

ANNUAL REPORT 2018

KRIBB

Korea Research Institute of
Bioscience & Biotechnology

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FOREWORD

Annual Report 2018

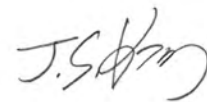
Korea Research Institute of Bioscience and Biotechnology (KRIBB) is the only government-funded research institute for biotechnology in Korea. Since the establishment in 1985, we have led the innovation in the field of biotechnology in Korea for the past 34 years, addressing the demand for national research development. We continue to establish strategies in order to provide solutions for global societal challenges such as food, medical services, environmental changes and lay the foundation for concrete results.

With our excellent team of researchers, latest research infrastructure and facilities, we are leading bioindustry and making accomplishments across a broad range of disciplines from the fundamental understanding of life phenomena to applied research and technology commercialization. Further, to remain viable in this ever changing environment, we are constantly innovating and responding to social needs. In this Annual Report, some of our research accomplishments from the year 2018 are highlighted.

Going forward, we will be at the forefront of creating future bio growth engines by acquiring new technologies and solving national and social agendas by obtaining national core technology. Moreover, we will work towards the advancement of biological infrastructure through enhancing consumer-oriented research infrastructure for nationwide use.

Please continue to support KRIBB, as we make a major leap forward.

Thank you.



Jang-Seong Kim, Ph.D.
President of 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

A Global Leader for
Healthy Life and
Bioeconomy

LIFE-ORIENTED

INNOVATION

FUTURE

EXCELLENCE

Creating Future Bio
Growth Engine

Solutions for
National Agenda

Advancing Biological
Infrastructure

GENERAL INFORMATION

FOUNDATION BASIS

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

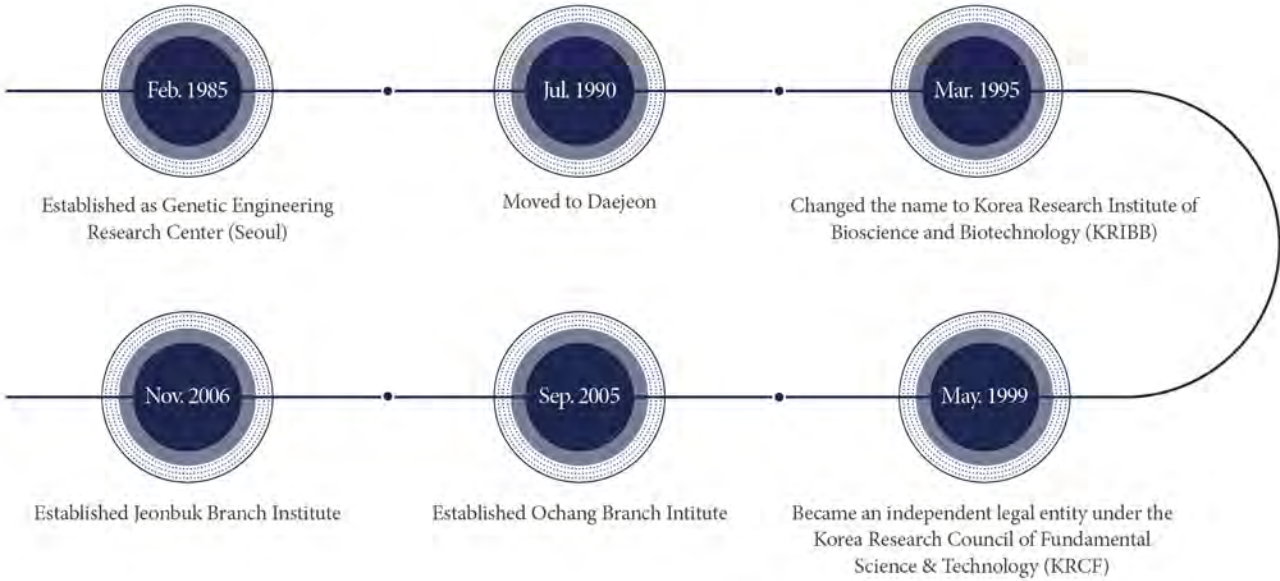
KEY FUNCTIONS

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



FACILITIES



Headquarter / 103,684m²



Ochang Branch Institute / 212,258m²



Jeonbuk Branch Institute / 160,709m²

BIOTECH FOR ECONOMIC GROWTH
AND BETTER LIVING STANDARDS

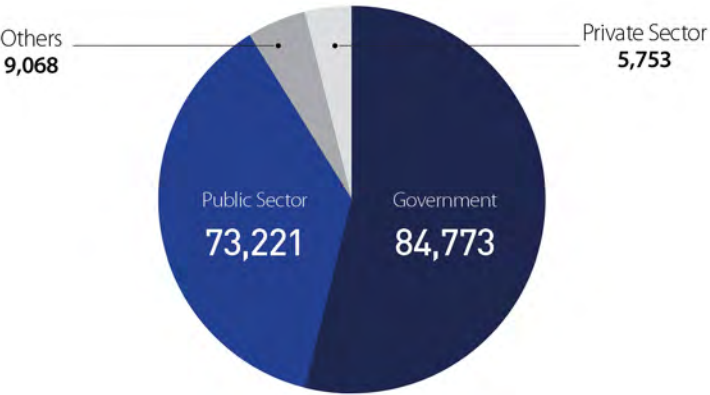
From fundamental research exploring basic facts about life to cutting-edging technologies, our work is aimed at creating new engines for economic growth and bringing concrete improvements in the quality of life.

Personnel
737

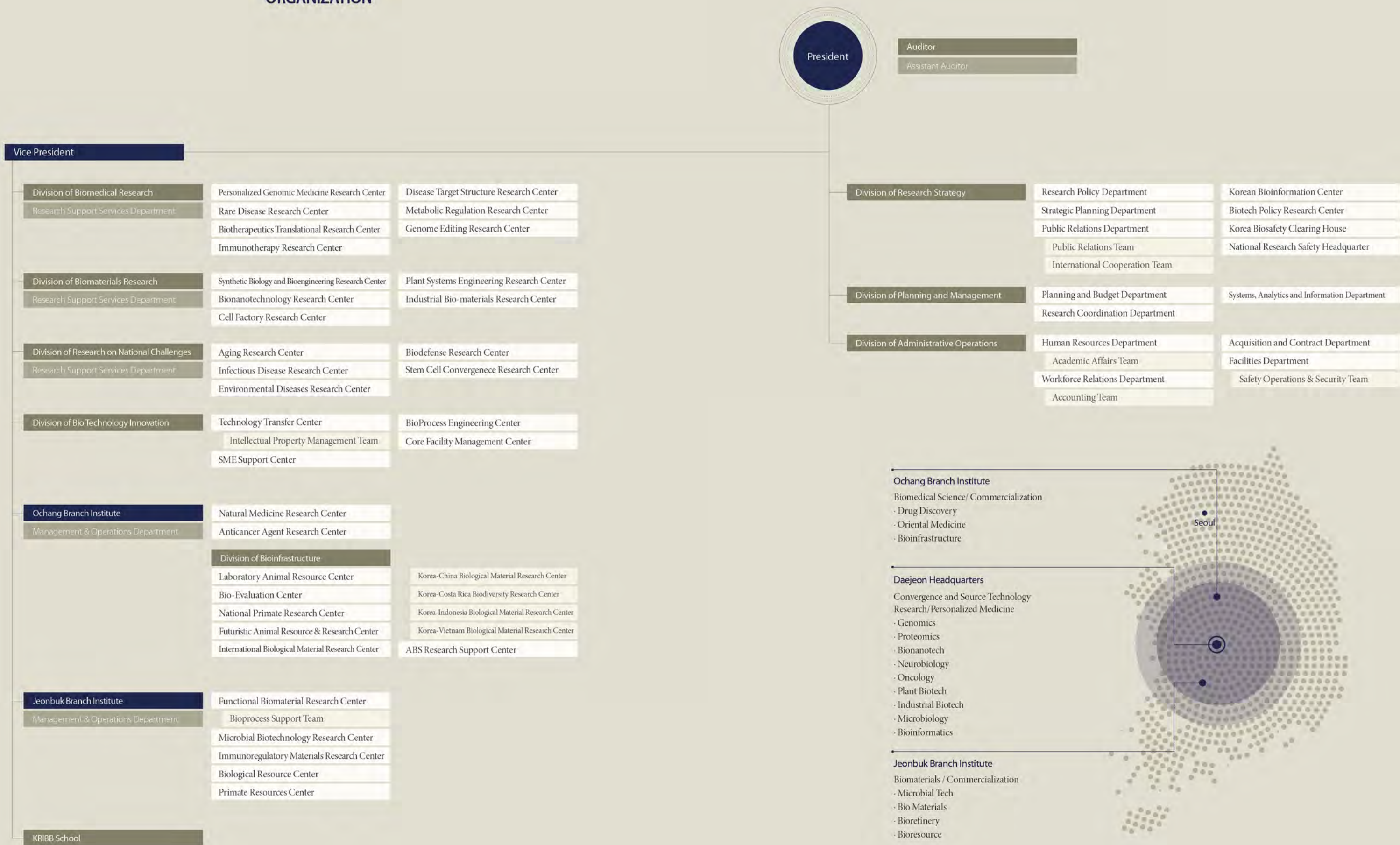
BRIEF OVERVIEW



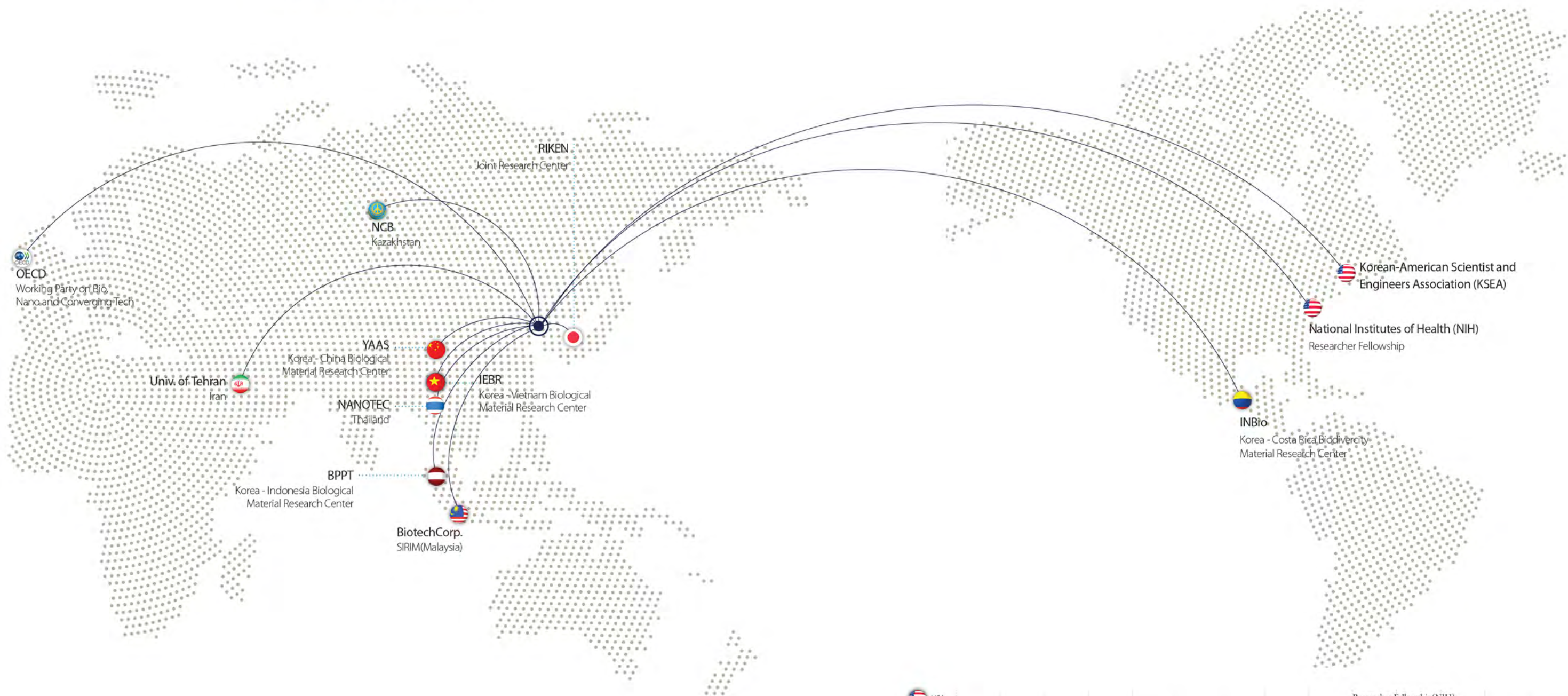
Research Expenses
(million KRW)
172,815



ORGANIZATION

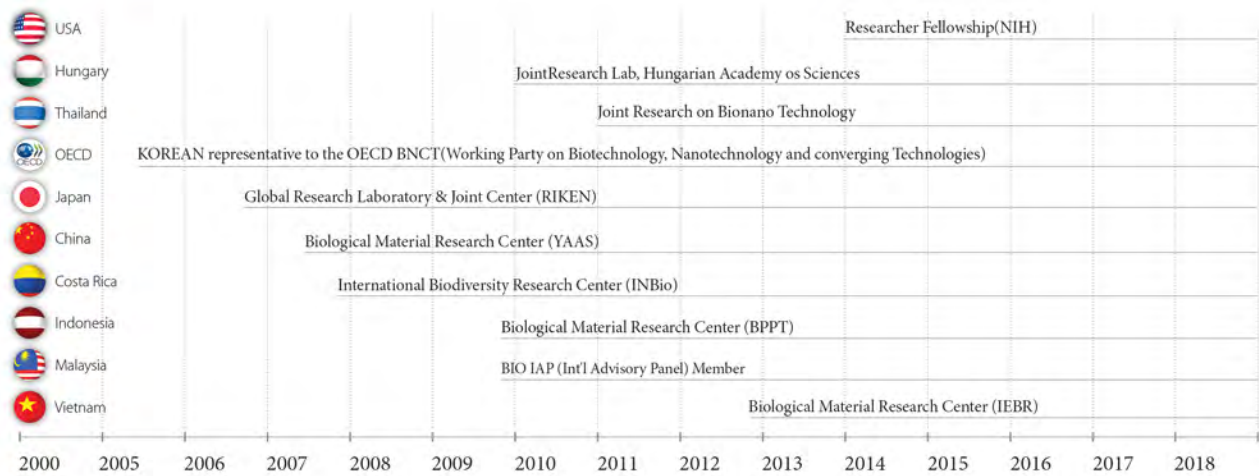


INTERNATIONAL NETWORK



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





FOCUS OF THE YEAR

16-25

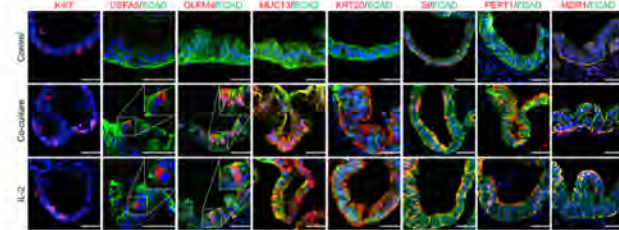


Research Highlights

News Highlights

Research Highlights

Interleukin-2 induces the *in vitro* maturation of human pluripotent stem cell-derived intestinal organoids



Immunofluorescent staining of control, co-cultured, and IL-2-treated hIOs with intestinal markers

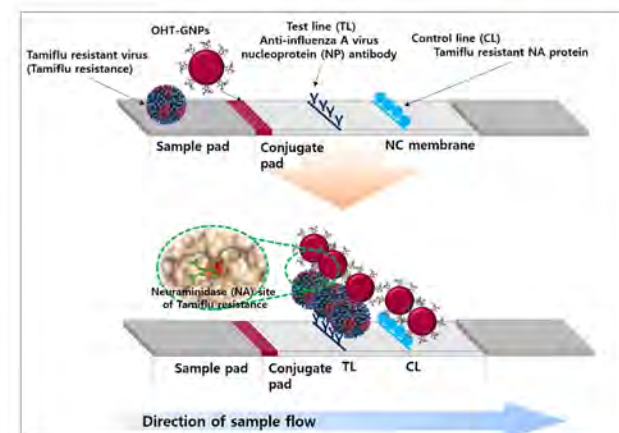
The first *in vitro* maturation technology for human intestinal organoids was developed by a team led by Dr. Mi-Young Son at Stem Cell Convergence Research Center by applying a novel 3D differentiation approach to human pluripotent stem cells. The team used 3D organoid differentiation and culture scheme to generate human pluripotent stem cell-derived intestinal organoids with a composition similar to that of human intestine.

In this study, co-culture system with immune cells was introduced to conventional 3D intestinal organoids to induce *in vitro* maturation. The mature intestinal organoids produced using this technology contained all four major intestinal cells: enterocytes, goblet cells, Paneth cells, and enteroendocrine cells. These cells expressed the markers representative of each cells' functions while exhibiting similar phenotypes and functions comparable to those of adult human intestine tissue. Immune cells in co-culture system released various cytokines to activate cellular responses such as immune reactions. Following the activation of T lymphocyte Jurkat T cells, a large amount of interleukin-2 (IL-2) was released, confirming that IL-2 is a key factor of co-culture system. In fact, direct treatment of intestinal organoids with IL-2 improved the phenotypic maturity and cellular functions. Either co-culture system with Jurkat T cells or IL-2 treatment of intestinal organoids was experimentally shown to activate the STAT3 pathway in epithelial cells of the organoids, which is known to regulate various genetic transcription processes in cells, thus playing

an essential role in cellular development, differentiation and growth. Co-cultured or IL-2 treated intestinal organoids contained the mature intestinal-specific cell types with the appropriate physiological functionalities, as evidenced by various functional assays as follows: drug reactivity of enterocytes in the mature enterocytes having functional efflux pump (P-gp assay), glucose absorption (Fluo-4AM assay), protein expression and function related to intestinal fibrosis (CFTR assay), mucus-secreting mature goblet cells, and functional enteroendocrine cells. Even after *in vivo* engraftment, *in vitro*-mature intestinal organoids retained their maturation status with normal karyotype. The study highlights the importance of increasing the phenotypic and cellular complexity of existing organoid culture systems and the appropriate physiological functionality to better model adult human organ systems *in vitro* for utilizing various aspects of *in vitro* and *in vivo* applications, such as a disease modeling, drug evaluation, pharmacological testing and potential clinical applications.

Kwang Bo Jung et al., "Interleukin-2 induces the *in vitro* maturation of human pluripotent stem cell-derived intestinal organoids", *Nature Communications*, 2018, DOI: 10.1038/s41467-018-05450-8

Rapid and simple detection of Tamiflu-resistant influenza virus: Development of oseltamivir derivative-based lateral flow biosensor for point-of-care (POC) diagnostics



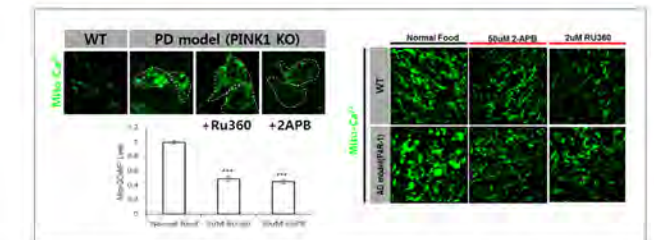
Conceptual diagram showing the Rapid Kit for detecting Tamiflu-resistant virus

A rapid test kit that can detect Tamiflu-resistant virus within 10 minutes was developed by a team led by Dr. Juyeon Jeong and

Dr. Eun-Kyung Lim at Bionanotechnology Research Center. An organic molecule that can selectively bind to the surface of Tamiflu-resistant virus was identified and applied it to a simple paper biodetector (lateral flow immunochromatography). In this study, an organic molecule with an oseltamivir derivative-based structure that specifically binds to a modified neuraminidase protein on the surface of Tamiflu-resistant virus was found. Through modeling analysis of neuraminidase reactivity, the analogue was shown to strongly bind to Tamiflu-resistant virus. The analogue on the surface of the gold nanoparticles binds to the neuraminidase protein on the surface of the Tamiflu-resistant virus, which causes the color change of the gold nanoparticles, enabling the detection of virus visually. Notably, newly developed immunoassay kit with analogue can visually detect the presence or absence of tamiflu-resistant virus within 10 minutes using a small amount of liquid (runny nose). The kit is convenient to use as the common influenza virus diagnostic kit or pregnancy test kit. When Tamiflu-resistant virus is present in samples from patients, two lines (test line and control line) will appear; when virus is not present, only control line will appear. Particularly, the color intensity of the test line varied according to the concentration of resistant virus, even when both Tamiflu-sensitive and Tamiflu-resistant viruses were present. Thus, this kit can be used to quantitatively analyze resistant viruses.

Seul Gee Hwang et al., "Rapid and simple detection of Tamiflu-resistant influenza virus: Development of oseltamivir derivative-based lateral flow biosensor for point-of-care (POC) diagnostics", *Scientific Reports*, 2018, DOI:10.1038/s41598-018-31311-x

Altered ER-mitochondria contact impacts mitochondria calcium homeostasis and contributes to neurodegeneration *in vivo* in disease models



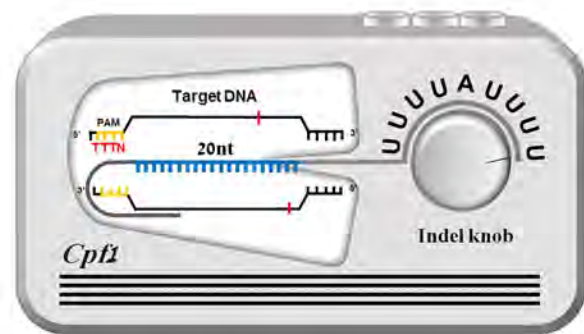
Rescue effect of calcium channel inhibitors in Parkinson's disease model (PD model, PINK1 KO, left) or Alzheimer's disease model (AD model, PAR-1, right). Detection of elevated mitochondrial calcium levels in a PD or AD model by using the mitochondrial calcium reporter, mito-GCaMP (green, Mito-Ca²⁺). When treating these models with calcium channel inhibitors (Ru360 or 2-APB), the aberrantly increased mitochondrial calcium level was restored to that in the WT control animal.

ER-mitochondria interactions leading to excessive increases in mitochondrial calcium levels are common causes of neurodegenerative diseases including Parkinson's and Alzheimer's disease. This was a collaborative study conducted by Dr. Kyu-Sun Lee at Bionanotechnology Research Center at KRIBB, Dr. Seongsu Lee at Korea Basic Science Institute and Prof. Bingwei Lu at Stanford School of Medicine.

Dr. Lee's team previously reported that the Miro, a mitochondrial transporting protein in neurons, plays a crucial role in mitochondrial calcium homeostasis (*Developmental Cell*, 2016). Miro protein is a common phosphorylated substrate of PAR-1 kinase, a gene known to cause Alzheimer's disease and PINK1, LRRK2 kinase, a gene known to cause Parkinson's disease. They confirmed that excessive increased mitochondrial calcium level both in Alzheimer's (PAR-1 overexpressing) and Parkinson's disease model (PINK1 knockout) by using a fluorescent reporter of mitochondrial calcium, mito-GCaMP transgenic *Drosophila* model. This abnormally increased mitochondrial calcium level lead to mitochondrial dysfunction and neuronal cell death in both neurodegenerative diseases. Notably, they suggested that mitochondrial calcium channel inhibiting compounds or gene regulation methods could be used as a therapeutic strategy for neurodegenerative diseases.

Kyu-Sun Lee et al., "Altered ER-mitochondria contact impacts mitochondria calcium homeostasis and contributes to neurodegeneration *in vivo* in disease models", *Proceedings of the National Academy of Sciences*, 2018, DOI: 10.1073/pnas.1721136115

Highly efficient genome editing by CRISPR-Cpf1 using CRISPR RNA with a uridylate-rich 3'-overhang



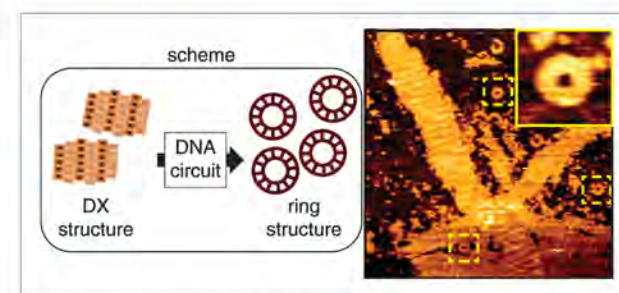
Schematic diagram showing the development of highly efficient CRISPR-Cpf1 through the application of 3'-end regulatory sequence

To enhance the efficiency of the CRISPR-Cpf1 system, next-generation genome editing tool was developed by a team led by Dr. Yong-Sam Kim at Genome Editing Research Center. The team successfully improved the efficiency of the CRISPR-Cpf1 system by adding a specific base sequence to the 3'-end of a guide RNA without physical or chemical treatment. It was shown that the addition of U4AU4 sequence to the 3'-end of the CRISPR RNA led to indel efficiency increase by up to 12-fold in human cells compared to the canonical CRISPR-Cpf1 system. This engineered CRISPR-Cpf1 system would enable genome engineering with higher efficiency, specificity, safety and low off-target effects. In this study, 115 genes were tested and Cpf1 was shown to have similar or higher editing efficiency compared to Cas9. Also, depending on target genes, Cas9 and Cpf1 showed different efficiencies. This indicates that each target gene requires different CRISPR systems for optimal efficiency and verifies that Cpf1 could complement Cas9 for genes that are difficult to be edited by Cas9, broadening the scope of CRISPR selection. To determine the mechanism of this effect, the binding affinity between Cpf1 protein and CRISPR RNA was compared. The optimized CRISPR RNA exhibited higher binding affinity towards Cpf1 protein than the non-optimized system, which is a unique feature for Cpf1. Conclusively, the editing efficiency of Cpf1 system was improved by using a relatively simple method of CRISPR RNA engineering, and the engineered system expanded the utility of CRISPR-Cpf1 in ge-

nome engineering and gene therapy.

