitor and modulate immune homeostasis. Secreted AmTARS triggers M2 macrophage polarization and orchestrates the production of anti-inflammatory IL-10 via its unique, evolutionary-acquired regions, which mediates specific interactions with TLR2. This interaction activates the MAPK and PI3K/AKT signaling pathways, which converge on CREB, leading to an efficient production of IL-10 and suppression of the central inflammatory mediator NF-κB. AmTARS restores IL-10-positive macrophages, increases IL-10 levels in the serum, and attenuates the pathological effects in colitis mice. Thus, commensal tRNA synthetases can act as intrinsic mediators that maintain homeostasis.

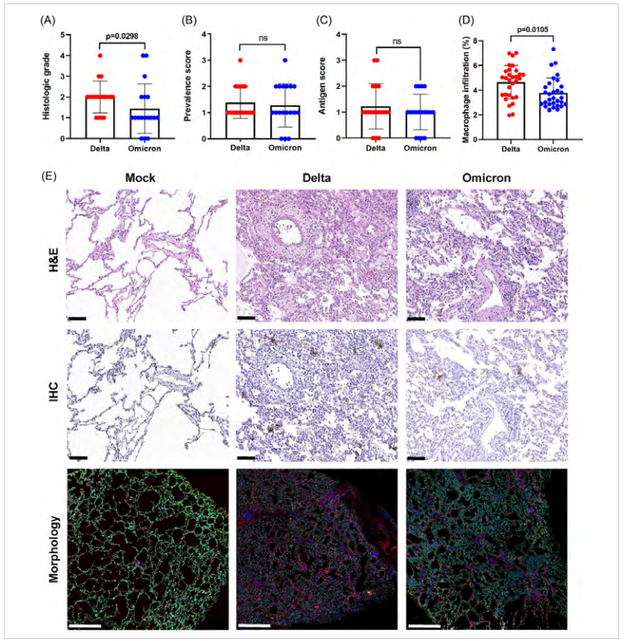


Dr. Jung Joo Hong

National Primate
Research Center

Comparative spatial transcriptomic profiling of severe acute respiratory syndrome coronavirus 2 Delta and Omicron variants infections in the lungs of cynomolgus macaques

Recently emerging severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) Omicron variants are generally less pathogenic than previous strains. However, elucidating the molecular basis for pulmonary immune response alterations is challenging owing to the virus's heterogeneous distribution within complex tissue structure. Here, we revealed the spatial transcriptomic profiles of pulmonary microstructures at the SARS-CoV-2 infection site in the nine cynomolgus macaques upon inoculation with the Delta and Omicron variants. Delta- and Omicron-infected lungs had upregulation of genes involved in inflammation, cytokine response, complement, cell damage, proliferation, and differentiation pathways. Depending on the tissue microstructures (alveoli, bronchioles, and blood vessels), there were differences in the types of significantly upregulated genes in each pathway. Notably, a limited number of genes involved in cytokine and cell damage response were differentially expressed between bronchioles of the Delta- and Omicron-infection groups. These results indicated that despite a significant antigenic shift in SARS-CoV-2, the host immune response mechanisms induced by the variants were relatively consistent, with limited transcriptional alterations observed only in large airways. This study may aid in understanding the pathogenesis of SARS-CoV-2 and developing a clinical strategy for addressing immune dysregulation by identifying potential transcriptional biomarkers within pulmonary microstructures during infection with emerging variants.

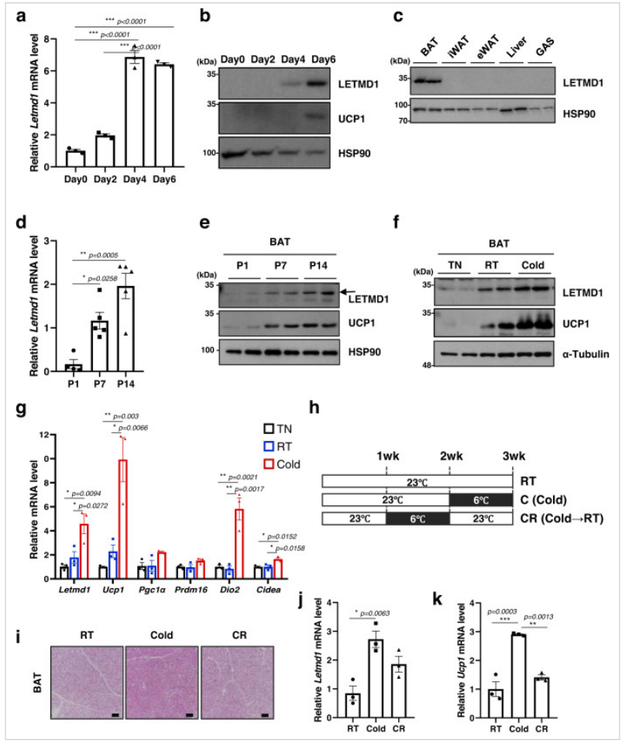


Dr. Won Kon Kim

Metabolic Regulation
Research Center

Mitochondrial matrix protein LETMD1 maintains thermogenic capacity of brown adipose tissue in male mice

Brown adipose tissue (BAT) has abundant mitochondria with the unique capability of generating heat via uncoupled respiration. Mitochondrial uncoupling protein 1 (UCP1) is activated in BAT during cold stress and dissipates mitochondrial proton motive force generated by the electron transport chain to generate heat. However, other mitochondrial factors required for brown adipocyte respiration and thermogenesis under cold stress are largely unknown. Here, we show LETM1 domain-containing protein 1 (LETMD1) is a BAT-enriched and cold-induced protein required for cold-stimulated respiration and thermogenesis of BAT. Proximity labeling studies reveal that LETMD1 is a mitochondrial matrix protein. Letmd1 knockout male mice display aberrant BAT mitochondria and fail to carry out adaptive thermogenesis under cold stress. Letmd1 knockout BAT is deficient in oxidative phosphorylation (OXPHOS) complex proteins and has impaired mitochondrial respiration. In addition, BAT-specific Letmd1 deficient mice exhibit phenotypes identical to those observed in Letmd1 knockout mice. Collectively, we demonstrate that the BAT-enriched mitochondrial matrix protein LETMD1 plays a tissue-autonomous role that is essential for BAT mitochondrial function and thermogenesis.

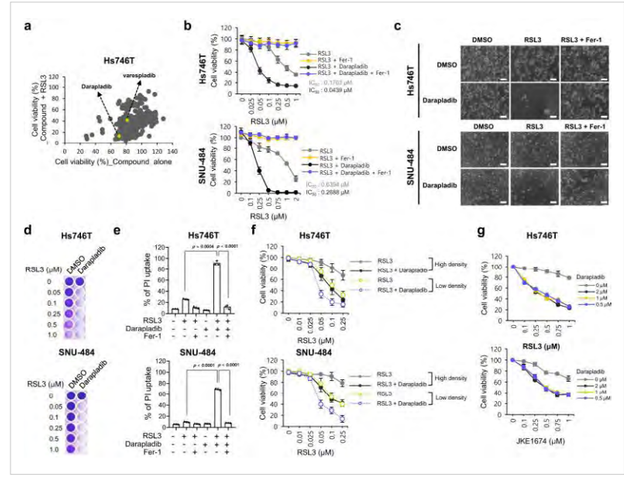


Dr. Mihee Oh

Biodefense
Research Center

The lipoprotein-associated phospholipase A2 inhibitor Darapladib sensitises cancer cells to ferroptosis by remodelling lipid metabolism

Arachidonic and adrenic acids in the membrane play key roles in ferroptosis. Here, we reveal that lipoprotein-associated phospholipase A2 (Lp-PLA2) controls intracellular phospholipid metabolism and contributes to ferroptosis resistance. A metabolic drug screen reveals that darapladib, an inhibitor of Lp-PLA2, synergistically induces ferroptosis in the presence of GPX4 inhibitors. We show that darapladib is able to enhance ferroptosis under lipoprotein-deficient or serum-free conditions. Furthermore, we find that Lp-PLA2 is located in the membrane and cytoplasm and suppresses ferroptosis, suggesting a critical role for intracellular Lp-PLA2. Lipidomic analyses show that darapladib treatment or deletion of PLA2G7, which encodes Lp-PLA2, generally enriches phosphatidylethanolamine species and reduces lysophosphatidylethanolamine species. Moreover, combination treatment of darapladib with the GPX4 inhibitor PACMA31 efficiently inhibits tumour growth in a xenograft model. Our study suggests that inhibition of Lp-PLA2 is a potential therapeutic strategy to enhance ferroptosis in cancer treatment.



Dr. **Jung Hwa Lim**

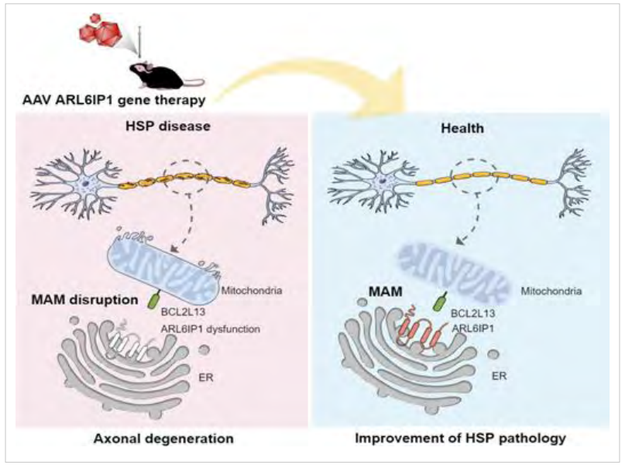
Stem Cell Convergenece Research Center

ARL6IP1 gene delivery reduces neuroinflammation and neurodegenerative pathology in hereditary spastic paraplegia model

ARL6IP1 is implicated in hereditary spastic paraplegia (HSP), but the specific pathogenic mechanism leading to neurodegeneration has not been elucidated. Here, we clarified the molecular mechanism of ARL6IP1 in HSP using in vitro and in vivo models.

The Arl6ip1 knockout (KO) mouse model was generated to represent the clinically involved frameshift mutations and mimicked the HSP phenotypes.

Notably, in vivo brain histopathological analysis revealed demyelination of the axon and neuroinflammation in the white matter, including the corticospinal tract. In in vitro experiments, ARL6IP1 silencing caused cell death during neuronal differentiation and mitochondrial dysfunction by dysregulated autophagy. ARL6IP1 localized on mitochondria-associated membranes (MAMs) to maintain endoplasmic reticulum and mitochondrial homeostasis via direct interaction with LC3B and BCl2L13. ARL6IP1 played a crucial role in connecting the endoplasmic reticulum and mitochondria as a member of MAMs. ARL6IP1 gene therapy reduced HSP phenotypes and restored pathophysiological changes in the Arl6ip1 KO model. Our results established that ARL6IP1 could be a potential target for HSP gene therapy.

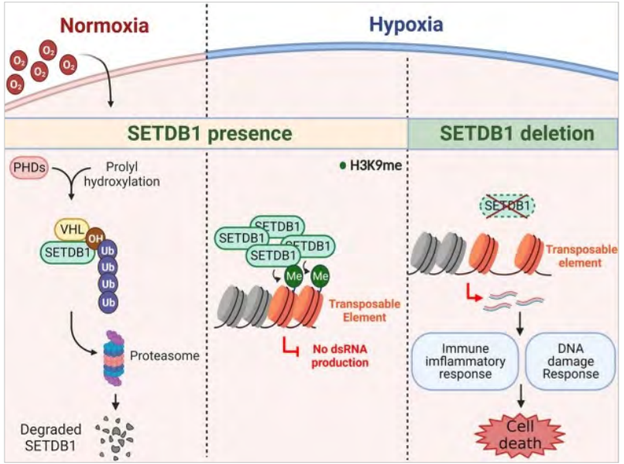


Dr. **Jeong-Hoon Kim**

Disease Target Structure Research Center

Hypoxia stabilizes SETDB1 to maintain genome stability

Von Hippel-Lindau (VHL) is a tumor suppressor that functions as the substrate recognition subunit of the CRL2VHL E3 complex. While substrates of VHL have been identified, its tumor suppressive role remains to be fully understood. For further determination of VHL substrates, we analyzed the physical interactome of VHL and identified the histone H3K9 methyltransferase SETBD1 as a novel target. SETDB1 undergoes oxygen-dependent hydroxylation by prolyl hydroxylase domain proteins and the CRL2VHL complex recognizes hydroxylated SETDB1 for ubiquitin-mediated degradation. Under hypoxic conditions, SETDB1 accumulates by escaping CRL2VHL activity. Loss of SETDB1 in hypoxia compared with that in normoxia escalates the production of transposable element-derived double-stranded RNAs, thereby hyperactivating the immune-inflammatory response. In addition, strong derepression of TEs in hypoxic cells lacking SETDB1 triggers DNA damage-induced death. Our collective results support a molecular mechanism of oxygen-dependent SETDB1 degradation by the CRL2VHL E3 complex and reveal a role of SETDB1 in genome stability under hypoxia.



03

RESEARCH DIVISIONS

[NST Convergence Research Groups]

Dr. Eun-Soo Kwon

Aging Convergence Research Center
Associate Director

eunsoo.kwon@kribb.re.kr

1. Introduction

Aging is one of the most complex biological processes yet to be poorly understood. Aging has been regarded as a common risk factor for most chronic diseases. In last decades, several interventions against aging and aging-associated diseases have been conducted using anti-aging plasma proteins, senolytic chemicals and potential dietary restriction mimetics. Aging Convergence Research Center (ACRC) is the research group dedicated to the fundamental science of aging and age-related diseases in KRIBB. ACRC are working on the projects focused on the development of diagnostic, therapeutic, and prevention of aging. To develop aging diagnostics, we have collected over 1,000 blood samples from individuals aged from 10s to 80s. Using bioinformatics, we are currently making aging clock based on DNA methylation patterns associated with age in human as well as mice. To reverse biological aging, we are developing anti-aging biologics derived from plasma proteins. Several promising candidates have already been validated in both cell and animal models. Furthermore, we explore 'in vivo' senescent cells and identify optimal targets for efficient senolytic technology.

2. Research Areas

- Developing an aging diagnostic technique based on epigenetics
  - Analysis of DNA methylome using genome-wide screening technique to identify aging-associated DNA methylation biomarkers.
  - Constructing the extensive epigenome database
- Identification and characterization of the blood-derived rejuvenating factors that reverse ageing processes
  - Analysis of the serum factors using multi-omics tools to achieve the slowing down of the aging process in old animals.
  - Seeking genetic factors and metabolites provided by the host-gut microbiota interactions that contribute to the longevity of the host using genome-wide gut microbiota library
  - A group of miRNA in the muscle of human biopsy and mouse models is coordinated by multi-omics analysis and examined to find out the role of those that change after exercise.
  - Identification of new genetic factors leading to muscle aging by analyzing lipid composition.
- Creating an in vivo senescent cell atlas
  - Quantitatively evaluate the burden of senescent cells in certain organs using tissue-specific premature and natural aging mouse models
  - Identifying in vivo senescent cells that adversely affect the aging micro-environment using (spatial) single-cell mRNA sequencing analysis
  - Discovering antigens specific to in vivo senescent cells through single-ell proteogenomics
- Elucidating the mechanisms underlying the accumulation of senescent cells in vivo
  - Identifying the key regulatory network in senescent cells through single cell transcriptional and epigenetic analysis
  - Identify immune evasion mechanisms specific to senescent cells
- Developing senescent cell-specific elimination strategies
  - Developing a novel senolytics modality that targets senescent cell-specific antigens to eliminate senescent cells
  - Developing strategies to restore immunosurveillance of senescent cells through co-culture system of senescent cells and immune cells
- Hematopoeitic stem cell (HSC) aging and rejuvenation
  - Aging mechanism and rejuvenation of HSCs
  - HSC fate decision
  - Recovery of immunity
  - Single cell-based multiome analysis
  - In silico virtual screening of small molecules for rejuvenation drug

3. Main Projects

- Developing aging clock to estimate biological aging in human and animal
  - Developing an aging diagnostic technique based on epigenetics
- Developing interventions that reverse and slow biological aging
  - Identification and characterization of the blood-derived rejuvenating factors that reverse ageing processes
  - Developing senescent cell-specific elimination strategies
  - In silico virtual screening of small molecules for rejuvenation drug
- Understanding biological aging processes
  - Creating an in vivo senescent cell atlas
  - Elucidating the mechanisms underlying the accumulation of senescent cells in vivo
  - Aging mechanism and rejuvenation of HSCs

4. Recent Achievements

- Development and Technology Transfer of Core Technology for Controlling Age-related Diseases (Technology Transfer, 2023)
  - Successfully discovered novel blood-based aging regulators and developed core technology for controlling age-related diseases based on these regulators.
  - Technology transferred for a fixed fee of 2.2 billion KRW.
- Identification of Genes Related to Muscle Function Improvement Regulated by Exercise and Caloric Restriction with Anti-aging Effects (Aging, 2023)
  - Identified genes regulated by exercise and caloric restriction in muscles and elucidated their mechanisms.
  - This research provides valuable insights into the molecular basis of muscle function improvement and has potential applications for developing novel anti-aging interventions.
- A new AMPK isoform mediates glucose-restriction induced longevity non-cell autonomously by promoting membrane fluidity (Nature Comm, 2023)
  - glucose restricted diets ameliorate neuro-degenerative diseases.
  - glucose restricted diets extend the lifespan in endocrine manners, including neuronal AMPK, neuropeptide, adipnectin receptor, PPARa, by modulating lipid metabolism.
- Overcoming cellular senescence through alternative lengthening of telomeres
  - Identification of a novel mechanism to overcome cellular senescence through an evolutionary conserved telomere lengthening mechanism
  - Elucidating molecular mechanisms of alternative lengthening of telomeres using multi-omics strategies
- Identification of Gut Microbiota Strains for Improving Muscle Function (Patent Application)
  - Identified gut microbiota that can mimic the muscle function-improving effects of exercise.
  - Old mice that ingested the culture medium of the identified gut microbiota showed improved muscle function.
  - This study suggests that gut microbiota manipulation could be a promising strategy for improving muscle function in the elderly.

[NST Convergence Research Groups]

Dr. Seung Jun Kim

Critical Diseases Diagnostics Convergence Research Center
Associate Director

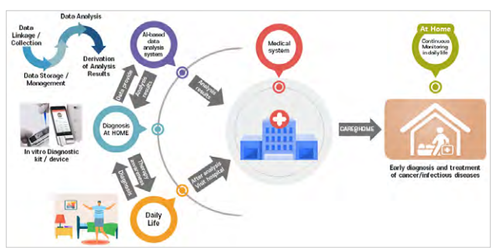
ksj@kribb.re.kr

1. Introduction

- In modern society, with the increasing survival rates through early detection of cancers and critical diseases, the paradigm of healthcare is transitioning from treatment to health management through diagnosis and prevention, and the market size of advanced technology-integrated diagnostic devices is rapidly expanding
- The Critical Diseases Diagnostics Convergence Research Center aims to address the current major healthcare situation and overcome the limitations of existing critical disease diagnoses by developing the UnTACT (Uninvasive Technology-oriented Autonomous Convenient Test) system. This system is designed to enable minimally or non-invasive early diagnosis technology, on-site diagnosis, and continuous monitoring capabilities.
- Our research center is currently progressing in the development of a next-generation healthcare system, the Smart Self-Diagnosis System, through the integration of BT (biotechnology), NT (nanotechnology), and ICT (information and communication technology). This includes the development of technology such as breath based bio-nano sensor development, artificial protein redesign for ultra-precise detection of disease biomarkers, CRISPR-based gene multiplex detection technology, nanopore-based single-molecule sensing technology for biomarker detection, and the development of an AI-based smart diagnostic analysis system

2. Research Areas

- Discovery of non/low-invasive virus target biomarkers
  - Discovery of at least 6 types of disease target biomarkers including 4 types of cancer (pancreatic cancer, biliary tract cancer, renal cancer, lung cancer), SARS-CoV, and novel/infectious variant viruses
- Development of ultra-precision/rapid biomarker detection technology
  - Development of ultra-precision/rapid sensing technology for early diagnosis and prevention of diseases such as cancer, infectious diseases, etc.
  - Development of sensors for biomarker detection (quantum sensors, nanopore sensors, artificial protein sensors)
- Establishment of portable self-diagnostic device and data integration management system
  - Establishment of portable self-diagnostic equipment and data integration management system to enhance the portability and usability of self-diagnostic equipment, ensuring the accuracy and reliability of detection results

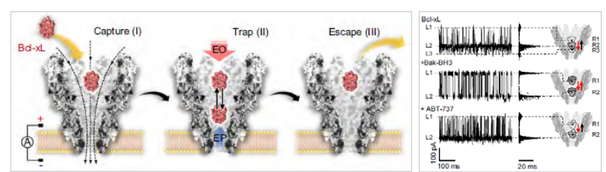


3. Main Projects

- Specific novel bio-marker discovery and selection capable of individually diagnosing, including four types of cancer (pancreatic, biliary tract, renal, and lung) and infectious viral diseases
  - Development of continuous analysis technology for non/low-invasive bio-marker discovery and self-diagnosis for non/low-invasive cancer diagnosis
  - Bio-marker discovery in non/low-invasive human-derived samples (blood, urine, breath, etc.) and presentation of a bio-marker panel with high sensitivity and specificity
  - Selection of at least one bio-marker for diagnosis of novel viral diseases (COVID-19, SARS-CoV) and development of a rapid diagnostic kit with high sensitivity and specificity
- Development of non/low-invasive biological sample collection and pre-processing technology
  - Portable and easy pre-processing system for non/low-invasive samples based on magnetic or electrophoretic methods
- Development of a diagnostic technology platform and for 4 cancers and unknown novel virus diagnosis using ultra-highly sensitive, accurate, precision, rapid, multi-sensing technology
  - Portable diagnostic technology based on room temperature operation using breath-based detection
  - Nanopore sensing technology for biomarker detection at the single-molecule level
  - Designed Artificial protein for highly sensitive sensor and on-site detection probe system
  - Highly sensitive CRISPR-based gene detection technology capable of rapid response to novel infectious diseases

4. Recent Achievements

- Single-molecule fingerprinting of protein-drug interaction using a funneled biological nanopore (Nat Commun. IF 17.69)
  - We developed a biological nanopore sensor using the YaxAB toxin for detecting proteins and protein-drug interactions (PDIs) at the single-molecule level. This nanopore allows label-free detection of interactions involving the anticancer protein Bcl-xL and small-molecule drugs. Its unique structure enables precise monitoring of PDIs, showing potential for cost-effective and efficient drug discovery against diverse targets.
- A versatile odor detection system based on automatically trained rats for chemical sensing
  - We developed an automated odor detection system using rats trained through operant conditioning. Our system achieved impressive results, with rats detecting 2,4-dinitrotoluene (DNT) at a 95% accuracy rate and maintaining their skills for up to four months post-training. This study introduces a highly effective method for specific odor detection, offering faster, more reliable, and accurate detection of various odors.
- Highly sensitive and specific detection of influenza A viruses using bimolecular fluorescence complementation (BiFC) reporter system
  - We developed a highly sensitive influenza A virus (IAV) detection system using bimolecular fluorescence complementation (BiFC), combining a galactose/glucose-binding protein (GGBP) with enhanced yellow fluorescence protein (eYFP). This system detects IAV through fluorescence reconstitution triggered by lactose binding to GGBP in the presence of neuraminidase (NA). With a linear dynamic range from 1 X 100 to 1 X 107 TCID50/mL and a detection limit of 1.1 X 100 TCID50/mL for IAV (H1N1), it offers ultra-high sensitivity. Our platform provides a simple, specific IAV detection method without the need for virus culture or RNA extraction.
- Enhancing the thermostability and activity of glycosyltransferase UGT76G1 via computational design
  - We performed computational design to enhance the thermostability and activity of diterpene glycosyltransferase UGT76G1, important for rebaudioside A production. The designed variants, 76_4 and 76_7, showed significant improvements: 76_4 exhibited a 9°C increase in thermal stability, 2.55-fold higher rebaudioside A production, and an 11% reduction in unwanted byproduct rebaudioside I. Variant 76_7 demonstrated a 1.91-fold increase in rebaudioside A production, maintained up to 55°C, highlighting the efficacy of structure-based design for industrial enzyme development.