Su Bin Moon et al., "Highly efficient genome editing by CRISPR-Cpf1 using CRISPR RNA with a uridylate-rich 3'-overhang", *Nature Communications*, 2018, DOI: 10.1038/s41467-018-06129-w

Kinetic Trans-Assembly of DNA Nanostructures



Schematic diagram showing the *in-situ* formation of DNA ring structure via the DNA circuit present in the solution from the DNA DX-tile, and two distinct nanostructures confirmed from AFM images

The formation of a secondary DNA nanostructure from one DNA nanostructure depending on an external signal was successfully demonstrated by Dr. Tai Hwan Ha at Bionanotechnology Research Center at KRIIBB, Dr. Junghoon Kim at Sungkyunkwan University and Dr. Sung Ha Park at Sung-kyunwan Advanced Institute of Nanotechnology. No previous studies have reported the formation of a dynamic structure that can lead to the formation of another nanostructure. Thus, these findings are important for applications in information transfer through DNA and nanotechnology development, as well as expanding the scope of DNA nanostructure use.

In this study, a DNA DX-tile was first produced on a circuit and placed in a solution containing a DNA circuit entities and transiently disabled precursors for DNA ring structures. When a DNA initiator strand was added to the solution, a single-stranded DNA oligomer tethered on the DX-tile released and reacted with its corresponding DNA circuit (dissolved in the solution) to activate the precursor structures to form the DNA ring structure that had been sealed. This led to the formation of a 30-nm DNA ring in the solution as confirmed by atomic force microscopy (AFM).

Jihoon Shin et al., "Kinetic Trans-Assembly of DNA Nanostructures", *ACS Nano*, 2018, DOI: 10.1021/acs.nano.8b04639

A synthetic microbial biosensor for high throughput screening of lactam biocatalysts

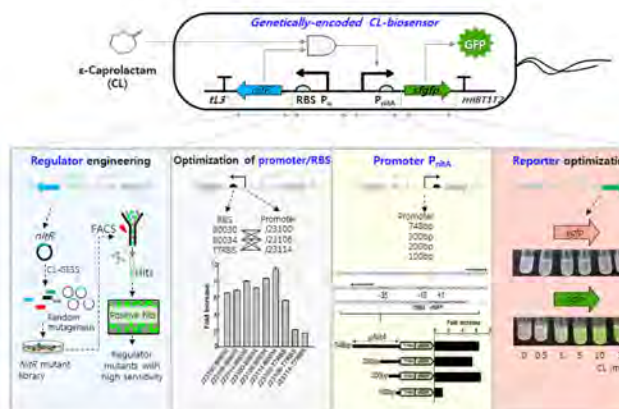


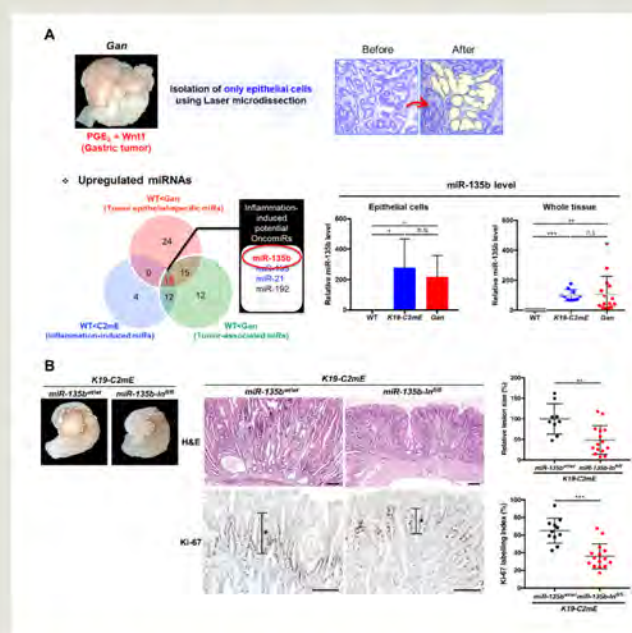
Diagram of artificial genetic circuit CL-GESS and its development process

Genes encoding a novel enzymatic function of synthesizing ϵ -caprolactam (a nylon monomer) were discovered in diverse microbial metagenomes of the west coast foreshore using artificial genetic circuit technology by a team led by Dr. Seung-Goo Lee at Synthetic Biology and Bioengineering Research Center. This study developed ϵ -caprolactam detectible genetic circuit (CL-GESS) as a biosensor. Microbial cells were equipped with CL-GESS that produces quantitative fluorescent signals upon detecting novel cyclizing enzymatic activity during nylon monomer synthesis. The cells as femto-liter volumed reactor conducted their normal enzyme reactions for a short period of time and were then screened with a fluorescence-assisted cell sorter (FACS) at a rate of thousands cells per second. Finally, cells exhibiting strong fluorescence that had activity of ϵ -caprolactam production were isolated. ϵ -Caprolactam is most widely used to produce nylon-6 and is mainly produced through Beckmann rearrangement of the cyclohexanone oxime in the presence of fuming sulfuric acid, at 90–120°C. Biorenewable routes towards ϵ -caprolactam from fermentation-derived 6-aminocaproic acid have gained attention. Although 6-aminocaproic acid biologically could be produced through biosynthetic pathways, complete biosynthetic pathways capable of synthesizing caprolactam are mostly unknown owing to the lack of enzymes able to catalyze the last ring-cyclization step. To identify biocatalysts in lactam biosynthesis, the team developed a caprolactam-detecting genetic enzyme screening system (CL-GESS). The *Alcaligenes*

faecalis regulatory protein NitR was adopted for the highly specific detection of lactam compounds against lactam biosynthetic intermediates. The team further systematically optimized the genetic components of the CL-GESS to enhance sensitivity, achieving 10-fold improvement. Using this highly sensitive GESS, the team screened diverse microbial metagenomes and found an enzyme that cyclizes 6-aminocaproic acid to ϵ -caprolactam. When an enzyme that mediates the conversion from 6-aminocaproic acid to caprolactam was present, the responsible microorganisms displayed fluorescence, and thus could be clearly distinguished from those without activity by FACS. Finally, based on the product confirmed by NMR, LC-MS, and IR analyses, the team concluded that the promiscuous enzyme catalyzed the cyclization of 6-aminocaproic acid in the absence of any cofactor. Basically, the screened CF3HBDs belong to the NAD(P)H-dependent short-chain dehydrogenase family, and they have cyclization activity as unexpected, promiscuous activity. Consequently, isolating a novel caprolactam-synthesizing enzyme from nature was successfully done; in-depth analysis of the enzyme structure and function showed that it has the unique function of synthesizing caprolactam without requiring any coenzyme.

Soo-Jin Yeom et al., "A synthetic microbial biosensor for high throughput screening of lactam biocatalysts", *Nature Communications*, 2018, DOI: 10.1038/s41467-018-07488-0

Interleukin 1 Upregulates MicroRNA 135b to Promote Inflammation-associated Gastric Carcinogenesis in Mice



(A) Identification of novel gene (miR-135b) in gastritis and gastric cancer mice
(B) Reduced size of gastric lesion in miR-135b knockout mice

A gene [microRNA-135b (miR-135b)], that plays a key role in gastric cancer pathogenesis, was identified using a spontaneous gastritis (*K19-C2mE*)/gastric cancer (*Gan*) mouse models and human gastric cancer samples in a collaborative study by Dr. Tae-Su Han at Biotherapeutics Translational Research Center at KRIBB, Prof. Dominic Chih-Cheng Voon and Prof. Masanobu Oshima at Kanazawa University in Japan, and Prof. Seong-Jin Kim and Prof. Han-Kwang Yang at Seoul National University. The collaborative team determined the roles of miR-135b in accelerating the progression of gastritis and early gastric cancer.

In this study, a strong up-regulation of miR-135b was observed in gastric epithelial cells during gastric inflammation and carcinogenesis, which was confirmed by laser microdissection and in situ hybridization. Moreover, the miR-135b expression was increased in human gastric cancer samples from TCGA (The Cancer Genome Atlas) database. Particularly, the miR-135b levels were already elevated in stage I early gastric cancer samples.

The gastric organoid culture with various cytokines treatment

showed that IL-1 strongly induced the miR-135b. Expression of miR-135b increased tumorigenicity, whereas suppression of miR-135b led to reduce oncogenic properties. Furthermore, the miR-135b directly inhibited tumor suppressors, *FOXN3* and *RECK*. Therefore, this study shows oncogenic functions of miR-135b and possibilities of miR-135b as a diagnostic marker for early detection of gastric abnormalities.

Tae-Su Han et al., "Interleukin 1 Upregulates MicroRNA 135b to Promote Inflammation-associated Gastric Carcinogenesis in Mice", *Gastroenterology*, 2018, DOI: 10.1053/j.gastro.2018.11.059

News Highlights

The Celebration of the 33rd Anniversary of the Foundation / February 1



The ceremony for the 33rd anniversary of KRIBB's foundation was held on February 1, 2018. The ceremony, which took place at Daejeon headquarters included three sub-events: award ceremony, opening remark from the president, and celebration performance. Employees who contributed to the development of KRIBB in the year 2018 were awarded. National Research Council of Science & Technology Presidential Awards were awarded to Dr. Kyung-Sook Chung, Director of Division of Research on National Challenges, for developing an original technology for the diagnosis and treatment of rare/incurable diseases and Joeun Kwak, a senior administrator of Workforce Relations Department for organizing the administrative system for Jeonbuk Branch Institute at the beginning of its establishment. Dr. Oh Seok Kwon of Infectious Disease Research Center was awarded with the Best Research Paper Award for his work on a new protein integrated electric biosensors (*ACS Nano*). The Best Technology Development Award was awarded to Dr. Ki-Sun Kwon of Aging Research Center for developing technology related to aging-related sarcopenia prevention and treatment drug.

Signboard Ceremony of Division of Bioinfrastructure / February 12



Division of Bioinfrastructure (Infra Division; Director Hyoung-Chin Kim), in charge of establishing and managing the public infrastructure of biological research resources, held a signboard ceremony on February 12 at Daejeon headquarters to celebrate its designation as the national 'Biological Resource Center' by the Ministry of Science and ICT (MSIT; Minister Young Min You). Infra Division established the Advanced bioResource Information System (ARIS), which collects, integrates, and manages information of all biological research resources obtained from seven resource banks officially designated by MSIT. Also, it is operated for the purpose of strengthening the utility of biological resources. Infra Division consists six centers, including Laboratory Animal Resource Center, Bio-Evaluation Center, National Primate Research Center, Futuristic Animal Resource & Research Center, International Biological Material Research Center, and ABS Research Support Center and strives to reinforce national competitiveness in biological research through R&D and the establishment of biological research resource infrastructure.

Science Technology Promotion and Information and Communication Advancement: Men of Merit Awards / April 20



To celebrate the 51st Science Day and 63rd Information and Communication Day, the Korean government award ceremony was held at the National Science Museum in Daejeon on April 20 by the Ministry of science and ICT. A total of three awards—an Order, a Medal, and a Presidential Citation—were awarded to researchers at KRIBB. The President Jang-Seong Kim was awarded with the Fifth Class Order of Science and Technology Merit for Progress in recognition of his contributions for developing an anti-angiogenic anticancer drug that is approved for clinical trials by the US Food and Drug Administration for the first time in Korea. Nam-Soon Kim, Associate Director of Rare Disease Research Center was awarded with a Medal of Science and Technology for her contributions in localization and construction of human genetic clones as research resource and for the development of a genomic platform technology for the diagnosis and treatment of rare cancers. Eun-Wie Cho, a senior researcher at Rare Disease Research Center, was awarded with a Presidential Citation for her contributions in advancement of biotechnology, for developing an *in vitro* cancer diagnostic test and investigating the functions of novel genes and proteins that govern the mechanisms underlying carcinogenesis and metastasis.

Inauguration of the 13th President Jang-Seong Kim / July 9



The inauguration ceremony of the 13th President Jang-Seong Kim was held on July 9. At the ceremony, the President Jang-Seong Kim pledged to dedicate all efforts to support the growth of KRIBB as a leading global biotechnology research institute and to solve national and social agendas by convergence research and public infrastructure innovation. He expressed his desire to contribute to growth of new industries and job creation by supporting laboratory establishment and biotechnology start-ups. The President Jang-Seong Kim will serve as the President of KRIBB until July 8, 2021.

University of Science and Technology Commencement Ceremony / August 23



Korea Research Institute of Bioscience and Biotechnology School (Representative Professor Seung Jun Kim, KRIBB School) of University of Science and Technology (UST) held the commencement ceremony on August 23 at KRIBB auditorium. In this fall commencement, KRIBB School conferred six doctoral and five master's degrees. The commencement was organized with celebration performance, degree conferment, and awards for outstanding graduates. Dr. Hyun Joo

Cho was awarded with the research institute founder award for accomplishing in-depth study on vasculotoxicity and *in vivo* distribution of graphene oxide, which was published in *Carbon* (Life Science- Ph.D. in Functional Genomics; Professor Jeong-Soo Lee). The excellence prize was awarded to Dr. Jong Hwan Kim (Life Science- Ph.D. in Functional Genomics; Professor Seon-Young Kim) for his work on epigenetic effect of vitamin C in neural stem cell differentiation through genome data analysis. Dr. Hyo Jung Yoo (Life Science- Ph.D. in Bioinformatics; Professor Jinhyuck Lee) was also awarded with the excellence prize for conducting a study on improving the three-dimensional protein structure based on computer simulations and protein big data.

* KRIBB School is a specialized biotechnology school of UST committed to training professionals in the field of biotechnology.

R&R Agreement Ceremony / September 7



The Ministry of Science and ICT (MSIT; Minister Young Min You) and 28 research institutes, including 25 research institutes under National Research Council of Science & Technology, signed a Memorandum of Understanding (MOU) defining the Role & Responsibility (R&R) of government-funded research institutes. R&R was proposed to address increasing demand about research institutes' contribution towards improving the quality of life, as their social obligations increased with changes by the Fourth Industrial Revolution. KRIBB set healthy life and advancement of national bioeconomy as its R&R and expressed its aim to focus on the development of biomedical technology and biomaterials. In addition, KRIBB plans to lead the biological infrastructure advancement.

National Primate Resources Center Completion Ceremony / November 6



The ceremony for the completion of National Primate Resources Center was held in Jeonbuk on November 6. The center was constructed to balance the supply and demand of primate resources and to establish a stable primate resource infrastructure in Korea. The center, which has a maximum breeding capacity of 3,000 primates, is expected to lay the foundation for supplying high-quality primate resources. The goal is to provide solutions for increasing demand of primates and to use primate resources for solving national agendas such as infectious disease (i.e. MERS).

Announcement of KRIBB's Vision / November 23



KRIBB established its mid and long-term goals based on the vision of 'a global leader for healthy life and bioeconomy'. Along with it, KRIBB identified future technology and core areas that it must work on. In this regard, KRIBB held Vision Announcement Ceremony on November 23 to present its future plans. According to its strategic direction, KRIBB set three mid and long-term goals of 'creating technology for new biomedicine', 'developing core technology for addressing societal agendas', and 'expanding bio start-ups for technol-

ogy innovation'. KRIBB will continue to push forward with its strategic goals.

2018 Bio Innovative Growth Convention / November 28



2018 Bio Innovative Growth Convention, hosted by the Ministry of Science and ICT and organized by Biotech Policy Research Center of KRIBB, National Research Foundation of Korea, and Commercialization Promotion Agency for R&D Outcomes, was held at Sejong University Convention Hall from November 28 to 29. The theme for the convention was 'Bioeconomy, Biotech Jobs' and the convention included various programs such as Innovative Growth Exhibition (exhibition and experience), Bio Future Forum (presentation and discussion of innovative growth strategies), and Business Partnering (technology partnering and recruitment) to help participants identify with the idea that bio innovation is the growth engine for the future.

Signing of MOU between KRIBB and Institut Pasteur Korea / December 4



KRIBB and Institut Pasteur Korea, a leading research institute in the field of infectious disease research, signed a Memorandum of Understanding (MOU) for collaboration in infectious disease research and new drug development on December 4. Two institutes will work cooperatively for joint research on infectious diseases and new drug development, exchange academic findings, and share equipment and facilities. Further, they plan to engage and perform joint research projects, mutually commission research, and provide technical guidance and consultation. This MOU is expected to have a significant impact on drug development for infectious diseases.

KRIBB Poster Festival / December 13



KRIBB hosted the 10th KRIBB Poster Festival from December 13 to 14. The Poster Festival started since 2007 and celebrated its 10th anniversary in 2018. The festival was organized to share research accomplishments within the institute and promote joint research and collaboration. Also, it is an annual event which serves as a social event among researchers. More than 130 posters were displayed in this event, and young researchers gave presentations of their research achievements in the 'Young Speaker' program.

2018 KRIBB Conference / December 14



KRIBB held 2018 KRIBB Conference entitled 'Technology for Life, Our Future' on December 13. The conference was organized into four sessions covering various biotechnology areas, including biomedicine, biomaterials, and bio ecosystems. Also, recent developments, accomplishments, and prospects of biotechnology were discussed. The conference brought together researchers to provide an opportunity to discuss and share key accomplishments and recent trends to facilitate convergence research among biotechnology fields. The keynote speaker Seong-jin Kim, the Vice President of Theragen Etex, gave a speech entitled, 'the story of TGF-β: from biology to clinical development'. KRIBB plans to host institute conference every year to provide opportunities for researchers to share their findings.

National Research and Development Advancement Award / December 28



KRIBB received an Order, a Prime Minister's Citation, and the Ministry of Science and ICT(MSIT) Citation at the '2018 Award Ceremony for Contributors to National Research and Development Advancement' held by the MSIT on December 28. An Order was awarded to Inpyo Choi, principal researcher at Immunotherapy Research Center for his contributions in

developing technology to rejuvenate aged hematopoietic stem cells, which served as a turning point in treatment of degenerative diseases, and providing an important foundation for treatment of incurable cancer by developing hematopoietic stem cell-induced cell therapeutics. KRIBB received a Prime Minister's Citation for its contribution towards Korea's bioscience and bioindustry advancement by obtaining an 'excellent' rating from the 2018 institutional evaluation, completing U.S. clinical trials of a new drug for chronic obstructive pulmonary disease, developing original technologies for treatment of aging and rare diseases, and dedicating efforts to expand research infrastructure for strengthening national competitiveness in biological research.

Establishment of INNOPOLIS Research Institute Spin-off Company T-MAC Co., Ltd. and Researcher-Business Start-up Cellapybio Co., Ltd



KRIBB operates various programs for supporting biotechnology start-up and building ecosystem for biotechnology field. As part of this effort, an INNOPOLIS Research Institute Spin-off Company T-MAC Co., Ltd. and a business start-up by researchers, Cellapybio Co., Ltd. were established. T-MAC Co., Ltd. was established on January 29, developing high-density blot array system. Cellapybio Co., Ltd. is a business start-up established by researchers on June 18 and concentrates on development of protein drugs and functional cosmetic materials.



DIVISION OF
BIOMEDICAL RESEARCH

28-41

Division of Biomedical Research consistently endeavors for healthy life by proposing ways to overcome incurable diseases, developing source technologies for biologics, and investigating innovative future technologies for personalized medical treatment.

- Personalized Genomic Medicine Research Center
- Rare Disease Research Center
- Biotherapeutics Translational Research Center
- Immunotherapy Research Center
- Disease Target Structure Research Center
- Metabolic Regulation Research Center
- Genome Editing Research Center

Personalized Genomic Medicine Research Center

The goal of the center is to develop original technologies for customized treatment of cancer based on genome-wide screening as well as genome and epigenome analysis. The center also focuses on prognostic and predictive biomarkers for lung, liver, and gastric cancers by conducting integrative analyses of the NGS genome, transcriptome, and epigenome data.

INVESTIGATORS

Kyung Chan Park / kpark@kribb.re.kr

- Large-scale screening and identification of cancer related genes
- Studies on regulation of metabolic reprogramming in cancer and inflammatory diseases

Misun Won / misun@kribb.re.kr

- Identification and functional verification of genes to develop therapeutic targets and overcome resistance to traditional therapeutics
- Studies on the mode of action of innovative anti-cancer agents

Dong Cho Han / dchan@kribb.re.kr

- Study of cancer cell stress responses, migration, meta-stasis, stemness, and drug resistance, using chemical biology

Seon-Young Kim / kimsy@kribb.re.kr

- Using single cell biology (transcriptomics and epigenomics) to understand cell differentiation and disease pathogenesis.
- Bioinformatics for multi-omics data analysis and integration

Mirang Kim / mirang@kribb.re.kr

- Epigenetic modifications that can affect cell behavior and cancer progression
- DNA methylation, histone modifications, and micro RNAs
- Single cell sequencing analysis of tumor heterogeneity and tumor microenvironment

Bo Kyung Kim / kimbk@kribb.re.kr

- Determining the feasibility of cancer-related gene expression control and therapeutic targets
- Analysis and verification of genes to overcome resistance to therapeutics

Jung-Ae Kim / jungaekim@kribb.re.kr

- Studies on epigenetic modifications involved in gene expression and genome stability, with regard to cancer progression
- Studies on the crosstalk between metabolic and epigenetic regulations
- Studies on the cellular heterogeneity associated with human diseases

Seon-Kyu Kim / seonkyu@kribb.re.kr

- Identification of prognostic and predictive signatures based on cancer genomics
- Software development for carrying out bioinformatics analyses

RESEARCH AREAS

- Development of bioinformatics tools and databases
- Genomic characterization of various cancers for prognostic and predictive biomarker discovery
- Integrative analysis of the NGS genome, transcriptome, and epigenome in large-scale data sets derived from various cancers
- Large-scale screening and identification of cancer-related genes
- Functional validation of candidate target genes and biomarkers for the development of therapeutics and diagnostics
- Discovery and characterization of active compounds for anti-cancer, anti-metastasis, and anti-relapse therapy

ACHIEVEMENTS

Enhancer remodeling and microRNA alterations are associated with acquired resistance to ALK inhibitors

Anaplastic lymphoma kinase (ALK) inhibitors are highly effective in patients with ALK fusion-positive lung cancer, but these patients invariably develop resistance towards them. The center investigated the dynamic changes in the transcriptome and enhancer landscape during the development of acquired resistance to ALK inhibitors. Histone H3 lysine 27 acetylation (H3K27ac) was profoundly altered during resistance development, and enhancer remodeling induced changes in the expression of both miRNAs and mRNAs. Decreased H3K27ac levels and reduced miR-34a expression were associated with the activation of target genes such as AXL. Panobinostat, a pan-histone deacetylase inhibitor, altered the H3K27ac profile and activated tumor-suppressor miRNAs such as miR-449, another member of the miR-34 family, and caused the synergistic induction of

anti-proliferative effects with ALK inhibitors in resistant cells. These findings suggest that strategies for targeting epigenetic pathways represent a potentially effective method for overcoming acquired resistance to cancer therapy.

Bioinformatic identification of prognostic biomarkers and web-based bioinformatic software development

The identification of practical biomarkers is profoundly important for predicting heterogeneous disease behavior. The center sought to identify prognostic biomarkers for various diseases, including cancers. Using serum data obtained from more than 100 sarcopenia patients, developed a practical risk scoring system to predict the risk of sarcopenia. The center also uncovered the fact that c-MYC drove brain-specific breast cancer metastasis after analyzing multiple cohorts of breast cancer patients. In addition, the center identified EHMT2 to be involved in cell proliferation via HSPD1 regulation in breast cancer patients. Apart from prognostic biomarker discovery, the center developed several practically useful bioinformatic resources, namely GENT2 and GSAseq. GENT2 is a platform for exploring gene expression patterns across normal and tumor tissues, and is a newly updated version of GENT. GSAseq is another useful tool used for the gene-set enrichment analysis of RNA-seq data for eight of the most studied species, including human, mouse, rat, yeast, A. thaliana, worm, fly, and E. coli species. By this study, it is believed that these resources, when used along with newly identified biomarkers and analysis toolkits, would provide more practically useful information for the development of clinical applications.

RNF25 promotes gefitinib resistance in EGFR-mutant NSCLC cells by inducing NF-κB-mediated ERK reactivation

Non-small cell lung cancer (NSCLC) patients with EGFR mutations initially respond well to EGFR tyrosine kinase inhibitors (TKIs), but eventually exhibit acquired or innate resistance to these therapies, typically due to gene mutations, such as the EGFR T790M mutation or a second mutation in the downstream pathways

of EGFR. Importantly, a significant number of NSCLC patients exhibit the development of resistance to TKI via unknown mechanisms; this underscores the need for more comprehensive studies that could reveal the underlying mechanisms. Here, the center investigated the synthetic lethality associated with gefitinib, using a genome-wide RNAi screening process in TKI-resistant EGFR-mutant NSCLC cells, and identified RNF25 as a novel factor that was associated with gefitinib resistance. The depletion of RNF25 expression substantially sensitized NSCLC cells to gefitinib treatment, while the forced expression of RNF25 augmented gefitinib resistance in sensitive cells. It was demonstrated that RNF25 mediates NF-κB activation in gefitinib-treated cells, which, in turn, induces the reactivation of the ERK signal, which causes drug resistance. The center identified the fact that ERK reactivation occurs via the function of cytokines such as IL-6, whose expression is transcriptionally induced in a gefitinib-dependent manner by RNF25-mediated NF-κB signals. This suggests that RNF25 plays an essential role in inducing gefitinib resistance in NSCLC cells, by mediating the cross-talk between the NF-κB and ERK pathways, and provides a novel target for combination therapy that could enable NSCLC cells to overcome the TKI resistance.

DDIAS suppresses TRAIL-mediated apoptosis by inhibiting DISC formation and destabilizing caspase-8 in cancer cells

The center reported that DDIAS protects cancer cells from tumor necrosis factor-related apoptosis-inducing ligand (TRAIL)-induced apoptosis by two distinct mechanisms in non-small cell lung cancer (NSCLC) and hepatocellular carcinoma (HCC) cells. DDIAS depletion sensitizes NSCLC and HCC cells to TRAIL-mediated apoptosis. Interestingly, the N terminus of DDIAS interacts with the death effector domain of Fas-associated protein death domain (FADD) and prevents its recruitment to the death-inducing signaling complex (DISC), thereby blocking caspase-8 activation. DDIAS knockdown also suppressed the epidermal growth factor-induced phosphorylation of p90 ribosomal S6 kinase (RSK) 2 and stabilized caspase-8, by preventing its ubiquitination and proteasomal degradation. Taken together, DDIAS has the dual function of inhibiting DISC formation as well as destabilizing caspase-8, thereby suppressing TRAIL-mediated apoptosis in cancer cells.

Understanding how histone H3K4 methylation is promoted by H2B ubiquitylation in a Set1 complex-dependent manner

H2B ubiquitylation (H2Bub)-dependent H3K4

methylation is mediated by the multi-subunit Set1 complex (Set1C) in yeast cells, but the mechanism by which Set1C subunits contribute to this histone modification remains unclear. Here, using reconstituted Set1Cs and recombinant H2Bub chromatin, we identified Set1C subunits and domains involved in the H2Bub-dependent H3K4 methylation process, thereby demonstrating that the Spp1 PHDL domain, in conjunction with the Set1 n-SET domain, interacts with Swd1/Swd3 and that this interaction is essential for H2Bub-dependent H3K4 methylation. Importantly, the presence of the Set1C a Spp1-Swd1 fusion bypasses the requirement for H2Bub during H3K4 methylation, which suggests that the role of H2Bub is to induce allosteric rearrangements of the subunit interaction network within the active site of Set1C that are necessary for methylation to occur. Moreover, the interaction between the Set1 N-terminal region and Swd1 renders the Spp1-lacking Set1C competent for H2Bub-dependent H3K4 methylation. Collectively, our results suggest that H2Bub induces conformational changes in Set1C that support H3K4 methylation activity.

Development of small molecular inhibitor of HSF1 and OCT4

HSF1 is the master transcription regulator of stress responses. Knock-out of HSF1 protects mice from tumor initiation and progression. We screened HSF1 inhibitors using cell-based reporter assays and identified KRIBB11 to be an inhibitor of cancer cell metastasis. Meanwhile, OCT4 is a main transcription factor that induces stemness in stem cells and is reported to be involved in cancer stem cells. We screened OCT4 inhibitors using cell-based reporter assays and identified KRIBB53, which binds to and enhances OCT4 degradation through the proteasome, causing the apoptosis of the OCT4-positive testicular germ cell tumor.

Technology transfer of tumor suppressor gene to develop gene therapy agent

A novel tumor suppressor was identified for the development of gene therapy. This novel tumor suppressor is involved in cancer metabolism and immune regulation, and its overexpression results in the inhibition of proliferation of cancer cells. In addition, overexpression of the tumor suppressor reduced the expression of HIF-1α, a major protein involved in tumor malignancies.

SELECTED PUBLICATIONS

Bcl-2-dependent synthetic lethal interaction of the IDF-11774 with the V0 subunit C of vacuolar ATPase (ATP6V0C) in colorectal cancer

Br J Cancer. 119(11):1347-57.

Misun Won and Bo-Kyung Kim

Enhancer remodeling and microRNA alterations are associated with acquired resistance to ALK inhibitors

Cancer Res. 78(12):3350-62.

Mirang Kim

KRIBB53 binds to OCT4 and enhances its degradation through the proteasome, causing apoptotic cell death of OCT4-positive testicular germ cell tumors

Carcinogenesis. 39(6):838-49.

Dong Cho Han and Byoung-Mog Kwon

RNF25 promotes gefitinib resistance in EGFR-mutant NSCLC cells by inducing NF-κB-mediated ERK reactivation

Cell Death Dis. 9(6):587.

Kyung Chan Park and Jung-Ae Kim

The lncRNA EPEL promotes lung cancer cell proliferation through E2F target activation

Cell Physiol Biochem. 45(3):1270-83.

Seon-Young Kim

Crosstalk among Set1 complex subunits involved in H2B ubiquitylation-dependent H3K4 methylation

Nucleic Acids Res. 46(21):11129-43.

Jung-Ae Kim

DDIAS suppresses TRAIL-mediated apoptosis by inhibiting DISC formation and destabilizing caspase-8 in cancer cells

Oncogene. 37(9):1251-62.

Misun Won

Vitamin C promotes astrocyte differentiation through DNA hydroxymethylation

Stem Cells. 36(10):1578-88.

Seon-Young Kim



Rare Disease Research Center

The center's goal is to establish world-class genomics-based technology platforms and use them for conducting biomedical research programs in order to achieve precision medicines for rare diseases, based on genomic big data. This would help with the analysis of large-scale NGS data for rare neuronal diseases, as well as the high-throughput identification and global functional analysis of genes associated with rare neuronal diseases, such as hereditary spastic paraplegia (HSP), ataxia, malformations of cortical development (MCD), and Lennox-Gastaut syndrome (LGS). The center also discovers targets and biomarkers in order to develop precise diagnostics and therapeutics for rare neuronal diseases.

INVESTIGATORS

Nam-Soon Kim / nskim37@kribb.re.kr

- Genomic and functional study of rare neuronal diseases
- Functional genomics of cancer
- Management of Korea Human Gene Bank (KHGB)

Jae-Ran Lee / leejr@kribb.re.kr

- Functional analysis of synaptic molecules related to rare neuronal diseases
- Discovery of biomarkers for early diagnosis of neurodevelopmental disorders

Eun-Wie Cho / ewcho@kribb.re.kr

- Cancer cell molecular biology and biochemistry
- Development of molecular diagnostics for rare neuronal diseases

Da Yong Lee / daylee@kribb.re.kr

- Neuroscience
- Developmental neurobiology

Dong Uk Kim / kimdongu@kribb.re.kr

- Systematic analysis of the cellular targets of bioactive molecules using the fission yeast genome-wide gene-deletion collection
- Studies on the cell biology underpinning protein misfolding diseases
- Research on neurodegenerative disease

Jeong-Ju Lee / snailee@kribb.re.kr

- Large-scale collection and distribution of human cDNA clones
- Operation of the Korea Human Gene Bank (KHGB)

Ji Yong Yoon / sererine@kribb.re.kr

- Functional study of genes associated with rare neuronal diseases



Associate Director Nam-Soon Kim / Tel. +82-42-879-8112 / E-mail nskim37@kribb.re.kr

RESEARCH AREAS

- Establishment of genome research infrastructure and technology platforms for rare neuronal diseases
- Construction of a genetic variants map and an integrated database for rare Korean neuronal diseases
- Large-scale screening and identification of genes related to rare neuronal diseases
- Identification of biomarkers and development of a gene panel for developing precise diagnostics for rare neuronal diseases
- Functional validation of candidate target genes for developing precise therapeutics for rare neuronal diseases
- Application of target genes in gene therapy for developing precise therapeutics for rare neuronal diseases
- Systematic analysis of the cellular targets of bioactive molecules using the fission yeast genome-wide gene-deletion collection

ACHIEVEMENTS

Construction of a genetic variants map of Korean HSP and ataxia

- Construction of a genetic variants map of Korean HSP from WES data of 88 HSP families, 116 affected individuals, and 25 healthy control subjects, using bioinformatic tools
- Construction of a genetic variant map for Korean ataxia, from WES data of 87 ataxia families, 95 affected individuals with non-polyglutamine ataxia, and 100 healthy control subjects, using bioinformatic tools
- These genetic variant maps revealed the genetic heterogeneity of Korean HSP and non-polyglutamine ataxia

Development of molecular diagnostics for HSP and Ataxia

- Development of an in-silico 113-gene panel for HSP, consisting of five X-linked genes, 21 autosomal dominant genes, and 54 autosomal recessive genes, extracted after referring to a genetic variant map of Korean HSP
- Development of a digital PCR-based method for the efficient and simple screening of a large genomic deletion in the spastin gene (*SPG4*), the main causative gene involved in HSP
- These technologies for HSP molecular diagnostics were transferred to companies
- Development of an in silico 242-gene panel for

ataxia, extracted after referring to a genetic variant map of Korean HSP

Construction of analysis pipeline of large volume NGS genome data for rare diseases

- Development of an integrated system for handling, processing, and analyzing large volumes of NGS genome data and multiple biological big data with different data structures
- Identification of various SNV/INDEL candidates associated with diseases using clinical samples and NGS data in public DBs
- Establishment of a technology for the integrated analysis of genome information and information standardization
- Construction of the CNV map and DBs for several diseases

Modeling of rare neuronal diseases using animal and patient derived iPSCs

- Development of animal models for rare brain diseases, including hereditary spastic paraplasia (HSP), tuberous sclerosis complex (TSC), and a rare multisystem genetic brain developmental disorder, a genetic brain disease involving the malfunctioning of cortical motor neurons
- Generation of iPSCs from the blood mononuclear cells of patients with Duchenne muscular dystrophy (DMD), a severe type of muscular dystrophy and intellectual disability
- Determining the various de novo mutations in nerve cell specific KIF1A motor domains that cause intellectual developmental disorders, spastic paralysis, axon disorders, and cerebellar atrophy

Construction of *S. pombe* genome-wide deletion mutant library

- A total of 4,836 heterozygous diploid deletion mutants, representing 98.4% of the genome of the organism and 3,400 haploid deletion mutants, with 95.3% genome coverage were deleted
- Providing an ideal way to approach research regarding gene functioning and drug target screening for large numbers of genes, by using pools of mutants

SELECTED PUBLICATIONS

Copine1 regulates neural stem cell functions during brain development

Biochem Biophys Res Commun. 495(1):168-73.
Da Yong Lee

Novel indazole-based MKK7-TIPRL interaction inhibitors as TRAIL sensitizers

Bull Kor Chem Soc. 39(10):1125-38.
Nam-Soon Kim

Hypoxia-inducible transgelin 2 selects epithelial-to-mesenchymal transition and γ -radiation-resistant subtypes by focal adhesion kinase-associated insulin-like growth factor 1 receptor activation in non-small-cell lung cancer cells

Cancer Sci. 109(11):3519-31.
Eun Wie Cho

Identification of anti-SF3B1 autoantibody as a diagnostic marker in patients with hepatocellular carcinoma

J Transl Med. 16(1):177.
Eun Wie Cho

A genome-wide screening of target genes against silver nanoparticles in fission yeast

Toxicol Sci. 161(1):171-85.
Dong Uk Kim

Biotherapeutics Translational Research Center

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

INVESTIGATORS

Jeong Ki Min / jekmin@kribb.re.kr

- Translational research for treatment of angiogenesis-related diseases and cancer
- Studies on vascular development and inflammation, new anticancer drug targets, and vascular stem cell differentiation

Yeon-Gu Kim / ygkim@kribb.re.kr

- Development of high therapeutic protein-producing mammalian cells
- Process development for therapeutic protein production in mammalian cells

Hyun Seung Ban / banhs@kribb.re.kr

- Identification of new anti-cancer target molecules using chemical biology and the development of materials that regulate function

Sang-Hyun Lee / leesh@kribb.re.kr

- Developing a validation and control technology for therapeutic targets using a multifunctional protein-based antibody library
- Translational research for the development of cancer control technology
- To understand the role of microglia chemotaxis and activation in neuroinflammation

Jong-Gil Park / jonggilpark@kribb.re.kr

- Validation of therapeutic targets for cardiovascular diseases
- Regulation of metabolic disorders

Jangwook Lee / jlee@kribb.re.kr

- Development and application of therapeutic biomacromolecules- on-demand for patients
- Targeted macromolecule delivery system for disease theragnosis (diagnosis and therapy)

Tae-Su Han / tshan@kribb.re.kr

- Identification and functional study of non-coding RNAs in cancer

Min-Gyeong Shin / shinmg@kribb.re.kr

- Development of serum-free suspension-based mammalian cell culture process
- Development of biopharmaceutical protein purification process

Jeong-Woong Lee / jwlee@kribb.re.kr

- Production of cloned pig
- Functional study of animal disease models

Chi-Yong Ahn / cyahn@kribb.re.kr

- Ecophysiology of microalgae and cyanobacteria (control of algal bloom)
- Optimization of mass cultivation of microalgae using wastewater

Hyun-Soon Kim / hyuns@kribb.re.kr

- Studies on plant-based expression system for the sustainable production of invaluable bio-materials

Suk Yoon Kwon / sykwon@kribb.re.kr

- Structural and functional genomics of plants
- Transformation of crop plants for enhancing agricultural traits



Associate Director Jeong Ki Min / Tel. +82-42-860-4137 / E-mail jekmin@kribb.re.kr

RESEARCH AREAS

Identification of a target that adjusts cancer/angiogenesis, blood vessel inflammation and development of a control technology

- Identification of a target based on multi-function antibody library system and development of antibody
- Regulating endothelium differentiation using stem cells

Development of biopharmaceuticals (antibody/AAV) for therapeutic angiogenesis and anti-cancer therapy

Mining of diagnostic/therapeutic targets for vascular/metabolic diseases and cancer

Determining the level of drug resistance and metastasis regulation and the development of a control technology

- Development of a new drug through translational research between basic and clinical research

Identification of non-coding RNAs as biomarkers for diagnosis and prognosis of cancer

Targeted therapeutic biomacromolecules (antibody/ protein/gene)

- Development of antibody-drug conjugates (Biobetter)
- Establishment of targeted drug delivery system

Identification of genes related to the production of immunodeficient pigs

- Research on the mechanism for factors that cause immune rejection response

Production of animal disease model and functional study- Production of transgenic and knockout animal using gene editing system

- Study of biomolecular and physiological mechanisms using an animal disease model

Wastewater treatment using microalgae

- Economical and efficient treatment of wastewater and biomass by cultivating microalgae
- Production of a biofuel and high-value compounds from microalgae

Algal bloom research

Ecophysiological and metagenomic study of the mechanisms of algal bloom in freshwater (green tide) and seawater (red tide); advanced monitoring of bloom and production of algal toxins, mal-odorous compounds, and their interaction with aquatic microorganisms.

Plant-based expression and production research

In-plant cell biotechnology for invaluable biomaterials

ACHIEVEMENTS

Providing cancer/blood vessel treatment after determining the function of new proteins regulating vascular homeostasis

- Development of technology that activates/controls angiogenesis based on the presence of certain antibodies
- Development of cell treatment technology based on the establishment of platform for regulating endothelial differentiation
- Identification of the phosphatase enzyme that regulates blood vessel inflammation/ permeability

Determination of the factors that regulate resistance to drugs and metastasis, development of control technology and establishment of basic-clinical translational research

Development of tumor-specific antibody-protein conjugates for therapeutic angiogenesis and anti-cancer therapy

- Development of antibodies to surface proteins for isolation of pluripotent stem cells
- Mining of diagnostic/therapeutic targets for biliary tract cancers

Development of biocompatible drug delivery system that can address adverse drug reactions and achieve targeted therapeutic success

Establishment of pig T- and B- cell knock out cell lines

Establishment of genetically modified cell lines to produce mini-pigs for xenotransplantation

Development of disease mouse models
Advanced cultivation of microalgae and wastewater treatment

- Collection of Korean algal strains with a high productivity for producing useful materials
- Development of cultivation systems and optimization of environmental conditions

Mechanism of algal bloom and its control

The genetic diversity of microalgae and their interactions with other microorganisms are being studied using metagenomic and ecoinformatics tools, to understand the detailed biological mechanisms for bloom formation. Environment-friendly methods are being developed to control algal bloom, based on ecological principles.

High-efficiency production of useful recombinant proteins by the transient expression of a plant cell suspension culture system

Establishment of plant cell and tissue culture for the over-production of secondary metabolites derived from native herbal plants

The high quality reference genomes of Cucurbit crops

Viral vectors for expression of foreign proteins in plants

SELECTED PUBLICATIONS

Co-amplification of EBNA-1 and PyLT through dhfr-mediated gene amplification for improving foreign protein production in transient gene expression in CHO cells

Appl Microbiol Biotechnol. 102(11):4729-39.
Yeon-Gu Kim

LJ-1888, a selective antagonist for the A3 adenosine receptor, ameliorates the development of atherosclerosis and hypercholesterolemia in apolipoprotein E knock-out mice

BMB Rep. 51(10):520-5.
Jong-Gil Park

Ectopic overexpression of porcine Myh1 increased in slow muscle fibers and enhanced endurance exercise in transgenic mice

Int J Mol Sci. 19(10):e2959.
Jeong-Woong Lee

o-carboranylalkoxy-1,3,5-triazine derivatives: synthesis, characterization, X-ray structural studies, and biological activity

Molecules. 23(9):e2194.
Hyun Seung Ban

DSG2 is a functional cell surface marker for identification and isolation of human pluripotent stem cells

Stem Cell Reports. 11(1):115-27.
Jeong Ki Min and Sang Chul Lee

Immunotherapy Research Center

The goal is to identify the differentiating factors between adult stem cells and immune cells, to develop a core platform technology for immune cell therapies that target cancer by researching their functions and a platform technology for anti-cancer antibody therapy and cancer diagnostics.

INVESTIGATORS

Suk Ran Yoon / sryoon@kribb.re.kr

- NK cell therapy, regulation of NK cell differentiation
- Role of NK cells in reproduction

Inpyo Choi / ipchoi@kribb.re.kr

- Differentiation of NK cells from hematopoietic stem cells
- Anti-tumor NK cell therapy based on NK differentiation

Tae-Don Kim / tdkim@kribb.re.kr

- Role of RNA in immune cell biology
- Development of CAR-NK cell therapy

Haiyoung Jung / haiyoung@kribb.re.kr

- Fate of hematopoietic stem cells

Jiyeon Noh / nohj16@kribb.re.kr

- NK cell migration and mechanism of anti-tumor targeting

Semi Kim / semikim@kribb.re.kr

- Mechanism of cancer development and metastasis
- Functional validation of novel therapeutic targets and development of molecular targeted therapy

Hee Gu Lee / hglee@kribb.re.kr

- Functional studies of target molecules in cancer cells

Hee Jun Cho / hjcho@kribb.re.kr

- Cancer progression and chemoresistance

Yee Sook Cho / yune@kribb.re.kr

- Pluripotency, reprogramming, differentiation, disease modeling

Young Il Yeom / yeomyi@kribb.re.kr

- Identification of cancer therapeutic targets

Dong Chul Lee / dclee@kribb.re.kr

- Identification of cancer therapeutic targets



Associate Director Suk Ran Yoon / Tel. +82-42-860-4239 / E-mail sryoon@kribb.re.kr

RESEARCH AREAS

NK cell therapy

- Development of platform technology for the differentiation of stem cells
- Development of platform technology for the regulation of NK cell differentiation
- Development of NK cell therapy for cancer treatment
- Development of CAR (chimeric antigen receptor)-NK cell therapy

Antibody therapy

- Development of therapeutic target antigens
- Development of human and humanized antibodies for cancer treatment
- Evaluation of therapeutic antibodies

Hematopoietic stem cell (HSC) aging

- Decision about HSC fate
- HSC aging mechanism and rejuvenation

Stem cell tech-based NK differentiation and production

Cellular reprogramming

- Reprogramming technologies for producing therapeutically-or disease-relevant human cells

Human pluripotent stem cells

- Human pluripotent stem cell-derived human cell production for disease modeling, drug discovery, and cell therapy

Cancer metabolism and metabolic signaling

- Identification of cancer targets and their roles in cell metabolism
- Identification of cancer biomarkers for targeted therapy
- Development of metabolism-directed anti-cancer agents

ACHIEVEMENTS

Molecular profiling of NK cell differentiation from stem cells

NK cells develop from hematopoietic stem cells (HSCs) in bone marrow. In order to understand the molecular regulation of NK cell development and activation, serial analysis of gene expression (SAGE), microarray, and NGS data of mRNA and noncoding RNAs have been obtained after stage-dependent NK cell differentiation and activation. These big data have been extensively used for the elucidation of basic roles, mechanistic insights, and molecular networks of differentially expressed

genes in NK cell development and activation.

Development of immune therapy techniques utilizing NK cells

The immunotherapy has been designed for cancer patients, based on the observations with regard to NK cell differentiation. The platform technology of NK cell therapy for cancer treatment has been established and used in clinical trials for incurable cancers. Recently, CAR-NK cell therapy has been developed in order to use it for biomarkers expressing solid tumors at the preclinical trial level.

Molecular mechanism of HSC aging and stress

The functions of HSCs are changed under the conditions of stress and aging. Reactive oxygen species are major players for bringing about the aging and stress response of HSCs. The molecular targets for HSC stress and aging have been identified and their functions have been investigated.

Stem cell technology-based NK cell production

The center has generated human induced pluripotent stem cells (iPSCs) from peripheral blood cells and developing the differentiation protocol for the efficient production of functional and cytotoxic NK cells. Further optimization of the protocol would enable to generate scalable cytotoxic NK cells, for treating different types of cancer and providing a genetically interchangeable platform to investigate the causes of cancer and potential targets for therapy.

SELECTED PUBLICATIONS

TXNIP regulates AKT-mediated cellular senescence by direct interaction under glucose-mediated metabolic stress

Aging Cell. 17(6):e12836.
Inpyo Choi and Haiyoung Jung

Protein phosphatase 1B dephosphorylates Rho guanine nucleotide dissociation inhibitor 1 and suppresses cancer cell migration and invasion

Cancer Lett. 417:141-51.
Hee Gu Lee and Yong Kyung Choe

Prostaglandin E2 secreted by thyroid cancer cells contributes to immune escape through the suppression of natural killer (NK) cell cytotoxicity and NK cell differentiation

Front Immunol. 9:1859.
Suk Ran Yoon and Inpyo Choi

MicroRNA-150 controls differentiation of intraepithelial lymphocytes through TGF- β

receptor II regulation

J Allergy Clin Immunol. 141(4):1382-94.
Tae-Don Kim and Inpyo Choi

Effects of the extracts from fruit and stem of *Camellia japonica* on induced pluripotency and wound healing

J Clin Med. 7(11):e449.
Yee Sook Cho and Jungwoon Lee

Peroxisome proliferator-activated receptor α agonist and its target Nanog cooperate to induce pluripotency

J Clin Med. 7(12):e488.
Yee Sook Cho

EphrinB1 promotes cancer cell migration and invasion through the interaction with RhoG-DI1

Oncogene. 37(7):861-72.
Hee Jun Cho

ESRP1-induced CD44 v3 is important for controlling pluripotency in human pluripotent stem cells

Stem Cells. 36(10):1525-34.
Yee Sook Cho

Disease Target Structure Research Center

Determination of three-dimensional structures of disease targets and development of highly efficient drug discovery platform technology for disease targets.

- Determination of structures and functions of disease target proteins
- Development of a drug discovery platform technology for disease targets
- Proteomics-based discovery and validation of disease targets
- Animal model-based research for the treatment of degenerative diseases
- Development of nanopore sensor technology

INVESTIGATORS

Sung Goo Park / sgpark@kribb.re.kr

- Mechanism and functions of apoptosis-related proteins
- Protease degradomics

Sunghyun Kang / skang@kribb.re.kr

- Proteomics and mass spectrometry

Sunhong Kim / sunhong@kribb.re.kr

- Cell signal transduction in mammalian cells and *C. elegans*
- GPCR drug discovery and PROTAC technology

Seung Jun Kim / ksj@kribb.re.kr

- Structural studies on anti-oxidant proteins and protein tyrosine phosphatases
- Drug development using 3-D structural information

Jeong Hee Moon / jhdal@kribb.re.kr

- Mass spectrometry, proteomics, protein dynamics, and protein quantification

Byoung Chul Park / parkbc@kribb.re.kr

- Target mining and validation using proteomics, signal transduction
- Translational research on immune diseases

Eui-Jeon Woo / ejwoo@kribb.re.kr

- Research on the structure and function of nucleic acid-binding proteins and CRISPR system
- Development of a functional control technology using structure-based protein engineering

Kweon Yu / kweonyu@kribb.re.kr

- Molecular genetics research on metabolic and neurodegenerative diseases using the drosophila model

Seung-Wook Chi / swchi@kribb.re.kr

- Nanopore sensor technology development, protein design, and engineering
- Structure-based drug development, structural biology of apoptosis-regulating anti-cancer proteins

Tae-Sung Yoon / yoonts@kribb.re.kr

- Neutron and X-ray crystallography, structural proteomics, astrobiology

Bonsu Ku / bku@kribb.re.kr

- Protein X-ray crystallography
- Structural studies on signaling-regulatory proteins

Jeong-Hoon Kim / hoonkim@kribb.re.kr

- Studies on the regulatory mechanisms of chromatin modifiers
- Protein degradation and development of PROTACs

Mi-Kyung Lee / miki@kribb.re.kr

- Structural and dynamics studies using NMR spectroscopy
- Analysis of biomolecule using solid-state and protein nanopores

Jeong-Soo Lee / jeongsoo@kribb.re.kr

- Research on neurology, blood vessel development, and nanotoxicity using zebrafish

Ho-Chul Shin / shinhc81@kribb.re.kr

- Protein X-ray crystallography
- Structural studies and development of drug screening system

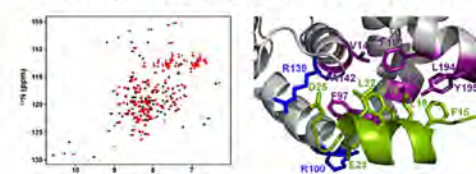
Hyun-Ju Cho / alleles@kribb.re.kr

- Human neurodegenerative disease modeling using zebrafish
- Application of zebrafish for nanotoxicity

Crystal image of P62/SQSTM1 PB1 domain



NMR structure of Bcl-X_L/p73-TAD16 peptide complex



RESEARCH AREAS

Research on structures and functions of disease target proteins

- Elucidation of structures and functions of therapeutic proteins involved in apoptosis, cell division, and carcinogenesis using X-ray crystallography and NMR spectroscopy
- Structure-based drug discovery against disease targets

Proteomics-based discovery and validation of disease target proteins

- Proteomics-based analysis of the apoptosis interactome
- Identification and validation of biomarkers related to atopic skin disease, asthma, and rheumatoid arthritis

Animal model-based research for treatment of degenerative diseases

- Development of animal models (drosophila and zebrafish) for the phenotypic screening of neurodegenerative diseases
- Animal model-based discovery and validation of new drug candidates for neurodegenerative diseases

Drug discovery by cellular signaling research

- Research on cellular signaling mechanism in various pathways, including cancer, inflammation, and metabolism
- Disease target discovery, validation, and assay development

Development of nanopore sensor technology for detecting proteins and nucleic acids

- Development of nanopore sensor platform technologies for drug screening and disease diagnosis

Nanotoxicity assessment using zebrafish

- *In vivo* toxicity assessment of various nanoparticles using zebrafish

ACHIEVEMENTS

Elucidation of structures and functions of kinases and phosphatases

- Determination of three-dimensional structures and functional mechanisms of over 20 phosphatases involved in cellular signaling, including apoptosis, cell division, and carcinogenesis.