- Insights into the recognition mechanism in the UBR box of UBR4 for its specific substrates
  - The N-end rule pathway regulates protein degradation via recognition of N-terminal amino acids (N-degrons) by E3 ligases like UBR4. Our study elucidates UBR4's unique mechanism for recognizing type-2 N-degrons, revealing specific interactions with aromatic residues and arginine. These findings offer insights into disease mechanisms associated with N-end rule pathway dysregulation.

[Korea Bioinformation Center (KOBIC)]

Dr. Haeyoung Jeong

Korea Bioinformation Center (KOBIC)
Associate Director

hyjeong@kribb.re.kr

1. Introduction

Korea Bioinformation Center (KOBIC) is a national center for biological research resources and information. We establish research environment infrastructure to facilitate biological data-driven research.

2. Research Areas

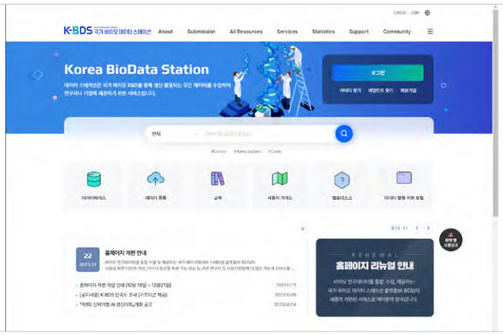
- Establishing infrastructure for collecting, distributing, and utilizing data from biological research
  - Construction and operation of an integrated platform (K-BDS; Korea BioData Station) to collect and distribute biological research data
  - Support for utilization of biological research data by providing cloud-computing service, data analysis service, and training courses
  - Cooperation and alignment with biological data management centers in both Korea and abroad
- Participating in the Korea National Genome Project
  - Participating in the Korea National Genome Project, which constructs a large-scale clinical and genomic data bank as an nationwide R&D infrastructure
  - Responsible for generating and analyzing genomics and other omics data
- Establishing national cluster of biological resources
  - Development and implementation of the strategies related to biological resources
  - Construction and operation of the information integration platform for biological resources (BioOne)

3. Main Projects

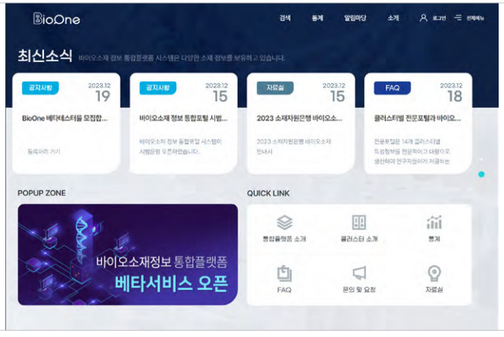
- Korea Biological Data Station (K-BDS) Project
- Korea National Genome Project
- Support for the National Cluster of Biological Resources Project

4. Recent Achievements

- Upgrade of Korea BioData Station (K-BDS)
  - Upgraded and launched the year 2023 version of Korea BioData Station (K-BDS) in December 2023
  - Major upgrades include specialization of data type-specific sub-homepages, improvement of interface, advancement of the procedures for submission, management, and provision of data



- Obtainment of official decision for the first phase of the Korea National Genome Project
  - Designed a project for the size of one million participants and obtained official decision for the first phase (2023-2028) of the project from Korean government
  - Construction and operation of the information integration platform for biological resources (BioOne)
- Development and launch of the pilot version of BioOne
  - Developed and launched the pilot version of BioOne platform in December 2023, which integrates information of biological resources and enables search and distribution application



[Digital Biotech Innovation Center]

Dr. Dae Soo Kim

Digital Biotech Innovation Center
Associate Director

kds2465@kribb.re.kr

1. Introduction

Recently, research in biohealth utilizing bio-big data is actively progressing. This research center is constructing a biohealthcare platform through the utilization of bio-big data to create a human organ map. This platform can be utilized for precision diagnosis, therapeutic development, and prognosis research.

2. Research Areas

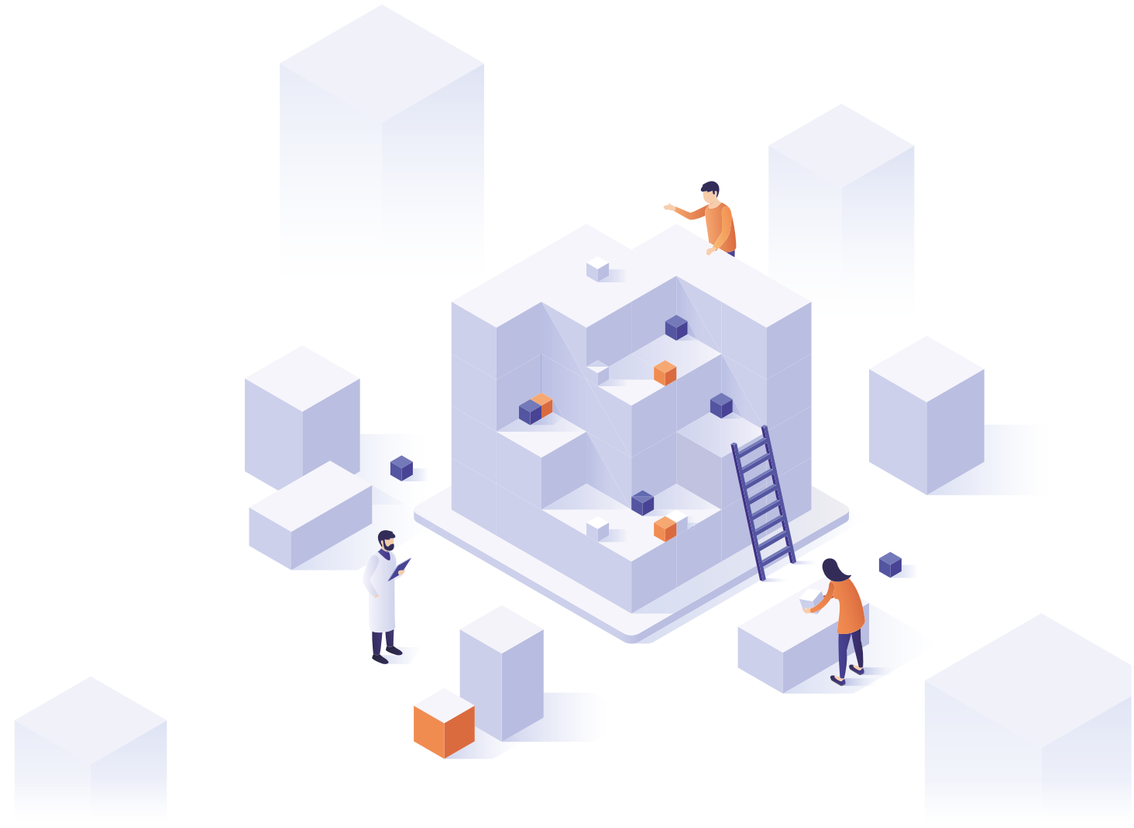
- Development of artificial intelligence-based genome analysis programs
- Identification of biomarkers and development of gene panel for precise diagnostics of metabolic diseases and cancer
- Development of an artificial intelligence-based computational framework for drug-target prioritization
- Integrative analysis of the whole genome, transcriptome, and epigenome in large-scale data sets derived from metabolic diseases and cancer
- Artificial intelligence-based analysis of pathological/diagnostic imaging data

3. Main Projects

- Establishing a human digital twin-based drug discovery platform using a multi-omic map of human tissues
  - The e-Human Atlas will transform our understanding of biology and disease, and could lead to major advances in the way illnesses are diagnosed and treated
- Construction of digital breeding platform for Hibiscus syriacus using artificial intelligence-based genome analysis
  - Development of flower color associated genetic markers and genes using correlation analysis of genotype and phenotype
- Development of artificial intelligence-based genome analysis programs and digital breeding platform
  - Development of artificial intelligence-based genome analysis programs
- Development of artificial intelligence-based bio bigdata analysis tools
  - Gene expression profiling interactive analysis and integrative analysis of genome by next generation sequencing platform

4. Recent Achievements

- Development of a quantitative prediction algorithm for target organ-specific similarity of human pluripotent stem cell-derived organoids and cells
  - The study aimed to develop a quantitative prediction algorithm to evaluate the target organ-specific similarity between human pluripotent stem cell (hPSC)-derived organoids and cells. The algorithm was designed based on the RNA sequencing data from hPSC-derived organoids and the corresponding human tissue samples. The algorithm was validated using different hPSC-derived organoids and showed high accuracy in predicting the target organ-specific similarity.
- Characterization of signature trends across the spectrum of non-alcoholic fatty liver disease using deep learning method
  - The study aimed to identify differentially expressed genes (DEGs) in non-alcoholic fatty liver disease (NAFLD) patients to determine different stages of the disease. The study found 103 DEGs in NAFLD patients, with 75 genes gradually increasing or decreasing in the NAFLD stage and 28 genes showing differences only in non-alcoholic steatohepatitis (NASH). The identified genes were used for deep-learning method with subset of features from lasso regression to obtain reliable determination performance in NAFL and NASH. The study also found significant differential expression of several candidate genes in liver cancer (LIHC), suggesting a potential relationship between NAFLD and hepatocellular carcinoma (HCC). The identified biomolecular signatures may improve clinical diagnosis and prognosis of NAFLD and enable therapeutic intervention.



[Synthetic Biology and Bioengineering Research Institute]

Dr. Dae Hee Lee

Synthetic Biology Research Center
Associate Director

dhlee@kribb.re.kr

1. Introduction

The Synthetic Biology Research Center (SBRC) at the Korea Institute of Biotechnology applies engineering principles to life sciences to construct novel biological systems through standardized bioparts. Our center brings together experts from diverse fields to advance the core technologies of synthetic biology, focusing on the Design-Build-Test-Learn (DBTL) cycle. Moreover, we've established a biofoundry beta to accelerate the DBTL cycle. This facility harnesses artificial intelligence for bio-design, develops bioparts, constructs genetic circuits, creates synthetic genomes, and leverages big data and deep learning for the production of biomaterials. Through these research activities, the SBRC aims to drive innovation and ecosystem development in the synthetic biology sector in Korea, contributing to the advancement of the bioindustry and the resolution of societal challenges.

2. Research Areas

- Development of Core Technologies in Synthetic Biology
  - Advancement of foundational technologies for synthetic biology aimed at the synthesis of intelligent genetic circuits and synthetic genomes
  - Development of industrially relevant enzymes through artificial intelligence-based protein design and molecular evolution techniques
  - Creation of intelligent cell control technologies via the integration of CRISPR gene editing tools with genetic circuits
  - Optimization of metabolic pathways and development of cell factories applying artificial intelligence-based biosystem design
- Establishment and Operation of the Biofoundry
  - Development of automation technologies for the biofoundry to facilitate the Design-Build-Test-Learn (DBTL) cycle in synthetic biology
  - Development of DNA design software and workflows to minimize errors in DNA assembly
  - Creation of synthetic microbes through artificial genome design and module assembly techniques
  - Enhancement of biofoundry capabilities through the establishment of standardized web-based databases for bioparts

3. Main Projects

- Development of Innovative Bioproduct Production Technologies
  - High-throughput screening using genetic circuits and improvement of proteins/enzymes through artificial intelligence
  - Discovery of useful enzymes derived from metagenomes using generative AI
  - Production of valuable compounds through optimization of metabolic pathways and cell factories based on the biofoundry infrastructure
- Development of Next-Generation Medical Technologies Based on Synthetic Biology
  - Development of probiotics for gut inflammation detection and recording using genetic circuits
  - Development of microbially based therapeutics for sensing and therapy regulation via CRISPR-based logic circuits
- Development of Technologies to Address Social Issues
  - Discovery and enhancement of enzymes for the degradation of non-degradable plastics
  - Development of biodegradable plastics that decompose at room temperature
  - Production of valuable biomaterials using microbes that utilize methane, a greenhouse gas
  - Development of bioparts and CRISPR gene-editing technologies for methanotrophs

4. Recent Achievements

- A highly efficient and versatile genetic engineering toolkit for a methanotroph-based biorefinery. Chem. Eng. J. 453, 139911 (2023). Dae-Hee Lee, Hyewon Lee and Seung-Goo Lee (IF 15.1)
  - Development of a high-efficiency synthetic biology technology for methanotrophs to convert methane, a greenhouse gas, into high-value biobased chemical materials
- Engineered Methylococcus capsulatus Bath for efficient methane conversion to isoprene. Bioresour. Technol. 393, 130098 (2023). Hyewon Lee and Seung-Goo Lee (IF 11.4)
  - Construction of a methanotroph-based cell factory for the production of isoprene, a raw material for rubber, from methane
- Development of novel recombinant peroxidase secretion system from Pseudomonas putida for lignin valorisation. Bioresour. Technol. 388, 129779 (2023). Bong Hyun Sung (IF 11.4)
  - Development of a novel protein secretion system in P. putida, secreting lignin peroxidase and demonstrating the potential for valorization of recalcitrant lignin
- Efficient valorization of food waste oils to renewable biodiesel by a Candida antarctica lipase B mutant that catalyzes the ester synthesis reaction in the presence of water. J. Clean. Prod. 428, 139336 (2023). Bong Hyun Sung and Jung-Hoon Sohn (IF 11.1)
  - Discovery of a highly active mutant of Candida antarctica lipase B that retains activity in the presence of water, an inhibitor of lipase action. This enables efficient production of biodiesel from low-grade waste oils by overproducing this lipase in yeast
- Identification of broad-spectrum neutralizing antibodies against influenza A virus and evaluation of their prophylactic efficacy in mice. Antiviral Res. 213, 105591. (2023) Sang Jick Kim (IF 10.103)
  - Development of therapeutic human antibodies broadly applicable to key subtypes (H1, H3, H5, etc.) of pandemic influenza A virus, demonstrating their prophylactic efficacy in mice

[Synthetic Biology and Bioengineering Research Institute]

Dr. Jeong-Heon Ko

Genome Editing Research Center
Associate Director

jhko@kribb.re.kr

1. Introduction

The genome editing research center as a pioneering department committed to driving innovation within the domain of gene editing technologies. This research center is endeavoring to a multifaceted exploration, including the refinement of genome editors, the advancement of gene therapy modalities, and the establishment of mouse models through gene-editing techniques.

2. Research Areas

• Advancement of gene editing technologies
- Development of ultra-small Cas enzyme engineered for enhanced efficacy and safety
- Development of technology to verify the accuracy of prime editors
- Improvement of efficiency in homology-directed repair to insert large gene fragments

• Development of gene therapy based on new genome editing technologies
- Development of novel genome editing tools for gene therapy applications
- Integration of genome editing technology into diagnostic platforms
- Validation of gene therapy through the utilization of gene-edited medium-sized animal models

• Development of glycan-humanized mouse model using glyco-gene editing technology
- Verification of the effectiveness of glycan-humanized mouse model
- Functional study of the role of non-human glycosyltransferase in human cancer

• Discovery of cancer biomarkers based on aberrant glycosylation
- Establishment of aglycosylated antibody-producing mice enabling quantification of tumor markers through aglycosylated antibody-lectin coupled immunoassays
- Discovery and validation of liver cancer marker based on aberrant glycosylation using aglycosylated antibody

3. Main Projects

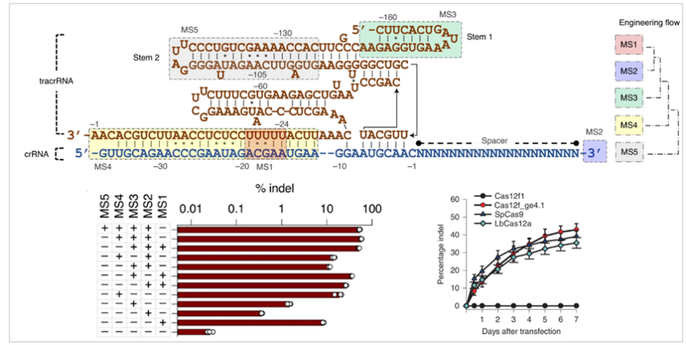
• Enhancement of the efficacy and specificity of genome editing technologies
• Development of new gene-editing tools for inserting large gene fragments
• Application of genome editing technologies to gene therapy and animal models

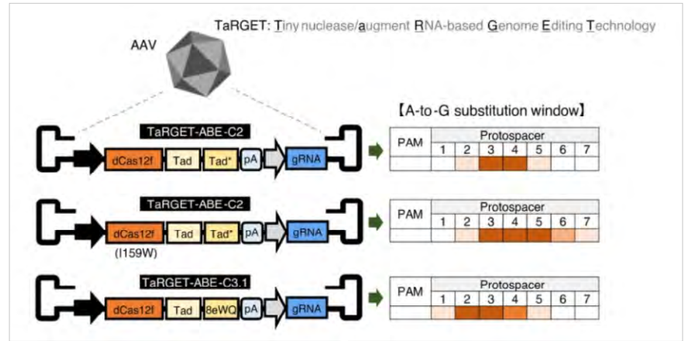
4. Recent Achievements

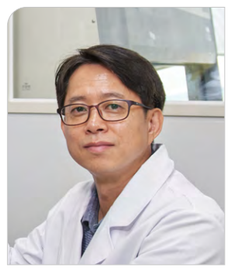
• Development of an ultra-small Cas enzyme achieving high efficacy and safety
- Gene-editing efficiency increased by 867-fold on average by optimizing the guide RNA of Cas12f1
- The optimized RNA, along with the ultra-small Cas enzyme Cas12f1, showed comparable editing efficiency to conventional editors.

• Establishment of hypercompact adenine base editors (ABE) based on the Cas12f1 variant with engineered RNA

- By combining Cas12f1 with engineered RNA, an AAV-deliverable genome editor without double-strand breaks is developed.
- The editing target range is expanded by engineering Cas12f or deaminases.







[Synthetic Biology and Bioengineering Research Institute]

Dr. Hee-Sik Kim

Cell Factory Research Center
Associate Director

hskim@kribb.re.kr

1. Introduction

In the era of climate crisis, new technological breakthroughs to mitigate greenhouse gases and bolster environmental sustainability remain imperative not just for the sake of stewarding ecosystem services, but seizing on new market opportunities. The center leads key initiatives in this core area with a primary goal of advancing microalgae-based carbon capture and utilization (CCU) technologies to enable effective transition to carbon-neutral bioeconomy. The center is also actively involved in major research efforts aimed at mitigating harmful algal blooms (HABs) as well as enabling effective biological treatment of plastic wastes. Furthermore, the center is dedicated to identifying and engineering a cell factory system capable of synthesizing valuable metabolites and proteins for a variety of industrial applications, including energy, environmental management, nutraceuticals, cosmetics, and pharmaceuticals. Through our multi-faceted endeavors, the center aspires to disseminate groundbreaking technologies and bioproducts in both the environmental and industrial sectors with a global reach.