Determination of structures of apoptosis regulating proteins and development of a structure-based multi-targeting strategy

- Determination of three-dimensional structures of apoptosis-regulating anti-cancer target proteins using NMR spectroscopy and structure-based development of multi-targeting anti-cancer therapeutics

Elucidation of growth-regulating microRNA

- Discovery of growth-regulating microRNA-9a by microRNA library screening
- Elucidation of the growth-regulating role of microRNA9a as a new target of sNPF/NPYR

Development of a novel screening technology for protein-protein interaction inhibitors using nanopores

Research for treatment of Alzheimer's disease using photoactivated porphyrins

High-resolution real-time imaging analysis to study the effect of graphene oxide nanoparticles on blood vessel development

Discovery of a novel immunomodulatory drug (IMiD) and the its application to PROTAC technology

Human disease modeling and identification of drug candidates using zebrafish

- Discovery of cerebrovascular function of *DYRK1A*, a human Down's syndrome candidate gene, in zebrafish *dyrk1aa* (*DYRK1A*) mutants
- Identification of drug candidates for cerebrovascular disorders in zebrafish *dyrk1aa* mutants
- Discovery of autism-associated *DYRK1A* function in zebrafish *dyrk1aa* mutants

Nanotoxicity assessment using zebrafish

- The nanotoxicity assessment of nanosized graphene oxide (NGO) and polystyrene (PS) nanoparticles using zebrafish embryos

SELECTED PUBLICATIONS

Identification of N-(5-(phenoxymethyl)-1,3,4-thiadiazol-2-yl)acetamide derivatives as novel protein tyrosine phosphatase epsilon inhibitors exhibiting anti-osteoclastic activity

Bioorg Med Chem. 26(18):5204-11.
Seung Jun Kim

Rapid and efficient western blot assay by rotational cyclic draining and replenishing procedure

Electrophoresis. 39(23):2974-8.
Sunghyun Kang and Tae-Sung Yoon

Cytoplasmic pro-apoptotic function of the tumor suppressor p73 is mediated through a modified mode of recognition of the anti-apoptotic regulator Bcl-XL

J Biol Chem. 293(51):19546-58.
Seung-Wook Chi

Solid-state nanopore analysis on conformation change of p53TAD-MDM2 fusion protein induced by protein-protein interaction

Nanoscale. 10(36):17227-35.
Seung-Wook Chi

Structural study reveals the temperature-dependent conformational flexibility of Tk-PTP, a protein tyrosine phosphatase from *Thermococcus kodakaraensis* KOD1

PLoS One. 13(5):e0197635.
Seung Jun Kim and Bonsu Ku

Metabolic Regulation Research Center

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 cellular mechanism 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.

INVESTIGATORS

Won Kon Kim / wkkim@kribb.re.kr

- Research on regulation of adipocyte differentiation and thermogenesis
- Research on trans-differentiation of adipocytes
- Research on metabolic diseases

Kwang-Hee Bae / khbae@kribb.re.kr

- Identification of metabolic disease treatment targets and functional research using proteomics
- Identification of stem cell differentiation and dedifferentiation related protein and functional research

Sang Chul Lee / lesach@kribb.re.kr

- Research on the mechanism of regulation in association with cancer metabolism
- Identification of the protein associated with metabolic disease based on the omics approach and an investigation of its function

Myung Hee Kim / mhh8n@kribb.re.kr

- Research on the mechanism and control of molecular pathology based on convergence technology

Byoung-Chan Kim / bckim@kribb.re.kr

- Research on the isolation and identification of anaerobic human microorganisms and their clinical application

Jungwon Hwang / jwhwang@kribb.re.kr

- Research on the pathogen-specific biochemical mechanism based on structural and cell biological approaches

Baek-Soo Han / bshan@kribb.re.kr

- Exploration of treatment for degenerative neural diseases, research on metabolic functions, and identification of factors regulating neural cell differentiation

Kyung Jin Oh / kjoh80@kribb.re.kr

- Understanding the insulin signal delivery system and energy metabolism of individuals with type 2 diabetes and obesity, and researching the associated regulations

Eun-Woo Lee / ewlee@kribb.re.kr

- Research on the ubiquitin pathways in metabolic disease and cancer metabolism
- Research on cell death pathways, including apoptosis, necroptosis, and ferroptosis



Associate Director Won Kon Kim / Tel. +82-42-860-4265 / E-mail wkkim@kribb.re.kr

RESEARCH AREAS

Research on the regulation of metabolic diseases

- Identification of metabolic energy system and regulatory mechanism of type 2 diabetes and obesity
- Identification of regulatory material associated with the transition from white adipose tissue to brown adipose tissue and determine their functions
- Screening and functional research of metabolic disease regulatory material based on the generation of a low molecular weight compound or natural product
- 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

Metabolic control research related to neurodegenerative diseases

- Research on metabolomics and animal models related to neuron functioning and neurodegenerative diseases

Research on the mechanism of cancer metabolism regulation

- Identification of target molecules associated with cancer metabolism by the regulation of compounds and functions
- Ubiquitination/deubiquitination-mediated control of cancer metabolism

Development of metabolic disease regulation technology utilizing microbiome analysis

- Development of treatment for obesity and diabetes that utilizes the intestinal microbiota

ACHIEVEMENTS

Research on the regulatory mechanism of adipocyte differentiation

- Discovery of the regulatory mechanisms and functions of white/brown adipocyte differentiation by protein phosphorylation and acetylation
- Identification of factors that control white/brown differentiation of adipose tissue in adipocytes using proteomic analysis and discovering its mechanism of action
- Identification of the protein that controls the conversion of white adipose tissue to brown adipose tissue and studying its function

Research on *in vivo* function of white and brown adipose tissue

- Understanding the role of novel regulatory proteins such as phosphatase in the adipose tissue and obesity using knock-out mice
- Identification of new targets for the control of brown adipocyte differentiation and studying its mechanism and function

Identification of new drug target protein to treat neurodegenerative diseases

- Identification of a new target protein drug to treat neurodegenerative diseases by analyzing changes in phosphorylated proteins during the destruction of neurons

Identification of new anti-vibriosis agent and investigation of associated mechanism of action

- Identification of sustainable anti-vibriosis agent, QStatin by target-based high-throughput screening
- Understanding the functional mechanism of QStatin using structural and biochemical analyses

Research on signaling and metabolic pathways in chemoresistant tumors and identification of new drug combinations

- Identification of specific signaling and metabolic pathways in chemoresistant tumors by transcriptomic, proteomic, and metabolomic approaches.
- Identification of new drug combinations by drug library screening

SELECTED PUBLICATIONS

Aminoacyl-tRNA synthetases, therapeutic targets for infectious diseases

Biochem Pharmacol. 154:424-34.
Myung Hee Kim

Structural basis of inactivation of Ras and Rap1 small GTPases by Ras/Rap1-specific endopeptidase from the sepsis-causing pathogen *Vibrio vulnificus*

J Biol Chem. 293(47):18110-22.
Myung Hee Kim

QStatin, a selective inhibitor of quorum sensing in *Vibrio* species

mBio. 9(1):e02262.
Myung Hee Kim

Genome Editing Research Center

Genome editing is a type of genetic engineering in which DNA is inserted, deleted, or corrected in the genome of a living organism using engineered nucleases or "molecular scissors." These nucleases create site-specific double-strand breaks (DSBs) at a desired locus, and the induced double-strand breaks are repaired through nonhomologous end-joining or homologous recombination, which results in targeted gene corrections and ablations. The center aims to develop a new genome-editing platform and improve CRISPR system to provide a sophisticated tool for genome engineering. These genome-engineering tools are used for basic research, including the functional study of genetics, generation of model organisms, and gene therapy. The associated techniques can also be applied to various research and development fields, including gene delivery, stem cells, nanotechnology, and cell therapy.

INVESTIGATORS

Yong-Sam Kim / omsys1@kribb.re.kr

- Development of new gene editing technology
- Improvement of CRISPR-based genome-editing technology

Yong Sung Kim / yongsung@kribb.re.kr

- Exploration of epigenetic target genes associated with cancer cell differentiation
- Development of epigenetic gene editing technology for target genes

Byoung-Mog Kwon / kwonbm@kribb.re.kr

- Exploration of genes related to diseases using biochemical and chemical genomics and identification of their function, utilizing gene editing technology

Dae-Yeul Yu / dyu10@kribb.re.kr

- Development of humanized mice for translational research
- Development of humanized liver mice for evaluation of HBV drug efficacy

Jeong-Heon Ko / jhko@kribb.re.kr

- Functional study of glyco-genes by genome editing in mouse

In-Sun Chu / chu@kribb.re.kr

- Development of biomarker and molecular subtypes of pan-cancer that are associated with prognosis and immunotherapy, using genomics data

Namshin Kim / deepreds@kribb.re.kr

- NGS-based genome platform development by the assessment of the genome variant and genic intolerance
- Development of genomic prediction algorithm and software using artificial intelligence
- Development of an open source platform for high-density genotyping technologies

Jinhyuk Lee / jinhyuk@kribb.re.kr

- Discovery of drug candidates and biomarkers based on big-data research

Yoonkyung Kim / ykim@kribb.re.kr

- Biocompatible dendrimers/polymers, nanomedicine (diagnosis, therapy), organic/supramolecular/medicinal chemistry

Bo Kyeng Hou / bkher71@kribb.re.kr

- Development of an integrated database and analysis software in bioinformatics
- Development of neural network and deep learning applications using bioinformatics and cheminformatics

Jeong Gu Kang / kang@kribb.re.kr

- Development of a method to regulate epigenetic target genes using gene editing technology

Se-Joo Kim / biosejoo@kribb.re.kr

- Phylogenetics and evolution of unicellular eukaryotes
- Evolution and adaptation of organisms living in chemosynthesis-based hydrothermal vent ecosystems

Boram Kim / kbr523@kribb.re.kr

- Organic/supramolecular chemistry, biocompatible dendrimers/polymers, nanomedicine (diagnosis, therapy)

Yu-Jin Lee / yujini@kribb.re.kr

- NGS-based drug target identification and validation
- Using gene editing technology for drug target validation

Do-Hyoung Kim / organic2@kribb.re.kr

- Biophysical characterization of IDPs (intrinsically disordered proteins) using NMR spectroscopy.

RESEARCH AREAS

Research on the advancement of gene editing technologies

- Research on the increase of efficiency of CRISPR/ Cas9 and CRISPR/cpf1 gene editing technologies
- Establishment of target regulation system of genes related to stem cells, diseases, and aging
- Using gene editing technology for drug target validation and determining the mode of action of new drug candidates

Development of human mimicking mouse model using glyco-gene editing technology

- Selection of the glyco-gene that causes differences in glycans between humans and mice and development of a mouse model by editing the selected gene.
- Verification of non-clinical appropriateness of the human mimicking mouse model

Development of new epigenetic targets for epigenetic editing to prevent gastric carcinogenesis

- Whole-genome epigenome analysis at multiple steps of gastric carcinogenesis
- Identification of epigenetic targets at pre-cancer and early stages of gastric cancer
- Development of epigenetic editing technology to prevent gastric cancer

Design, synthesis, and applications of new organic, supramolecular, and dendritic compounds for the diagnosis and treatment of diseases

Discovery of new migrastatic compounds

- Developing of a proof-of-concept for a metastatic target molecule in an animal model
- Validation of binding sites of new drug candidates using gene editing technology

Identification of molecular subtype of bladder cancer associated with prognosis and immunotherapy

Macro-molecular mechanics studies related to proteins and chemical structures

- Drug candidate/biomarker discovery, in silico/big data biology, protein-chemical interaction, molecular design, protein structure modeling, in silico synthetic biology

Development of genome informatics technologies using deep learning

- Interpretation of genomic variants using deep learning
- Precision genomic prediction using an artificial neural network
- Genome big-data analyses technologies in cloud environment

ACHIEVEMENTS

Development of a highly efficient CRISPR-Cpf1 system

- CRISPR-Cpf1 was improved by engineering a crRNA with uridynylated tail.
- Improved Cpf1 can complement or substitute Cas9-based genome editing.

Development of new nano-sized compounds for the diagnosis of cancer and retinal diseases

Development of new epigenetic targets in pre-cancer and early gastric cancer

- Identification of hypermethylated and hypomethylated targets in intestinal metaplasia and gastric cancer
- Hypermethylated targets with the highest reliability were proven to be GI hormone receptor genes
- Hypomethylated targets in intestinal metaplasia would be provided with new target genes with protooncogenic activity, to prevent the development of gastric cancer

SELECTED PUBLICATIONS

2'-hydroxycinnamaldehyde inhibits cancer cell proliferation and tumor growth by targeting the pyruvate kinase M2

Cancer Lett. 434:42-55.

Byoung-Mog Kwon and Dong Cho Han

A gene expression signature of FOXM1 predicts the prognosis of hepatocellular carcinoma

Exp Mol Med. 50(1):e418.

In-Sun Chu

Whole genome MBD-seq and RRBS analyses reveal that hypermethylation of gastrointestinal hormone receptors is associated with gastric carcinogenesis

Exp Mol Med. 50(12):156.

Yong Sung Kim

Inhibitory effect of raspberry ketone on α -glucosidase: docking simulation integrating inhibition kinetics

Int J Biol Macromol. 113:212-8.

Jinhyuk Lee

Highly efficient genome editing by CRISPR-Cpf1 using CRISPR RNA with a uridynylate-rich 3'-overhang

Nature Communications. 9(1):3651.

Yong-Sam Kim





DIVISION OF
BIOMATERIALS RESEARCH

44-53

Division of Biomaterials Research is making an effort to develop biotechnological processes for the production and utilization of industrial biomaterials, pharmaceuticals and bio-nanomaterials by manipulating bacteria, microalgae, plants, and nano-interfaces. In addition, the division is aiming to achieve the industrialization of cell factory based on synthetic biological processes. The division is committed to the beginning of new era in global bioindustries in the 21st century.

- Synthetic Biology and Bioengineering Research Center
- Bionanotechnology Research Center
- Cell Factory Research Center
- Plant Systems Engineering Research Center
- Industrial Bio-materials Research Center

Synthetic Biology and Bioengineering Research Center

Synthetic Biology and Bioengineering Research Center (SBBRC) develops biological systems and assembles them into practical and useful engineering tools. The key is the development of artificial genetic circuit devices using bio-parts, modeling/simulation, and CRISPR technology. The range of potential applications encompasses but is not limited to biocatalyst/enzyme engineering, biofuel/chemical production, diagnostics, and therapeutics.

INVESTIGATORS

Seung-Goo Lee / sglee@kribb.re.kr

· Genetic circuits for synthetic biology, enzyme engineering, bio-imaging

Jung-Hoon Sohn / sohn4090@kribb.re.kr

· Yeast-based platform technology for protein secretion, bio-diesel lipase

Heung-Chae Jung / hcjung@kribb.re.kr

· Microbial physiology, protein surface expression

Sang Jick Kim / sjick@kribb.re.kr

· Phage display for antibody library building, protein medicine

Bong Hyun Sung / bhsung@kribb.re.kr

· Genome engineering, cascade enzyme systems for carbon fixation

Dae-Hee Lee / dhlee@kribb.re.kr

· CRISPR interference for synthetic biology, genome evolution

Haseong Kim / haseong@kribb.re.kr

· Systems biology, bioinformatics, and genetic circuit design for synthetic biology

Soo-Jin Yeom / sujin258@kribb.re.kr

· Protein/enzyme engineering, synthetic biology

Hyewon Lee / hlee@kribb.re.kr

· Biosensors, Biochips

Jung-Hoon Bae / hoon@kribb.re.kr

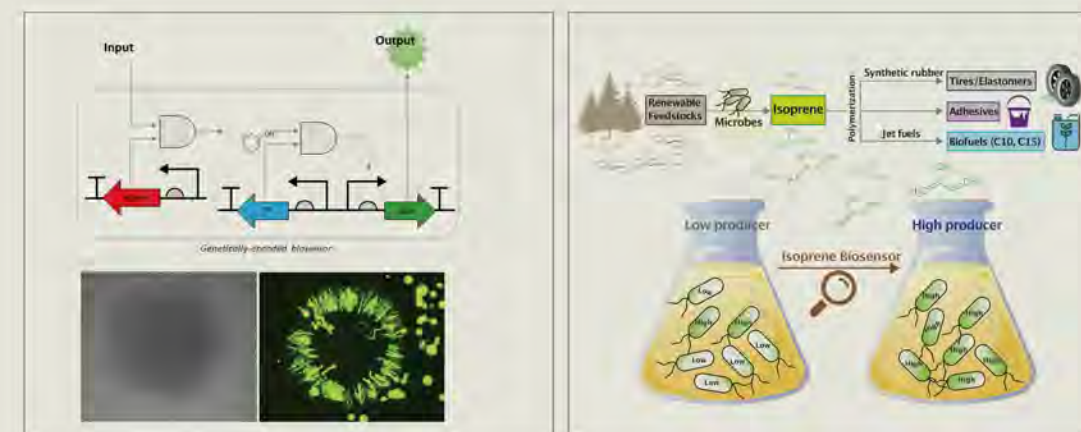
· Yeast metabolic engineering, recombinant protein production

Eugene Rha / josephin@kribb.re.kr

· Genetic engineering, smart library design

Mi-Jin Kim / mijin111@kribb.re.kr

· Yeast metabolic engineering, fermentation



RESEARCH AREAS

Synthetic biology and genetic devices

- Artificial genetic circuits for high-throughput screening of enzymes and biological pathways
- CRISPR interference-based regulation of cellular networks for microbial cell factories

Systems biology

- Machine learning approaches for standardization of microbial genetic circuits
- In silico modeling and simulation of transcription/translation processes

Microbial cell factory

- Development of microbial cell factories for producing sustainable biochemicals and bioplastics
- Yeast and bacterial expression systems for pharmaceutical proteins, industrial enzymes, and antimicrobial peptides

Enzyme engineering for industrial biocatalysts

- Development of novel functional enzymes: methane oxidation, C1-conversion and ligation, plastic degradation, and lipase for biodiesels
- Cascade enzyme reactions for artificial photosynthesis

ACHIEVEMENTS

Development of artificial genetic circuits for synthetic biology advances

- Artificial genetic circuits for detection of enzyme activity in a single cell
- High-throughput screening for engineering enzymes and biosynthetic pathways using flow cytometry
- New genetically encoded biosensors for monitoring of caprolactam, isoprene, cellobiose, etc in engineered *E. coli*

Development of biocatalysts for industrial applications

- First instance of identification of a lactam-synthetic cyclic amidase
- Molecular and biochemical characterization of novel isoprene synthase from *Metrosideros polymorpha*
- Evolution of new enzyme specificity genetic circuit-based rapid screening

Development of intelligent metabolic control devices

- CRISPR interference-based metabolic control of microbial cells for the production of natural compounds and for redirecting metabolic flux
- Artificial metabolon-equipped microbial cell factory for improving biochemical production
- Enzymatic production of biodiesel and consolidated bioprocessing for bio-based chemical production from various types of feedstock.

Development of novel protein expression system

- Development of antibiotic-free protein expression system for long-term stability and tightly controlled production
- Controlled aggregation and increased stability of enzymes by cellulose binding domain fusion
- Construction of yeast protein factory by genome-wide screening of the TFP library and efficient secretion of difficult-to-express proteins and enzymes.

SELECTED PUBLICATIONS

A genetically encoded biosensor for monitoring isoprene production in engineered *Escherichia coli*

ACS Synth Biol. 7(10):2379-90.
Seung-Goo Lee and Dae-Hee Lee

Low-pH production of D-lactic acid using newly isolated acid tolerant yeast *Pichia kudriavzevii* NG7

Biotechnol Bioeng. 115(9):2232-42.
Jung-Hoon Sohn

A synthetic microbial biosensor for high-throughput screening of lactam biocatalysts

Nature Communications. 9(1):5053.
Seung-Goo Lee and Soo-Jin Yeom

Development of *Bacillus methanolicus* methanol dehydrogenase with improved formaldehyde reduction activity

Sci Rep. 8(1):12483.
Jung-Hoon Sohn and Bong Hyun Sung

Bionanotechnology Research Center

Bionanotechnology Research Center aims to develop effective biosensor technology for hazard detection and disease diagnosis based on interfacing bio-contents and nanomaterials. For enabling continuous and convenient detection of hazards and human diseases, the center develops new biomarkers, innovative nanomaterials, and integrated system. The center also focuses on development of theragnostic nanotechnology to achieve precision medicine development for healthy future.

INVESTIGATORS

Kyu-Sun Lee / ekuse74@kribb.re.kr

· Development of *in vivo* model for validating the therapeutics and nanomedicine

Moonil Kim / kimm@kribb.re.kr

· Bioelectronics, living Biosensor

Tai Hwan Ha / taihwan@kribb.re.kr

· Nanobiomaterials for biosensor and biochips, DNA nano-technology

Yong-Beom Shin / ybshin@kribb.re.kr

· Development of nano and optics-based platform for detection/diagnosis

Myung Kyu Lee / mklee@kribb.re.kr

· Bionanotechnology, biochemistry

Chang-Soo Lee / cslee@kribb.re.kr

· Nanobiomaterials for nanobiosensor and nanomedicine

Juyeon Jung / jjung@kribb.re.kr

· Antibody development and engineering for diagnostic and therapeutic applications

Taejoon Kang / kangtaejoon@kribb.re.kr

· BioNano convergence research on disease diagnosis, therapy, environmental monitoring, and food safety

Eun-Kyung Lim / eklim1112@kribb.re.kr

· Development of nano-bio materials for diagnosis and treatment of diseases

Ju Young Byun / bjiy8349@kribb.re.kr

· Bionanosensors based on paper-chips

RESEARCH AREAS

Bio-contents and nano structure interfacing technology for detecting biological hazards (infectious germs and virus) and genetic diseases

- Development of highly efficient biomaterials (antibodies, peptides, oligonucleotides etc.) for the detection of hazards and genetic mutations
- Optimizing bio-contents for the detection of infectious and genetic diseases
- Highly efficient interfacing technology between bio-contents and nano structures

Integrated monitoring system technology to detect hazards and diseases

- Sensor and signal transducer technology to detect hazards
- Signal amplification technology for detecting hazards using biosensors
- Bioelectronics, bionanosensor, and optic-based platform for the detection of hazards and diseases

Innovative nanomaterials for drug delivery and disease diagnostics

- Highly sensitive detection system for chronic, infectious, and genetic diseases based on nano-technology
- Development of nanomaterials for a highly efficient drug delivery system

ACHIEVEMENTS

Development of DNA nanostructures for generating another structure in-situ, in response to signaling cascades

Starting from one type of DNA nanostructure, DNA strand displacement circuits were designed to interact and pass the information encoded in the initial structure in order to mediate self-assembly of a different type of structure, which would be the structure representing the final output, whose self-assembly depends on the type of circuit triggered. Therefore, by integrating the structural and dynamic paradigms of DNA nanotechnology, the center presented rationally designed synthetic platform that functions in an analogous manner, to create complex DNA nanostructures.

Convergence of multivalent antibody and nanoparticle for the advanced immunoassay

Multivalent immunoprobes can improve the sensitivity of biosensors because an increased valency can strengthen the binding affinity between the receptor and target biomolecules. The center developed the surface-enhanced Raman

scattering (SERS)-based immunoassay, using multivalent antibody-conjugated nanoparticles (NPs) for the first time. Multivalent antibody-NP conjugates (MANCs) improved the sensitivity of SERS-based immunoassays by 100 times as compared to that of standard antibody-NP conjugates. It is anticipated that MANCs will increase the feasibility of practical SERS-based immunoassays.