2. Research Areas

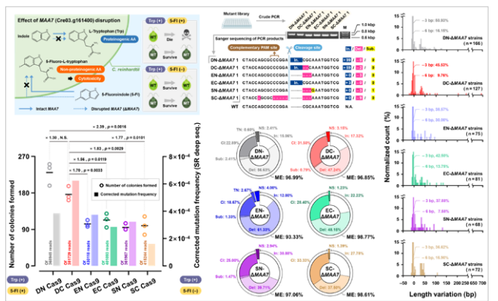
- Development of microalgal cell factories
  - Screening of novel pharmaceutical, nutraceutical, and cosmetic ingredient from microalgae and microbes.
  - Synthetic biology-based cellular and metabolic engineering of microalgae for high-value biomaterial production.
  - Development of a high-performance clustered regularly interspaced short palindromic repeats (CRISPR) RNA-guided nucleases system for the efficient gene editing of microalgae
  - Omics research of microalgae to modulate biosynthetic pathways
- Advancement of microalgae-based carbon capture and utilization (CCU) technology
  - Development of microalgal strains with high carbon fixation capability under different facility operation scenarios
  - Enabling lab-to-field transition of microalgae-based CCU technology through bioprocess engineering, proccess integration, and techno-economic assessment
  - Improvement of biorefinery technology to construct circular bioeconomy system based on microalgae product portfolio
  - Trophic conversion of microalgae for valorization of various carbon sources
- Microalgae-based environmental engineering
  - Development of plastic-degrading microalgae and their application for remediating the trophic transfer of microplastics
  - Phytoremediation: Microalgae-based pollutant removal from wastewaters
  - Synthetic communities: Assembling synergistic microbial consortium for environmental remediation
- Microalgae-related microbiome research
  - Study of microbiome and their interaction network during cyanobacterial blooms and development of novel methods for bloom control
  - Freshwater ecosystem health assessment based on multi-meta-omics of microbiome
  - Microbiome on aquatic plants and their interaction with cyanobacteria

3. Main Projects

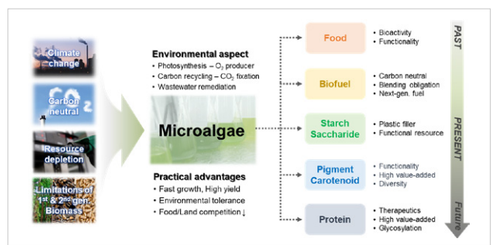
- Microbial cell factory for industrial and environmental applications
  - Development of algal lutein-based eye-healthy functional food
  - Development of algal violaxanthin-based anti-wrinkle functional cosmetics
  - Development of microbial pigments and biomaterials for cosmetics
  - Genetic engineering of microalge for plastic biodegradation with synthetic microbiome
- Development of carbon reduction technologies utilizing microalgae
  - Development of biofillers and various high-value product lines based on microalgae CCU technology.
  - Establishment of an optimal production process for microalgae biomass and securing economic viability.
  - Development of microalgae-based biorefinery technologies for the production of a diverse range of bioproducts.
- Microalgae-related microbiome research
  - Investigation of key bacteria and their interaction mechanisms contributing to cyanobacterial blooms
  - Multi-meta-omics study of aquatic microbiome determining ecosystem health
  - Control of cyanobacterial bloom, using biological interaction mechanisms

4. Recent Achievements

- The patent assignment for anti-wrinkle cosmetics application to ASKLabs (2023, total amount: $1,000,000)
  - Novel microalgae having high productivity for lutein (Korean Patent No. 10-2023-0023614))
- Designer microalgal biorefinery
  - Toward a zero-waste microalgal biorefinery: Complete utilization of defatted Chlorella biomass as a sole heterotrophic substrate for Chlorella sp. HS2 and an improved composite filler Chem. Eng. J. 480:147998 (2023)
- Bloom control by cyanobactericidal bacteria
  - Effective control of harmful Microcystis blooms by paucibactin A, a novel macrocyclic tambjamine, isolated from Paucibacter aquatile DH15. J Cleaner Production 383, 135408 (2023)
- Overproduction of microalgal nuetral lipid
  - Inhibition of monogalactosyldiacylglycerol synthesis by down-regulation of MGD1 leads to membrane lipid remodeling and enhanced triacylglycerol biosynthesis in Chlamydomonas reinhardtii Biotechnol Biofuels Bioprod vol.15, 88 (2022)
- Improvement of gene editing frequency in microalgae through optimization of CRISPR-Cas9 system
  - Gene editing frequency was dramatically increased via improving cell wall and nuclear membrane permeability
  - Nuclear import mechanism in microalgae was elucidated by harnessing the recent in silico tools



Patent applications (KR10-2023-0061795, PCT/KR2023/006493, WO 2023/224327 A1)



Improvement of gene editing frequency in microalgae through optimization of CRISPR-Cas9 system

[Division of Biomedical Research]

Dr. Kyung Chan Park

Personalized Genomic Medicine Research Center
Associate Director

kpark@kribb.re.kr

1. Introduction

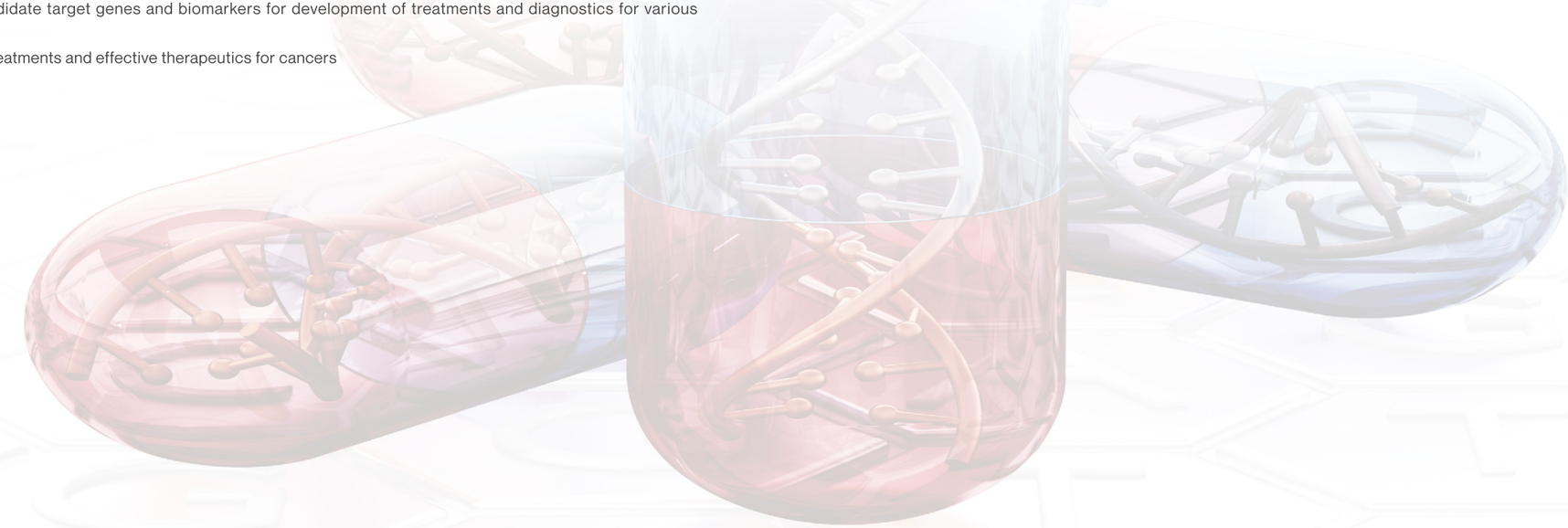
This research center is discovering novel biomarkers that can diagnose/ control primary and metastatic cancers based on the genome, and developing anticancer treatment technologies through functional analysis. We are producing multi-genomics data by using next-generation sequencing platform and also developing targeted anticancer drugs through bio big data-based biomarker discovery and validation.

2. Research Areas

- Development of bioinformatics tools and databases
- Multiomics analyses of various cancers to develop prognostic and predictive biomarkers and therapeutic targets
- Genome assembly and pan-genome construction for precision and personalized medicines.
- Maintenance and upgrade of NGS platform generating multiomics data
- Large-scale screening and identification of cancer-related genes
- Research on cancer dormancy
- Functional validation of candidate target genes and biomarkers for development of treatments and diagnostics for various cancers
- Development of innovative treatments and effective therapeutics for cancers

3. Main Projects

- Construction of genomics-based technical hub for cancer study
  - Development of bioinformatics tools
  - Development of gene expression database for tumor styudy (GENT3)
  - Development of cancer proteogenomic database portal
  - Construction of Korean reference pan-genomes
  - Discovery of somatic mutations based on whole genome data.
- Korea National Genome Project
  - Generating and management the whole genome sequencing data from the severe cancers and rare disease
  - Making the standard operating procedures and quality control index for generating the multiomics data
- Discovery and validation of novel therapeutic targets of non-smoking lung cancer by multiomics analysis
  - Integrative data analysis of multiomics data(transcriptome, proteome) for non-smoking lung cancer tissues
  - Screening of shRNA library for novel genes selected from the integrative analysis of multiomics data
  - Validation of the novel therapeutic target genes derived from shRNA library screening
- Study for cancer dormancy
  - Establishment and therapeutic application of lung/pancreatic cancer in vivo models for the study of cancer dormancy
  - Establishment of a lung cancer-inducing transgenic mouse model that can detect dormant cancer cells
  - Production & analysis of single cell transcriptome and epigenome data for the study of cancer dormancy
  - Identification & validation of cancer dormancy biomarkers
- Understanding mechanisms and treatment of chronic pancreas/liver disease related to inflammation
  - Identification of novel regulatory genes in progression of chronic inflammatory liver disease
  - Elucidating the pathophysiological mechanism for treatment of hepatic fibrosis and liver cancer
  - Identification of the novel role of NDRG3 in the progression of acute pancreatitis and chronicization
  - Identification of pathophysiological mechanisms for the treatment of pancreatitis/fibrosis and pancreatic cancer



4. Recent Achievements

- A 23-Gene Prognostic Index Predicts Progression and Bacillus Calmette-Guérin Response in Non–muscle-invasive Bladder Cancer
  - Advances in high-throughput technology have provided insight into non-muscle invasive bladder cancer (NMIBC); however, predicting clinical behavior and treatment responses remains challenging. This study develop a prognostic index (PI) for predicting progression and responses to intravesical Bacillus Calmette-Guérin therapy in NMIBC.
  - A total of 1,789 progression-associated genes were identified in a training cohort and their prognostic significance was confirmed in the validation cohorts using the deep learning algorithm.
  - Pathway enrichment and immunohistochemical analyses identified a 23-gene signature comprising established prognostic transcription factors and novel genes. Incorporating these genes into the PI revealed a significant association between it and NMIBC progression.
  - Multivariate analysis and subset stratification according to stage and grade confirmed the PI score as an independent risk factor (HR: 4.95, 95% CI=1.54–15.885; p=0.007).
  - The PI score effectively identified patients who would benefit from intravesical BCG therapy.
  - This study introduces a 23-gene-based PI as a potential diagnostic tool for predicting NMIBC progression and the response to BCG therapy. The findings suggest that the PI holds promise for identifying high-risk NMIBC patients and guiding personalized treatment choices.
- Estrogen Signaling as a Putative Target for Never-Smoker Lung Adenocarcinoma Patients without EGFR Mutation and ALK Fusion from Proteogenomic Characterization. Cancer Research
  - Never-smoker lung adenocarcinoma (NSLA) is prevalent in Asian populations, and is even more in women. EGFR mutations and ALK fusions are major alterations observed in NSLA.
  - Genome analysis revealed that TP53 (25%), KRAS (22%), ROS1 fusion (14%), and SETD2 (11%) were the most frequently mutated genes in NENA patients. Proteogenomic impact analysis revealed that STK11 and ERBB2 somatic mutations had broader effects on cancer-associated genes in NSLA without EGFR and ALK alteration (NENA).
  - Through DNA copy-number alteration analysis, we identified 22 prognostic proteins, influencing transcriptomic and proteomic changes. Gene set enrichment analysis revealed that the estrogen signaling emerged as the key pathway activated in NENA
  - Saracatinib, an Src inhibitor, was suggested as a potential drug for targeting activated estrogen signaling in NENA, and was experimentally validated in vitro using cell line model.
  - In this study, we enhanced our understanding of the etiology of NENA NSLA through the proteogenomic landscape, based on which we proposed saracatinib as an effective drug.
- CYB5R3 functions as a tumor suppressor by inducing ER stress-mediated apoptosis in lung cancer cells via the PERK-ATF4 and IRE1α-JNK pathways
  - Cytochrome b5 reductase 3 (CYB5R3) is involved in various cellular metabolic processes, including fatty acid synthesis and drug metabolism. However, the role of CYB5R3 in cancer development remains poorly understood.
  - Here, we show that CYB5R3 expression is downregulated in human lung cancer cell lines and tissues. CYB5R3 suppresses lung cancer cell growth, and CYB5R3 deficiency promotes tumorigenesis and metastasis in mouse models.
  - CYB5R3 upregulated the expression of apoptosis- and endoplasmic reticulum (ER) stress-related genes and induces the generation of reactive oxygen species and caspase-9-dependent intrinsic cell death. In addition, CYB5R3 increased the production of nicotinamide adenine dinucleotide (NAD+) and oxidized glutathione (GSSG).
  - CYB5R3 is mainly localized in the ER, where CYB5R3-dependent ER stress signaling is induced via activation of protein kinase RNA-like ER kinase (PERK) and inositol-requiring enzyme 1 alpha (IRE1α). Moreover, NAD+ activates poly (ADP-ribose) polymerase16 (PARP16), an ER-resident protein, to promote ADP-ribosylation of PERK and IRE1α and induce ER stress.
  - The findings highlight the importance of CYB5R3 as a tumor suppressor for the development of CYB5R3-based therapeutics for lung cancer.
- Epigenetic Activation of Tensin 4 Promotes Gastric Cancer Progression
  - Tensin 4(TNS4), a member of the Tensin family of proteins, is localized to focal adhesion sites, which connect the extracellular matrix and cytoskeletal network.
  - We identified the promoter region of TNS4 was hypomethylated in GC cell lines that showed upregulation of TNS4. We also found a significant negative correlation between TNS4 expression and CpG methylation in 250 GC tumors based on The Cancer Genome Atlas (TCGA) data.
  - This study elucidates the epigenetic mechanism of TNS4 activation and functional roles of TNS4 in GC development and progression and suggests a possible approach for future GC treatments.
- Glycogen storage disease phenotypes accompanying the perturbation of methionine cycle in NDRG3-deficient mouse livers
  - NDRG3 is a unique pro-tumorigenic member among NDRG family genes, mediating growth signals. Here, we investigated the pathophysiological roles of NDRG3 in relation to cell metabolism by disrupting its functions in liver.
  - Mice with liver-specific KO of NDRG3 (Ndrg3 LKO) exhibited glycogen storage disease (GSD) phenotypes including excessive hepatic glycogen accumulation, hypoglycemia, elevated liver triglyceride content, and several signs of liver injury.
  - They suffered from impaired hepatic glucose homeostasis, due to the suppression of fasting-associated glycogenolysis and gluconeogenesis. Consistently, the expression of glycogen phosphorylase (PYGL) and glucose-6-phosphate transporter (G6PT) was significantly down-regulated in an Ndrg3 LKO-dependent manner.
  - Transcriptomic and metabolomic analyses revealed that NDRG3 depletion significantly perturbed the methionine cycle, redirecting its flux towards branch pathways to upregulate several metabolites known to have hepatoprotective functions.
  - Mechanistically, Ndrg3 LKO-dependent downregulation of glycine N-methyltransferase in the methionine cycle and the resultant elevation of the S-adenosylmethionine level appears to play a critical role in the restructuring of the methionine metabolism, eventually leading to the manifestation of GSD phenotypes in Ndrg3 LKO mice.
  - Our results indicate that NDRG3 is required for the homeostasis of liver cell metabolism upstream of the glucose-glycogen flux and methionine cycle and suggest therapeutic values for regulating NDRG3 in disorders with malfunctions in these pathways.

[Division of Biomedical Research]

Dr. Myung Hee Kim

Microbiome Convergence Research Center
Associate Director

mhk8n@kribb.re.kr

1. Introduction

- The gut microbiota has been established as an invisible organ forming its multidirectional connecting axis with other organs. The interaction between host and microbiota plays a pivotal role in both health and disease.
- The mechanisms through which gut microbiota exerts its beneficial or detrimental impacts remain largely undefined. The Microbiome Convergence Research Center is dedicated to studying the role of microbiota in health and disease, and developing microbiome-based therapeutics to address unmet clinical needs.

2. Research Areas

- The gut microbiome in health and diseases
  - Addressing fundamental questions about how commensal microbiota contribute to the host immune system
  - Understanding the pathogenesis of microbiota dysbiosis in disease development and progression
  - Utilizing microbiota for disease diagnosis and treatment
- Understanding mechanisms of host and microbiome/microbe interactions
  - Identification of host targets interacting with microbiome
  - Uncovering molecular mechanisms of host-microbiome/microbe interactions based on structural biochemical, immunological and cell biological technologies
  - Animal model-based evaluation of host-microbiome interactions
- Industrial utilization of microbiome
  - Analysis of economic animal microbiome and symbiotic systems for the sustainable development goals (SDGs)
  - Development of soil probiotics based on synthetic biology and microbial biodiversity
  - Degradation of chemical polymers by microbiome resources

3. Main Projects

- Uncovering the role of human microbiome in health and disease, and its application in the therapeutic drug development
  - Understanding the involvement of microbiota in the health and disease, and utilizing microbiota for disease treatment
- Understanding the interactions of the microbiome and the host in neurological disorders and tumorigenesis using disease animal models
  - Identification of roles of the microbiome and microbial products that control the neurodegenerative diseases and the lung cancer in vivo
- Molecular mechanisms of cancer metastasis and relapse regulated by hybrid EMT and generation of a novel anti-cancer therapeutic strategy
  - Investigating the molecular mechanisms of cancer stemness and therapy resistance regulated by hybrid EMT process

4. Recent Achievements

- Secreted Akkermansia muciniphila threonyl-tRNA synthetase functions to monitor and modulate immune homeostasis (Cell Host & Microbe 2023, Corresponding author Dr. Myung Hee Kim)
  - Threonyl-tRNA synthetase (AmTARS) of the gut-associated bacterium Akkermansia muciniphila is secreted and functions to monitor and modulate immune homeostasis.
  - Secreted AmTARS targets macrophages and activates the anti-inflammatory TLR2-CREB axis.
  - AmTARS restores macrophage homeostasis, increases IL-10, and attenuates colitis in mice.
- UBAP2 plays a role in bone homeostasis through the regulation of osteoblastogenesis and osteoclastogenesis (Nature Communications 2023, Co-first author Dr. Jeong-Soo Lee)
  - Osteoporosis is a condition characterized by decreased bone mineral density (BMD) and reduced bone strength, leading to an increased risk of fractures.
  - UBAP2 was identified as a novel risk variant for susceptibility to osteoporosis-related traits.
  - UBAP2 has a critical role in bone homeostasis through the regulation of bone remodeling.
- Phosphocode-dependent glutamyl-prolyl-tRNA synthetase 1 signaling in immunity, metabolism, and disease (Experimental & Molecular Medicine 2023, Corresponding author Dr. Myung Hee Kim)
  - Glutamyl-prolyl-tRNA synthetase 1 (EPRS1) is the most evolutionarily derived component within the multi-tRNA synthetase complex that plays a critical role in immunity and metabolism (beyond its catalytic role in translation) via stimulus-dependent phosphorylation events.
  - This review describes on the role of EPRS1 signaling in inflammation resolution and metabolic modulation. The involvement of EPRS1 in diseases such as cancer is also discussed.
- TMPRSS4, a type II transmembrane serine protease, as a potential therapeutic target in cancer (Experimental & Molecular Medicine 2023, Corresponding author Dr. Semi Kim)
  - Cancer-associated expression and oncogenic roles of TMPRSS4 and its clinical significance

[Division of Biomedical Research]

Dr. Nam-Soon Kim

Rare Disease Research Center
Associate Director

nskim37@kribb.re.kr

1. Introduction

Precision medicine for rare neuronal disease based on omics big data considered to be a better option for next generation. To develop technologies related to these, this research center is focusing on the construction of genomics-based technology platforms, identification of the therapeutic target genes and diagnostic biomarkers, and application to diagnosis and treatment for rare neuronal disease as shown belows.

2. Research Areas

- Identification of therapeutic target genes and diagnostics biomarkers for Precision medicine of rare neuronal diseases
  - Establishment of genome research infrastructure and technology platforms for rare neuronal diseases
  - Functional validation and application onto gene therapy of candidate target genes for precise therapeutics development of rare neuronal diseases
  - Identification of biomarkers and development of gene panel for precise diagnostics of rare neuronal diseases
- Identification of regulation mechanism for neuronal development and discovery of biomarkers for early diagnosis of neurodevelopment disorder
  - Molecular functions of synaptic proteins that regulate neuronal development
  - Production of animal model to infer the cause of neurondevelopmental disorders
  - Discovery of serum biomarkers for early diagnosis of neurodevelopmental disorders
- Investigation of the effects of microplastics on the brain and metabolism
  - Establishment of microplastics as environmental risk factors in developmental disorder
  - Investigation of the effects of microplastic exposure on metabolic changes and related phenotypes
  - Investigation of the molecular mechanisms underlying the biological effects of microplastics
- Studies on Amyotrophic Lateral Sclerosis and Drug Target identification
  - A yeast TDP-43 proteinopathy model: Exploring the molecular determinants of TDP-43 aggregation and cellular toxicity
  - Target identification and mechanism of action in drug discovery
  - Target deconvolution using yeast gene-deletion collection
- Identification of therapeutic targets for incurable diseases and development of specific antibodies.
  - Discovery of therapeutic targets for drug-resistant cancers and development of target-specific response antibodies.
  - Exploration of therapeutic targets for viral infections and development of virus-specific antibodies.
  - Development of diagnostics and therapies based on target-specific antibodies.

3. Main Projects

- Development of Genome-based Platform Technologies for Precision Medicine of Rare Neurological Diseases
  - Constructtion of a genome mutation map and integrated database for rare neurological diseases.
  - Identification of diagnostic biomarkers and treatment target genes related to rare neurological diseases.
  - Application to diagnosis and treatment of rare neurological diseases.
- Identification of molecular mechanism of synaptic proteins that regulate neuronal development and synaptic formation
  - Production of animal model for analysis of phenotype and transcriptome/proteome to identify the pathogenesis of neurodevelopmental disorders
- Investigation of effects of microplastic exposure on the brain and metabolism
  - Investigation of the molecular mechanism underlying microplastic-induced brain dieseases
  - Investigation of the molecular mechanism underlying microplastic-induced body weight increase
- A study on ALS disease using fission yeast model
  - Study on the relationship between ALS disease and TDP43 Protein
- Development of fundamental technology for the prevention and treatment of national disaster virus infections
  - Development of global fundamental technology for preventing and treating national disaster viral infections based on basic research aimed at elucidating the mechanisms and causes of viral infections.

4. Recent Achievements

- Characteristics of genetic variations and identification of a novel therapeutic target rare neurological diseases in Korean families
  - The emerging genetic diversity of hereditary spastic paraplegia (HSP) in Korean patients.
  - Identification of novel candidate genetic variations and networks associated with LGS in Korean LGS Families.
  - TREX1 deficiency induces ER stress-mediated neuronal cell death by disrupting Ca2+homeostasis
- Nanoplasmonic immunosensor for the detection of SCG2, a candidate serum biomarker for the early diagnosis of neurodevelopmental disorders
  - Discovery of serum biomarker for the early detection of neurodevelopmental disorders
  - Development of highly sensitive diagnostic methods using a small amount of infant body fluids
- Determination of the mechanism underlying abnormal weight gain and brain disorder induced by microplastic exposure
  - Maternal exposure to microplastics causes cognition deficit
  - Maternal exposure to microplastics causes abnormal increase of the body weight in progeny
  - Microplastic ingestion induces body weight increase by altering lipid species in maternal breastmilk and progeny plasma and the distribution of gut microbiota (Jeong et al., Environment International, In revision)
- Development and characterization of SARS-CoV-2 virus-specific monoclonal antibodies
  - Identification of Novel Neutralizing Monoclonal Antibody against SARS-CoV-2 Spike S2 subunit with broad neutralizing activity (Heo CK et al., Front Immunol. 2023.8;14:1307693.).
  - Identification and application of noncompeting monoclonal antibodies broadly binding to the nucleocapsid proteins of SARS-CoV-2 variants (Heo CK et al, Sens Actuators B Chem. 2023;380:133331).
- Construction of S. pombe Genome-wide Deletion Mutant Library
  - A total of 4,836 heterozygous diploid deletion mutants representing 98.4% of the organism genome and 3,400 haploid deletion mutants with 95.3% genome coverage are deleted.
  - Providing an ideal way to approach research in gene function and drug target screening for large numbers of genes by using pools of mutants

[Division of Biomedical Research]

Dr. Jangwook Lee

Biotherapeutics Translational Research Center
Associate Director

jlee@kribb.re.kr

1. Introduction

The Biotherapeutic Translational Research Center (BTRC) is focused on fostering personalized treatment for rare and incurable diseases through development and implementation of new therapeutic platform technology and translational research studies. The primary mission of the BTRC is to stimulate disease-overcoming clinical and translational research that seeks to enhance the care of cancer, diabetes, and cardio-/neurodegenerative diseases. All BTRC faculty are dedicated to several translational projects aimed at design, discovery, and development of tailored biotherapeutics in cancer, vascular, and metabolic research.

2. Research Areas

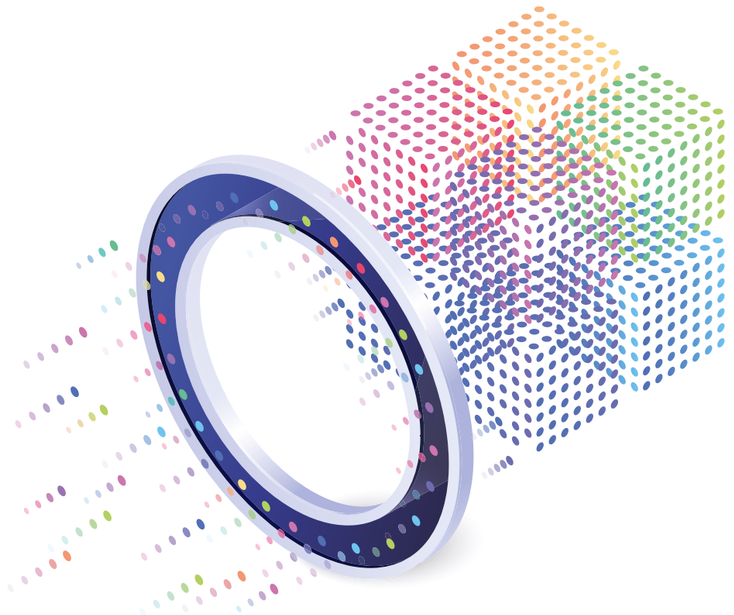
- Mining of therapeutic targets for cancer and vascular/metabolic diseases
  - Discovery, validation and control technology of tumor therapeutic targets by transcriptome and genome analysis
  - Focus on the evaluation of targets and drugs for atherosclerosis, aortic aneurysm, type 2 diabetes, non-alcoholic fatty liver disease (NAFLD), and obesity using in vivo and in vitro models
- Development of Biopharmaceuticals (antibody/protein) for cancer and vascular/metabolic diseases
  - Discovery of disease-specific target-controlled antibodies
  - Development of bispecific antibodies, fusion protein, and antibody-drug conjugates
- Process development for the efficient biopharmaceutics production
  - Establishment of high antibody-producing mammalian cells
  - Development for culture process for serum-free suspended mammalian cells
- Development of antibody/exosome-based molecular diagnostic system
  - Discovery of novel antibodies targeting disease-specific antigens
  - Discovery of early diagnostic markers for disease using exosomal microRNAs
- Research on drugs targeting tumor microenvironment
  - Platform technology development for cancer immunotherapy
  - Development of drugs controling HIF-1-centric cancer metabolism
- Exosome engineering for disease therapy and diagnosis
  - Exosome engineering for surface molecules and contents
  - Hybrid exosome engineering by memebrane fusion with liposome
  - Discovery of selective inhibitors for exosome secretion
- Production of transgenic and knockout animal using gene editing system.
  - Biomolecular and physiological mechanism study using animal disease model
  - Research on the mechanism of factors that cause immune rejection response
  - Identification of gene related to the production of immunodeficient pigs

3. Main Projects

- Platform technology development for high efficient targeted antibody
  - Development of bispecific antibodies and combination therapy technology for the treatment of next-generation cancer and vascular diseases
  - Development of bispecific antibodies inducing tumor-vessel normalization to improve the therapeutic efficacy of immunotherapy
  - Development of novel immuno-oncology therapy based on antibodies and macrophages
- Developmet of small molecule-based anti-cancer drugs
  - Development of anti-cancer drugs regulating cancer metabolism
  - Development of anti-cancer drugs to overcome drug resistance
  - Development of G-protein coupled receptors-targeted drugs
- Development of a remedy for particulate matter-induced aggravation of metabolic underlying disease

4. Recent Achievements

- Licensing-out of Tie2-agonistic antibodies inducing therapeutic angiogenesis and blood vessel normalization
  - Foundation of a spin-off biotech company from KRIBB and technical licensing-out
- Intracellular Glucose-Depriving Polymer Micelles for Antiglycolytic Cancer Treatment. Adv Mater. 2023 Mar;35(10):e2207342.
- Endothelial PTP4A1 mitigates vascular inflammation via USF1/A20 axis-mediated NF-κB inactivation. Cardiovasc Res. 2023 May 22;119(5):1265-1278.
- Hepatic PTP4A1 ameliorates high-fat diet-induced hepatosteatosis and hyperglycemia by the activation of the CREBH/FGF21 axis. Theranostics 2023; 13(3):1076-1090.
- Identification of repurposed drugs regulating function of G-protein coupled receptors and development of diagnostic system for the receptors



[Division of Biomedical Research]

Dr. Suk Ran Yoon

Immunotherapy Research Center
Associate Director

sryoon@kribb.re.kr

1. Introduction

Recently, gene-engineered immune cell therapies have emerged as advanced treatment for cancer. Natural killer (NK) cells are a type of innate immune cells that represent a unique biology in cancer immune surveillance. This research cneter has been dedicated to the development of anti-tumor NK cell therapy since the early 2000s and has extended its efforts to include the development of chimeric antigen receptor (CAR)-NK cells and T cells, antibody therapies, cytokine production, hematopoietic stem cell (HSC) aging and rejuvenation, HSC differentiation and platelet cell therapy. We are committed to advancing diverse technologies in immune and blood cell-based therapies.

2. Research Areas

- Natural Killer (NK) cell immunotherapy for refractory cancer
  - Establishment of anti-cancer immunotherapy platform based on NK cell differentiation
  - Advancement of NK cell therapy through the regulation of NK cell activation
  - Development of cryopreservation method for NK cell therapy
- Development of chimeric antigen receptor (CAR)-NK cell and gene therapy
  - Establishment of cell culture method for NK cell expansion
  - Development of NK cell specific CAR construct for NK cell activation
  - CAR-NK cell therapy using gene delivery system
- Novel therapeutic candidates for anti-tumor immunotherapy
  - Development of modulating molecules of NK cell anti-cancer efficacy
  - Development of fusion cytokine for NK cell activation
  - Investigation of immunomodulatory substances for therapeutic candidates
  - Development of human and humanized antibodies for cancer treatment
- Hematopoietic stem cell (HSC) differentiation and aging
  - Molecular hematopoiesis and blood disorders
  - Development of platform for stem cell-derived platelet generation
  - HSC aging mechanism and rejuvenation
- Cell fate reprogramming
  - Cell fate conversion to immune cells
  - Characterization of reprogrammed cells
  - Efficacy and safety of reprogrammed cells

3. Main Projects

- Development of NK cell therapy for refractory cancer
  - NK cell expansion and storage for therapeutic purpose
  - Development of synthetic cytokine for anticancer therapy of NK cells
  - Development of advanced technology for enhancing therapeutic efficacy of induced NK Cells
- Next-generation CAR-NK cell therapy and gene delivery system
  - Development of NK cell specific CAR construct for treating refractory cancer
  - Identifying single-chain variable fragment against novel tumor antigen
  - Preclinical studies with high efficient NK cell
- Study of mechanisms for the cancer immunotherapy
  - Researches on NK cell immune checkpoint and molecular mechanisms
  - Mechanisms of immune suppression in refractory cancer
  - NK cell exhaustion by tumor microenvironment
- Hematopoietic stem cell (HSC) differentiation and aging study
  - Generation of HSC-derived functional immune cells and platelets
  - Molecular mechanisms of immune cell aging and rejuvenation
  - Novel approaches for development of immune cell targeting senescent cell

4. Recent Achievements

- The infusion of ex vivo, interleukin-15 and -21-activated donor NK cells after haploidentical HCT in high-risk AML and MDS patients-a randomized trial. Leukemia (2023) (Suk Ran Yoon and Inpyo Choi)
  - Administration of donor-derived NK cells after haploidentical hematopoietic stem cell transplantation (haplo-HSCT) in patients with acute myeloid leukemia (AML) and myelodysplastic syndromes (MDS) resulted in a 50% reduction in disease progression compared to the non-administered group, confirming enhanced anti-cancer efficacy due to increased graft-versus-leukemia effect.
- NgR1 is an NK cell inhibitory receptor that destabilizes immunological synapse. Nat. Immunol. (2023) (Tae-Don Kim)
  - Investigation of a novel class immune checkpoint NgR1 in anti-cancer effect of NK cells
- Deficiency of thioredoxin-interacting protein results in age-related thrombocytopenia due to megakaryocyte oxidative stress. J. Thromb. Haemost. (2023) (Haiyoung Jung and Ji-Yoon Noh)
  - Essential role of TXNIP in mitochondrial biogenesis and polyploidization for promoting megakaryopoiesis
  - Age-dependent thrombocytopenia in the absence of TXNIP due to exhaustion of megakaryocytes in the BM
- Astragalus Complanatus Ethanol Attenuates Septic Shock by Exerting Anti-Inflammatory Effects on Macrophages Int. J. Mol. Sci. (2023) (Hee Jun Cho and Hee Gu Lee)
  - The role of Astragalus Complanatus extracts on Sepsis
  - Identification of the mechanism of action of Astragalus Complanatus extracts to alleviate sepsis
- Novel anti-CD5 and EphA2 chimeric antigen receptor and immune cells expressing the same and use thereof. Technology Transfer, (2023) (Tae-Don Kim and Sooyun Lee)
  - Development of cancer-specific CD5 and EphA2 targeting CAR-NK therapy
- Method for producing directly reprogrammed natural killer cells and uses thereof (Patent registration, 2023) (Yee Sook Cho)
  - Development of Technology for Manufacturing Human Natural Killer Cells for Anti-cancer Therapy via Cellular Reprogramming

[Division of Biomedical Research]

Dr. Sung Goo Park

Disease Target Structure Research Center
Associate Director

_sgpark@kribb.re.kr

1. Introduction

This research center have been focused on the development of new drugs by the basis of protein 3-D structure oriented screening of disease targets and biological validation of screened targets.

2. Research Areas

• Target identification & validation for drug discovery
- Drug discovery using targeted protein degradation (PROTAC and molecular glue)
- Protein X-ray crystallography
- Structural studies on signaling-regulatory proteins
- Development of nanopore sensor technology for detection of protein-protein interaction, protein-nucleic acid interaction, proteins, peptides, and small molecules
- Development of nanopore sensor platform technologies for drug screening and disease diagnosis.
- Development of new drugs regulating Wnt signal through artificial protein
- Development of hypersensitivity immunosuppressants through artificial cytokine

3. Main Projects

• Development of nanopore platform technology for drug discovery (funded by KRIBB Initiative Program)
- Development of sensing platform for discovering low-cost, high-efficiency new drugs by developing single-molecule-based analysis technology for disease targets based on the new nanopore sensing principles

• Development of drug discovery platform based on targeted protein degradation
- Identification/validation of novel drug targets
- Development of PROTAC and molecular glue

• CRISPR/Cas12-based pathogenic RNA virus self-diagnosis technology development

4. Recent Achievements

• Hypoxia stabilizes SETDB1 to maintain genome stability Nucleic Acids Res
- Drug discovery using targeted protein degradation (PROTAC and molecular glue)

• Single-molecule fingerprinting of protein-drug interaction using a funneled biological nanopore Nature Comm
- Development of nanopore sensor platform technologies for drug screening and disease diagnosis

• Structural basis for proapoptotic activation of Bak by the noncanonical BH3-only protein Pxt1 PLoS Biol
- Structural studies on signaling-regulatory proteins

[Division of Biomedical Research]

Dr. Won Kon Kim

Metabolic Regulation Research Center
Associate Director

wkkim@kribb.re.kr

1. Introduction

Metabolic Regulation Research Center (MRRC) is designed to conduct basic scientific and translational research to control metabolic diseases, including diabetes, obesity, neurodegenerative disease, and cancer. The center aims to understand the mitochondria and cell signaling as well as metabolic network between organs (fat, liver,muscle, cranial nerve, etc.) through omics analysis and in vivo analysis. Further, the center also supports and promotes multidisciplinary studies to develop the core technology for controlling metabolic diseases.

2. Research Areas

- Identification of metabolic energy system and regulatory mechanism of type 2 diabetes and obesity
- Identification of regulatory mechanism associated with the transition from white adipose tissue to brown adipose tissue
- Screening and functional research of metabolic disease regulatory material based on the generation of a low molecular weight compound or natural product
- Elucidating the pathophysiological mechanism of Metabolic dysfunction-associated fatty liver disease (MAFLD) and Metabolic dysfunction-associatedsteatohepatitis (MASH)
- Pathophysiology and energy metabolism in skeletal muscle
- Analysis of the functional change in major metabolic organs and signal delivery systems under the metabolic abnormality and improvement conditions using animal models
- Identification and functional research of network regulation factors among metabolic organs through omics analysis
- Research on lipid metabolism and ferroptosis in cancer and cardiovascular diseases

3. Main Projects

- Development of Mitochondria and Energy Metabolism based Therapeutics for the Treatement of Metabolic Disease
  - Development of mitochondrial control technology through the regulation of mitochondrial function and cellular metabolism
  - Development of mitochondrial control technology by mitochondrial transplantation
  - Development of original technology for metabolic disease treatment based on mitochondrial function control/transplantation
- Discovery of therapeutic targets for improving liver failure associated with type 2 diabetes and obesity
  - Discovery of new therapeutic targets for metabolic dysfunction-associated fatty liver disease (MAFLD) and metabolic dysfunction-associatedsteatohepatitis (MASH)
  - Discovery of the targets for controlling the progreassion from MAFLD/MASH to HCC
  - Discovery of the targets for regulating hepatic glucose metabolism
- New drug development for metabolic diseases treatment
  - Discovery of small molecule compounds/antibodies that promotes mitochondrial activity
  - Discovery of small molecule compounds/antibodies targeting novel mechanisms for metabolic diseases
- Understanding metabolic pathway of chemorefractory group through metabolomic analysis and development of therapeutic strategy
  - Identification of matabolites and metabolic enzymes through combined transcriptomic/proteomic/metabolomic analysis using chemoresistant and chemosensitive cancer cells
  - Identification of new drug combinations targeting cancer metabolism for the treatment of chemoresistant tumors
  - Understanding of cellular metabolism underpinning ferroptosis and development of therapeutic strategy

4. Recent Achievements

- Novel protein indentification involved in regulation of of brown fat theromegenesis
  - Identification of Letmd1, a new factor that can regulate energy homeostasis in brown fat
  - Confirmation of new location of letmd1 protein in mitochondria
- Identification of new targets for metabolic dysfunction-associated fatty liver disease (MAFLD)
  - First research report and intellectual property rights acquisition on the occurrence and progression of metabolic abnormality-related fatty liver disease (MAFLD) due to regulation of expression of diabetes gene TCF7L2
- Generation of preclinical animal models and discovery of new targets related to the progression from MAFLD/MASH to
  - Generation of a mouse model that ensures predictability and rapidity of liver cancer formation for research on progression from MAFLD/MASH to Hepatocellular carcinoma (HCC)
- Elucidating the role of phospholipid recyling by lipoprotein-associated phospholipases A2 (Lp-PLA2) in ferroptosis through metabolomics analysis
  - Identification of darapladib, an Lp-PLA2 inhibitor that was tested in phase III clinical trial for cardiovascular diseases, as a ferroptosis-sensitizing drug
  - Elucidating the role of Lp-PLA2 that cleaves pro-ferroptotic phospholipids through metabolomic and biochemical approaches

[Division of Research on National Challenges]

Dr. Kyung-Sook Chung

Infectious Disease Research Center
Associate Director

kschung@kribb.re.kr

1. Introduction

Infectious diseases, including antibiotic-resistant superbacteria and acute viral diseases such as influenza and COVID-19, pose significant health challenges. To address these threats, our department focuses on studying bacterial resistance mechanisms and uncovering novel interactions between viruses and the host immune system. Based on these basic studies, we are also trying to identify new antibacterial agents and develop new viral vaccines, adjuvants and therapeutic options.

2. Research Areas

- Discovery and development of anti-bacterial compounds
  - Multidrug-resistant bacteria and bacterial persister
  - Lipid nanoparticle based antimicrobial
  - in vivo model for efficacy evaluation
  - Discovery and development of novel compounds against superbacteria
- Interaction between respiratory viral proteins and host innate immunity
- Genetic and mucosal vaccine and adjuvants against viral infectious diseases
- Development of antigen-specific antibody for applying diagnosis and therapeutics
- Antigenicity and biological characteristics of influenza virus with zoonotic potential
- Mechanisms of regulating antibody immunity in B cells
- Nano-/Supramolecular Biomedicine via Organic Synthesis
  - Development of probes for bioimaging and carriers for tumor/retina targeting
  - Development of lipids for nonviral delivery agents (mRNA vaccine and gene therapy)

3. Main Projects

- Development of compounds against bacterial persister
- Establishment of global infectious disease network (GloPID-R)
- Development of fundamental technology for prevention and therapy of viral disease
- Development of antimicrobial strategies through host immune control
- Discovery and mechanistic study of novel antibiofilm compounds for the treatment of multidrug-resistant bacteria
- Development of new high-performance multivalent mRNA nanocarriers
- Pilot study on the development of lipid nanoparticle-based gene delivery platform for ocular administration
- High-efficiency organic supramolecular reversible fluorescence photoswitch for high-resolution imaging in living systems

4. Recent Achievements

- Exploitation of a novel adjuvant for polymyxin B against multidrug-resistant Acinetobacter baumannii
  - Development of PA108 as a polymyxin B adjuvant
- Deciphering gut microbiota in patients with severe sepsis and septic shock
  - Identification of core gut microbiota determining susceptibility to sepsis
- Cellular and molecular pathogenesis mechanisms by influenza viral proteins
- Development of lipid nanoparticle system to control sepsis-causing strains
  - Patent application on lipid nanoparticle that controls bacteria by delivering the CRISPR-Cas system
- Development of antigen-specific antibody for applying COVID-19 diagnosis and therapeutics
  - Development of nucleocapsid-specific monoclonal antibodies for SARS-CoV-2 and their diagnostic applications on an automatic microfluidic device
  - Development of a high-throughput centrifugal microsystem for enzyme-linked immunosorbent assay to detect SARS-CoV-2
- Regulating host cell metabolism to control bacterial toxin pathogenicity
- Modulating Lipid Nanoparticles with Histidinamide-Conjugated Cholesterol for Improved Intracellular Delivery of mRNA (Adv. Healthcare Mater. 2023)
- Reversible Near-Infrared Fluorescence Photoswitching in Aqueous Media by Diarylethene: Toward High-Accuracy Live Optical Imaging (Small 2022)
- Tuning Surface Functionalities of Sub-10 nm-Sized Nanocarriers to Target Outer Retina in Designing Drug Delivery Agents for Intravitreal Administration (Biomaterials 2020)
- Discovery of a novel antibiofilm target, the nitrite transporter, in Pseudomonas aeruginosa.

[Division of Research on National Challenges]

Dr. Seon-Jin Lee

Environmental Diseases Research Center
Associate Director

sjlee@kribb.re.kr

1. Introduction

- Welcome to the Environmental Disease Research Center. Our ultimate mission is to unravel the mechanism of multi-organ failure triggered by environmental pollutants, such as fine dust, and to craft defense technologies to mitigate this damage. Our commitment is to enhance the quality of life for our citizens.
- Our core responsibilities include safeguarding public health by investigating the accumulation of fine dust within the human body. We analyze the diseases it causes and research control strategies. Our work involves the creation of disease models induced by fine dust, the standardizing of analyses on its impact within the body, and the identification of new damage prediction factors for each organ due to fine dust. We are also engaged in the study of disease network mechanisms and the development of pioneering technologies to control damage.
- In addition, we clarify the interrelationship between harmful environmental factors, including air pollution and exposure to pollutants, and human health. We actively collaborate with international institutions to share knowledge and technologies that can solve new challenges related to environmental disease-causing substances.
- Through our research endeavors, we aim to establish efficient disaster response research and development policies for diseases caused by fine dust. We strive to be the driving force for the nation's next-generation growth by developing control technologies for multi-organ damage. We are working towards enhancing our competitiveness in the prevention, diagnosis, and treatment of diseases related to multi-organ damage, as well as in the development of related product technologies. Above all, we aim to bolster our social safety nets.

2. Research Areas

- Analysis of the disease-related impact and the accumulation of fine dust (particulate matter (PM)) within the body
  - Physical and chemical properties of fine dust (PMs), and 3D shape analysis
  - Analysis of pathogenesis and impact of harmful substances induced by PMs
- Discovery of regulatory targets and therapeutic candidates for controlling diseases caused by PMs
  - Discovery of candidate substances for regulating macrophage inflammatory responses induced by PMs
  - Verification of medicinal samples capable of controlling inflammatory responses caused by PMs
- Discovery of molecular targets for the diagnosis/treatment of diseases caused by PMs
  - Analysis of harmful genes induced by PMs through single-cell genomic analysis of lung tissue
  - Analysis of damage prediction/diagnostic markers and transcription factor expression patterns for respiratory diseases mediated by PMs
- Analysis of multi-organ damage and elucidation of mechanisms based on disease models induced by PMs
  - Analysis of signal transduction regulatory mechanisms in intestinal diseases induced by PMs
  - Analysis of candidate substances for regulating Caspase-1 activity and mechanisms after exposure to PMs
- Analysis of the significance and safety of disease control substances based on animal models
  - Construction of animal models for cancer metastasis due to various types of cancer caused by PMs
  - Analysis of genomic changes and significance in stem cell-based models under the influence of PMs
  - Discovery of respiratory microbiomes controlling opportunistic pathogens induced by PMs

3. Main Projects

- Investigation of particulate matter(PM10/2.5)-mediated multiorgan failure
  - In response to the health hazards from PMs, we aim to protect public health by constructing disease models induced by PMs, analyzing the impact of PMs in the body, discovering new damage prediction factors for each organ, researching disease network mechanisms, and developing specific diagnostic/treatment candidates, damage control technology and multi-organ damage response technology induced by PMs
- The evaluation of developmental technique and regulatory analysis of particulate matter-induced GI tract damage
  - Analyzing biological impacts and developing immune regulation methods in a PM-induced inflammation model. Comparing key genes involved in damage and analyzing their control networks. Conducting drug screenings for inflammation control in various inflammation models and identifying potential substances.
- Development of candidate substances and markers for controlling diseases induced by PM10/2.5
  - Discovery analysis of essential biomarkers of diseases induced by environmental pollutants and establishment of validation assays or control system in various environmental diseases

4. Recent Achievements

- The development of diagnostic marker for the particulate matter-related disease
  - Specific upregulation of extracellular miR-6238 in particulate matter-induced acute lung injury and its immunomodulation (J. Hazard. Mater. 2023, 445, 130466)
- Finding of particulate matter-induced cancer metastasis mechanisms
  - Particulate matter promotes cancer metastasis through increased HBEGF expression in macrophages (Exp. Mol. Med. 2022, 54(11), 1901-1912)
- Physical and chemical properties of PMs and 3D shape analysis
  - Three-dimensional label-free visualization of the interactions of PM2.5 with macrophage & epithelial cells using optical diffraction tomography (J. Hazard. Mater. 2023, 456, 131678)
- Analysis of the impact of PMs accumulation in the body and the possibility of control regulation
  - Differential particle and ion kinetics of silver nanoparticles in the lungs and biotransformation to insoluble silver sulfide (J. Hazard. Mater. 2023, 452, 131223)
- Analysis of the characteristics of bacteria carried by PMs and host damage mechanism
  - P. stutzeri PM101005 inhaled with atmospheric particulate matter induces lung damage through inflammatory responses (Environ. Pollut. 2023, 317, 120741)

[Division of Research on National Challenges]

Dr. Baek-Soo Han

Biodefense Research Center
Associate Director

bshan@kribb.re.kr

1. Introduction

- Research and development planning in the field of bio-defense
- Policy research and R&D project planning related to biological weapons/terrorism
- Technology exchange and collaboration with military-related institutions (Agency for defense development, Army, KIST Future Defense National Technology Strategy Center, etc.)