Development of lateral flow biosensor for tamiflu resistant virus detection

The center has developed novel nanoprobe for the Tamiflu-resistant virus. Oseltamivir derivative-modified gold nanoparticles (OHT-GNPs) exhibit a higher binding affinity for Tamiflu-resistant virus that shown in a simple colorimetric assay for detecting the Tamiflu-resistant virus. Moreover, the OHT-based lateral flow assay (LFA) allows the rapid and easy detection of Tamiflu resistance, as the limit of detection (LOD) is $5 \times 10^2 \sim 10^3$ PFU per test.

Development of *in vivo* mitochondrial calcium monitoring system for studying the pathogenesis of neurodegenerative diseases

The center confirmed that the aberrant elevation of mitochondrial calcium levels occurs in animal models of Alzheimer and Parkinson's diseases, the most common neurodegenerative diseases, using an *in vivo* biosensor and mito-GCaMP transgenic animals. These findings have important implications for understanding the pathogenic mechanism and therapeutic interventions of neurodegenerative diseases.

SELECTED PUBLICATIONS

Multivalent antibody-nanoparticle conjugates to enhance the sensitivity of surface-enhanced Raman scattering-based immunoassays

ACS Appl Mater Interf. 10(44):37829-34.
Taejoon Kang and Juyeon Jung

3-input/1-output logic implementation demonstrated by DNA algorithmic self-assembly

ACS Nano. 12(5):4369-77.
Tai Hwan Ha

Kinetic trans-assembly of DNA nanostructures

ACS Nano. 12(9):9423-32.
Tai Hwan Ha

Single-step LRET aptasensor for rapid mycotoxin detection

Anal Chem. 90(1):716-22.
Ju Young Byun

Fast and sensitive near-infrared fluorescent probes for ALP detection and 3d printed calcium phosphate scaffold imaging *in vivo*

Biosens Bioelectron. 105:151-8.
Chang-Soo Lee and Oh Seok Kwon

High-performance nanogap electrode-based impedimetric sensor for direct DNA assays

Biosens Bioelectron. 118:153-9.
Yong-Beom Shin

Fabrication of silver nanoparticles in titanium dioxide/poly(vinyl alcohol) alternate thin films: a nonenzymatic hydrogen peroxide sensor application

Electrochimica Acta. 292:749-58.
Chang-Soo Lee

neurodegeneration *in vivo* in disease models

Proc Natl Acad Sci. 115(38):e8844-53.
Kyu-Sun Lee

Rapid and simple detection of Tamiflu-resistant influenza virus: development of oseltamivir derivative-based lateral flow biosensor for point-of-care (POC) diagnostics

Sci Rep. 8(1):12999.
Eun-Kyung Lim and Juyeon Jung



Cell Factory Research Center

Slowly but surely, bioproducts with a sustainable life cycle are being preferred. Hence, the center identifies and develops a cell factory system that is capable of producing useful metabolites and proteins for industries, including energy, environment, nutraceuticals, cosmetics, and pharmaceuticals. The center currently focuses on the production of these products from microalgae and yeast using genetic, ecological, and fermentation engineering. The center's goal is to research these organisms and associated processes, and develop novel and highly efficient technologies/products from the resources.

INVESTIGATORS

Hee-Sik Kim / hkim@kribb.re.kr

- Development and application of cell factories
- Research on microalgae-based bioenergy and other bio-products
- Algal-bacterial interactions and their impending applications

Hee-Mock Oh / heemock@kribb.re.kr

- Ecophysiological and genomic research of microalgae and cyanobacteria for cyanobacterial bloom control and algal biofuel production

Jae-Wha Kim / wjkim@kribb.re.kr

- Establishment of external factors that are involved in bio regulation and immunity activation associated with disease and securing candidate materials

Chi-Yong Ahn / cyahn@kribb.re.kr

- Ecophysiology of microalgae and cyanobacteria (control of algal bloom)
- Optimization of mass cultivation of microalgae using wastewater

Hyung Gwan Lee / trustin@kribb.re.kr

- Microbial taxonomy and genetic engineering of microalgae
- Omics studies for identification of metabolic pathways and metabolic engineering

Yong Jae Lee / leeyj@kribb.re.kr

- Protein engineering and recombinant protein expression in microorganisms
- Genetic engineering and directed evolution of microorganisms

RESEARCH AREAS

Development of microalgal cell factory

- Genetic and ecological engineering for strain improvement and cultivation
- Omics studies on metabolism, signaling, and regulation
- Development of high-efficiency production system based on exploring novel engineered systems for cultivation and harvest of microalgae

Production of microalgae-based biofuel/biomaterials

- Screening of novel pharmaceutical, cosmetic, and nutraceutical compounds obtained from microalgae
- Economic and efficient production of biodiesel and high-value biomaterials from microalgae based on physiological, genetic, and omics research

Algal bloom research

- Ecophysiological and metagenomic study of the mechanisms of algal bloom in freshwater (green tide) and seawater (red tide)
- Advanced monitoring of bloom and production of algal toxins, mal-odorous compounds, and their interaction with aquatic microorganisms

ACHIEVEMENTS

Increased lipid productivity in microalgae used for industrial application. A three-pronged strategy for achieving high lipid productivity with enhanced growth.

- Collection of strains from Korean wilderness with high lipid productivity
- Ecosystem engineering of algal production systems using beneficial bacteria
- Genetic engineering of algal metabolic and signaling pathways

Construction of omics information and genetic network

The whole genomes of two novel microalgae have been sequenced. Genomic information would provide valuable clues useful for driving the commercialization of microalgae for the maximum production of lipids and carotenoids through genetic modifications.

Mechanism of algal bloom and its control

Genetic diversity of microalgae and their interactions with other microorganisms are being studied using metagenomic and ecoinformatics tools, to understand the detailed biological mechanisms of bloom formation. Environmental-friendly methods based on ecological principles are being developed to control algal bloom.

SELECTED PUBLICATIONS

Optimized co-production of lipids and carotenoids from *Ettlia* sp. by regulating stress conditions

Bioresour Technol. 258:234-9.
Hee-Mock Oh

1-palmitoyl-2-linoleoyl-3-acetyl-rac-glycerol (PLAG) reduces hepatic injury in concanavalin A-treated mice

J Cell Biochem. 119(2):1392-405.
Jae-Wha Kim

The ancient phosphatidylinositol 3-kinase signaling system is a master regulator of energy and carbon metabolism in algae

Plant Physiol. 177(3):1050-65.
Hee-Sik Kim

Application of biosurfactant from *Bacillus subtilis* C9 for controlling cladoceran grazers in algal cultivation systems

Sci Rep. 8(1):5365.
Hee-Sik Kim

PLAG alleviates chemotherapy-induced thrombocytopenia via promotion of megakaryocyte/erythrocyte progenitor differentiation in mice

Thromb Res. 161:84-90.
Jae-Wha Kim

Improving water quality using settleable microalga *Ettlia* sp. and the bacterial community in freshwater recirculating aquaculture system of *Danio rerio*

Water Res. 135:112-21.
Hee-Mock Oh and Chi-Yong Ahn



Plant Systems Engineering Research Center

The center focuses on development of important platform technology for plant biotechnology and industrial transgenic plants. These include studies on plant genomes and metaboloms, determining functionally important genes, and developing molecular tools to improve plant traits. Furthermore, the center generates industrial transgenic plants with an enhanced tolerance to environmental stresses in marginal lands, to develop a plant-based global green technology and establish international cooperation network. Further, the center currently focuses on development of in-plant cell biotechnology for the production of invaluable bio-pharmaceuticals and bio-materials. The goal is to investigate these organisms and associated processes, and develop sustainable technologies/products from these resources.

INVESTIGATORS

Hyun Soon Kim / hyuns@kribb.re.kr

- Establishment of plant-based expression system for sustainable production of invaluable bio-materials
- Potato biotechnology

Sang-Soo Kwak / sskwak@kribb.re.kr

- Development of industrial plants (sweet potato, alfalfa, poplar etc.) exhibiting enhanced tolerance to multiple stresses for sustainable agriculture in global marginal lands

HyeRan Kim / kimhr@kribb.re.kr

- Using genetics and genomics to enhance plant secondary metabolite contents
- Development of genomic technologies to build reference genomes and explore useful genomes

Sung Ran Min / srmin@kribb.re.kr

- Development of transgenic plants for determining agricultural traits via nuclear and plastid transformation
- Establishment of optimal culture system for *in vitro* large scale production of medicinal plants

Stephen Beungtae Ryu / sbryu@kribb.re.kr

- Lipid-based signaling of plants in response to abiotic and biotic stresses
- Production of natural rubber using Russian dandelion

Haeng-Soon Lee / hslee@kribb.re.kr

- Development of biotech plants with enhanced tolerance to abiotic stresses

Suk Yoon Kwon / sykwon@kribb.re.kr

- Structural and functional genomics of plants
- Transformation of crop plants to enhance agricultural traits

Jae Sun Moon / jsmoon@kribb.re.kr

- Molecular plant-microbe interactions
- Development of oligo chips for pathogen diagnosis

Jeong Mee Park / jmpark@kribb.re.kr

- Molecular mechanisms of pathogens - induced cell death
- Plant immunity to viruses

Hye Sun Cho / hscho@kribb.re.kr

- Studies of the roles and fine-tuning mechanisms of post-translational regulation (PPase) in response to environmental stress and the application of genes to improve crop productivity

Won-Joong Jeong / wonjoong@kribb.re.kr

- Regulation of gene expression for improvement of algal biomass

Jae Heung Jeon / jeonjh@kribb.re.kr

- Development of optimal system for the mass production of the seeds or seedlings of useful vegetative crops
- Potato biotechnology

Jeongyeo Lee / leejy@kribb.re.kr

- Functional characterization of the genes associated with secondary metabolite contents and plant nutrients, using molecular genetics and genomics approaches

Hyo-Jun Lee / hyojunlee@kribb.re.kr

- Studies on plant responses to mechanical stimuli
- Studies on wound-induced plant regeneration
- Identification of signaling pathways useful for the adaptation to environmental changes in potato

RESEARCH AREAS

- Studies on structural and functional genomics of plants
- Studies on post-translational modifications in plants
- Generation of biotech plants with an enhanced tolerance to multiple stresses
- Studies of omics to achieve increase in the storage ability of sweet potato
- Functional studies on the IbOrange gene, in terms of abiotic stress tolerance
- Studies on plant-microbe interactions and their utilizable technology
- Studies on light and circadian clock signaling networks in plants
- Cooperative study of plant-based global green technology with China, Kazakhstan, etc.
- Establishment of sustainable biomass
- Development of high-efficiency production system
- Lipid signaling network and production of natural rubber
- Studies on molecular mechanisms of plant regeneration

ACHIEVEMENTS

Development of transgenic plants with enhanced tolerance to multiple environmental stresses

The center characterized tolerance to drought, high salt, low temperature, and oxidative stress using a transgenic sweet potato overexpressing IbOrange, IbCBF3, AtP3B etc. In addition, transgenic poplar plants with increased plant growth and salt stress tolerance were generated by the down-regulation of GIGANTEA-like genes.

Functional studies of the IbOrange gene involved in accumulation of carotenoids

Transgenic sweet potato plants overexpressing the IbOrange gene showed a strong heat stress tolerance at 47 °C. IbOrange exhibiting a high chaperone activity regulates photosynthesis under heat stress by stabilizing IbPsbP, in addition to also stabilizing IbPSY protein. It is one of the most important genes involved in the carotenoid biosynthetic pathway of the sweet potato.

Development of salt tolerance transgenic plant

The center developed transgenic tobacco plants with enhanced salt stress tolerance by introducing an alcohol dehydrogenase gene (ADH) from *Synechocystis* PCC6906

Investigating cell death mechanism of plants related to disease resistance

- Isolation of novel leaf-inhabiting endophytic bacteria that showed antagonistic activities against phytopathogens
- The center has characterized genes related to the cell death mechanism of plants that were involved in resistance to bacterial and viral diseases, using virus induced gene silencing technology.

Studies on enhancing plant secondary metabolite contents

- Characterized sugar metabolism related genes in strawberry fruits
- Profiling of the major phenolic compounds and their biosynthesis genes in *Sophora flavescens* Aiton

Development of molecular and genomics tools to improve plant traits

- Development of SNP markers to distinguish between day-neutral and short day strawberries and low progoitrin, or high glucobrassicin content cabbages
- Development of anthracnose resistant strawberry resources

Increased lipid productivity in microalgae for biofuel production

- Three pronged strategy for achieving high lipid productivity with enhanced growth
- Collection of strains from Korean wilderness with high lipid productivity
- Ecosystem engineering of algal production systems using beneficial bacteria
- Genetic engineering of algal metabolic and signaling pathways

Construction of omics information and genetic network

The whole genomes of two novel microalgae have been sequenced. Genomic information will provide valuable clues to drive the commercialization of microalgae for the maximum production of lipid and carotenoids through genetic modifications.

Investigation of fine-tuning mechanism of immunophilins to adapt to environmental stress in Arabidopsis and rice

- Classification of rice immunophilin genes (29 FKBP and 26 CYPs belonging to the PPase family) was achieved for the first time in monocots, along with the identification of a number of immunophilins related to environmental stresses
- Molecular characterization and physiological roles of novel immunophilins in environmental stress adaptation
- Development of breeding materials and crops

- against future climate change, using immunophilins
- RNA-guided genome editing in immunophilins for functional genomics

Lipid signaling and production of natural rubber

- Lipid-derived signaling in systemic acquired resistance in plants
- Commercialization of lipid signals for multi-resistant crops
- New variety of Russian dandelion showing a 3-fold increase in yield of rubber

SELECTED PUBLICATIONS

Genome-wide analysis of alternative splicing in an inbred cabbage (*Brassica oleracea* L.) line 'HO' in response to heat stress
Curr Genomics. 19(1):12-20.
Hye Sun Cho and Hyun Soon Kim

Stress-induced expression of the sweetpotato gene IbLEA14 in poplar confers enhanced tolerance to multiple abiotic stresses

Environ Exp Bot. 156:261-70.
Sang-Soo Kwak

Elevated inorganic carbon concentrating mechanism confers tolerance to high light in an arctic *Chlorella* sp. ARM0029B

Front Plant Sci. 9:590.
Won-Joong Jeong

Transcriptome profiling and characterization of drought-tolerant potato plant (*Solanum tuberosum* L.)

Mol Cells. 41(11):979-92.
Hyun Soon Kim

Overexpression of alfalfa Orange gene in tobacco enhances carotenoid accumulation and tolerance to multiple abiotic stresses

Plant Physiol Biochem. 130:613-22.
Sang-Soo Kwak



Industrial Bio-materials Research Center

Recently, the use of environmentally friendly functional bio-materials in bio-industrial applications is considered to be better than chemical materials that have been used in industrial fields extensively. Thus, based on biodiversity of microorganisms, insects, plants, and natural resources, the center is determining new bio-materials, including enzymes, health functional foods, pharmaceuticals, cosmeceuticals, biopesticides, and biological processes as shown below.

- Highly active enzymes from diverse organisms, including insect gut microbiota
- Natural resources for health functional foods and cosmeceuticals
- Biopesticide candidates from natural resources
- Microbial libraries (bacteria, actinomycetes, fungi, and yeasts)
- Business build-up based on biodiversity information
- Technologies to solve social issue such as livestock malodor

INVESTIGATORS

Kwang-Hee Son / sonkh@kribb.re.kr

- Enzymes for industrial uses from biodiversity
- Microbial genomics and bioinformatics
- Natural products obtained from plants used as skin whitening agents

Chang-Jin Kim / changjin@kribb.re.kr

- Exploitation of microbial resources (Actinomycetes)
- Screening of secondary metabolites and development of useful biomaterials

Ho-Yong Park / hypark@kribb.re.kr

- Using highly active enzymes and bio-materials obtained from insects and microbes for industrial applications (food, cosmetics, livestock industry etc.)
- Qualified production of edible and medicinal insects
- Bio-insecticides for the control of agricultural and forest pests by insect-pathogenic microbes

Tae-Sook Jeong / tsjeong@kribb.re.kr

- Screening, *in vivo* efficacy testing, and study of the mechanism of bioactive materials and substances for the prevention and treatment of metabolic syndrome (including obesity, diabetes, fatty liver, hyperlipidemia, and atherosclerosis) and using these in development of health functional foods and nutraceuticals

Kee-Sun Shin / ksshin@kribb.re.kr

- Evaluation of microbial activities for industrial applications
- Yeast physiological analysis, biodiversity, and evolution

Do Young Kim / kdy119@kribb.re.kr

- Development of industrially valuable biocatalysts, bio-active compounds, and biopolyesters
- Metagenomic analysis of the invertebrate gut microbiome

Seokho Kim / kims@kribb.re.kr

- Search and development of bio-materials useful for treating cancers and liver fibrosis
- Study of the value of bio-materials through *in vivo* experiments

Dong-Jin Park / dongjin@kribb.re.kr

- Screening, isolation and production of bioactive compounds from actinomycetes
- Classification and identification of actinomycetes

Yoonjung Ju / chizcake@kribb.re.kr

- Studies on the value of evaluating microbial resources for industrial applications
- Screening of secondary metabolites and development of useful biomaterials



Associate Director Kwang-Hee Son / Tel. +82-42-860-4553 / E-mail sonkh@kribb.re.kr

RESEARCH AREAS

Development of bio-materials based on biodiversity and FT (fusion technology)

- Identifying unique highly active enzymes and bio-materials from insect and related microorganisms (gut microbiome etc.)
- Biocatalysts used to resolve the biorecalcitrance of biomass
- Environmentally friendly bio-pesticide production using insect-pathogenic microbes
- Reduction of odor in livestock farms using enzymes, microbes, and bio-material complexes

Development of health functional foods for metabolic syndrome control

- Development and study of health functional materials and active components from natural and edible resources for prevention and treatment of metabolic syndrome

Construction of mass utilization system of value-created microbial resources for industrial applications

- Investigation of the production of useful microbial enzymes, antimicrobial activities, plant growth promoting activities, etc.
- Production of microbial broths, extracts, and proteomes
- Generation of LC/MS profiles for microbial metabolomes
- Construction of DBs for storing information about microbial characterization and products

Development of biomaterial for enhancing immunotherapy against pancreatic cancer

- Development of therapeutic agents for pancreatic cancer by inducing the activation of NK cells
- Generation of NK cells for clinical applications
- Development of novel strategy for enhancing immunotherapy, including natural compound and antibody engineering

ACHIEVEMENTS

Protein-degrading enzyme, Arazyme

From the gut-bacteria pool of the Korean black widow spider, a salt tolerant and cold tolerant enzyme, Arazyme, was developed. The core technology and the protein producing strain were transferred to a biospecific company, which resulted in the creation of various industrial materials, biocosmetics, and feed enzymes.

NSP (non-starch polysaccharides)-degrading enzymes

Although wooden components (including cellulose, hemicellulose, and lignin) are known to be major biomasses on earth, their usage is limited because of their recalcitrance. As biocatalyst used to cut and degrade the NSP, the center developed xylanase system and related products to gain share of the feed market.

Development of functional materials from black-soybean-leaf extract for prevention and treatment of hyperlipidemia and hepatic steatosis, and investigation of their molecular mechanism

Extracts of black-soybean-leaf extract (EBL) are enriched in quercetin glycosides and isorhamnetin glycosides. EBL supplementation decreased body weight and fasting glucose, insulin, and triglyceride levels, and suppressed hepatic steatosis in mice with high-fat-diet-induced obesity and diabetes. EBL improved plasma adiponectin levels and hepatic AMPK activation. EBL has potential as safe and effective supplement against obesity, type 2 diabetes, and fatty liver.

Technology transfer of *Aspergillus niger* F22 and its applications for biological control of *Meloidogyne incognita*

Plant-parasitic nematode infection is a major problem in crop production. In the course of screening nematode biological control agents, the center isolated a fungal strain, *A. niger* F22, exhibiting strong nematocidal activity on *M. incognita*. The center later devised a suitable formulation useful for developing industrial applications and handling of bio-agent with increased efficacy.

NHP (NK cell Homing Protein)-body

- NK cell therapy is limited by tumor cell inhibition of NK cells that are homed into the tumor site. Therefore, we developed an antibody based NK cell homing protein, named NK cell homing protein-conjugated antibody.
- Increasing NK cell infiltration into tumor tissues improved the response to this cancer immunotherapy.

SELECTED PUBLICATIONS

Genetic and functional characterization of a novel GH10 endo- β -1,4-xylanase with a ricin-type β -trefoil domain-like domain from *Luteimicrobium xylanilyticum* HY-24

Int J Biol Macromol. 106:620-8.

Ho-Yong Park and Kwang-Hee Son

Stackebrandtia soli sp. nov., a novel actinobacterium isolated from a soil sample

Int J Syst Evol Microbiol. 68:1215-9.

Chang-Jin Kim



DIVISION OF RESEARCH ON
NATIONAL CHALLENGES

56-65

Division of Research on National Challenges contributes to the safety and higher quality of life by developing key source technologies in the field of biotechnology, to provide a preemptive response to social agendas, such as infectious diseases, aging, climate change and environmental changes that affect the lives of people.

- Aging Research Center
- Infectious Disease Research Center
- Environmental Diseases Research Center
- Biodefense Research Center
- Stem Cell Convergence Research Center

Aging Research Center

The center investigates the molecular mechanisms of the aging processes with regard to cellular changes and organ degeneration. The center is also responsible for developing fundamental technologies for the prevention of aging, aging-associated diseases and generation of therapeutics, using a multi-omics analysis, followed by functional validation.

INVESTIGATORS

Eun-Soo Kwon / eunsoo.kwon@kribb.re.kr

- Molecular biology of aging and aging-related diseases using *Caenorhabditis elegans*
- Inter-species regulation of longevity by gut microbes

Ki-Sun Kwon / kwonks@kribb.re.kr

- Systems biology of sarcopenia and age-related diseases
- Signal transduction associated with muscle aging

Yong-Kook Kang / ykkang@kribb.re.kr

- Epigenetic mechanism of muscle aging

Sung Sup Park / sspark@kribb.re.kr

- Understanding the pathogenesis of muscle dysfunction

Young Kyo Seo / ykseo@kribb.re.kr

- Regulation of age-dependent inflammation in muscles
- Energy metabolism in muscle aging

Kwang Pyo Lee / kplee@kribb.re.kr

- Molecular mechanisms of myoblast (satellite cell) differentiation, dysfunction, and diseases (aging and sarcopenia)
- Developing therapeutics for aging-associated diseases using plasma factors

Yong Ryoul Yang / dearyang@kribb.re.kr

- Age-related diseases in mouse models
- Identification of rejuvenating plasma factors and their molecular mechanisms

Jung Sun Park / jspark@kribb.re.kr

- Production of transgenic animal models related to aging

Seung-Min Lee / lsjhm99@kribb.re.kr

- Isolation of therapeutic targets of aging-associated diseases
- Developing therapeutics for aging-associated diseases using plasma factors

Ju Yeon Kwak / kjy9070@kribb.re.kr

- Developing blood biomarkers for aging and aging-related diseases and their applications

RESEARCH AREAS

- Systems biology of sarcopenia and age-related diseases
- Discovery of new genes involved in the aging process and study of associated signaling pathways
- Discovery of rejuvenating factors to reverse the processes of aging
- Functional identification of age-related genes using animal models
- Development of drug candidates and biologics for the control of age-associated diseases

ACHIEVEMENTS

- Identification of the rejuvenating factors that are able to reverse aging in old animals: analysis of serum factors and gut microbes by using proteomics tools and a genome-wide library, in order to achieve the slowing down of the aging process in old animals.
- Identification of muscular microRNAs that are associated with age: study of the function of miRNAs that are downregulated in old muscle tissues and their targets, in order to achieve improved muscular function in old animals.
- Development of drug candidates to treat muscle-wasting disease: discovery of chemical compounds that improved the regenerative capacity of old mice. Recently, the technology transfer of a drug candidate to a biotech company was done.

SELECTED PUBLICATIONS

Age-associated bimodal transcriptional drift reduces intergenic disparities in transcription

Aging. 10(4):789-807.

Yong-Kook Kang

3'-Sialyllactose as an inhibitor of p65 phosphorylation ameliorates the progression of experimental rheumatoid arthritis

Br J Pharmacol. 175(23):4295-309.

Eun-Soo Kwon

Determination of oocyte-manipulation, zygote-manipulation, and genome-reprogramming effects on the transcriptomes of bovine blastocysts

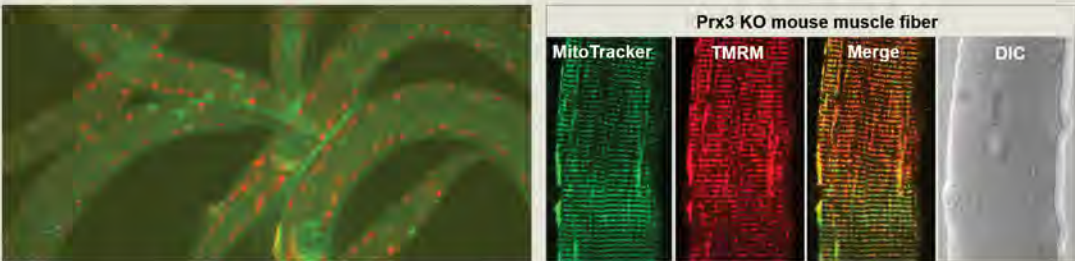
Front Genet. 9:143.

Yong-Kook Kang

Prediction of sarcopenia using a combination of multiple serum biomarkers

Sci Rep. 8(1):8574.