2. Research Areas

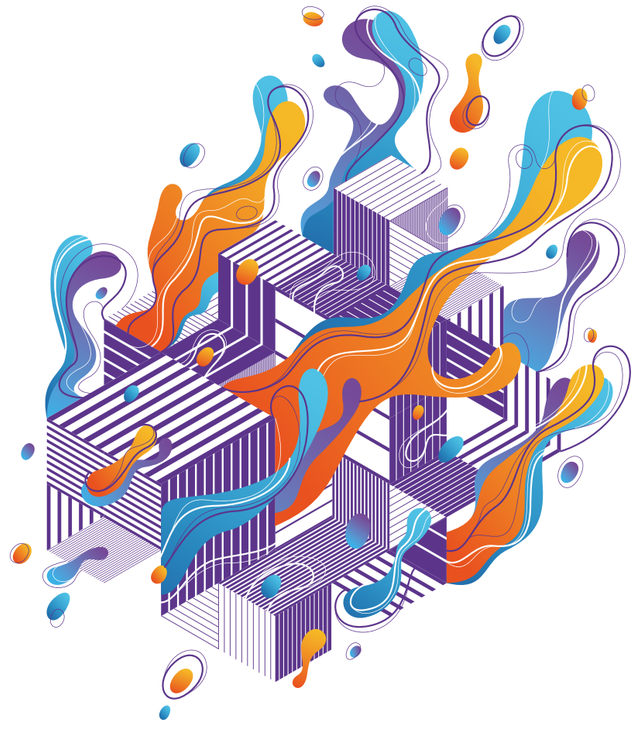
- Development of biomarkers for early and rapid response of biological agents and establishment of basic technology for micro human simulation for hazard identification,
- Development of wearable sensors for monitoring the physical condition of future soldiers
- Research on the development of the point-of-care diagnosis device for detecting biochemical and toxic materials using bionanoelectronics
- Development of drug delivery system for detoxification of biochemical agents
- The effectiveness of wearable sensors and drug delivery systems can be validated through primate-based animal models

3. Main Projects

- Next-Generation Biodefense Research Laboratory
  - Development of core source technologies necessary for the development of next generation prevention, diagnosis and treatment system and future wearable integrated biodefense system to respond to future biological weapon threat and bioterrorism threat
- Development of Nuclear, weapon for mass destruction response technology
  - Joint research and project planning with ADD, Army and Defense Acquisition Program Administration
  - Development of defense technology for biological agents
- Diagnostic technology development for bio-weapon defense
  - Design and production of antigens for biological agents
  - Diagnostic antibody against biological agents
  - Development of antibody-based bio-defensive diagnosis and therapy

4. Recent Achievements

- Development of immune cell differentiation technology with human embryonic stem cells
  - Investigation of characteristics of differentiated immune cells and development and confirmation of QA/QC techniques
- Ultrasensitive Stress Biomarker Detection Using Polypyrrole Nanotube Coupled to a Field-Effect Transistor
  - We describe rapid and sensitive cortisol detection based on a conducting polymer (CP) nanotube (NT) field-effect transistor (FET) platform. The synthesized polypyrrole (PPy) NT was functionalized with the cortisol antibody immunoglobulin G (IgG) for the sensitive and specific detection of cortisol hormone. The anti-cortisol IgG was covalently attached to a basal plane of PPy NT through an amide bond between the carboxyl group of PPy NT and the amino group of anti-cortisol IgG.
  - We believe that our approach can serve as an alternative to time-consuming and labor-intensive health questionnaires; it can also be used for diagnosis of underlying stress-related disorders.
- Molecular evolution of dengue virus types 1 and 4 in Korean travelers
  - Dengue virus (DV) is a mosquito-borne virus that is endemic to many tropical and subtropical areas. Recently, the annual incidence of DV infection has increased worldwide, including in Korea, due to global warming and increased global travel. We therefore sought to characterize the molecular and evolutionary features of DV-1 and DV-4 isolated from Korean overseas travelers.
  - In this study, the molecular, phylogenetic, and evolutionary characteristics of Korean DV-1 and DV-4 isolates were evaluated for the first time.



[Division of Research on National Challenges]

Dr. Mi-Young Son

Stem Cell Convergence Research Center
Associate Director

myson@kribb.re.kr

1. Introduction

The research goal of this center is to conduct fundamental research that includes investigations into differentiation mechanisms by utilizing various differentiated cells and organoids derived from pluripotent stem cells, as well as applied research for various purposes such as disease modeling, drug development, personalized therapy, and tissue regeneration.

2. Research Areas

- Development of regenerative therapies based on stem cell-derived organoids
  - Human intestinal organoid-based regenerative therapy with the enhanced in vivo engraftment and regeneration by microenvironment modulation
  - Non-clinical safety and efficacy evaluation using animal models with various intestinal diseases
- Development of biomimetic 3D human tissue and networking platform for predicting drug toxicity and efficacy
  - Establishment of bio-mimetic network circulation culture system (NOCS)
  - Modeling 3D human diseases based on stem cells and organoid technology for personalized therapeutics
  - Development of in silico prediction systems for the differentiation or functional status of organoids
  - Technology for PK/PD assessment based on NOCS
- Development of advanced biopharmaceuticals
  - Functional mechanism research of genetic diseases and development of gene therapy treatments
  - Development of cell therapy technology through cell fate conversion techniques
  - Advancement of gene delivery techniques for gene therapy

3. Main Projects

- Development of advanced biomedical technology for orphan diseases
  - Development of advanced Biomedicine targeting orphan diseases such as gene therapy, cell therapy, and genome editing
  - Development of patient-derived organoid model and animal model for evaluating the efficacy of gene therapy, cell therapy, and genome editing based on AAV (adeno-associated virus) vector systems
- Development of personalized disease model based on the networking organoid circulating culture system (BIG project of the KRIBB Research Initiative Program)
  - Establishment of in vivo mimicking drug evaluation platform to study accurate human drug response using highly matured organoids/ engineered tissues and NOCS
  - Development of new PK/PD assay based on NOCS for the alternative preclinical test
- Development of human gut organoid based microbiome research platform and microbiome therapeutics (The Bio & Medical Technology Development Program of the National Research Foundation)
  - Establishment of a research platform based on human gastrointestinal organoids to study the entire human microbiota
  - Development of novel microbiome therapeutics for the treatment of non-alcoholic steatohepatitis and GI disorders using human organoid-based screening platform
- Development of organoid platform for safety evaluation (Research program of the Ministry of Food and Drug Safety)
  - Development of drug safety evaluation platform using liver- and intestine organoids
  - Validation of organoid-based drug safety evaluation platform and development of test giudeline for hepatotoxicity prediction

4. Recent Achievements

- Epigenetic regulation of SMAD3 by histone methyltransferase SMYD2 promotes lung cancer metastasis (Exp Mol Med, , 2023, 1-13.)
  - Discovery of the lung cancer metastasis-inducing histone methyltransferase SMYD2 and presentation of an inhibition mechanism for lung cancer metastasis
- Particulate matter 10 exposure affects intestinal functionality in both inflamed 2D intestinal epithelial cell and 3D intestinal organoid models (Front Immunol, 2023, 14.)
  - 2D human intestinal epithelial cell and 3D human intestinal organoid models could be powerful in vitro platforms for the evaluation of the causal relationship between PM exposure and abnormal human intestinal functions.
- Integrative analysis of single-cell RNA-seq and ATAC-seq reveals heterogeneity of induced pluripotent stem cell-derived hepatic organoids (iScience, 2023, 26.9.)
  - Analysis of multicellular liver organoids reflecting diverse cell compositions of liver tissue
- Human small intestinal epithelial model and its manufacturing method
  - Technology Transfer to OrganoidScience Co., Ltd.
- Prediction of absorption of orally applicable peptide/protein drug candidates fused with macromolecule transduction domain using 2D human small intestinal epithelium model
  - Technology Transfer to ProCell Therapeutics, Inc

[Division of Research on National Challenges]

Dr. Juyeon Jung

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Bionanotechnology Research Center
Associate Director

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jjung@kribb.re.kr

1. Introduction

- Based on the strategy of integrating novel biomarker discovery and innovative bionano contents, Bionanotechnolgy Research Center develops new biomedical technologies, aiming at prompt, effective control on emerging infectious diseases, chronic, incurable diseases, and a range of hazards.
- By leveraging on fusion technologies between innovative bionano contents, Bionanotechnology Research Center develops cutting-edge biosensors for diagnosis of diseases and hazards and theragnostic technologies connecting diagnosis and therapy. With such endeavors, Bionanotechnology Research Center pursues customized, precision medicine to realize healthy, future society.

2. Research Areas

- Development of bionano fusion technologies against chronic, incurable diseases and infectious diseases
  - Discovery of biomarkers and target biomolecules to fulfill customized, precision medicine
  - Development of interfacing technologies between nano- and bio-contents
  - Optimization of in-vivo signal transduction/amplification technologies
- Application technology development of bionano contents for diagnosis and therapy
  - Development of bionano-composite materials for efficient drug delivery and sensitive in-vivo imaging
  - Development of targeting technologies to maximize in-vivo diagnostic and therapeutic efficacy
  - Securement of technologies connecting pre-clinical tests and clinical validation to the commercialization

3. Main Projects

- Development of theragnosis platforms based on bionanotechnologies
- Securing of biocontents and analytic platform technology development for the diagnosis of infectious diseases
- One Health-based research on the basics/mechanisms of zoonotic viruses originating from humans, animals, and the environment
- Development of real-time, point-of-care detection systems
- Development of real-time monitoring systems and smart disinfection/ hygiene systems for domestic animal diseases

4. Recent Achievements

- Hybrid CRISPR/Cas protein for one-pot detection of DNA and RNA
  - Clustered regularly interspaced short palindromic repeats (CRISPR)-based diagnostics have been limited in universal nucleic acid (DNA and RNA) detection because different types of Cas proteins were required, depending on types of nucleic acid targets. Cas12 is needed for DNA detection whereas Cas13 is needed for RNA detection. Herein, we developed a novel hybrid Cas protein capable of simultaneously detecting both DNA and RNA in a single tube. Using wild-type (WT) and N501Y mutant severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) as detection models, the CRISPR/hybrid Cas system successfully detected both virus strains with a detection limit of 10 viral copies per reaction without cross-reactivity. Furthermore, it accurately detected WT SARS-CoV-2 and N501Y mutant variants in clinical samples. The hybrid Cas protein is expected to be utilized in molecular diagnostic methods for infectious diseases, tissue and liquid biopsies, and other nucleic acid biomarkers.
- Artificial nucleic acid circuit with argonaute protein (ANCA) for one-step, amplification-free, and isothermal detection of antibiotic-resistant bacteria
  - Recently, endonucleases have been widely used in molecular diagnostics. Here, we report a strategy to exploit the properties of Argonaute (Ago) proteins for molecular diagnostics by introducing an artificial nucleic acid circuit with Ago protein (ANCA) method. The ANCA is designed to perform a continuous autocatalytic reaction through cross-catalytic cleavage of the Ago protein, enabling one-step, extraction-free, amplification-free, and isothermal DNA detection. The ACNA fulfilled carbapenemase-producing Klebsiella pneumoniae (CPKP) detection in human urine and blood samples. In conjunction with a three-dimensional nanopillar structure, it detected CPKP swabbed from surfaces. Importantly, it accurately diagnosed CPKP in rectal swab specimens from infected patients with 100% sensitivity and 100% specificity, supporting that the ACNA would contribute to preventing nosocomial infections.
- Ferritin-nanocaged copper arsenite minerals with oxidative stress-amplifying activity for targeted cancer therapy
  - We report copper(II) arsenite-encapsulated ferritin nanoparticles (CuAS-FNs) as oxidative stress-amplifying anticancer agents. The CuAS-FNs were fabricated through CuAS mineralization in the cavity of FNs. The formation of crystalline CuAS complex minerals in the FNs was systematically identified using various analytical tools including X-ray photoelectron spectroscopy (XPS) and transmission electron microscopy (TEM)-associated energy-dispersive X-ray spectroscopy (TEM-EDS). The CuAS-FNs showed pH-dependent release behavior in which the CuAS mineral was effectively retained at physiological pH while it was dissociated to release arsenite and Cu^{2+} ions at lysosomal pH. At lysosomal pH, the release rate of arsenite ($HAsO^{32-}$) and Cu^{2+} ions from the CuAS-FNs more accelerated than at physiological pH. Upon transferrin receptor-1-mediated endocytosis, the CuAS-FNs simultaneously released arsenite and Cu^{2+} ions in cells. The released arsenite ions increased the intracellular concentration of hydrogen peroxide (H_2O_2), which led to the elevation of hydroxyl radicals (·OH) via Fenton-like reaction constituted by Cu^{2+} and H_2O_2. Thus, the CuAS-FNs target cancer cells with FNs' recognition ability and kill them by amplifying the radical level through the synergistic actions of Cu^{2+} and arsenic ions. The CuAs-FNs effectively suppressed MCF-7 tumors without systemic in-vivo toxicity, indicating that they are a promising class of Fenton-like catalytic nanosystem for cancer treatment.
- An immuno-magnetophoresis-based microfluidic chip to isolate and detect HER2-Positive cancer-derived exosomes via multiple separation
  - Exosomes are useful for cancer diagnosis and monitoring. However, clinical samples contain impurities that complicate direct analyses of cancer-derived exosomes. Therefore, a microfluidic chip-based magnetically labeled exosome isolation system (MEIS-chip) was developed as a lab-on-a-chip platform for human epidermal growth factor receptor 2 (HER2)-positive cancer diagnosis and monitoring. Various magnetic nanoclusters (MNCs) of different degrees of magnetization were synthesized, and antibodies were introduced to capture HER2-overexpressing and common exosomes using immunoaffinity. MNC-bonded exosomes were separated into different exits according to their magnetization degrees. The MEIS-chip efficiently separated HER2-overexpressing exosomes from common exosomes that did not contain disease-related information. The simultaneous separation of HER2-and non-HER2-overexpressing exosomes provided a means of analyzing high-purity HER2-overexpressing exosomes while minimizing the contribution of non-target exosomes, reducing misdiagnosis risk. Notably, common exosomes served as a negative control for monitoring real-time changes in HER2 expression. These findings support the application of MEIS-chip for cancer diagnosis and treatment monitoring via effective exosome isolation.
- Rapid and simultaneous multiple detection of a tripledemic using a dual-gate oxide semiconductor thin-film transistor-based immunosensor
  - The simultaneous infection with a tripledemic—simultaneous infection with influenza A pH1N1 virus (Flu), severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and respiratory syncytial virus (RSV)—necessitates the development of accurate and fast multiplex diagnostic tests. The coronavirus disease 2019 (COVID-19) pandemic has emphasized the importance of virus detection. Field-effect transistor (FET)-based immuno-biosensors have a short detection time and do not require labeling or polymerase chain reaction. This study demonstrates the rapid, sensitive detection of influenza A pH1N1, SARS-CoV-2, and RSV using a multiplex immunosensor based on a dual-gate oxide semiconductor thin-film transistor (TFT), a type of FET. The dual-gate oxide TFT was modified by adjusting both top and bottom gate insulators to improve capacitive coupling to approximately 120-fold amplification, exhibiting a high pH sensitivity of about 10 V/pH. The dual-gate oxide TFT-based immunosensor detected target proteins (hemagglutinin (HA) protein of Flu, spike 1 (S1) protein of SARS-CoV-2, and fusion protein of RSV) of each virus, with a limit of detection of approximately 1 fg/mL. Cultured viruses in phosphate-buffered saline or artificial saliva and clinical nasopharynx samples were detected in 1-μL sample volumes within 60 s. This promising diagnostics has a great potential as point-of-care tests to enable a prompt, sensitive response to future pandemics and multiplex detection without pretreatment.

[Division of Research on National Challenges]

Dr. Hye Sun Cho

Plant Systems Engineering Research Center
Associate Director

hscho@kribb.re.kr

1. Introduction

We aim to establish foundational technologies for crop improvement to adapt to climate change by understanding how plants respond to their environment, utilizing gene regulation and genome editing techniques. This research center is focusing on crop trait design, including regeneration, molecular biology, omics, and protein modeling.

2. Research Areas

- Studies on molecular mechanisms of plant response to environmental stresses
  - Understanding the physiological processes of plants under stress conditions
  - Exploring relevant useful genetic resources
- Advancement of plant regeneration techniques
  - Identification of molecular mechanisms of plant cell regeneration
  - Development of new technologies to improve regeneration efficiency universally
- Establishment of plant systems biology-based platform for bio-materials production and trait improvement
  - Development of plant omics and bioinformatics
  - Induction or modification of metabolic pathways in plants
  - Optimization of genetic curcuits for efficient reprogramming

3. Main Projects

- Improving photosynthetic efficiency to accelerate production of plant bioproducts
  - Enhancing photosynthetic efficiency via protein engineering and genetic modification of photosynthetic machinery
- Plant engineering for adaptation to climate change
  - Identifying key genes involved in heat stress response and developing climate-resilient crops using genome editing technology
- Establishment of transformation and regeneration hubs to put genome editing technology to crops
  - Creating a technological hub focused on plant regeneration/transformation to facilitate the application of genome editing in crop improvement
- Designing plants for high-value bioresource production
  - Advancing plant platforms and plant systems biology-based technologies to optimize the production of industrial bio-material

4. Recent Achievements

- Elucidation of molecular mechanism of spliceosomal OsFKBP20-1b in RNA splicing
  - The nuclear spliceosome-associated OsFKBP20-1b highlights a novel gene regulating RNA splicing under stress conditions through stabilization of SR45 and SR34 splicing
- Uncovering the RNA splicing regulation of CYP18-2 involved in heat stress adaptation
  - Elucidation of the role of CYP18-2 in RNA splicing regulation: as a splicing factor within the BACT spliceosome complex through a crucial role for ensuring the production of adequate levels of alternative spliced transcripts to enhance thermotolerance
- Determining shoot regeneration efficiency in potato genotypes through WUSCHEUL
  - By comparing 12 potato genotypes, we identified the expression level of potato WUSCHEL as a determining factor for shoot regeneration efficiency
- Demonstration of the superior performance of plant-derived FMDV antibody-HRP as a diagnostic agent
  - HRP-fused FMDV antibodies expressed in plant exhibit significantly higher HRP activity as diagnostic reagents compared to those expressed in CHO cells

[Division of Biotechnology Innovation]

Dr. Hong-Weon Lee

Technology Transfer Center
Associate Director

hwlee@kribb.re.kr

1. Introduction

The Technology Transfer Center (TTC) at KRIBB offers a range of programs designed to enhance the applicability and commercial potential of KRIBB's intellectual property portfolio, encompassing both tangible and intangible assets.

2. Research Areas

KRIBB's Technology Transfer Center (TTC) offers several programs to support the development and commercialization of its intellectual property (IP):

• IP-INNO : This program provides comprehensive support, from initial research planning in laboratories to patent application for resulting inventions, ensuring the creation of strong and competitive IP.
• TECH-UP : This program bridges the gap between academic research and industry needs. It helps refine KRIBB-developed technologies by incorporating valuable feedback from industry experts, making them more commercially viable.
• IP Biz : This program focuses on maximizing the success of technology transfer and commercialization. It offers various services, including marketing, negotiation assistance, and technical support for transferred technologies.
• Technology Valuation and IP Management : TTC actively manages research outputs and associated records. Additionally, they perform comprehensive evaluations of IP assets intended for commercialization, ensuring informed decision-making.

3. Main Projects

• Biotechnology Commercialization Programs: This program fosters technological innovation, aiming to generate outstanding research achievements in the field of biotechnology.
• Technology Transfer Acceleration Programs: These programs facilitate the successful transfer and commercialization of promising technologies, bridging the gap between research and the market.
• Research Outputs and Invested Technology Evaluation: This program assesses the value and technological feasibility of research outputs and invested technologies.

4. Recent Achievements

• Recent Increases in Technology Licensing Revenue and Contract Value through the Technology Commercialization Innovation Platform(IP-Pro, Tech-Up, IP Biz) :
  - 51.1% Rise in Technology Licensing Revenue : Revenue grew from 6.28 billion KRW (2018~2020) to 9.49 billion KRW (2021~2023).
  - 710.3% Surge in Technology Transfer Contract Value : Contract value increased from 28.82 billion KRW (2018~2020) to 233.54 billion KRW (2021~2023).
• Three Successful Technology Transfer Contracts Exceeding 10 Billion KRW :
  - OnecureOOO Co., Ltd(2023.5., 18.7 billion KRW), TSOOO Co., Ltd(2023.7., 11.7 billion KRW), TSOOO Co., Ltd(2023.8., 10 billion KRW)
• Efficient Creation of Technology Transfer Successes : Follow-up R&D and Commercialization Support for Promising Tevchnologies
  - Successful technology transfer contracts worth 13.83 billion KRW, approximately 17 times the invested budget (0.8 billion KRW).

[Division of Biotechnology Innovation]

Dr. Ohsuk Kwon

The SME Support Center
Associate Director

oskwon@kribb.re.kr

1. Introduction

The SME Support Center was established to foster bioindustry in Korea through providing technical and business support to SMEs. We aim to ensure creation and scale-up of new biotechnology ventures, and to provide the necessary supports for the growth of these SMEs. To achieve our vision and mission, we develop and operate various programs based on budgets, equipment and facilities, and researcher in KRIBB. We also run governmentally funded projects and employ networks with various players in the Korean and grobal business ecosystems such as talented business experts, venture capitals, and public and private sector players.

2. Main Projects

• Creation and Acceleration of Bio-Ventures

The Center operates the biotech-specialized business incubator Bio-Venture Center (BVC) to foster early-stage bio-ventures by providing space as well as administrative and entrepreneurial services. In addition, the Center runs the KRIBB Bio-Startup Booster Program to accelerate the growth of bio-ventures.

- The KRIBB Bio-Startup Booster Program : Total solution program to support successful creation and growth of bio-ventures, including Tech-Mining (Discovering of business items and potential entrepreneurs), Startup School (Entrepreneurial training), Startup Consulting (business model development and growth/ exist planning), Incubation (supporting space/ infrastructure), Accelerating (supporting for investment attraction and product development)
- Open innovation for bio-venture creation : Arrangement and support for joint bio-venture creation between KRIBB researchers and outside business experts
- Bio-Venture Center (BVC) : Accelerating the settlement and growth of early stage bio-startups by providing designated space/ infrastructure and startup incubation programs

• Coordination of R&BD Collaboration

Since 2015, the Center has been coordinating R&BD collaboration program between the innovative biotech companies and KRIBB researchers. Participating companies receives R&BD support from KRIBB research team based on their growth stage and business target.

- Hidden Champions Program : Support for new product development to enter the global market
- Pre-Hidden Champions Program : Support for product diversification to lead the domestic market
- Techin-Biz Program : Support for process and manufacturing innovation of early stage bio-startups
- Leading Regional Innovation Companies Program : Support for strengthening technology competitiveness of early stage bio-startups located in the regions with KRIBB branch campus

• Support for KRIBB Family Company

Since 2017, the KRIBB has designated closely collaboation innovative biotech companies as KRIBB Family Companies. In 2022, 34 companies were newly added, which gives rise to totally 239 ones. The center support the KRIBB Family Companies through various activities such as R&D collaboration, licensing of KRIBB technologies, and technical and business mentoring.

• Strengthening Bioindustry Ecosystems

In order to stimulate the business idea exchange and shared business growth, the Center promotes networking events and programs with biotech enterprises.

- KRIBB Tech-Biz Partnering Program : Partnering events with regional biotech SMEs consist of seminars for technology and support program, mentoring for technical and business problem, and networking.

[Division of Biotechnology Innovation]

Dr. Eun Gyo Lee

Bioprocess Engineering Center
Associate Director

eglee@kribb.re.kr

1. Introduction

The BioProcess Engineering Center (BPEC), established in 1995, serves as a collaborative infrastructure for the biotechnology industry, academia, and research institutions. Since its inception, BPEC has utilized a diverse range of industrial equipment to support collaborative research and development, provide equipment assistance, conduct research on biopharmaceutical and biochemical material process development, support the production of prototypes, and contribute to the training of personnel in the field of biotechnology.

To achieve these objectives, BPEC has developed and possesses key process technologies, including animal cell-based biopharmaceutical protein expression, cell line construction, animal cell suspension culture, high-purity separation and purification of therapeutic proteins, recombinant protein analysis, industrial strain development for microbes, microbial fermentation technology, downstream process development, and large-scale production technology.

BPEC plays a crucial role in advancing the commercialization processes related to biopharmaceutical and material development for bio-companies. By supporting research and prototype production, BPEC accelerates the productization timeline for companies, contributing to the enhancement of the competitiveness of domestic biotechnology industrial technologies.

2. Research Areas

- Support for the industrial process development and prototype production of biopharmaceuticals/biochemicals
- Core technology development for the industrialization of biopharmaceuticals and biochemicals
- Establishment of advanced infrastructure for the industrialization support of biopharmaceuticals/biochemicals
- Support for the utilization of industrial research equipment in industry-academia collaboration
- Training for Industrial Personnel

3. Main Projects

- Support for process development and prototype production for biocompany demand
  - Mass production technology for VLP (Virus-Like Particle) and i mmunostimulant based on Escherichia coli
  - Optimization of Lab-scale cultivation for microbial-derived polysaccharides production
  - Process development of bispecific antibody production for T cell activation (Cyron therapeutics)
  - Process development of growth factors production for cell therapeutics manufacturing (xcell therapeutics)
  - Development of allogeneic CAR-T cell therapy with switch receptor for cancer immunotherapy
  - Process development of adeno-associated viral vector production for gene therapy
- Development of core process technologies for commercialization of biomaterials
  - Establishment of a microbial fermentation data collection and monitoring system
  - Development of mRNA In Vitro Transcription (IVT) and high-purity purification process technology for vaccines and cell therapy
- Support of bioprocess equipment utilization: 500 cases
- Training of biochemical and pharmaceutical industry experts: 20 trainees

4. Recent Achievements

- Technology transfer performance
  - Enzyme production technology for gene therapy (Pharmicell, 2020)
  - Production technology for E. coli-based VLP and immunity boosters (Careside, 2023)
  - Cell lines for monoclonal antibody production (Hankook Korus Pharm, 2022)
- Production of a 135-residue long N-truncated human keratinocyte growth factor 1 in Escherichia coli. Microbial Cell Factories. 2023 May 11;22(1):98
- Octyl syringate is preferentially cytotoxic to cancer cells via lysosomal membrane permeabilization and autophagic flux inhibition. Cell Biology and Toxicology. 2023 Feb;39(1):183-199

[Division of Biotechnology Innovation]

Dr. Chang-Gi Kim

Bio-evaluation Center
Associate Director

cgkim@kribb.re.kr

1. Introduction

In order to support the industrialization of new organisms (such as living modified organisms and genome-edited organisms), the Bio-Evaluation Center continues to develop technologies for molecular genetic analysis, human and environmental risk assessment, and evaluation and also established the highest level of human and physical infrastructure in the country using biotechnology. By supporting genetic characterization, risk assessment, and approval throughout the entire process from the development of new organisms to commercialization, we aim to establish ourselves as a hub center for the evaluation of domestic bioproducts safety using this infrastructure.

2. Research Areas

- Developing and establishing risk assessment techniques for living modified organisms
  - Expanding the host type and introduced gene format in living modified organisms including plants and yeast
- Support for development and production approval of living modified organisms for commercialization
  - Support to genetic analysis, human- and environment risk assessment for domestically developed living modified organisms
- Introducing cut-edge techniques to risk assessment of living modified organisms
  - Introducing and applying state-of-art technologies, such as Digital PCR, Next-generation sequencing, etc., into risk assessment procedure of living modified organisms

3. Main Projects

- Bioevaluation infra-building and support project of organisms for industrialization
- Development of risk assessment technology and standards for industrial genetically modified organisms
- Improvement and risk assessment of plastic-degrading living modified microalgae
- Extablishment of production technology for the manufacture of useful human glycolipids and development of new materials
- Risk assessment of genetically modified microorganisms
- Environmental risk assessment of non-food LM crop
- Development of antibiotics risk assessment system in agricultural environment
- Development of evaluation of biodegradability and performance of degradation additive for mulching film

4. Recent Achievements

- Bio-Evaluation Support for living modified organism
  - Support to acquire approval from the regulatory authority of living modified microorganisms for food or industrial use
  - Support to acquire international approval from the regulatory authority of living modified microorganisms for industrial use
  - On-going support for risk assessment of 23 events of domestically developed living modified microorganisms

[Division of Biotechnology Innovation]

Dr. Hyun Woo Oh

Core Research Facility & Analysis Center
Associate Director

hwoh@kribb.re.kr

1. Introduction

The Core Research Facility & Analysis Center establishes joint research equipment, and provides close-quarters research support services so that research departments within the institute can efficiently utilize expensive equipment, and conducts various research activities. We are promoting technological innovation based on the research excellence of our researchers.

2. Research Areas

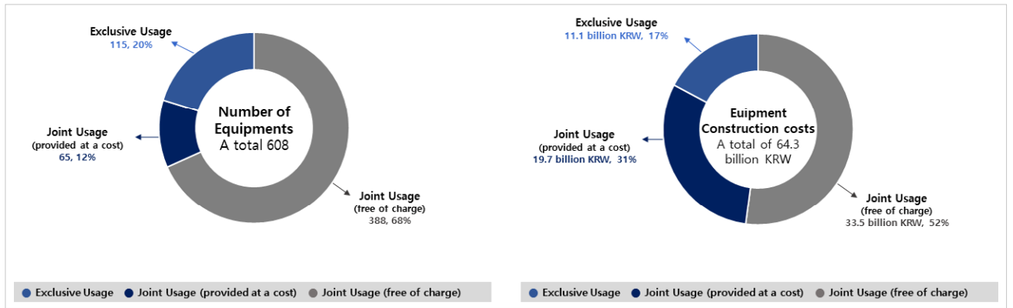
- Operation of integrated research equipment room and common equipment room for efficient joint-usage of research equipments
- Establishment and operation of joint utilization system to enhance shared usage of research equipments
- Survey and asset inspection for the shared research equipments (once a year)
- Implementation of projects linked to the integrated portal(ZEUS) for National research facility equipment utilization
- Increase joint-usage research equipments and improve management efficiency
  - Stabilization of a mobile app(Biocore) that can be accessed in real-time at the research site
  - Implementation of additional function for research equipment location map
- Enable to identify the status of research equipment for joint-usage
  - Survey the demand for jointly used equipment and perform an on-site survey of assets
- Expand the integration room and common equipment room for efficient use of research equipments
  - Establishment of Central Analysis Laboratory (in Ochang subdivision) at the basement of Biomedical Building
- Supports proteome and structural data analysis of biosamples using common equipment
  - Identification of proteins and compounds by Mass Spectrometry(MS)
  - Structural analysis of proteins and various biomolecules using Cryo-TEM

3. Main Projects

- Establishment and construction of mid- to long-term plans for research facility equipment and operation planning
- Operation and management of jointly utilized equipment and internal and external support
- Support for bio information production and analysis using jointly utilized equipment
- Operation and training of personnel dedicated to research equipment

4. Recent Achievements

- Comprehensive survey of jointly used research equipment(as of 2023)



- Support for excellent research results using protein mass spectrometry system
  - Protein that interact with the SETDB1 gene, which is functionally involved in various aspects of tumor formation, was identified using a mass spectrometry system (Nucleic Acids Res. 2023 Nov 10;51(20):11178-11196)
  - Identification of proteins present in phytochrome B, an actual photoreceptor called photobody using a mass spectrometry system (Nat Commun. 2023 Mar 27;14(1):1708)
- Support for excellent research results through cryo-TEM analysis
  - Demonstrating the functional from of TRPV1-nanodisc by showing the 2D structure of the TRPV1-nanodisc complex which is reusable electronic tongue based on a TRPV1 (Adv Mater. 2023 May 35(19):e2206198)

[Ochang Branch Institute]

Dr. Sei-Ryang Oh

Natural Medicine Research Center
Associate Director

seiryang@kribb.re.kr

1. Introduction

- Plant-derived natural products have been traditionally used for phytomedicine, and are still actively used today as raw materials for new drug candidates, natural medicines, functional foods, and functional cosmetics.
- Natural Products Research Center manages the largest natural product extract bank (Natural Products Central Bank) in Korea providing standard extracts derived from domestic & foreign plants and their information, and discovers active constituents form plants to develop effective raw materials into pharmaceuticals and functional foods that are effective in chronic diseases.

2. Research Areas

- Management of Natural Product Central Bank
  - Securing natural materials derived from domestic/overseas plants and manufacturing standard extracts
  - Establishment of integrated information on materials/analysis/efficacy of domestic native plants
  - Provision of standard extracts and information of searching program
- Development of raw materials for treatment of chronic diseases
  - Research for effective targets of respiratory/metabolic diseases, evaluation of efficacy of natural products, and efficacy mechanism
  - Research on separation and structural analysis of active natural compounds
  - Discovery of food and drug source materials and standardization of raw materials from domestic/foreign plants

3. Main Projects

- Development of natural raw materials for treatment of chronic diseases
  - Discovery and efficacy evaluation of active natural products in chronic disease models from plant-derived natural products
  - Standardization of food and pharmaceutical raw materials from plant sources
  - Development of natural products for the treatment of atopic skin and dry eyes using ABO blood-type antigen expression control technology
  - Development of new concept intractable infectious disease control technology through regulation of Gram-negative bacteria Type III protein secretion system (T3SS)
  - Research on the role and mechanism of action of RHBDF2 protein in pulmonary fibrosis
  - Research on the utilization of neutrophil-specific mechanisms to alleviate chronic lung inflammation tailored to elderly women
  - Securing crop metabolite data using UPLC-QTOP/MS
  - Research on the intracellular function of Psen-2 and development of selective inhibitors
- Operation of natural products cluster development project
  - Securing natural materials derived from domestic and overseas plants, distribution of standard extracts, and information utilization services
  - Management of natural products resources as a Natural Product Central Bank in the Natural Products Cluster Project by linking other banks and organizations

4. Recent Achievements

- Establishment of an utilization platform of natural product information
  - Establishment of a platform to utilize integrated material/analysis/efficacy information of standard extracts derived from domestic and overseas plant materials
- 1,5-Dicaffeoylquinic acid from Pseudognaphalium affine ameliorates dry eye disease via suppression of inflammation and protection of the ocular surface
  The Ocular Surface 29 (2023) 469-479
- Cinnamomum verum extract inhibits NOX2/ROS and PKCδ/JNK/AP-1/ NF-κB pathway-mediated inflammatory response in PMA-stimulated THP-1 monocytes
  Phytomedicine 112 (2023) 154685
- Comparisons of phenolic compounds and antioxidant activities during different growth stages in Artemisia gmelinii Weber ex Stechm with UPLC-QTOF/MS based on a metabolomics approach
  Industrial Crops & Products 202 (2023) 116999
- Daphnetin Alleviates Bleomycin-Induced Pulmonary Fibrosis through Inhibition of Epithelial-to-Mesenchymal Transition and IL-17A
  Cells 12 (2023) 2795

[Ochang Branch Institute]

Dr. Jae-Hyuk Jang

Chemical Biology Research Center
Associate Director

jangjh@kribb.re.kr

1. Research Areas

- Discovery of novel microbial secondary metabolites employing genome mining for drug development
- Construction of microbial secondary metabolites library
- The role of primary cilia in anticancer drug resistance
- Modulation of Cancer Associated Fibroblasts (CAF) for cancer therapeutics development
- Cancer cell division mediated by cell signaling
- Target identification and validation of bio-active secondary metabolites

2. Main Projects

- Discovery of bioactive novel microbial secondary metabolites for drug development
  - Through enforced activation of biosynthetic cryptic gene clusters
  - Studying the enzymatic machinery for the biosynthesis of secondary metabolites and development of new drugs candidates
  - Construction of artificial biosynthetic pathway for useful bioactive compounds
  - Construction of microbial secondary metabolites library
- Identification of bioactive compounds regulating tumor cell proliferation, apoptosis, autophagy, and metastasis
- Modulation of Cancer Associated Fibroblasts (CAF) for cancer therapeutics development
- Regulation of anticancer drug resistance by primary cilia
  - Elucidating the role of primary cilia in anticancer drug-resistant cells
- Establishment of patient-derived cancer organoid and development of drug efficacy test system using cancer organoid

[Ochang Branch Institute]

Dr. Hyunjoo Cha-Molstad

Nucleic Acid Therapeutics Research Center
Associate Director

hcha@kribb.re.kr

1. Introduction

The Nucleic Acid Therapeutics Research Center at the Korea Research Institute of Bioscience and Biotechnology is dedicated to advancing proprietary nucleic acid-based vaccines and therapeutic platforms with potential applications in prophylactic vaccines, therapeutic vaccines, and non-vaccine therapies. Our center is currently focusing on the development of core technologies, including conventional mRNA, self-amplifying RNA (saRNA), and circular RNA, as well as next-generation nucleic acid delivery systems such as lipid nanoparticles, to achieve robust and long-lasting expression of antigens and targets. Additionally, we are actively identifying novel anti-disease targets that can be effectively addressed by our cutting-edge RNA-based platforms, aiming to combat a wide range of conditions, including infectious diseases, cancer, rare incurable diseases, and age-related diseases. To achieve these goals, we leverage our expertise in molecular biology, medicinal chemistry, bioengineering, chemical engineering, cancer biology, and immunology. Our current research areas include the development of COVID-19 RNA vaccines, pan-sarbecovirus RNA vaccines, universal influenza RNA vaccines, pancreatic cancer RNA therapeutic vaccines, and therapies for pancreatic cancer and spinal muscular atrophy (SMA).

2. Main Projects

- Establishment of Next-Generation mRNA Vaccine and Therapeutics Platforms
- Development of Pan-sarbecovirus and Universal Influenza mRNA Vaccines
- Development of All-In-One Nucleic Acid Technology for Diagnosis, Treatment, and Vaccination of Pancreatic Cancer
- Development of ASO Therapeutic Technology
- Development of Core Technology for Next-Generation Nucleic Acid Therapeutic Modalities

3. Recent Achievements

- Development of Core Technology for Next-Generation mRNA Vaccines and Therapeutics (2023)
- Development of Screening Technology for Coronavirus Neutralizing Antibodies and Therapeutic Agents (2023)
- Development of Technology for Comprehensive Identification of Intracellular N-terminal Arginylated Proteins (2023)
- Development of UBR-based PROTAC for Treating Lung Cancer (2023)
- Elucidation of Hepatitis C Virus Proliferation Mechanism and Identification of Therapeutic Candidates (2022)
- Development of Autoimmune Disease Treatment Technology and Global Technology Transfer (2021)

[Division of National Bio-Infrastructure]

Dr. Ki Hoan Nam

Laboratory Animal Resource & Research Center
Associate Director

namk@kribb.re.kr

1. Introduction

The goals of the center are to establish a national infrastructure for laboratory animal resources and a public/intramural service core for animal experimentations. For these purposes, we have been collecting mouse resources, developing quality control technologies, generating animal models for human diseases, and providing animal resources and services to researchers in biomedical research fields since 1984. Recently, we started running a broad-based primary mouse phenotyping system which was established in cooperation with Korea Mouse Phenotyping Consortium (KMPC) and International Mouse Phenotyping Consortium (IMPC). In addition, we have established infrastructure for non-clinical evaluation and lead optimization of drug candidates using laboratory animals and have been providing research support to bio-health companies and researchers. Especially, our center has been designated as the exclusive center for mouse resources and Central Bank of Model Animal Cluster by Ministry of Science and ICT in 2019 and 2020, respectively.

2. Research Areas

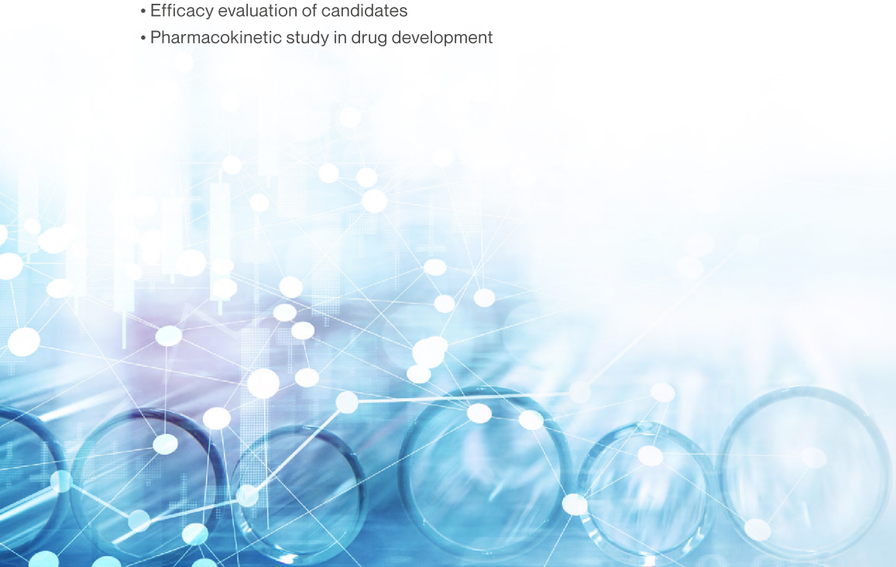
- Collection, maintenance, production and distribution of laboratory animal resources for research communities
- Permanent preservation of laboratory animal resources as frozen resource
- Quality control of laboratory animals (microbiological and genetic monitoring, microbiological clearing of animals contaminated with pathogens)
- Phenotyping of mutant mice
- Development of animal models for human diseases and animal experiment support
- Establishment of infrastructure for non-clinical evaluation of drug candidates
- Efficacy evaluation of candidates
- Pharmacokinetic study in drug development

3. Main Projects

- KRIBB Initiative Program
  - Running of the mouse resource bank
  - Establishment of animal models for cancers (humanized, orthotopic, etc.) and acute lung injury
  - Research Support for Animal Experiments
  - Establishment of animal models for non-clinical evaluation of new drug candidates and research support for industry, academy and research institute
  - Establishment of next-generation animal model platform for evaluation of advanced biopharmaceuticals
- Korea Mouse Phenotyping Center Project
  - Archiving KMPC mutant mice and proving quality control service to KMPC program
  - Broad-based mouse basic phenotyping of KMPC mouse
- [NRF] Studies on the regulation of arthritis by orphan nuclear receptor
  - Functional analysis of orphan nuclear receptors in osteoarthritis
- [MOTIE] High-Throughput 3D Multifunctional Tissue-based Screening Service of Efficacy and Safety for Drug Discovery
  - Organoid-based pharmacokinetic evaluation platform
- [Industry-Sponsored Research & Self-Supporting Account System] Research support for industry, academy and research institute
  - Technical assistance for efficacy evaluation of drug candidates (small molecules, therapeutic antibodies, cell therapeutics etc.)

4. Recent Achievements

- Running an Exclusive Center for Mouse Resource in Korea
  - Designated as a Central Bank for Model Animal Cluster by MSIT since 2020
- The largest laboratory animal resource bank in Korea
  - Deposits of laboratory animal resources: more than 2,200 strains
  - Distribution of laboratory animal resources: more than 8,000 animals
- Center for quality control of laboratory animals
  - Health monitoring: more than 6,000 animals
  - Animal clearing: more than 140 strains
- Research supports for animal experiments
  - IACUC-approved animal experiments: 150 items
  - Pathological experiments: 900 cases/10,736 specimens
- Technical assistance for non-clinical evaluation of new drug candidates
  - Efficacy evaluation of new drug candidates: 883 cases
  - Pharmacokinetic study in drug development: 279 cases



[Division of National Bio-Infrastructure]

Dr. Jae Won Huh

National Primate Research Center
Associate Director

huhjw@kribb.re.kr

1. Introduction

National Primate Research Center(NPRC) has been constructed specialized facilities for primates-based research as per international standards, securing and maintaining primate resources, expanding advanced equipment and professionals, and upgrading the management system. NPRC will support industry-academia-research institutes through advanced imaging equipment such as 3T MRI, PET-CT, and Micro PET-CT, and by establishing a support system for research on novel drugs, stem cells, and gene therapy. NPRC ako aim to develop disease models and construct efficacy evaluation systems through joint research. In addition, NPRC aim to function as support infrastructure for research on the rapid response and resolution of significant social health issues by establishing our animal biosafety level 3(ABL3) research facility. Through this, NPRC aim to support research for the prevention and treatment development of deadly, infectious diseases such as the novel Coronavirus(COVID-19), Middle East Respiratory Syndrome(MERS), Severe Acute Respiratory Syndrome(SARS), and Zika virus disease(Zika) and zoonosis, that have resulted in significant global health crises.