Ki-Sun Kwon



Infectious Disease Research Center

Infectious diseases have become a serious medical and social problem recently. Bacterial resistance against major antibiotics is causing bacteria to evolve into untreatable 'superbacteria.' Additionally, acute viral diseases such as influenza viruses and MERS, which are associated with high morbidity and mortality, are posing a threat to public health. Therefore, it is necessary to formulate plans to counter current and future infectious diseases. To combat superbacteria using the new insights gained by the study of induced resistance, the genomic library, small RNAs, and novel antibacterial lead compounds, the center is actively engaged in identifying novel antibacterial targets and innovative antibacterial compounds. For taking prophylactic measures against viral diseases, the center is developing new vaccines, adjuvant technologies, and anti-viral strategies based on virology, immunology, and structural biology. Further, the center also investigates microbe-host interactions to understand and manage viral/bacterial pathogenesis better.

INVESTIGATORS

Choong-Min Ryu / cmryu@kribb.re.kr

· Antimicrobial Resistance, bacteria-host interactions, plant immunity

Soo-Keun Choi / sookeun@kribb.re.kr

· Genetics and genomics of gram-positive bacteria

Dae Gwin Jeong / dgjeong@kribb.re.kr

· Structure-based development of recombinant viral protein vaccines
· Rapid viral diagnosis using the antigen and antibody detection technique

Haeyoung Jeong / hyjeong@kribb.re.kr

· High-throughput sequencing and analysis of microbial genomes
· Genomic epidemiological study of nosocomial infection-related bacteria

Won-Gon Kim / wgkim@kribb.re.kr

· Discovery and development of new antibacterials
· Microbial natural product chemistry/biosynthetic engineering

Jae Gu Pan / jgpan@kribb.re.kr

· Molecular microbial physiology and antimicrobial genomics

Haryoung Poo / haryoung@kribb.re.kr

· Development of vaccine adjuvants and study of the immune response generated towards them
· Development of a cervical cancer vaccine using lactobacillus as a vehicle

Doo-Jin Kim / goldjdj@kribb.re.kr

· Genetic vaccines against infectious viral diseases
· Interaction between influenza virus and host immune system

Sun-Woo Yoon / syoon@kribb.re.kr

· Pathogenesis and genetic characterization of influenza viruses
· Development of influenza vaccine technologies using the reverse genetics system

Hye Kwon Kim / khk1329@kribb.re.kr

· Viral infectious diseases in animals
· Identification and characterization of novel viruses

Ji Hyung Kim / kzh81@kribb.re.kr

· Antibiotic resistance and virulence in aquatic pathogens
· Zoonotic bacterial diseases in animals

Jun-Seob Kim / junkim83@kribb.re.kr

· Control of multi-drug resistance (superbacteria)
· Bacterial persistence (Non-inherited antibiotic resistance)

Sung-Kyun Park / skpark@kribb.re.kr

· Metabolic control of B cell activation, microbe-immune cell interaction

Oh Seok Kwon / oskwon79@kribb.re.kr

· Development of point-of-care tests for monitoring infectious diseases

RESEARCH AREAS

- Antibacterial discovery and target identification using the genomic library
- Microbial genome analysis and recombineering for enhanced antibiotic production
- Small RNA biology and induced resistance in the pathogenic bacteria
- Bacterial display of enzymes and antigens: directed evolution
- Bacterial acetylproteomes
- Bacteria-host interactions
- Development of a high throughput protein expression system
- Development of new vaccines against infectious diseases, including influenza and MERS
- Development of novel vaccine adjuvants and the investigation of their immunomodulatory mechanisms
- Basic research on pandemic influenza, including surveillance and genetic characterization
- Research on emerging and re-emerging viral infectious diseases

ACHIEVEMENTS

Superbacteria-related

- Engineering of NRPS gene clusters from *Paenibacillus polymyxa* and over-producing strains of peptide antibiotics
- High expression of polymyxin and fusaricidin biosynthetic gene clusters and engineering to generate novel derivatives.
- Discovery of new anti-Gram negative compounds with a new mode of action from a microbial library
- Generation of new analogues by the biosynthetic engineering of *Streptomyces* gene clusters
- Role of volatile organic compounds in bacterial communication
- *Galleria mellonella* genomics and its application in antimicrobial drug screening
- Spore display system for enzymes and vaccines
- Developing novel display systems for enzymes and antigens in *Bacillus* spores.
- Bacterial acetylproteomes and the systematic identification of post-translationally acetylated proteins in bacteria.
- Genome engineering of *Bacillus subtilis* through a highly efficient microbial genome engineering method, using the CRISPR/Cas9 system

- Dissecting probiotic *Paenibacillus*-plant interactions and their genome analysis
- Understanding and applying plant growth promoting rhizobacteria-elicited plant growth promotion and induced resistance.

Infectious virus-related

- Development and technology transfer of avian influenza vaccine
- Investigation of the immunomodulatory and anti-viral functions of bacterial outer membrane vesicles (OMVs)
- Molecular mechanisms of development of intraepithelial lymphocytes
- Isolation and characterization of influenza viruses from domestic wild birds, dogs, horses, and human patients.
- Development and clinical study of a cervical cancer vaccine
- Precision sequencing and analysis of microbial reference genomes, using contemporary genome sequencing technologies, after taking genealogy and evolution into account

SELECTED PUBLICATIONS

Surface-modified polymer nanofiber membrane for high-efficiency microdust capturing

Chem Eng J. 2018;204-13.
Oh Seok Kwon

Pseudomonas syringae evades phagocytosis by animal cells via type III effector-mediated regulation of actin filament plasticity

Environ Microbiol. 20(11):3980-91.
Choong-Min Ryu and Young-Jun Park

Characterization of an oleaginous unicellular green microalga, *Lobosphaera incisa* (Reisigl, 1964) strain K-1, isolated from a tidal flat in the Yellow Sea, Republic of Korea

Front Microbiol. 9:2159.
Ji Hyung Kim

Stereoisomers of the bacterial volatile compound 2,3-butanediol differently elicit systemic defense responses of pepper against multiple viruses in the field

Front Plant Sci. 9:90.
Choong-Min Ryu

Thermotherapy for Na⁺/I⁻ symporter-expressing cancer using anti-Na⁺/I⁻ symporter antibody-conjugated magnetite nanoparticles

J Ind Eng Chem. 63:359-65.
Oh Seok Kwon

Dysregulated T-helper type 1 (Th1): Th2 cytokine profile and poor immune response in pregnant ferrets infected with 2009 pandemic influenza A(H1N1) virus

J Infect Dis. 217(3):438-42.
Sun-Woo Yoon

Terrein is an inhibitor of quorum sensing and c-di-GMP in *Pseudomonas aeruginosa*: a connection between quorum sensing and c-di-GMP

Sci Rep. 8(1):8617.
Won-Gon Kim



Environmental Diseases Research Center

Exposure to environmental pollutants and unhealthy environments contributes to a wide range of adverse health outcomes in our community; hence, these have received national recognition. The primary objective of Environmental Disease Research Center is to conduct research on the pathogenesis mechanism by which environmental factors cause or influence human disease and development, in order to develop innovative methods for early detection, prevention, and control of environmentally related diseases. The proposed center focuses on the study and analysis of essential biomarkers of diseases induced by environmental pollutants, and on establishing a validation or control system for various environmental diseases. In particular, the center focuses on the development of novel targets and therapeutic candidates specific to particulate matter-mediated cell responses.

INVESTIGATORS

Young-Jun Park / pyj71@kribb.re.kr

- Research on metabolic control and control of infectious diseases using the macrophage, which is involved in innate immunity

Doo-Byoung Oh / dhoh@kribb.re.kr

- Protein therapeutics, glycan analysis, and remodeling

Dae-Soo Kim / kds2465@kribb.re.kr

- Bioinformatics: Gene expression profiling interactive analysis and integrative analysis of the genome using a next generation sequencing platform

Seon-Jin Lee / sjlee@kribb.re.kr

- The regulatory and functional study of autophagy and disease-related genes
- Validation of novel therapeutic target drugs in pathological mouse animal model

Moo-Seung Lee / msl031000@kribb.re.kr

- Characterization of enterohemorrhagic E.coli Shiga toxins that cause renal failure
- Efficient production of recombinant antimicrobial hybrid peptides and therapeutic proteins that prevent pathogens from infecting the host
- Understanding microbial toxin-host interaction

Jungwoon Lee / jwlee821@kribb.re.kr

- Cellular and molecular regulatory mechanisms that decide stem cell fate
- Environmental influence on stem cells involved in development, regeneration, and disease progression

Jinyoung Jeong / jyjeong@kribb.re.kr

- Fabrication of nanomaterials and nanostructures for biosensors
- Environmental and toxicological effects of nano- and micro-materials

Baek-Soo Han / bshan@kribb.re.kr

- Exploration of treatments for degenerative neural diseases, research on metabolic functions, and identification of factors regulating neural cell differentiation

Jun-Seob Kim / junkim83@kribb.re.kr

- Control of multi-drug resistance (superbacteria)
- Bacterial persistence (Non-inherited antibiotic resistance)

Jong-Gil Park / jonggilpark@kribb.re.kr

- Validation of therapeutic targets for cardiovascular diseases
- Regulation of metabolic disorders

RESEARCH AREAS

- Establishment of infrastructure for genome research and technology platforms for studying environmental diseases
- Assessment of ecotoxicological effects of particulate matter in human organs
- Development of particulate matter-induced pulmonary disease in mouse model and validation of novel therapeutic targets
- The regulatory and functional study of autophagy and disease-related genes
- Pathogenesis of environmental-related disease
- Investigation of particulate matter (PM10/2.5)-mediated multi-organ failure
- Development of stem cell models for environmental disease
- Metabolic control and control of infectious diseases using the macrophage, which is involved in the generation of an innate immune response
- Research on the mechanism for controlling the metabolism using macrophages
- Identification of the mechanism for deterring infectious disease development and controlling the signaling process using macrophages
- Study of environmental microbe (microbial toxin) - host interactions

ACHIEVEMENTS

- A liver-specific gene expression panel predicts the differentiation status of in-vitro hepatocyte models
- Gene selection tool (GST): Development of the R-based tool for genetic disorders based on the sliding-window proportion test, using whole-exome sequencing data
- Beclin 1 deficiency is associated with increased hypoxia-induced angiogenesis
- Discovery of small molecules that control stem cell fate
- Discovery of the deterrent effect of inflammation via iNOS control
- Research about the possibility of controlling obesity and diabetes
- Discovery of the signaling system for TXNIP in obese and diabetic individuals
- Bacterial toxin-mediated induction of multi-functional host signaling

SELECTED PUBLICATIONS

Pseudomonas syringae evades phagocytosis by animal cells via type III effector-mediated regulation of actin filament plasticity
Environ Microbiol. 20(11):3980-91.
Young-Jun Park and Choong-Min Ryu



Biodefense Research Center

Recently, there has been a global epidemic of new and transformed infectious diseases, and the possibility of bio-terrorism has been increasing. Futurists are expecting the spread of pandemic disease and biological terrorism using high-risk pathogens to be a major cause of human catastrophes. Terrorism can occur with the aid of biochemical weapons worldwide, regardless of the time of exposure and it takes a lot of time to check the presence of infections and prepare after their occurrence. In particular, somewhat inadequate level of scientific and technological knowledge is required in the domestic chemical, biological, and radiological fields for the development of small and remote alarms for detection and identification, which should enhance the level of protection biological warfare. Therefore, Biodefense Research Center is planning and conducting the following studies:

- Development of preventive, diagnostic, and therapeutic technologies to preemptively respond to biological agent threats
- Development of a wearable integrated biological defense system for the future soldier and its validation through a primate model

INVESTIGATORS

Doo-Byung Oh / dboh@kribb.re.kr

- Protein therapeutics, Glycan analysis and remodeling

Choong-Min / Ryu cmryu@kribb.re.kr

- Understanding the host-microbe interactions that lead to the development of drugs against infectious diseases

Sang-Rae Lee / srlee@kribb.re.kr

- Establishment of an efficacy test system with nonhuman primate disease models

Tai Hwan Ha / taihwan@kribb.re.kr

- Development of biosensors for biochemical warfare through novel nanomaterials
- Development of a drug delivery mechanism to load anti-dotes for chemical warfare

Doo-Jin Kim / golddj@kribb.re.kr

- Genetic vaccines against infectious viral diseases
- Interaction between influenza virus and host immune system

Baek-Soo Han / bshan@kribb.re.kr

- Development of a micro human body simulation system for the early evaluation of bio-markers

Sun-Woo Yoon / syoon@kribb.re.kr

- Pathogenesis and genetic characterization of influenza viruses
- Development of influenza vaccine technologies using the reverse genetics system

Jangwook Lee / jlee@kribb.re.kr

- Development and application of therapeutic biomacromolecules-on-demand for patients
- Targeted macromolecule delivery system for disease theragnosis (diagnosis and therapy)



RESEARCH AREAS

- Development of brain disease models (stroke, dementia, Parkinson's disease) with nonhuman primates
- Novel mechanism of influenza viral pathogenesis through interactions with the host immune system
- Differentiation of various organs with human stem cells and development of a system for the evaluation of drug efficacy and toxicity
- Inter-kingdom genomics-inspired molecular understanding of host-microbe interactions for combating pathogens
- Basic research on pandemic influenza, including surveillance and genetic characterization
- Research on emerging and re-emerging viral infectious diseases
- Targeted drug delivery system and therapeutic biomacromolecules (antibody/protein/gene)
- Various aptamer-based opto-electronic sensor systems and DNA based nanotechnology

ACHIEVEMENTS

- Development of potential antibiotic compound, its molecular targets, and platform technology
- Molecular mechanisms of development of intraepithelial lymphocytes
- Identification of the role of protein tyrosine phosphatases during neuronal differentiation
- Development and technology transfer of a novel avian influenza vaccine
- Isolation and characterization of zoonosis in domestic wild birds, dogs, horses, and human patients.
- Development of biocompatible drug delivery system that can address an adverse drug reaction and achieve targeted therapeutic success
- Development of chemical methods for facile optical mercury sensors on flexible substrates.

Stem Cell Convergence Research Center

The research goal of the center is to understand stem cell functions and disease mechanisms, in order to develop therapeutics for the treatment of human diseases. The center focuses on the generation of 3D human disease model systems using reprogrammed cells such as patient-derived induced pluripotent stem cells (iPSCs) for developing personalized and in vivo-mimetic disease models. In addition, the center developed an alternative method for animal testing, named as the 'Networking Organoid Culture System (NOCS)', which involves different types of organoids, such as the intestine, liver, heart, brain, etc.

INVESTIGATORS

Janghwan Kim / janghwan.kim@kribb.re.kr

- Differentiation and transdifferentiation into neural cells
- Disease modeling and development of therapeutics
- Common mechanisms of reprogramming

Mi-Young Son / myson@kribb.re.kr

- Disease modeling based on induced pluripotent stem cells
- Stem cell-based 3D gastrointestinal organoids as models of human development and disease

Kyung-Sook Chung / kschung@kribb.re.kr

- Functional validation of novel GPCR proteins and de-velopment of therapeutics
- Disease modeling based 3D-liver spheroid/organoid
- *In vitro* human hepatocyte-based experimental systems for the evaluation of drug metabolism and drug toxicity

Cho Rok Jung / crjung@kribb.re.kr

- Functional validation of disease related genes and development of therapeutics
- Development of a three-dimensional cell-based disease model

Myung Jin Son / mjson@kribb.re.kr

- Metabolic and mitochondrial regulation during cell fate transition
- Modeling normal- and disease-state livers using organoid systems

Mi-Ok Lee / molee@kribb.re.kr

- Genetically engineered iPSC-based disease modeling
- 3D human tissue modeling using human pluripotent stem cells

Jung Hwa Lim / jhwa@kribb.re.kr

- Functional analysis of disease related genes
- Development and evaluation of small cancer drug molecules
- Evaluation of therapeutic gene transfer for combating genetic diseases

Hyun-Soo Cho / chohs@kribb.re.kr

- Development of prediction pipeline for hPSC-derived cells
- Functional analysis of epigenetic modifiers in hPSC-derived cells and cancers

Hyun Mi Kang / hmkang@kribb.re.kr

- Development of disease model based on 3-dimensional cells
- Research on generation/differentiation of kidney organoids

Kyung Hee Noh / trollius@kribb.re.kr

- Novel mechanism of action of the ubiquitination enzyme
- Development of novel oral bioavailability method

Young-Joo Jeon / jeonyj@kribb.re.kr

- Molecular analysis of disease targets identified using patient iPSCs

- Proteomic analysis and identification of novel drug targets

Areum Baek / areumbaek@kribb.re.kr

- Basic research in the field of stem cells and life sciences
- Management of research-related systems

Jiwon Ahn / jiwon@kribb.re.kr

- Functional validation of disease-related target genes for the development of therapeutics and diagnostics
- Research on 3D culture system based hepatotoxicity

RESEARCH AREAS

- Development of core technologies involved in the cell fate change between somatic cells and stem cells
- Modeling 3D human diseases based on stem cells, reprogramming, and organoid technology
- *In silico* prediction systems for differentiation or determining the functional status of *in vitro* models
- Development of a biomimetic 3D human tissue and networking platform for predicting drug toxicity and efficacy
- Characterization of genes related to various diseases such as cancer and the development of therapeutic interventions such as small molecules, gene therapy, regenerative cells, and tissues

ACHIEVEMENTS

A novel and safe small molecule enhances hair follicle regeneration by facilitating metabolic reprogramming

The knowledge about stem cell metabolism and the specific regulation of bioenergetics during the hair regeneration process is insufficient at present. Here, the center reported the hair regrowth-promoting effect of a newly synthesized novel small molecule, IM176OUT05 (IM), which activates stem cell metabolism. IM treatment mildly inhibited mitochondrial oxidative phosphorylation and concurrently increased glycolysis levels, which accelerated the induction of stemness during the early phase of reprogramming. More importantly, the topical application of IM accelerated hair follicle regeneration, by stimulating the progression of the hair follicle cycle to the anagen phase and increased the hair follicle number in mice. Overall, these results show that the novel small molecule IM promotes tissue regeneration, specifically for hair regrowth, by restructuring the metabolic configuration of stem cells.

Developing scalable cultivation systems of hepatic spheroids for drug metabolism via genomic and functional analyses

The center established a process for the mass production of functionally enhanced hepatic spheroids by a systematic comparison of three different culture/formation modes. It was found that shear stress has positive effects on hepatic differentiation and the maintenance of hepatic function, upon culturing cells in a DMSO-containing differentiation medium or serum-free medium formulation. The removal of DMSO, which acts as a differentiating factor in the presence of serum and mild shear stress, resulted in the deterioration of hepatic function, but serum-free formulation showed a greater level of shear stress dependence on hepatic function. Finally, SFUs may serve as a mass production tool in hepatic spheroids with enhanced functionalities.

Interleukin-2 induces the *in vitro* maturation of human pluripotent stem cell-derived intestinal organoids

Human pluripotent stem cell (hPSC)-derived intestinal organoids (hIOs) form 3D structures that are organized into crypt and villus domains, making them excellent *in vitro* model systems for studying human intestinal development and disease. However, hPSC-derived hIOs still need to undergo *in vivo* maturation to completely recapitulate the adult intestine, and the mechanism of maturation for doing so remains elusive. Here,

it was shown that co-culture with human T lymphocytes induces the *in vitro* maturation of hIOs, and that the STAT3-activating interleukin-2 (IL-2) is the major factor that induces maturation. The hIOs exposed to IL-2 closely mimic the adult intestinal epithelium and show expression levels that are comparable to those of mature intestinal markers, and show increased intestine-specific functional activities. Even after *in vivo* engraftment, the hIOs matured *in vitro* retain their maturation status. The results of our study demonstrate that STAT3 signaling can induce the maturation of hIOs *in vitro*, thereby circumventing the need for animal models and *in vivo* maturation.

Missense mutation of the SPAST protein (I344K) results in a loss of ATPase activity and prolongs the half-life, and is implicated in autosomal dominant hereditary spastic paraplegia.

The spastin protein (SPAST), which contains an (AAA) domain and ATPase with diverse cellular activities, regulates microtubule dynamics. Missense mutations of the SPAST gene are frequently detected in patients with hereditary spastic paraplegias (HSPs), and represent the main reason for the loss of SPAST function; however, the pathogenicity of mutant SPAST is heterogeneous. Here, SPAST variant with I344K mutation (I344K-SPAST) was identified in a Korean family with an autosomal dominant-type HSP. The center investigated the role of the I344K-SPAST in HSP, to determine the therapeutic mechanism. The I344K-SPAST mutation prolonged the half-life of the protein, as compared to that of wild-type SPAST (WT-SPAST) in cells, by modulating post-translational modifications, for proteasomal degradation. Though I344K-SPAST was localized in the microtubules, its microtubule severing and ATPase activity was lesser than that observed for WT-SPAST. The presence of mutant M87 isoforms harboring the same mutation as I344K-M1 SPAST also increased the protein stability and loss of MT severing activity, but its pathogenicity was lower than that of I344K-M1 SPAST in neurite outgrowths. An overexpression of I344K-SPAST resulted in microtubule accumulation, following the inhibited neurite growth in neuroblastomas, neural progenitor cells, and mouse primary cortical neurons. Conversely, the pathogenic effects of I344K-SPAST were reduced by the overexpression of WT-M1 SPAST in a dose dependent manner, because WT-SPAST could interact with I344K-SPAST. Our data therefore provide the proof-of-concept for the fact that the genetic transfer of WT-M1 SPAST might serve as a valid therapeutic option for HSPs.

System for screening of novel prognostic and diagnostic markers using an *in silico* epigenetic panel in cancer patients

Different systems of molecular classification have been developed for several types of cancers to reduce needless treatment, by dividing cancer patients into low- and high-risk progression groups. However, these methods do not account for all the pathological features of cancers, and constant investigations into novel prognostic/therapeutic markers are thus required. In this study, the center screened prognostic and diagnostic markers using an *in silico* epigenetic panel with RNA-seq results derived from the TCGA portal. Using target genes, the center validated the possibility of using prognostic/ diagnostic markers with multiple cancer patient cohorts. In conclusion, results might assist in the development of novel therapeutic strategies for cancer patients.

SELECTED PUBLICATIONS

Missense mutation of SPAST protein (I344K) results in loss of ATPase activity and prolonged the half-life, implicated in autosomal dominant hereditary spastic paraplegia

Biochim Biophys Acta Mol Basis Dis. 1864(10):32-21-33.

Cho Rok Jung

EHMT2 is a metastasis regulator in breast cancer

Biochem Biophys Res Commun. 496(2):758-62.

Hyun-Soo Cho

A novel and safe small molecule enhances hair follicle regeneration by facilitating metabolic reprogramming

Exp Mol Med. 50(12):160.

Myung Jin Son and Kyung-Sook Chung

In vitro and *in vivo* imaging and tracking of intestinal organoids from human induced pluripotent stem cells

FASEB J. 32(1):111-22.

Mi-Young Son and Janghwan Kim

Interleukin-2 induces the *in vitro* maturation of human pluripotent stem cell-derived intestinal organoids

Nature Communications. 9(1):3039.

Mi-Young Son, Janghwan Kim and Cho Rok Jung





DIVISION OF
BIO TECHNOLOGY INNOVATION

68-71

Division of Bio Technology Innovation is composed of Technology Transfer Center, SME (small-to-medium enterprises) Support Center, and Biotechnology Process Engineering Center.

- Technology Transfer Center
- SME Support Center
- BioProcess Engineering Center

Technology Transfer Center

The mission of Technology Transfer Center (TTC) is to support and encourage the dissemination of technology related intellectual property resulting from the scientific and technical programs of KRIBB and carry out research for further development and commercial exploitation. TTC is responsible for the identification and protection of technological assets. Once these technologies are protected effectively, marketing initiatives are used to facilitate their adoption and commercial uptake. Dissemination is mainly carried out after licensing. The terms and conditions of the licensing agreements are adapted on a case-by-case basis, depending on the specific situation of the licensee, maturity of the technology, and expected markets. In specific cases, if the technology arising because of a research project has business potential, the TTC also supports the creation of a start-up. To support biotechnological innovation in Korea, TTC also analyzes and values biotech-related intellectual property, to support the creation of start-up or technology transfer. TTC also conducts the technological evaluation of new biotech companies on the KOSDAQ (Korea Securities Dealers Automated Quotation) list.

STAFF

Hong-Weon Lee / hwlee@kribb.re.kr
Ph.D, Associate Director

Eun-Seok Jang / esjang@kribb.re.kr
Assistant Manager

Jeong Hyun Choi / choijh16@kribb.re.kr
Ph.D, IP Management

Hyung-Cheol Kim / hcgim@kribb.re.kr
Ph.D, Technology Transfer Commercialization

Seung-Hyun Park / wiclever@kribb.re.kr
Technology Transfer Commercialization

Sang-Jun Kim / sjkim@kribb.re.kr
Ph.D, Paper · Laboratory Notebook

MAIN FUNCTIONS

Intellectual Property Management: Building strong patent portfolio

- Consulting on intellectual property filling / office action / maintenance
- Screening of excellent ideas / know-how / technology
- Scientific affairs to internal and external collaboration

Technology transfer

- Technology valuation / marketing
- Technology licensing-out

Technology commercialization

- Support joint ventures (Institute Enterprise)
- Analysis and valuation of biotech-related IP
- Technological evaluation for KOSDAQ list

ACHIEVEMENTS

Creating/securing superior technology

- Number of Registered Patents (accumulated, 2014-2018)

Year	Domestic	Overseas	Total
2018	1,078	524	1,602

Technology transfer commercialization

- 377 intellectual property transfers to industry have been carried out, as of the year 2018
- Established in-house joint venture, 'Nano Biotech' in November 2015, between KRIBB, Natural F&P Inc., and Next BT Inc.
- Established in-house joint venture, 'DK Bio' in May 2016, between KRIBB and DAMY Chemical Inc.
- Established in-house joint venture, 'Huvet' in November 2017, between KRIBB and Huvet Inc.
- Established in-house joint venture, 'T-Mac' in November 2018, between KRIBB and C-Mac Inc.