2. Research Areas

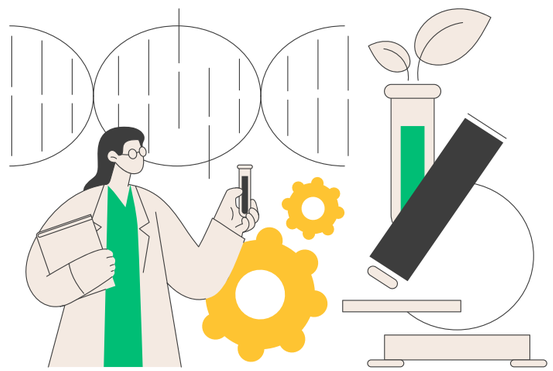
- Construction of a system to secure SPF primate resources
- Establishing a system to secure stable SPF primate resources essential to discover new biologic medical products, regenerative cell therapy and research neurological and infectious diseases
- Development of research system based on SPF primate resources for industry-academia-research institute support
- Management and standardization of SPF primate resources
- Construction of an international-grade SPF primate breeding facility and development of management system to establish national standard operating procedure(SOP)
- Standardization of health monitoring system to maintain SPF primate resources
- Construction of a comprehensive SPF primate resource management systems
- Research on primate model for efficacy evaluation
- Establishing an efficacy evaluation system to discover new drugs, biomaterials, and vaccines based on SPF primate resources
- Developing evaluation system using imaging/molecular biological/histopathological/behavioral/cognitive functional assay
- Development of primate disease models
- Development of induced disease model based on SPF primate resources(neurodegenerative disease, drug addiction, aging, and infectious disease)
- Research on the efficacy evaluation system for drug, biomaterial, and vaccine candidates using primate disease models
- Animal Biosafety Level 3(ABL3) facility for research support
- Support for research on infectious diseases, animal diseases, bioterrorism, and super bacteria on a national disaster scale
- Providing expertise and technology related to primates-based research
- Providing researchers with specialized skills and information on primate care and related-facilities

3. Main Projects

- Establishing primate research infrastructure and facilitate cooperation with industries, academia and research institutes
  - Developing research infrastructure for preclinical primate model, standardization and quality improvement of primate care, and facilitating cooperation with industry, academia, and research institutes
- Developing non-human primate models of human infectious disease required for the industry-academia-research institute
  - Establishing primate model system for infectious diseases research
  - Establishing the efficacy evaluation system for diagnosis/treatment agents and vaccines development using primate models of infectious diseases
- Establishment of customized drug efficacy evaluation platform based on comparative analysis of primate degenerative brain
  - Developing the platform for the generation, analysis, and utilization of comparative medical data for degenerative brain diseases
  - Supporting for development of degenerative brain disease models for customized healthcare technology and establishing effective verification platform
- Development of animal models of neurodegenerative diseases
  - Establishment of neurodegenerative disease primate model and related efficacy evaluation system

4. Recent Achievements

- Establishment of primate models for COVID-19 research
  - World's fourth development of COVID-19 Primate Infectious Disease Model(USA, China, Netherlands, South Korea)
  - SARS-CoV-2 virus acquisition, isolation, purification and amplification technology establishment
  - Support for development of vaccine and medicine targeting COVID-19 using the ABL3 research facility and the COVID-19 primate model
- Improvement of the breeding environment and management system of primate resources in consideration of animal welfare
  - Establishing an advanced breeding environment with social housing for primate social interaction
  - Providing living space conforming to international standards in accordance with USA and EU guidelines
- Establishment of primate disease models and support the industry, academia, and research institutes
  - Establishing and support the disease models of AD, PD, Stroke.
  - Establishment of evaluation system for new drug candidates using primates



[Division of National Bio-Infrastructure]

Dr. Sun-Uk Kim

Futuristic Animal Resource & Research Center
Associate Director

sunuk@kribb.re.kr

1. Introduction

Futuristic Animal Resource & Research Center, a core infrastructure for mini-pig resources, was established with the purpose of establishing a national high-tech infrastructure with world-class resources, materials, equipment, facilities, technology, information, and manpower and supporting/leading research and development activities related to rapid response/resolution of current and future issues in science and technology, national society, and industrial economy, thereby contributing to securing/preempting national competitiveness in advanced biotechnology, promoting/expanding universal public healthcare/welfare, and revitalizing/fostering industrial ecosystems.

2. Research Areas

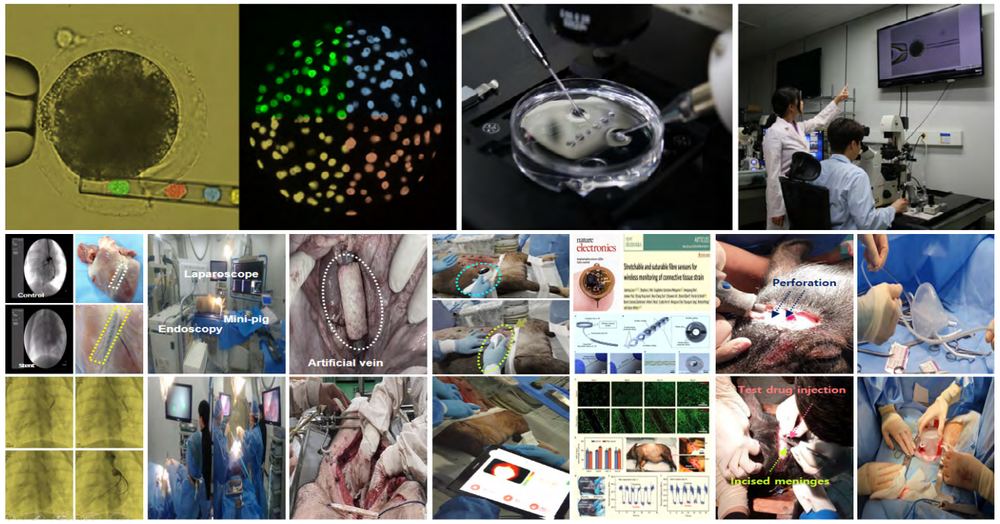
- Establishment of a system to secure, standardize, value-enhance and support mini-pig resources/materials/technologies/information
  - Promoting the establishment of a comprehensive management system for mini-pig resources, materials, and data
- Promotion of the creation, evaluation, and utilization of mini-pig models for biomedical research and development
  - Supporting for transgenic/induced model mini-pigs and non-clinical evaluations
- Establishment and support of (advanced) regenerative medicine/biotechnology R&D support systems and non-clinical platforms
  - Establishment of advanced regenerative medicine R&D infra/technology for artificial blood, artificial organs, etc.
  - Activation of support for (advanced) biotechnology R&D, including gene therapy, cell therapy, and new drugs
- Establishment and support of non-clinical evaluation platforms for (advanced/convergent) medical devices, equipment and techniques
  - Promotion of support for non-clinical evaluation of (advanced/convergent) medical devices, equipment, and techniques based on minipig models
- Establishment and operation of a consumer needs-driven/lead support system
  - Enhancement of demand research/needs-based support
  - Establishment of forward-looking/demand-driven support system

3. Main Projects

- Project for ‘Development of universal/customized artificial blood using mini-pig resources’
  - Establishment of artificial blood core resources and infrastructure
  - Development of artificial blood production technology
  - Non-clinical evaluation of artificial blood
- Project for ‘Mini-pig resouce base bank’
  - Enhancement of demand research/needs-based support
  - Establishment of forward-looking/demand-driven support system

4. Recent Achievements

- Development of Korea’s first artificial bladder implant model using mini-pigs and achievement of non-clinical success (2023)
- Support of the development of the world’s first ligament rehabilitation sensor utilizing mini-pigs (2021, Nat. Electronics)
- Global level of cloned minipig production efficiency (2021-2023)
- Advancement of developmental biotechnology and animal cloning-based technology (2023, J Anim Sci Biotech, JCR<5%)
- Registeration of overseas patent for Korea’s first large animal model (small size/dwarfism) (2023)



[Division of National Bio-Infrastructure]

Dr. Kweon Yu

Bio-Resource Central Bank
Associate Director

kweonyu@kribb.re.kr

1. Introduction

The Bio-Resource Central Bank Center deals with three clusters of the model animals, plants and microbe. Functioning as a central repository for bio-resources, it plays a pivotal role in the development of the infrastructure for the bio-resources through close collaboration with other bio-banks and relevant centers.

2. Research Areas

• Model Animal Central Bank
- As a central bank of physical resources/model animals, it engages in roles of resource standardization and maintains exclusive oversight of mouse resources.

• Microorganism Central Bank
- Its objective is to explore novel microbial resources, emphasizing their inherent value, and furthering their utilization across the red, white, and green bio sectors.

• Natural Product Central Bank
- It endeavors to create a hub-and-spoke type of cluster model, connecting a central bank, other bio-banks and relevant centers, and offers standardized natural raw materials and customized information utilization services.

3. Recent Achievements

• Model Animal Central Bank
- Acquisition of KOLAS certification on biological resources

• Microorganism Central Bank
- Operation of a portal site for the microbial cluster (https://kctc.kribb.re.kr/come)

• Natural Product Central Bank
- Standardization of natural product materials and information : Establishment of standard operating procedures

Model Animal Central Bank

Microorganism Central Bank

Natural Product Central Bank

[Division of National Bio-Infrastructure]

Dr. Sangho Choi

International Biological Material Research Center
Associate Director

decoy0@kribb.re.kr

1. Introduction

IBMRC was established in 2006 by the Korean government as an infrastructure to support biotechnology research in Korea. Through the operation of an open website, IBMRC is actively providing information and materials to industry, academia, and research institutes to support the creation of high-quality research results.

2. Research Areas

• Retain Biological Materials: 40,000 no.
• Deposits of voucher specimens: 103,000 herbarium specimens
• Distribute 241,080 no. of materials to research organizations, such as universities, research institutes, and private companies (2023)
• Support for bulk materials for industrialization candidates: 12 cases (2023)
• Discovering of taxa closely related to highly active materials: 2 cases (2023)
• Establishment of cooperation system with industry: 3 cases (2023)
• Implementation of technology transfer to company 1 case (2023)

3. Recent Achievements

• Operation and management of four collaborative biological material research centers
- Korea-China Biological Material Research Center (Kunming)
- Korea-Costa Rica Biological Material Research Center (Heredia)
- Korea-Indonesia Biological Material Research Center (Tangerang)
- Korea-Vietnam Biological Material Research Center (Hanoi)

• Establishment and operation of massive sample supply system
- Pistacia weinmannifolia massive cultivation farm (Kunming, China)
- Diospyros blancoi massive cultivation farm (Guacimo, Costa Rica)
- Lagestroemia ovalifolia, Ficus villosa massive cultivation farm (Lampung, Indonesia)

• International collaborative research
- Status of International Partnership (2023): 11 countries, 13 Institutions
- 39 countries, 54 Institutions (accumulated)
- Joint research consultations with overseas local research institutes: 13 institutes
- Exchange program of 3 scientists from Ecuador, Mongolia, Nepal

[Division of National Bio-Infrastructure]

Dr. Kyong-Cheol Ko

Korea Preclinical Evaluation Center
Associate Director

kcko@kribb.re.kr

1. Introduction

The Korea Preclinical Evaluation Center (KPEC) is a “mission-oriented” center that focuses on continuous, preemptive, and rapid response to emerging infectious diseases (EIDs). This research center continuously establishes a national preclinical evaluation support system and provides support for preclinical evaluation based on the needs of industry-academia-research institute collaborations. Its goal is to accelerate the development of treatments and vaccines and advance the ecosystem surrounding them.

2. Research Areas

- Supporting preclinical trials for industry-academia-research institute collaboration to develop treatments and vaccines for emerging infectious diseases (EIDs)
  - Efficacy assesment of therapeutic and vaccine candidates using Biosafety Level 3 (BL3)/Animal Biosafety Level 3 (ABL3) facilities (in vitro and in vivo)
    - · Cell-based basic efficacy evaluation
    - · Efficacy evaluation using small animals (mouse, hamster and ferret)
    - · Efficacy evaluation using non-human primates (Rhesus macaque, Cynomolgus macaque)
    - · Efficacy evaluation using human organoids (lung etc.)
  - Safety assesment (GLP toxicity evaluation) of therapeutic and vaccine candidates
  - Pharmacokinetic evaluation of therapeutic and vaccine candidates
    - · Assesment of the POC (Proof of Concept) and ADME (Absorption, Distribution, Metabolism and Excretion) properties using radioisotopes
    - · Pharmacokinetic study using small animals
    - · Pharmacokinetic study using non-human primates
  - Clinical predictive evaluation using Digital Preclinical Platform (DPP)
- Enhancement of research infrastructure for EIDs response
  - Expansion of ABL3 facilities for primate research in response to high-risk infectious diseases.
  - Establishment of high-cost medical equipment such as PET-CT
- Priorization of response to infectious diseases and advencement of preemptive preclinical evaluation method
  - Selection of candidates for infectious diseases that can cause a pandemic
  - Advancement of preemptive infection model* platform development
    *Cell, Human organoid, Mice, Hamster, Ferret, Primate, etc.
- Establishment of Digital Preclinical Platform (DPP)
  - Establinshing the DPP by the production and utilization of preclinical data
  - Securing and providing clinical prediction technology using real-time modeling & simulation technology
- Advancement of rapid evaluation platform using human organoids
  - Establishment of a human organoid model to overcome inter-species differences and enable rapid preclinical verification
- Establishing of a Pandemic Emergency Bank (PEB) to secure a library of excellent candidate substances
  - Stockpiling of excellent candidate substances, adjuvants and control drugs verified by KPEC

3. Main Projects

- Establishment of National Preclinical Support System
  - To enhance the country’s disaster response capacity for infectious diseases, systematic supporting for the efficacy and safety evaluation of therapeutic and vaccine candidates developed by industry-academia-research institute collaboration to contribute to fast entry into clinical trial
  - Preemptive development of infectious models and enhancement of research infrastructure for EIDs response
  - Establishment of a system for the production and utilization of preclinical infectious disease trial data

4. Recent Achievements

- Establishment of a ‘one-stop preclinical support platform’ against EIDs
- Support for preclinical evaluation of treatment and vaccine candidates for COVID-19 in industry-academia-research institute collaboration
  - A total of 3,164 preclinical evaluations for treatments of infectious diseases and vaccine candidates have been supported. (2,146 cases for treatment candidates, 1,018 cases for vaccine candidates) * Last Updated December 2023
  - 19 candidates have entered clinical trials and 2 candidates have been approved as products
- Prioritization of response to infectious diseases
  - Selection of candidates for infectious diseases that can cause a pandemic (COVID-19, MERS, Influenza, SFTS, SARS, Zika)
- Promotion of the expansion of ABL3 facilities
  - Commencement of design service for ABL3 facility expansion (as from December 2023)
  - Geotechnical survey for the ABL3 facilities (as from Feburary 2023)

Figure 1

Figure 2

[Division of National Bio-Infrastructure]

Dr. Young Hyo Chang

Bio-Infrastructure Policy Support Center
Associate Director

yhchang@kribb.re.kr

1. Introduction

Bio-Infrastructure Policy Support Center is the secretariat of Division of National Bio-Infrastructure, which is the “Competent Authority for Biological Research Resources of the Ministry of Science and ICT (MSIT)”, and supports the establishment and execution of policies related to Biological Research Resources. As a designated center for responding to and supporting the Nagoya Protocol (ABS) of the MSIT, we also operate ABS Help-Desk for researchers. Another primary responsibility is to manage the following three committees with institutional authority, in terms of legal regulations for ensuring bio-safety: Institutional Review Board (IRB), Institutional Animal Care and Use Committee (IACUC), and Institutional Bio-safety Committee (IBC). We also research taxonomy and cultures probiotic anaerobic bacteria to cope with ABS.

2. Research Areas

- Support for establishing policies for Biological Research Resources and develop institutional policies for Division of National Bio-Infrastructure to reinforce its roles
- Research on ABS laws and regulations in line with global trends or emerging issues
- Promotion of ABS by holding public seminars
- Provision of consulting services on the access and use of domestic and foreign genetic resources
- Management of three KRIBB ethics boards (IRB, IACUC and IBC)
- Research on taxonomy of anaerobic bacteria to cope with ABS and develop authentic probiotics of Korean origin

3. Main Projects

- Support for establishing policies for Biological Research Resources and develop institutional policies for Division of National Bio-Infrastructure to reinforce its roles
- Consigned affairs on behalf of the Ministry of Science and ICT (MSIT) for their role as Competent National Authority & Checkpoint under the Nagoya Protocol
  - Supports the MSIT to provide public services for processing ‘Report on Access to Domestic Genetic Resources’, ‘Procedural Compliance Report on Foreign Genetic Resources’, and etc.
  - In charge of ‘ABS Help-Desk’(online and telephone consultation)
- Consigned affairs on behalf of the Ministry of Science and ICT (MSIT) for the Export Approval in accordance with the Act on the Acquisition, Management, and Utilization of Biological Research Resources
  - Review on the preparation of lists of objects subject to approval for shipment to other countries, Receipt and processing of Export Approval applications, etc.
- Promotion of public awareness of the Nagoya Protocol
  - Publishes ‘ABS Brief’(online newsletter) every month
  - Publishes ‘ABS Guide’(paperback series) every year
  - Convenes public events (e.g., symposium, seminars, etc.) for ABS awareness raising
- Management of three institutional ethics boards
  - Institutional Review Board (IRB), Institutional Animal Care and Use Committee (IACUC), Institutional Bio-safety Committee (IBC)

4. Recent Achievements

- Organization of public events for the Division of National Bio-Infrastructure
  - Joint promotion at Korean Society for Biochemistry and Molecular Biology (May 2023/KSBMB), etc.
  - KRIBB Conference (October 2023)
  - Bio-Infrastructure Advisory Committee meeting (April 2023)
- Holding policy seminars in response to current issues of the Nagoya Protocol
  - (The 2nd) ‘Scope and Use of DSI form the Perspective of Researchers’ (April 2023, Seoul)
  - (The 3rd) ‘DSI Benefit-Sharing Mechanism from the Perspective of Researchers’ (September 2023, Daejeon)

- Attending and presenting at an international symposium
  - ‘Asian Academic ABS Forum – ABS Symposium 2023’ (October 2023, Tokyo)

- Holding three KRIBB ethics boards
  - IRB: 2 annual meetings (45 reviews conducted by the public IRB of the MOHW)
  - IACUC: 27 meetings with 355 reviews
  - IBC: 5 meetings with 14 reviews
- Research Paper
  - Seon Lee, Young-Hyo Chang, “A Legal study on possible elements in designing the benefit-sharing mechanism on DSI under the CBD”, Korea Law Review, Vol. 111 (2023.12).
  - Jayoung Paek, Lu Bai, Young-Hyo Chang (et al), The novel immunobiotic Clostridium butyricum S-45-5 displays broad-spectrum antiviral activity in vitro and in vivo by inducing immune modulation. Front. Immunol., vol.14 (2023.10).
  - Lu Bai, Jayoung Paek, Young-Hyo Chang (et al), Description of Fusibacillus kribbianus gen. nov., sp. nov., a fusiform anaerobe isolated from pig feces. Anaerobe, Vol 84 (2023.12).

[Jeonbuk Branch Institute]

Dr. Young Bae Ryu

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Functional Biomaterial Research Center
Associate Director

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ybryu@kribb.re.kr

1. Research Areas

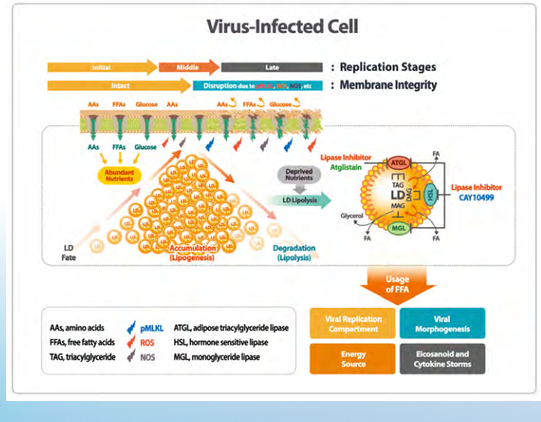
• Development and commercialization of functional biomaterial-based foods and drugs in response to the current fast-changing ear
- Discover and evaluate the efficacy of functional biomaterial in response to the fast-changing era
- Establishment of food and drug evaluation models and the development of appropriate biomaterial (immune response, metabolic disease, etc.)
- Identification and profile of functional biomaterials by using spectroscopic instrumental analysis (NMR, MSMS, etc.)
- Isolation of extracellular nano like vesicles from natural resources and evaluation of their biological effective

• Evaluation and support of ABL3-facility-based responses to national disasters and novel infectious diseases
- Efficacy assessment of COVID-19 vaccine/treatment using small-animal models for infection (hamster, ACE2-TG mouse, etc.)
- Secure new variations of infectious pathogens and ABL3 facility operation and maintenance

2. Recent Achievements

• Discover and evaluate the efficacy of functional biomaterial in response to the fast-changing era
- Oleanolic acid acetate inhibits mast cell activation in ovalbumin-induced allergic airway inflammation (Allergy Asthma and Immunology Research)
- Efficacy evaluation of Streptomyces nigrescens KA-1 against the root-knot nematode Meloidogyne incognita (Biological Control)
- Estrogenic active Ecklonia cava extract improves bone loss and depressive behaviour in OVX mice (Journal of Functional Foods)

• ABL3 facility-based evaluation and technology transfer of lead candidates for infectious disease treatment
- Therapeutic strategy targeting host lipolysis limits infection by SARS-CoV-2 and influenza A virus (Singnal Transduction and Targeting Therapy, 2022)
- Ocular tropism of SARS-CoV-2 in animal models with retinal inflammatory via neuronal invasion following intranasal inoculation (Nature Communications, 2022)
- (Technology transfer) Evaluation technology to assess the efficacy single and combination of candidate drugs for COVID-19 treatment



[Jeonbuk Branch Institute]

Dr. Seonghun Kim

Microbial Biotechnology Research Center
Associate Director

seonghun@kribb.re.kr

1. Introduction

The emphasis of the Center for Microbial biotechnology research center is to develop novel technology for improving the efficiency and quality of industrial microorganisms and microbial processes in the production of food and feed ingredients, biochemicals and biofuel, and bio-agro-products to ensure sustainable bio-economy.
Our activities are centered on both fundamental and applied biotechnology, with the view to establishing a basis for effective microbial cell factories in industrial biotechnology.