SME Support Center

In Korea, biotech startups and small-to-medium enterprises (SMEs) compete with large companies, make inroads into the global market and are at the forefront of efforts to drive the nation's economic growth and create high-quality jobs. However, biotech SMEs have to overcome various barriers at every stage of growth. The primary goal of SME Support Center is to support Biotech Business Ecosystems in order to accelerate business innovation and growth. To achieve this goal, SME Support Center develops and implements various strategies, programs, and network based on human resources, infrastructure, and funds provided by KRIBB.

STAFF

Ohsuk Kwon / oskwon@kribb.re.kr
Associate Director

Joong Su Kim / joongsu@kribb.re.kr
Biotech SME support specialist

Hyo Kon Chun / hkchun@kribb.re.kr
Biotech SME support specialist

Heungchae Jung / hcjung@kribb.re.kr
Biotech SME support specialist

Kyong-Cheol Ko / kcko@kribb.re.kr
Biotech SME support specialist

Soon-Han Kwon / soonhan@kribb.re.kr
Manager

Seung-Hui Lee / seunghui@kribb.re.kr
Researcher

So Yeon Shin / syshin@kribb.re.kr
Researcher

Donghun Hyun / donghun@kribb.re.kr
Researcher

MAIN FUNCTIONS

Strengthening biotech business ecosystems

- To conduct KRIBB Family Business Program, to achieve cooperation of 200 Biotech SMEs (~'21)
- To conduct the Tech-Clinic Program, in order to provide solutions for technological difficulties
- KRIBB Research Center – Biotech SME Partnership Program strengthens technological competitiveness between Biotech SMEs
- To train commercialization specialists and dispatch KRIBB researchers to Biotech SMEs

Fostering 50 global future leader biotech companies ('19-'21)

- 5 Hidden Champions : Support new product development
- 10 Pre-Hidden Champions : Support product diversification
- 20 Techin-Biz Companies : Support process innovation
- 15 Leading regional innovation companies : Support technology competitiveness strengthening

Accelerating biotech startups

- Customized Researcher Startup Support Program provides entrepreneurship education and training with regard to business plan preparation, inauguration, and business incubation
- Bio-Venture Center Operation accelerates the settlement and growth of early stage biotech startups (by providing designated spaces and startup incubation programs for technological business incubators, technological innovation centers, and companies cooperating under KRIBB programs)

ACHIEVEMENTS

Establishment of biotech business ecosystems

- Bio-convergence in Daejeon, Bio-medicine in Chungcheongbuk-do, and Eco-friendly biomaterials in Jeollabuk-do, with 300 Biotech SMEs
- Generation of common agendas and development of B2B business models
- Operation of KRIBB Bio-Mentoring System: Technological innovation and problem solving (42 cases), attracting investment and financing (41 cases)

Operation of growth stage specific support programs ('15~'18)

- Global Hidden Champion Program (5 projects)
- Pre-Global Hidden Champion Program (15 projects)
- Techin-Biz Program (30 projects)

Operation of demands-based support programs for biotech SMEs

- Demands-Based KRIBB-Biotech Cooperative R&D Program (15 projects)
- KRIBB Research Center-Biotech SME Partnership Program (74 companies with 25 KRIBB research centers)

Acceleration of biotech startups

- Bio-Venture Center (3-story building with a total of 2,970 m2 and 35 business incubation units)
- 66 Biotech Startups graduated since 2000 (12 listed on the KOSDAQ)
- 21 Biotech Startups in Bio-Venture Center achieved total annual sales of 19.5B KRW in 2018

BioProcess Engineering Center

BioProcess Engineering Center (BPEC) is a skilled division that provides engineering solutions for technical issues in biological processes. Since 1995, the center plays a unique role in Korea's industrial biotechnological R&D ecosystem, by transforming scientific proof of concepts into value propositions in the field, including the microbial fermentation, biotransformation, and downstream processing of biochemical materials. In addition, the center established research facilities for animal cell culture, to efficiently respond to the recent explosive growth in the biopharmaceutical industry. The center has been carrying out the mass production and commercialization of protein drugs using animal cells, while gaining more knowledge about advanced biotechnology. Nowadays, the center is providing a range of support services to strengthen domestic bio-industry capabilities, for example, it provides support for the industrialization of results obtained during research and equipment utilization, in addition to professional manpower training.

INVESTIGATORS

Eun-Gyo Lee / eglee@kribb.re.kr

- Biochemical engineering
- Biologics manufacturing
- Animal cell culture/separation and purification

Hong-Weon Lee / hwlee@kribb.re.kr

- Fermentation physiology and Microbial engineering
- Bioprocess engineering

Eui-Sung Choi / choi4162@kribb.re.kr

- Metabolic engineering
- Enzyme engineering
- Yeast biotechnology

Jung-Oh Ahn / ahnjo@kribb.re.kr

- Biochemical engineering
- Molecular breeding of yeast and bacterial cells

Woo Young Jeon / wyjeon27@kribb.re.kr

- Microbial metabolic engineering

Hyeok-Won Lee / tntn7616@kribb.re.kr

- Support for pilot-scale upstream equipment

Jin Gyeom Lee / jhlee@kribb.re.kr

- Support for pilot-scale downstream equipment

Min jeong Jang / tkekrh@kribb.re.kr

- Industrial strain development & metabolite analysis

Won Kyo Kim / wonkyo@kribb.re.kr

- Support for pilot-scale upstream equipment

Kyoung-hwa Ryu / khryu@kribb.re.kr

- Support for biological pilot-scale downstream equipment

Soonyong Park / sympark@kribb.re.kr

- Process development for large-scale mammalian cell cultures using bioreactors

Sung-Hwa Seo / seosh87@kribb.re.kr

- Support for recombinant protein production

Hyeonkyeong Kim / hkkim@kribb.re.kr

- High protein expression system/ biopharmaceutical cell line development

Eun-Sil Kim / eskim@kribb.re.kr

- Biopharmaceutical cell line development



Associate Director Eun-Gyo Lee / Tel. +82-43-240-6633 / E-mail eglee@kribb.re.kr

RESEARCH AREAS

Microbial fermentation and scale-up research for biomaterials production

- Development of a novel gene expression system in microorganisms
- Development of industrial strains for producing biomaterials
- Process development and scale-up of research for biomaterial production

Mammalian cell culture for biopharmaceuticals production

- Development of stable cell lines producing biopharmaceuticals
- High-density cell culture of mammalian cells
- Process design for quality control.

Separation and purification technology

- Optimization of chromatography and membrane processes
- Protein/organic acid purification
- Scale-up of separation and purification processes

ACHIEVEMENTS

Development of a new cell line for production of monoclonal antibodies by CHO cells

Chinese hamster ovary (CHO) cells are one of the most widely used host cells for therapeutic protein production. Because of clonal variation, it is necessary to develop an efficient high-throughput cell screening system for a large number of analytes. Recently, the center developed an efficient screening method based on the reconstitution of split GFP to select high antibody producing CHO cells, using FACS analysis. Based on a correlation between antibody production and fluorescence intensity after the reconstitution of GFP, the fragment complementation system for split GFP has the potential to act as a powerful tool for antibody production in CHO cells.

Process development of mammalian cells for biopharmaceuticals production

Mammalian cell culture has become the dominant system for the production of biopharmaceuticals, including therapeutic proteins and live virus vaccines. The center is currently developing a cell line in a serum-free suspension culture, serum-free medium with hydrolysates, and developing feeding strategies for fed-batch cultures in a number of mammalian cell lines, such as CHO, baby hamster kidney (BHK), and human embryonic kidney (HEK)-293 cells. Further-

more, the center has developed chromatographic purification technologies and high-throughput precision analysis techniques, based on a design of experiment (DOE) analysis.

Microbial engineering for recombinant protein production

The demand for recombinant proteins has increased, as more applications in several fields have become a commercial reality. The center has developed microbial strains producing industrial enzymes, antigenic proteins, and virus-like particles for veterinary vaccines, growth factors for cosmetics, and bioreceptors for diagnostic kits. In order to nurture a commercially viable process for generating the final products, the microbial fermentation and protein purification processes at the pilot-plant scale were optimized.

Yeast biotechnology for polymeric bio-monomer production from plant oil

Growing environmental concerns have attracted attention on efforts to produce bio-based plastics from renewable sources. However, past efforts mostly focused on short-chain polymeric monomers that were based on sugars. Plant oils represent renewable sources for the production of medium to long-chain hydrocarbons, many of which are able to emulate the properties of petrochemicals or enable the production of new industrial chemicals. The center has developed an n-alkane-assimilating diploid *Candida tropicalis*, for achieving the biotransformation of plant oil-derived fatty acids into dicarboxylic acid compounds (dodecanedioic acid and sebacic acid), which act as polymeric monomers. Subsequent fed-batch processes carried out using this engineered strain allowed us to achieve a molar yield of above 98% and a final titer of above 100 g/L at the pilot scale. In addition, the center has developed biosynthetic pathways for medium- to long-chain α , ω -diols, α , ω -diamines, and ω -amino fatty acids from plant oil-derived fatty acids and their derivatives in the cheese-ripening yeast *Yarrowia lipolytica*. This has made it possible to use yeast to produce all the long chain monomers for polyamide and polyester production, in accordance with their corresponding substrates.

SELECTED PUBLICATIONS

Effect of decanoic acid and 10-hydroxydecanoic acid on the biotransformation of methyl decanoate to sebacic acid

AMB Express. 8(1):75.
Hong-Weon Lee

Microcrystalline cellulose for delivery of recombinant protein-based antigen against erysipelas in mice

Biomed Res Int. 2018;7670505.
Jung-Oh Ahn

Ty1-fused protein-body formation for spatial organization of metabolic pathways in *Saccharomyces cerevisiae*

Biotechnol Bioeng. 115(3):694-704.
Eui-Sung Choi

Development of a promising microbial platform for the production of dicarboxylic acids from biorenewable resources

Biotechnol Biofuels. 11:310.
Hong-Weon Lee

High-level recombinant production of squalene using selected *Saccharomyces cerevisiae* strains

J Ind Microbiol Biotechnol. 45(4):239-51.
Eui-Sung Choi



OCHANG
BRANCH INSTITUTE

74-77

Ochang Branch Institute conducts studies to enhance the pipeline and platform for the development of new bio-drugs at the national level. Its major research areas include the assessment of medicinal resources based on metabolomic analysis of natural products, and the establishment of systems to discover new physiologically active substances. The institute is also involved in identifying inhibitors and clinical candidates for targeting diseases. It is also supporting researchers by providing bio-resource infrastructures, such as laboratory mice, miniature pigs, and primates and a bio-evaluation system for drug efficacy and GMO safety tests .

- Natural Medicine Research Center
- Anticancer Agent Research Center

Natural Medicine Research Center

The center aims to develop a platform for digital-based big data analytics based on natural products in Korean medicinal plants and natural drug candidates obtained from plant sources that are effective against chronic diseases, such as asthma/COPD, cancers, and spinal muscular atrophy.

INVESTIGATORS

Sei-Ryang Oh / seiryang@kribb.re.kr

- Identification of biologically active compounds from natural resources
- Metabolomic research of medicinal plants for carrying out origin discrimination and standardization of natural drugs.

Hyeong-Kyu Lee / hykylee@kribb.re.kr

- Pharmacognosy and natural product chemistry
- Drug discovery from natural products

Hyun-Sun Lee / leehs@kribb.re.kr

- Pharmacognosy and natural product chemistry
- Drug discovery from natural products

Kyung-Seop Ahn / ksahn@kribb.re.kr

- Evaluation of the anti-inflammatory and anti-asthmatic activity of natural products
- Identification of new bio-markers for asthma/COPD

Hyun-Jun Lee / hjlee7@kribb.re.kr

- Innate and adaptive immune mechanisms of pulmonary disease treatment
- Discovery of drug candidates for respiratory disease treatment

Jong-Pyung Kim / kimjp@kribb.re.kr

- Development of natural substances for cosmeceuticals and nutraceuticals
- Development of drug candidates for the prevention/treatment of neurological disorders

Jae-Hyuk Jang / jangjh@kribb.re.kr

- Discovery of bioactive metabolites from microorganisms and plants
- Determination of the structure of bioactive compounds

Sungchan Cho / sungchan@kribb.re.kr

- Unveiling the molecular mechanism of incurable diseases
- Discovery of drug candidates for the treatment of incurable diseases

Su Ui Lee / iamsuui@kribb.re.kr

- Development of cell-based assays for drug discovery
- Exploring the mechanism of action of bioactive compounds

Sung-Kyun Ko / ksk1230@kribb.re.kr

- Chemical biology and drug discovery
- Target protein identification and target molecule interaction

Hyung Won Ryu / ryuhw@kribb.re.kr

- Isolation, characterization, and biological evaluation of natural products of plants
- Metabolite analysis of the dynamic metabolic response of living plant systems

Mun-Ock Kim / mokim@kribb.re.kr

- Development of *in vitro* and *in vivo* screening systems for drug discovery
- Study of mechanism based on cancer cell death

RESEARCH AREAS

Natural product chemistry for digital-based big data analytics

- Isolation of active constituents using analytical instruments from medicinal plants
- Elucidation of natural compound structure using 1D and 2D NMR
- Chemical identification of the plant specialized metabolites using QToF-MS
- Digital-based big data analytics from the chemical structures of plant metabolites

Drug candidate discovery for chronic respiratory diseases

- Establishment of bioassay/screening systems based on the molecular targets of chronic respiratory diseases, such as asthma/COPD/pulmonary fibrosis
- Research on molecular mechanisms of bioactive compounds
- Evaluation of therapeutic effects of natural products in animal models of pulmonary diseases

Cancer immunotherapeutic agent screening

- Screening of bioactive compounds regulating tumor cell proliferation, autophagy, and metastasis
- Screening of bioactive compounds inhibiting indole 2,3-oxygenase (IDO)
- Screening and development of an immunogenic cell death inducer
- Identification and validation of cellular targets for cancer immunotherapy

Discovery of drug candidate for the treatment of spinal muscular atrophy (SMA)

- Identification of bioactive compounds that could correct the defect of SMN splicing
- Pharmacological validation of bioactive compounds in the SMA mouse model

ACHIEVEMENTS

Identification of natural products against chronic diseases

The center has isolated active natural compounds that act as therapeutic candidates from plant sources and evaluated their biological activities during inflammation, asthma/COPD, cancer, and metabolic disorder.

Construction of plant extract bank

Management of plant extract bank (with extracts of over 5,000 samples from domestic plants), and provide the extracts to researchers for screening active materials and employ a long extraction/fractionation/purification process.

Industrial research

The center has licensed out two natural drug candidates (asthma/COPD: Yungjin Pharm Co. Ltd, 2011.05.16., atherosclerosis: Korea Bio Medical Sciences Institute, 2015.03.23.) and one lead compound composed of synthetic pharmaceuticals for treating chronic inflammation (A-ju Pharmaceutical Co. Ltd, 2015.07.02). The phase IIa (U.S.A. FDA 2017.08.01) trials were successful for the natural drug candidate for COPD. For developing nutraceuticals, the original candidates (compounds from *Pistacia weinmannifolia*) were licensed out to a company (BTC Co. Ltd, 2016.06.29.).

Discovery of drug candidate for Alzheimer's disease and technology transfer to Korean pharmaceuticals

Dr. Sungchan Cho's team has successfully discovered potent and selective small molecule inhibitors of DYRK1A, a less explored and increasingly highlighted kinase target associated with several incurable diseases, such as Alzheimer's disease, Down's syndrome, diabetes, and cancers. The technologies employing DYRK1A inhibitors have been separately transferred to a Korean pharmaceutical and biotech venture worth billions of won, which includes running royalties on the sales. Based on the close collaborations with several companies, DYRK1A inhibitors have currently been under further development, and it is expected that US IND approval would be sought for a fast-moving drug candidate within this year. This success was selected as one of the most outstanding achievements of 2018 by KHIDI (Korea Health Industry Development Institute).

SELECTED PUBLICATIONS

Fisetin inhibits TNF- α /NF- κ B-induced IL-8 expression by targeting PKC δ in human airway epithelial cells

Cytokine. 108:247-54.
Su Ui Lee

Polyacetylene from *Dendropanax moribifera* alleviates diet-induced obesity and hepatic steatosis by activating AMPK signaling pathway

Front Pharmacol. 9:537.
Mun-Ock Kim and Su Ui Lee

Lignans isolated from flower buds of *Magnolia fargesii* attenuate airway inflammation induced by cigarette smoke *in vitro* and *in vivo*

Front Pharmacol. 9:970.
Sei-Ryang Oh

Evaluation of phytochemicals in *Agastache rugosa* (Fisch. & C.A.Mey.) Kuntze at different growth stages by UPLC-QToF-MS

Ind Crop Prod. 112:608-16.
Sei-Ryang Oh and Hyung Won Ryu

3,4,5-Trihydroxycinnamic acid attenuates lipopolysaccharide (LPS)-induced acute lung injury via downregulating inflammatory molecules and upregulating HO-1/AMPK activation

Int Immunopharmacol. 64:123-30.
Kyung-Seop Ahn and Sei-Ryang Oh

Selective oncolytic effect in Epstein-Barr virus (EBV)-associated gastric carcinoma through efficient lytic induction by *Euphorbia* extracts

J Funct Foods. 42:146-58.
Sungchan Cho

Copper oxide nanoparticles induce collagen deposition via TGF- β 1/Smad3 signaling in human airway epithelial cells

Nanotoxicology. 12(3):239-50.
Kyung-Seop Ahn



Anticancer Agent Research Center

The center strives to discover new anti-cancer agents that are derived from microorganisms and chemical libraries, and identify their cellular targets for the development of novel front-line chemotherapeutic agents. Research utilizes chemical biology techniques based on metabolomics, genomics, proteomics, and cellulomics technologies, in combination with expertise in N-end rule mediated protein degradation (epiproteomics), PLK-linked cytokinesis, and tumor cell specific metabolism for the development of medicinal and bio-functional compounds.

INVESTIGATORS

Bo Yeon Kim / bykim@kribb.re.kr

· Cancer molecular cell biology
· Epiproteomics

Jong Seog Ahn / jsahn@kribb.re.kr

· Microbiology and cell biology
· Chemical biology

Sangku Lee / sangku@kribb.re.kr

· Organic chemistry
· Organic synthesis, medicinal Chemistry

Young-Soo Hong / hongsoo@kribb.re.kr

· Natural product biosynthesis and engineering
· Genome mining for new bioactive molecule discovery

Nak-Kyun Soung / soungnak@kribb.re.kr

· Cancer cell biology
· Cell division, anti-cancer drug discovery

Hyunjoo Cha-Molstad / hcha@kribb.re.kr

· Molecular cell biology
· Protein degradation, protein arginylation, and cancer

Kyung Ho Lee / leekh@kribb.re.kr

· Molecular cell biology
· Cell cycle, primary cilia, Wnt signaling pathway

In-Ja Ryoo / ijrwoo@kribb.re.kr

· Natural product chemistry
· Bioassay system

Jun-Pil Jang / jpjang@kribb.re.kr

· Natural product chemistry
· Development of bioactive compounds inhibiting indole 2,3-oxygenase (IDO) and protein arginine deiminase (PAD) from natural sources

Joonsung Hwang / hwangj1@kribb.re.kr

· Cell and developmental Biology
· Dermatology, animal disease models, genetically modified animals

RESEARCH AREAS

Anti-cancer agent screening

- Screening new bioactive compounds regulating tumor cell proliferation and metastasis
- Identifying their cellular targets and optimizing the anti-cancer candidates
- Evaluation of the efficacy of drug candidates using animal disease models
- Research on structure-activity relationship
- Development of drug candidates

Construction of microbial secondary metabolites

- Discovery of bioactive secondary metabolites from microorganisms

- Compiling a library of secondary microbial metabolites

Cancer target discovery and functional mining of anti-cancer targets

- Research on cancer cell division and its regulatory proteins, polo-like kinase, (PLK), and centrosome
- Studies on the relationship between centrosome biosynthesis and cancer
- Wnt signaling-related cell cycle regulation and tumorigenesis/metastasis
- Regulation of primary cilium formation in cancer cells
- Investigation of disease mechanisms using genetically modified animals

Research on protein degradation focused on the N-end rule pathway

- Cancer therapeutic drug development through the targeting of the N-end rule pathway
- Regulation of tumor development via protein arginylation
- Cancer-specific proteolytic signaling mediated by the N-end rule pathway

Natural Product Biosynthesis and Engineering

- Genome mining for new bioactive molecule discovery
- Construction of an artificial biosynthetic pathway of bioactive compounds in the microbe

ACHIEVEMENTS

Discovering of bioactive secondary metabolites from microorganism

Structurally unique and diverse secondary metabolites from microorganisms have been an invaluable source of drugs and molecular probes over several decades. The center has focused attention on the exploration of less chemically studied microorganisms, which are potentially prolific sources of novel chemistry. The research team isolated 1,500 Actinomycetes and fungal strains from soil samples or marine sediments and screened their secondary metabolites. The preliminary process of chemical screening of EtOAc extracts by LC-MS could enable to select the candidate microorganisms, which are rarely found in public and in-house databases, for the production of unusual metabolites. These metabolites were identified to be glycoside anthraquinone aturanosides possessing 6-O- α -L-rhamoside, catenulisporolides, glycosylated triene macrolides, enamidomines of cyclic lipopeptides, pentaminomycins of hydroxyarginine containing hexapeptides, phomalichenones, α -pyrone derivatives, and Ulleungdin, a lasso peptide.

Identification of a novel cancer cell migration pathway

The elevated expression of human enhancer filamentation 1 (HEF1) is an essential stimulus for the metastasis of various solid tumors. Here, the center reported that CK1 δ phosphorylates HEF1 at Ser-780 and Thr-804, and that these phosphorylation events promote a physical interaction between polo-like kinase 1 (Plk1) and HEF1. It was found that this interaction is critical for the translocation of HEF1 to focal adhesions (FAs) and for inducing the migration of HeLa cells. These findings provide critical mechanistic insights into the HEF1-Plk1 complex-dependent localization of HEF1 to FAs underlying the metastatic process, and might therefore contribute to the development of new cancer therapies.

Autophagic proteolysis modulated by the N-end rule pathway

The center's research has led to the discovery that the N-end rule pathway, which was previously associated exclusively with the ubiquitin-proteasome system (UPS), functions as the crossroad between cellular stress sensing and autophagy. These findings have shed light on how cells sense proteotoxic stress, induced by the loss of proteasome function and, in response, induce autophagy. The results clearly demonstrate that under proteotoxic stress, BiP/

GRP78, an ER chaperone, is retrotranslocated into the cytoplasm and N-terminally arginylated by arginyltransferase 1 (ATE1). Through its N-arginine, BiP binds to the ZZ domain of p62/sqstm1, a critical autophagic cargo receptor. This interaction facilitates p62 aggregation, autophagic co-delivery, and the degradation of p62 and its associated cargo. Using this mechanism, cells maintain cellular homeostasis and promote cell survival, in response to devastating stresses.

Construction of artificial biosynthetic pathway of bioactive compounds in microbe

The biological synthesis of plant-specific polyketides has attracted increasing levels of attention due to their proven beneficial properties and health-promoting effects. Engineered *E. coli* containing artificial phenylpropanoid biosynthetic pathways were established for the production of plant-specific metabolites. The lab is interested in studying the biosynthesis of various pharmaceutically important natural products, including but not limited to plant-specific polyketides and bacterial type III polyketides.

Development of anti-cancer agents by chemical synthesis

The center has obtained small molecular compounds from chemical libraries and secured new materials through structural modifications of the compounds, which improved the structural specificity and pharmacological properties of the compounds. In addition, the center is studying the target of a substance, by investigating its mechanism of action.

PLK4 regulated centrosome biogenesis via a centrosomal protein with a weight of 131 kDa.

The center identified Cep131 to be a novel substrate for the major centrosomal kinase PLK4, and studied the mechanism by which it causes the replication of the centrosome through phosphorylation. In addition, these results suggest that the inhibited Cep131 could be a candidate protein for anti-cancer activity.

SELECTED PUBLICATIONS

Optimization of artificial curcumin biosynthesis in *E. coli* by randomized 5'-UTR sequences to control the multienzyme pathway

ACS Synth Biol. 7(9):2054-62.

Young-Soo Hong

PARK7 modulates autophagic proteolysis through binding to the N-terminally arginylated form of the molecular chaperone HSPA5

Autophagy. 14(11):1870-85.

Bo Yeon Kim

Pentaminomycins A and B, hydroxyarginine-containing cyclic pentapeptides from *Streptomyces* sp. RK88-1441

J Nat Prod. 81(4):806-10.

Jong Seog Ahn and Jae-Hyuk Jang

Ulleungdin, a lasso peptide with cancer cell migration inhibitory activity discovered by the genome mining approach

J Nat Prod. 81(10):2205-11.

Jong Seog Ahn and Jae-Hyuk Jang

Catenulisporolides, glycosylated triene macrolides from the chemically underexploited actinomycete *Catenulispora* species

Org Lett. 20(22):7234-8.

Jong Seog Ahn and Jae-Hyuk Jang

N-terminal arginylation generates a bimodal degron that modulates autophagic proteolysis

Proc Natl Acad Sci. 115(12):e2716-24.