2. Research Areas

- Microbial metabolic engineering
  - Production of microbial metabolites
  - Metabolic engineering of industrial microorganisms
- Bioconversion technology
  - High throughput screening of novel biocatalysts
  - Directed evolution of industrial enzymes
- Gut microbiome researches
  - Development of novel methodologies for evaluation of gut microbiome
  - Evaluation of prebiotics and probiotics resources for human and animal health
- Biochemical and bioprocess engineering
  - Production of biochemicals for sustainable materials
  - Development of green technologies from renewable sources

3. Main Projects

- Development and commercialization of well-aging biomaterials based on agro-bio microbiome
- Development of industrial miroorganisms by using random substitution of genetic codes in the 5'coding region
- Development of novel lectins for identification of bacterial glycan epitopes in gut microbiota
- Development of Bio-based Glycolic Acid Production and Polymerization Process for Polyglycolic Acid Production

4. Recent Achievements

- Biochemical characterization and cytotoxicity of polylactosamine-extended N-glycans binding isolectins from the mushroom Hericium erinaceus
  - The mushroom Hericium erinaceus expresses isolectins with different glycan binding specificities; of these, the ricin B-like lectin HEL1 and HEL2 (HEL2a and HEL2b) can bind fucosylated N-glycans and core 1 O-glycans, respectively.
  - These biochemical properties indicate that rHEL3 isolectins may be used as unique lectins for detecting poly-LacNAc-extended glycans, which are known to be over-expressed in leukemia or metastatic melanoma cells, in cancer diagnostic assays and anti-cancer therapies.
- Production of 1,2-propanediol from glycerol in Klebsiella pneumoniae GEM167 with flux enhancement of the oxidative pathway
  - We developed K. pneumoniae GEM167ΔadhE/pBR-1,2PDO, a novel bacterial strain that has blockage of ethanol biosynthesis and biosynthesized 1,2-PDO from lactic acid when glycerol is carbon source.
  - K. pneumoniae GEM167 has potential for the production of additional valuable chemical products from metabolites produced through oxidative pathways.
- Lipid mediators derived from DHA alleviate DNCB-induced atopic dermatitis and improve the gut microbiome in BALB/c mice
  - We determined the potential therapeutic benefits of lipid mediators (LM, 17S-monohydroxy DHA, resolvin D5, and protectin DX in a ratio of 3:47:50) produced by soybean lipoxygenase from DHA.
  - Our findings suggest that LM represents a potential therapeutic agent for improving AD symptoms through its ability to suppress inflammatory cytokines and alter the composition of gut microbiota.
- Agarolytic pathway in the newly isolated Aquimarina sp. bacterial strain ERC-38 and characterization of a putative β-agarase
  - Marine microbes, particularly Bacteroidetes, are a rich source of enzymes that can degrade diverse marine polysaccharides.
  - Aq1840, which is closest to ZgAgaC within the glycoside hydrolase 16 family, is involved in at least the initial agar degradation step prior to the metabolic pathway that uses agarose as a carbon source for growth of the strain.

[Jeonbuk Branch Institute]

Dr. Song-Gun Kim

Biological Resource Center
Associate Director

gkim@kribb.re.kr

1. Introduction

The Biological Resource Center (BRC) is the largest biorepository in the country, systematically collecting and preserving essential materials for biotechnology research and industrialization, including standard and patented microorganisms, animal and plant cell lines, microalgae, embryos, and genomic research materials. We provides these resources to researchers both domestically and internationally. Additionally, BRC is enhancing the acquisition and upgrading of various biological resources by building a network among domestic and international Biological Resource Centers (BRCs), improving the informatization of biological resources, and strengthening support functions for external collaboration.

2. Research Areas

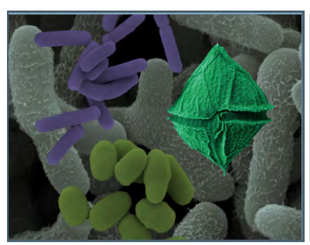
- Acquisition and management of biological resources
  - Collect and preserve key biological resources for research activities
  - Distribute biological resources to academia, research, and industry
  - Develop platform technologies for isolation, long-term preservation and application of useful biological resources
  - Support for storage, preservation, and distribution of patented microorganisms
- Support for network infrastructure construction and bioresources- related services and training
  - Building local and global networks for biological resources
  - Support for training workshops, conferences, and consultations
- Develop microbial infrastructure systems and applications to support the healthcare industry
  - Establish human and animal gut microbiome banks
  - Supporting gut microbiome research and industry
- Development and management of valuable plant cell resources
  - Development, collection, preservation, and distribution of plant cell resources (callus, adventitious roots, shoot and micro-tubes)
  - Mass production of valuable plant cell resources using bioreactors
  - High-level production of useful metabolites by eliciting response from plant cells
- Developing platform technology for the localization of medical cannabis
  - Developing elite plant cell lines to mass-produce valuable substances from medical cannabis
  - Establishing metabolite cultivation techniques to enhance cannabinoid content in cell culture and indoor farms

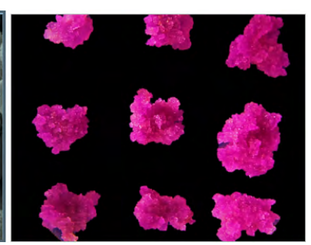
3. Main Projects

- Enhancement of infrastructure for biological resources and customized service thereof
  - Collection, quality control, long-term preservation and distribution of type strains and patent microorganisms
  - Research and development to strengthen utilization of biological resources
- Advancement of Central Microbial Resource Center of the Ministry of Science and ICT
  - Operation of a portal specializing in microbial resources
  - Services for utilization of microbiological resources
- Development of the standard bank and support of Korean gut microbiome
  - Optimization of isolation/cultivation/preservation technology and construction of an integrated database of the gut microbiome (obligate anaerobic) of healthy Koreans
  - Support domestic microbiome research and commercialization by operating a world-class gut microbiome bank
  - Build a platform to support the acquisition and utilization of human-derived probiotic strains
  - Support demand-driven discovery and industrial cultivation of functional probiotics
- Advancement of Acquisition, Management and Application of Biological Research&Development Products
  - Continuous deposit and management of bioresource research results and resources to promote utilization of bioresource
  - Establish a database of quality and characteristic information of microbial research results and provide various utilization support services for utilizing research results
  - Expanding the integrated research and development support system and improving the bioresource research results
- Establishment of plant cell resources and its application
  - Acquisition, development and long-term preservation of plant cell resouces
  - Developing technologies to enhance production of useful metabolites by modulating plant metabolic fluxes
  - Establishment and industrialization of a mass culture system for plant engineered cell resources using bioreactors
- Localization of medical hemp material for establishment of research base for food and medicine development
  - Establishment of a research center for the localization of functional raw materials using medical hemp based on advanced biotechnology
  - Development of food and pharmaceuticals such as treatments for rare and incurable diseases and geriatric diseases for the aging

4. Recent Achievements

- A new omega-3 rich euglenoid Eutreptiella sp. from the Korean coastal waters
  - The morphology, phylogeny and MALDI-TOF MS of an unspecified euglenoid strain was examined
  - This new isolate could be used in aquaculture and nutraceuticals without any risk
- Chondrinema litorale gen. nov., sp. nov., of the phylum Bacteroidota, carrying multiple megaplasmids isolated from a tidal flat in the West Sea, Korea
  - We isolated a bacterial strain from red algae living in tidal flats and performed physiological and genetic analyses. We proposed that this microorganism represents a new genus and new species
- ECM-targeting bacteria enhance chemotherapeutic drug efficacy by lowering IFP in tumor mouse models
  - Development and verification of bacteria with the capability to degrading the extracellular matrix of tumor.
  - Validation of the enhanced anticancer efficacy achieved by ECM-targeting bacteria in breast and pancreatic tumor mouse models.
- Adenosine monophosphate enhances callus regeneration competence for de novo plant organogenesis
  - Based on the effect of AMP on plant regeneration, we optimized cell and tissue culture methods for improving protoplast regeneration efficiency in plant
- A nostoxanthin-producing bacterium, Sphingomonas nostoxanthinifaciens sp. nov., alleviates the salt stress of Arabidopsis seedlings by scavenging of reactive oxygen species
  - Isolation of a novel nostozanthin-producing endophytic strain, named AK-PDB1-5T, from the leaves of Abies koreana collected from Mount Halla, Jeju, South Korea.
  - Potential use as s biomaterials to mitigate climate change stress on plants





[Jeonbuk Branch Institute]

Dr. Ji-Su Kim

Primate Resources Center
Associate Director

kimjs@kribb.re.kr

1. Introduction

Recently, non-human primate resources have become a very valuable resource internationally. Primate Resources Center(PRC) intends to introduction of SPF primate resources for bio (medicine and vaccine) research and establish its production base. High-quality primate colonies through the breeding primates group, and establish group breeding SOP to establish a cross-ministerial support infrastructure for primate research through the establishment of a cooperative network at home and abroad.

2. Research Areas

- Maintenance, production, and distribution of non-human primate resources
  - Establishment and preservation of laboratory non-human primate resources
  - Constructing stable breeding colony for non-human primates resources
- Establishment and development of SPF non-human primate resources
  - Quality control of laboratory non-human primates (infectious viruses and bacterial monitoring)
  - Acquiring and distributing SPF non-human primate resources to industrial, academic and research institutions
- Standardization in non-human primate accommodation, care and use for non-human primate research
  - Maintaining quality standards for non-human primate breeding, handling, training, environment enrichments
  - Establishing a standard operating procedure (SOP) by providing guidelines for the veterinary care and welfare assessment of non-human primate resources at the international level
- Behavioral analysis for non-human primate disease models
  - Constructing disease models for incurable non-human primate diseases, which have metabolic pathways most similar to human, and thus developing new drugs and applications for organ and regenerative research
  - Establishing methods for analyzing behavioral patterns in a non-human primate models
- Collaboration and support for industrial-academical-institutional research groups using non-human primates
  - Provide other researchers with expertise and information on care methods and facilities for large-scale reproduction of non-human primates, and conducting collaborative research to develop related specific technologies in industry, university, institute and hospitals

3. Main Projects

- Infrastructures for securing and supporting primate resources
- Primate resources biobank for biomedical and basic science
- Creating and verifying monkey and pig models of human genetic diseases using advanced genome editing tools

4. Recent Achievements

- Establishment of production system for non-human primate resources
  - Production of 2 species macaque monkey (cynomolgus monkey, rhesus monkey)
- Creation of natural/artificial nursing environment for pregnant macaques
  - Achieved 50% production rate of macaca monkeys (Cynomolgus monkey and Rhesus monkey) throughout an own breeding system in Primate Resources Center
- Research support of non-human primate resources/materials to national partners of industry, university, institute and hospitals (COVID-19, Organ transplantation research etc.)
  - We supported macaque monkeys (weight, age, sex etc.) that customers needed through a strict quarantine process.
  - We supported macaque monkey materials (blood origin and cell lines, tissues) for various research
- Development of in vitro fertilization (IVF) monkey production and gene target editing monkey production technology through assisted reproductive technology (ART).
  - Development of superovulation and surrogate mother synchronization technology by checking hormone (E2, P4 etc.,) levels in serum
  - Establishment of primate derived IVF embryos production and in vitro culture technology
  - Development of primate embryo transplantation and pregnancy diagnosis (ultrasonic diagnostics) technology

[Division of Research Strategy]

Dr. Heoung-Yeol Kim

Biotech Policy Research Center
Associate Director

yeolhee@kribb.re.kr

1. Introduction

• Nominated and established by the Ministry of Science and ICT in 2004, the Biotech Policy Research Center is a non-profit organization devoted to the research and development of biotech policy and policy alternatives. And in April 2021, our center was designated as a specialized institution for biotechnology policy based on Article 24 of the Biotechnology Support Act. Our mission is mainly threefold :
- To provide government officers with accurate, relevant, and timely information on biotech trends.
- As a think tank, to develop biotech R&D strategy to help government officers.
- To build networks with opinion leaders as an idea platform.

• We run a portal site(BIOIN, www.bioin.or.kr) to enhance public understanding of biotechnology and biotechnology policies and also a BT innovative linkage platform (BICS, www.bics.or.kr) to faciliate Bio Discovery to Market activities.

2. Research Areas

• Policy Planning
- To plan comprehensive national policy and strategies to foster the research and development of biotechnology.

• Policy Research
- To investigate technology, industry, infra and institutional policy information and to conduct relevant statistics, patent maps, and bibliometric analysis.

• Dissemination of Knowledge and Issues
- To provide systematic knowledge and issues regarding biotechnology and biotechnology policy at large through portal sites (www.bioin.or.kr).

• Public Relations
- To publish biotechnology white papers and to organize public workshops to enhance public understanding of biotechnology.

3. Main Projects

• Policy Planning :
- Planning for Digital- Biotechnology Strategy.
- Planning for National Synthetic Biology Initiative.
- Planning for the forth Biotechnology Fostering Basic Plan – Science Technology based.
- Planning of large-scale projects for Survey and analysis of national R&D programs.
- Research on BT regulatory issues and operation of “Bio Regulatory SINMUNGO”
- Supporting the establishment of Biotechnology Fostering Implementation Plan
- Research on continuous research methods for achievements (technology, industry, investment) for vitalization of the bio-industry.
- Analysis of the status of small and medium-sized bio venture companies to discover ways to revitalize the bio-industry ecosystem.

• Emerging Technology Forecast and Statistical Development
- Discovery promising and emerging BT technologies that will affect the industrial and technological fields in the next 5 to 10 years.
- Publishing annual reports on domestic and overseas statistical data on biotechnologies categorized by investment, human resources, industry, and technology.

• Expert Network & International Collaboration
- To OECD Korea Workshop“Policy directions for critical health technology innovation and access”
- To operate the “BIO Innovative Growth Convention”, BT Forum and Exhibition.
- To participate in the annual Session of the OECD Working Party on Biotechology, Nanotechnology and Converging technology(BNCT).
- To support Special Committee on Biotechnology / Infectious Disease
- To support the Bio-regulatory TF

• Policy information portal (Website)
- BioIN : A one-stop portal website to provide Bio information related to various technology, industry trends and policies. (https://www.bioin.or.kr)
- BICS (Biotechnology Innovation Connect Service) : Bioeconomy monitoring and networking platform (https://www.bics.re.kr)
- SBKIH (Synthetic Biology Knowledge Information Hub) : Synthetic Biology monitoring and networking platform (https://www.bics.re.kr/synbio_korea)

[Division of Research Strategy]

Dr. Gicheol Kim

Korea Biosafety Clearing House
Associate Director

kgccc@kribb.re.kr

1. Introduction

Based on Cartagena Protocol on Biosafety(CPB) and LMOs Act, Korea Biosafety Clearing-House carries out professionally the collection and exchange of the information on living modified organisms(LMO) and Biotechnology to promote and facilitate public awareness, education and participation concerning the safe transboundary movements, handing and use of LMOs, contributing to the sound development of bioindustry in Korea

2. Research Areas

- Implementation of the Cartagena Protocol & LMO Act
- Improvement of Public Awareness & Communication
- Risk Review for LMOs for Industrial Use
- Implementation of the Nagoya Protocol & Genetic Resources Act

3. Main Projects

- Implemetation of the Cartagena Protocol and Operation of the Biosafety Clearing House
  - Implementation of the Cartagena Protocol on Biosafety
  - Implementation of LMO Act and Policy Support
  - Public Communication and Information Management
- Safety Management for LMOs for Industrial Use
  - Risk Review for LMOs for Industrial Use and Safety Management for Related Facilities
  - Awareness-Raising and Capacity Building of Safety Management in the industry
- Establishment of Industry Support System related to the Nagoya Protocol

4. Recent Achievements

- Actively Producing LMO information and Communicating with Stakeholders
  - Publishing KBCH Briefings and National Reports (39 cases)
  - Operating the Youtube Channel(GMO TV) (Upload: 69 cases)
  - Operating the GMO Portal (https://www.biosafety.or.kr)
  - Operating Publications(5 cases), Public Panel, and KBCH Forum Seminar(3 times), SMART LMO Reporters etc
- Operating Biosafety Management for LMOs for Industrial Use
  - Helding the LMO risk review committee (8 times)
  - Publishing the risk assessment guideline for the contained use of biosafety level 1 LMOs
  - Conducting the R&D Project for Upgrading Risk Assessment and Risk Review for LMOs for industrial use
- Revising the LMO Act and Operating the Association of Related Agencies
  - Support for laying a revised the LMO Act to the National Assembly
  - Holding the National Biosafety Committee and Research meetings (12 times)
- Strengthening the Asia cooperation network(Asia Biosafety Family)
  - Implementing the BCH Capacity Building Project
  - Operating the ABF Portal
- Establishment of Industry Support System related to the Nagoya Protocol
  - Investigation and analysis of overseas biological resources usage status in bio-industry (In-depth investigation of overseas biological resources brokerage companies)
  - Publication of comprehensive manual on 10 years of Nagoya Protocol implementation
  - Operating the ABS webpage and publishing the legal guidebook for the Nagoya Protocol to provide information and raise awareness in the industry

[Division of Research Strategy]

Dr. Young-Hee Roh

National Research Safety Headquarters(NRSH)
Associate Director

rohyh@kribb.re.kr

1. Introduction

- In recent years, new hazards are constantly emerging due to the development of science and technology and the increase in interdisciplinary research, and the risks in the laboratory have become more complex and diversified.
- The National Research Safety Headquarters(NRSH) was established in April 2015 to serve as a specialized organization to ensure that researchers in science and technology laboratories and LMO research facilities conduct safe research activities. The NRSH has being carried out lab & LMO safety management projects supported from Ministry of Science and ICT.

2. Research Areas

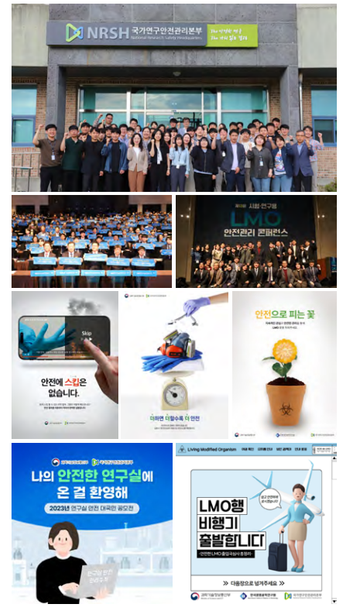
- Ensuring a safe research environment and preventing accidents
  - Identifying and improving factors contributing to safety in LMO research through facility inspections and comprehensive surveys
  - Conducting on-site inspection of laboratories in the field of science and technology to identify safety management vulnerabilities and guide improvement measures
  - Supporting the establishment of autonomous safety management systems at research sites
- Support for establishing a safety management system of LMOs for R&D (Expecially in the operation of governmental compliance procedures and the development of policy & standards, etc.)
  - Assistance in the operation of the license system related to research facilities and import & export of LMOs for R&D
  - Establishment and dissemination of biosafety standards for LMO research facilities and biological materials (microorganisms, animals, plants, etc.)
- Development of safety management policies and systems for science and technology laboratories
  - Legal operation and policy support for Act on the Establishment of Safe Laboratory Environment
  - Establishment of national laboratory safety management policy and system
  - Development of laboratory-specific safety standards and guidelines
  - Supporting the establishment of an organization dedicated to lab safety and the improvement of lab environment, and operating certification system for exemplary labs
- Conduct safety training (online and offline) and develop educational content
  - Operate statutory safety training and training by target, research material, and field
  - Development and distribution of educational contents (e-learning, textbooks, videos)
- Fostering a culture of safety by hosting lab & LMO-related occasions and public relations
  - Planning and operating programs(content contests, conference, safety events, etc.) to promote a culture of safety
  - Conduct promotional activities through online communication tools, such as social media(YouTube, Instagram, etc.) and newsletters
- Establishment and operation of an information system to provide intelligent safety information
  - Development and provision of LMO administrative information portal, chatbot, LMS (Lab Management System), and mobile app

3. Main Projects

- LMO Safety Management
  - Establishing the foundation for a safe research environment for LMOs for testing and research to ensure the safety of researchers
  - Enhance public confidence in LMO and promote development of biotechnology research
- Laboratory Safety Management
  - Create safety environments of laboratories in universities, research organizations, and etc. to prevent safety-related accidents and improve research productivity
- Establishment of a safety management plan
  - Established and performed the 4th Safety Management Plan on LMO for R&D and Basic Plan for Creating a Safe Laboratory Environment(2023-2027)
  - Supporting the development of short-, medium-, and long-term implementation plans of Ministry of Science and ICT
  - Establishment and implementation of major policies and strategies in the field of lab & LMO safety management(inspection, education, safety culture, etc.)

4. Recent Achievements

- Laying the foundation as a specialized safety management institution
  - Designated as an organization specializing in the 'Safe Laboratory Environment Establishment Project' (Ministry of Science and ICT)
  - Designated as an auxiliary organization for Public Institution Safety Management Rating Evaluation (Ministry of Economy and Finance)
  - Designated as an educational institution specializing in biosafety management (Korea Disease Control and Prevention Agency)
- Amending laws, and developing guidelines for lab & LMO safety management
  - Amendment of the public announcement on Transboundary Movement of Living Modified Organisms(amended on '23.11.13.)
  - Amendment of Act on the Establishment of Safe Laboratory Environment(amended on '23.10.31.)
  - Publishment of revised edition to 'Validation Guidance For The Plant Research Facility(BL3)', and development of 'Safety Guideline in Procedure of Genetically Modified Animal Research'
  - Development and publication of "Manual for establishment of high-pressure gas safety management system in laboratory', 'Safety management guidelines for laboratory animal handling laboratories', and 'FAQ on Act on the Establishment of Safe Laboratory Environment'
- Conducting on-site inspections and safety management consulting
  - Field inspection, survey, and safety management consulting for LMO research facilities
  - Conducting institution-specific safety management guidance and supervision that considers the institution's characteristics(conducting on-site inspections for 400 targeted institutions under concentrated management, consulting for the establishment of safety management systems in 200 small-scale corporate research institutes)



- Enhancing safety consciousness through education and dissemination of a safety culture
  - Development and distribution of lab & LMO safety education contents(lab: 833, LMO: 177)
  - Organized safety-related events, such as Lab Safety Week and LMO Safety Conference, and operated recognition programs for meritorious individuals and organizations in the field of lab & LMO safety
- Providing lab & LMO safety information
  - Improving user access to information through the operation of a mobile APP and chatbot(SAFI-bot)

KRIBB

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