Bo Yeon Kim

The endoplasmic reticulum-residing chaperone BiP is short-lived and metabolized through N-terminal arginylation

Sci Signal. 11(511):eaan0630.

Bo Yeon Kim





DIVISION OF
BIOINFRASTRUCTURE

80-91

The activities of Division of Bioinfrastructure are establishing and running the infrastructures for useful biological materials and live animals in Korea, to increase the utilization of the resources and to strengthen the bio-researches and bio-industries. It is consisted of three key functions to promote national R&D in the field of bioscience and biotechnology: the infrastructure for biological resources involved with resources of human DNA clones, microorganisms, mice, minipig and primates; Infrastructure for biological resources from abroad; and the infrastructure for utilization of living modified organisms (LMOs) and the implementation of access and benefit sharing (ABS).

- Laboratory Animal Resource Center
- Bio-Evaluation Center
- National Primate Research Center
- Futuristic Animal Resource & Research Center
- International Biological Material Research Center
- ABS Research Support Center

Laboratory Animal Resource Center

The goals of the center are to establish national infrastructure for laboratory animal resources and a public/intramural service core for animal experimentations. For these purposes, the center has been collecting mouse resources, developing quality control technologies, generating animal models for human diseases, and providing animal resources and services for researchers in biomedical research fields since 1984. Recently, the center started producing genetically engineered mice (GEM) and 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, the center has established infrastructure for non-clinical evaluation and lead optimization of drug candidates using laboratory animal resources and have been providing research support to bio-health companies and researchers.

INVESTIGATORS

Hyoung-Chin Kim / hckim@kribb.re.kr

- Experimental Animal Medicine,
- Toxicology of Drug Development
- Health Safety of LMOs

Chul-Ho Lee / chullee@kribb.re.kr

- Development and functional validation of animal models for human diseases
- Genetic quality control of laboratory animals

Ki-Hoan Nam / namk@kribb.re.kr

- Laboratory Animal Science/Immunology
- Reproductive engineering/Phenotyping of mutant mice

Won-Kee Yoon / wkyoon@kribb.re.kr

- Veterinary Pathology
- Genetic monitoring of laboratory animals
- Health Safety of LMO

Young-Suk Won / yswon@kribb.re.kr

- Bacteriology
- Health monitoring of laboratory animals

Jung Hwan Hwang / coccs99@kribb.re.kr

- Development of genetically altered laboratory animal models
- Phenotyping of functional genes associated with metabolic diseases

Kyung-Shim Kim / kskim@kribb.re.kr

- Development and phenotyping of animal models for brain and neurological diseases
- Discovery of bioactive materials for human brains and neurological diseases

Yong-Hoon Kim / milknut@kribb.re.kr

- Support for veterinary care and histopathological diagnosis
- Functional phenotyping of cardiovascular and liver disease models

Hoyoung Ghang / kangho@kribb.re.kr

- Genome and phenome association study with model animals
- Bioinformatics

Jong Soon Kang / kanjon@kribb.re.kr

- Molecular Pharmacology
- Efficacy evaluation of drug candidates

Kyeong-Ryoon Lee / kyeongrlee@kribb.re.kr

- Drug Metabolism and Pharmacokinetics (DMPK)
- PK-PD modeling and simulation



Associate Director Hyoung-Chin Kim / Tel. +82-43-240-6100 / E-mail hckim@kribb.re.kr

RESEARCH AREAS

- Collection and maintenance of laboratory animal resources.
- Production, expansion and distribution of laboratory animal resources for research communities.
- Permanent preservation of laboratory animal resources as frozen resources.
- Establishment of a laboratory animal database.
- 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
- Research support for animal experiments
- Functional validation of the genes associated with human diseases
- Provision of the basics of laboratory animal experimentation techniques to animal technicians and researchers
- Establishment of infrastructure for non-clinical evaluation of new drug candidates
- Efficacy evaluation of new drug candidates
- DMPK evaluation of new drug candidates

ACHIEVEMENTS

The largest laboratory animal resource bank in Korea

- Deposits of laboratory animal resources: 1,216 strains
- Distribution of laboratory animal resources: 7,804 animals

Center for quality control of laboratory animals

- Health monitoring: 5,570 animals
- Mouse genotyping: 4,717 animals
- Animal clearing: 141 strains

Training workshop for laboratory animal techniques

- The 41th Laboratory Animal Workshop was held on November 14-15, 2018.

International cooperation with ICLAS, RIKEN and IMPC

- ICLAS: International Council for Laboratory Animal Science.
- RIKEN BRC: RIKEN BioResource Center
- IMPC: International Mouse Phenotyping Consortium.

Support for animal experiments

- IACUC-approved animal experiments: 156 cases
- Service for pathological diagnosis: 53 cases
- Service for hematology and blood biochemistry: 89 cases

Non-clinical evaluation of drug candidates

- Efficacy evaluation of drug candidates: 4,253 cases
- DMPK evaluation of drug candidates: 443 cases

SELECTED PUBLICATIONS

Hepatocyte SHP deficiency protects mice from acetaminophen-evoked liver injury in a JNK-signaling regulation and GADD45 β -dependent manner

Arch Toxicol. 92(8):2563-72.
Chul-Ho Lee

Multi-paratopic VEGF decoy receptor have superior anti-tumor effects through anti-EGFRs and targeted anti-angiogenic activities

Biomaterials. 171:34-45.
Jong Soon Kang

Small activating RNA induced expression of VHL gene in renal cell carcinoma

Int J Biochem Cell Biol. 97:36-42.
Jong Soon Kang

Piperlongumine activates Sirtuin1 and improves cognitive function in a murine model of Alzheimer's disease

J Funct Foods. 43:103-11.
Kyung-Shim Kim and Chul-Ho Lee

Metformin inhibits the development of L-DOPA-induced dyskinesia in a murine model of Parkinson's disease

Mol Neurobiol. 55(7):5715-26.
Kyung-Shim Kim and Chul-Ho Lee

Small heterodimer partner negatively regulates C-X-C motif chemokine ligand 2 in hepatocytes during liver inflammation

Sci Rep. 8(1):15222.
Chul-Ho Lee

Bio-Evaluation Center

The mission of Bio-Evaluation Center is to support development and commercialization of organisms, which were developed using biological engineering tools (gene transformation, cell fusion, or genome editing, etc.). To achieve this goal, the center has established human and physical infrastructure for research and bio-evaluation, consisting of molecular genetic analysis techniques, human- and environment-risk assessment techniques, facilities, and experts. The benefits and risks of organisms for industrialization (living modified organisms, exotic plants, and organisms developed by genome editing or cell fusion, etc.) are evaluated through the entire process from development to commercialization using the established infrastructure, in order to acquire approval from the regulatory authority. The center also advises industries to carry out the optimization and standardization of the process at the developmental stage.

INVESTIGATORS

Soon-Chun Jeong / scjeong@kribb.re.kr

- Molecular genetic characterization of organisms for industrialization
- Plant genetics and genomics

Chang-Gi Kim / cgkim@kribb.re.kr

- Environmental risk assessment of organisms for industrialization
- Plant ecology

Jung-Ho Park / jungho@kribb.re.kr

- Risk assessment of organisms for industrialization
- Protein engineering

Ju Seok Lee / juseoklee@kribb.re.kr

- Molecular genetic analysis of organisms for industrialization
- Soybean genetics

In-Soon Park / bis74@kribb.re.kr

- Molecular genetic characterization of organisms for industrialization



RESEARCH AREAS

Organisms for industrialization

- Living modified organisms (LMOs), exotic plants, and organisms developed by genome editing or cell fusion, etc
- Genetic analysis
- Environmental risk assessment
- Human risk assessment

ACHIEVEMENTS

Development of the infrastructure required for conducting genetic analysis and risk assessments of organisms to be used for industrialization.

Genetic analysis and evaluation technique development

Development of evaluation techniques for genetic analysis and human- and environment-risk assessment, for domestically developed transgenic organisms (soybean, tobacco, and microorganisms).

Bio-evaluation support

Support companies to conduct genetic analysis and evaluate the risk from various transgenic organisms (cabbage, lettuce, water melon, poplar, soybean, rice, and microorganisms)

SELECTED PUBLICATIONS

Levels of Cry1Ac1 protein in herbivorous and predatory arthropods in fields of *Bacillus thuringiensis* cabbage

J Asia-Pac Entomol. 21:1048-53.
Chang-Gi Kim

Survival of *Escherichia coli* harboring nucleic acid-hydrolyzing 3D8 scFv during RNA virus infection

Regul Toxicol Pharmacol. 94:286-92.
Jung-Ho Park

National Primate Research Center

National Primate Research Center (NPRC) was established as a major national non-human primate infrastructure to support industry/academia/research institute, including those involved in xenotransplantation, regenerative medicine, and new-drug discovery for incurable diseases.

INVESTIGATORS

Yeung Bae Jin / ybjin@kribb.re.kr

- Pathologic diagnosis and veterinary clinical care for non-human primates
- Development and pre-clinical evaluation of non-human primate models for human disease

Sang-Rae Lee / srlee@kribb.re.kr

- Development of brain disease models (stroke, dementia, Parkinson's disease) using non-human primates
- Establishment of an efficacy test system with brain disease models
- Development of infectious disease models with non-human primates

Jae-Won Huh / huhjw@kribb.re.kr

- Comparative genomics of humans and non-human primates
- Molecular genetics and primatology
- Identification and molecular characterization of non-human primate genes

Young-Hyun Kim / kyh@kribb.re.kr

- Maintaining quality standards of non-human primate resources by SPF health monitoring
- Comparative analysis of human and non-human primate genomes
- Identification and molecular characterization of non-human primate genes

Kang-Jin Jeong / nemo9426@kribb.re.kr

- Reproduction and maintenance of SPF primates
- Quarantine of non-human primates
- External support services

Youngjeon Lee / neurosci@kribb.re.kr

- Neuroscience and behavioral science
- Development and pre-clinical evaluation of non-human primate models for Alzheimer's disease and Parkinson's disease

Jung Joo Hong / hong75@kribb.re.kr

- Comparative immunology of human and non-human primates
- Understanding the immunologic mechanisms involved in immunization and vaccination using an infectious model of a non-human primate
- Analyzing the safety and efficacy of immune modulators in *in vitro* and *in vivo* non-human primate models

Sang-Je Park / parksj@kribb.re.kr

- Virus monitoring of SPF primate
- Molecular genetics of human and non-human primates
- Quantitative analysis of various species genes

Bon-Sang Koo / porco9@kribb.re.kr

- Veterinary preventive medicine
- Veterinary clinical diagnosis and care for non-human primates and minipigs
- Pathologic and molecular characterization of infectious agents using *in vitro* and *in vivo* systems, including minipigs and non-human primates
- Biosafety management of animal biosafety level 3 facility

Jong-Hee Lee / jonglee@kribb.re.kr

- Stem cell biology of non-human primates and minipigs
- Understanding the developmental and disease mechanisms and the provision of new therapeutics using stem cell technology from non-human primate and minipig models

Seung Hwan Lee / lsh080390@kribb.re.kr

- Development of an effective transgenic animal model using target-specific genome engineering
- Development of a disease model and therapeutic agent by using non-human primates and minipigs
- Development of minipig models for heterologous organ transplantation

Chang-Yeop Jeon / jcy7959@kribb.re.kr

- Bio-medical engineering and radiology
- MR imaging in the development of brain disease models (stroke, Alzheimer's disease, and Parkinson's disease) with non-human primates

Seung-Ho Baek / bsh82@kribb.re.kr

- Molecular imaging using PET-CT

Hwal-Yong Lee / lhy3650@kribb.re.kr

- Reproduction and maintenance of SPF primates

Sung-Hyun Park / ck2816@kribb.re.kr

- Reproduction and maintenance of SPF primates

Won-Suk Choi / choiws@kribb.re.kr

- Reproduction and maintenance of SPF primates

Yoo-Jung Ahn / ayj0610@kribb.re.kr

- Support and management for industrial/academic/research purposes was obtained on using non-human primates and advanced video equipment

Han-Na Kim / hnkim@kribb.re.kr

- Clinical pathological diagnosis for non-human primates and minipigs
- Biosafety management and research support of the animal biosafety level 3 facility

RESEARCH AREAS

Acquisition, propagation, and distribution of specific pathogen free (SPF) non-human primate resources

Acquiring and distributing SPF non-human primate resources to industries/academia/research institutes

Standardization of the processes of handling and regulating lab requirements for non-human primate research

- Maintaining quality standards of non-human primate resources by monitoring bacteria, viruses, and other general health parameters.
- Establishing a standard operating procedure (SOP) by providing guidelines for the breeding and management of non-human primate resources at the international level.

Xenotransplantation research

Transplanting organs (e.g. pancreatic islets, hearts) from transgenic germ-free minipigs into SPF non-human primates, and analyzing the efficacy and safety of the organs transplanted.

Regenerative medical research and applications

Using non-human primate disease models in studies involving cell and gene therapy, and evaluating their efficacy and safety for the treatment of incurable diseases.

Pre-clinical efficacy assessments of newly developed drug candidates

Applying various biodrugs and biomaterials to SPF non-human primates, to evaluate their efficacy.

Evaluation of immunogenicity and safety of vaccine candidates

Testing and assessing the immunogenicity, efficacy, and safety of AIDS and other vaccines.

Development of disease models

- Constructing disease models for incurable non-human primate diseases, which have metabolic pathways that are similar to those of humans, and thus developing new drugs and applications for organ and regenerative research
- Developmental biotechnologies and applications
- Establishing cell resources, including embryonic stem cells, tissue cells, and applying them to cell therapies, nuclear transfers, and the study of molecular mechanisms

Genome research and the establishment of genomic database and support for animal biosafety level 3 (ABL 3) research facilities

Support for infection experiments in non-human primates/minipigs/rodents in preparation of national disaster-level infections/diseases/zoonoses/bio-terror attacks/super bacterial infections

Collaboration and support for nationwide non-institutional research involving non-human primates

Providing specialized technologies and information about non-human primate care and facilities to researchers, and conducting collaborative research for the development of related technologies.

ACHIEVEMENTS

Procurement of SPF non-human primate resources, maintenance, breeding of healthy SPF animals, and pre-clinical evaluation of biomedical technologies

NPRC currently houses the following SPF non-human primates: rhesus monkeys, cynomolgus monkeys.

Transfer of non-human primate-related resources and techniques to national partners of industry/academia/research institute

NPRC shares its non-human primate-related expertise with researchers nationwide, in fields such as neuroscience, pharmacokinetics, etc. NPRC provides services for the upkeep of SPF non-human primates, including microbiological

monitoring, quarantine, and maintenance workshops, and train the personnel (e.g. veterinarians and breeders) who work with non-human primates.

Establishment of disease models using non-human primates

Establishment of production technology for three brain disease models (stroke, Alzheimer's disease, and Parkinson's disease). The MRI and PET-CT systems at NPRC can be used for the establishment of a noninvasive evaluation system for non-human primate brain disease models.

Collaboration with national and international research teams

The center has conducted collaborative studies in various fields, including xenotransplantation and conducted the pharmacokinetic evaluation of therapeutic drugs against aplastic anemia. The center is currently collaborating with world-renowned researchers in the fields of embryo implantation/development and working with domestic companies for the development of minipigs that would be useful in organ xenotransplantation.

Construction of self-sustaining non-human primate resource research facilities to prepare for a turbulent supply of primate resources (Primate Resource Center, Jeonbuk Jeongeup Science-Industry Town)

SELECTED PUBLICATIONS

Successful application of human-based methyl capture sequencing for methylome analysis in non-human primate models

BMC Genomics. 19(1):267.

Jae-Won Huh and Young-Hyun Kim

A novel voxel-wise lesion segmentation technique on 3.0-T diffusion MRI of hyperacute focal cerebral ischemia at 1 h after permanent MCAO in rats

J Cereb Blood Flow Metab. 38(8):1371-83.

Sang-Rae Lee

Oleuropein isolated from *Fraxinus rhynchophylla* inhibits glutamate-induced neuronal cell death by attenuating mitochondrial dysfunction

Nutr Neurosci. 21(7):520-8.

Sang-Rae Lee

Effects of acute and chronic methamphetamine administration on cynomolgus monkey hippocampus structure and cellular transcriptome

Toxicol Appl Pharmacol. 355:68-79.

Sang-Rae Lee



Associate Director Yeung Bae Jin / Tel. +82-43-240-6317 / E-mail ybjin@kribb.re.kr

Futuristic Animal Resource & Research Center

Futuristic Animal Resource & Research Center (FARRC) has been established for contributing to the vitalization of future bio-industries, including new bio-drug discovery, xenotransplantation and regenerative medicine. Further, the center works to address national/social issues, such as artificial blood and foot-and-mouth disease by developing research support system that could be utilized across the government ministries, based on national mini-pig infrastructure that combines the world's best resources, materials, technologies, instruments, facilities, and specialists.

INVESTIGATORS

Sun-Uk Kim / sunuk@kribb.re.kr

- Establishment of developmental biotechnology and regenerative medicine in mini-pigs
- Development and derivation of research resources from mini-pigs
- Establishment of a phenotyping system in mini-pigs

Bong-Seok Song / sbs6401@kribb.re.kr

- Establishment of developmental biotechnology for the generation of transgenic mini-pigs
- Production of early porcine embryos with a high developmental competence

Young-Ho Park / pyh2877@kribb.re.kr

- Development of vector system for transgenesis in mini-pigs
- Establishment of molecular phenotyping system in mini-pigs

Bo-Woong Sim / embryont@kribb.re.kr

- Establishment of high efficiency production system for transgenic mini-pigs
- Development of advanced developmental biotechnology in mini-pigs

Kyung-Seob Lim / dvmlim96@kribb.re.kr

- Veterinary clinical diagnosis and care for large-to-medium experimental animals
- General surgery of large-to-medium experimental animals
- Support veterinary service and pre-clinical tests for biomedical research, using large-to-medium experimental animals

Phil-Yong Kang / gt1300@kribb.re.kr

- Reproduction and maintenance of SPF mini-pigs

Hee-Chang Son / son1989@kribb.re.kr

- Reproduction and maintenance of SPF mini-pigs

RESEARCH AREAS

Obtainment and standardization of specific pathogen free (SPF) mini-pig resources

- Obtained mini-pig resources and developed a new breed
- Standardization of mini-pig resources by SPF/+health monitoring

Supply of mini-pig resources/materials/techniques/information

- Development and support transgenesis techniques in minipigs
- Generation and support transgenic/cloned mini-pigs
- Generation and support an induced/transgenic disease model using mini-pigs
- Development and support mini-pig research resources, including tissues, cells, bloods, nucleic acids, etc.

Industry/academia/research institute support

- Basic biomedical research: neuroscience, genomics, bioinformatics, developmental biotechnology, etc.
- Advanced biotechnology: new bio-drug discovery, xenotransplantation, stem cell medication, regenerative medicine, etc.
- National/social issues: national-wide infectious diseases, bioterrorism, chronic incurable diseases, etc.

Establishment of research needs-customizing/leading infrastructure

- Establishment of user-customizing infrastructure after the analysis of on/off-line research needs
- Establishment of infrastructure required by the user, based on expectations from future research fields

ACHIEVEMENTS

Reproduction and maintenance of SPF mini-pigs

- The center has obtained mini-pigs through breeding and maintenance, under a stable SPF environment.

Derivation of research resources from SPF minipigs

- Support industry/academia/research institute demands and establish somatic cell nuclear transfer method- somatic cell lines were established from a variety of mini-pig tissues.

Establishment of transgenesis/cloning system in mini-pigs

- Transgenic mini-pigs were successfully generated by the production of cloned embryos, embryo transfer into foster mothers, delivery by caesarian section and artificial nursing, indicating the successful establishment of the transgenesis/cloning system in mini-pigs.

SELECTED PUBLICATIONS

Anti-inflammatory effect of gallic acid-eluting stent in a porcine coronary restenosis model

Acta Cardiol Sin. 34(3):224-32.

Kyung-Seob Lim

Melatonin improves the meiotic maturation of porcine oocytes by reducing endoplasmic reticulum stress during *in vitro* maturation

J Pineal Res. 64(2):12458.

Sun-Uk Kim

The effects of kinase modulation on *in vitro* maturation according to different cumulus-oocyte complex morphologies

PLoS One. 13(10):e0205495.

Sun-Uk Kim



International Biological Material Research Center

The center aims to procure biological materials from four overseas regional centers and their neighboring countries through legal routes, within the scope of international collaborative research projects. The mission is to provide researchers with a variety of materials, including indigenous medicinal knowledge and to establish nation's core infrastructure for developing new natural drugs and nutraceuticals, along with other commercially important natural products.

INVESTIGATORS

Sangho Choi / decoy0@kribb.re.kr
· Biodiversity, environmental Science

Sangwoo Lee / ethnolee@kribb.re.kr
· Ethnobotany, biodiversity

Jin-Hyub Paik / jpaik@kribb.re.kr
· Plant Taxonomy, biodiversity

Soo-Yong Kim / soodole@kribb.re.kr
· Plant molecular biology, biodiversity

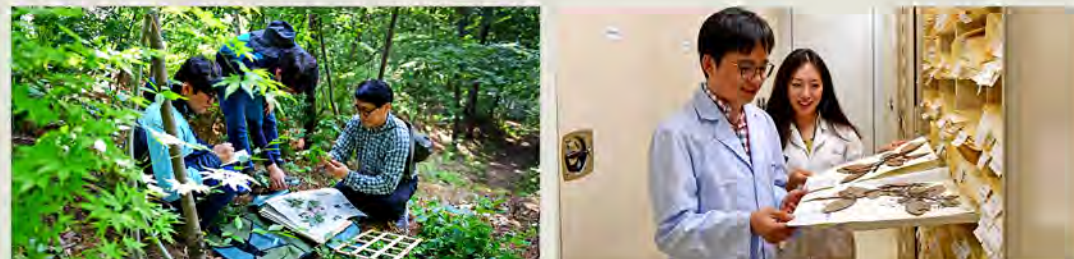
Sangmi Eum / eomsm@kribb.re.kr
· Plant taxonomy, biodiversity

Dong-Keun Yi / lydian78@kribb.re.kr
· Plant systematics, bioinformatics, biodiversity

Kyu Jong Lee / kjlee@kribb.re.kr
· Crop cultivation, crop physiology, crop growth modeling

Mijin Park / mjpark@kribb.re.kr
· Management of four regional research centers and extraction of supplies

Changyoung Lee / changags@kribb.re.kr
· Ethnobotany, biodiversity



Associate Director Sangho Choi / Tel. +82-42-879-8340 / E-mail decoy0@kribb.re.kr

RESEARCH AREAS

- Operation and management of four collaborative biological material research centers for the collection and preparation of biological materials worldwide
- Establishment and operation of comprehensive system and database for managing biological materials and related traditional medicinal knowledge procured from four regional centers and their neighboring countries
- Study of the standardization of highly active biological materials (large-scale cultivation and quality control) for establishment and operation of supply system for leading research groups within the scope of the assigned project
- Phylogenetic analysis and development of DNA barcode for the identification of medicinal plants
- Study of the information-related resources (biological resource access and benefit sharing, related laws, system and local information) for promoting cooperation and utilization among industries

ACHIEVEMENTS

Establishment and operation of International Biological Material Research Center (IBMRC)

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

- Retained biological materials: 34,000 no.
- Deposits of voucher specimens: 80,000 herbarium specimens

Operation and management of four collaborative biological material research centers

- Korea-China Biological Material Research Center (Kunming)
- Korea-Costa Rica Biodiversity Research Center (Heredia)
- Korea-Indonesia Biological Material Research Center (Tangerang)
- Korea-Vietnam Biological Material Research Center (Hanoi)

Establishment and operation of a massive sample supply system

- A massive *Pistacia weinmannifolia* cultivation farm (Kunming, China)
- A massive, open *Diospyros blancoi* cultivation farm (Guacimo, Costa Rica)
- A massive, open cultivation farm for culturing *Lagestroemia ovalifolia* and *Ficus villosa* (Lampung, Indonesia)

International collaborative research

- Status of International Partnership (2018): 36 countries, 43 institutions

Exchange program

- 7 scientists from Vietnam, Indonesia, and Kazakhstan

Books and report

- Useful flowering plants in Nicaragua
- Medicinal plants of Northern LAOS Vol. 1

SELECTED PUBLICATIONS

Enrichment of genomic resources and identification of simple sequence repeats from medicinally important *Clausena excavata*

3 *Biotech.* 8(3):133.
Sangho Choi

Quantification of arbutin in plant extracts by stable isotope dilution gas chromatography-mass spectrometry

Chromatographia. 81(3):533-8.
Sangho Choi

ABS Research Support Center

ABS Research Support Center, an executive office of the Competent National Authority for biological resources management, plays a main role in the provision of comprehensive services for obtaining access to genetic resources and benefit-sharing (ABS) rules under the supervision of the Ministry of Science and ICT (MSIT). The center operates the 'ABS Help-Desk' to provide valuable information about Nagoya Protocol issues and the 'Advanced bioResource Information System (ARIS)' for the convenient utilization of biological resources and information. The Center also studies taxonomy and cultures probiotic anaerobic bacteria to cope with ABS. Another primary responsibility is to manage the following three committees with institutional authority, in terms of legal regulations for ensuring biosafety: Institutional Review Board (IRB), Institutional Animal Care and Use Committee (IACUC), and Institutional Biosafety Committee(IBC).

INVESTIGATORS

Young Hyo Chang / yhchang@kribb.re.kr

- Management of ABS Research Support Center
- Operation of ABS help-desk
- Research on laws, regulations, and current international trends on ABS agenda

Han Chul Lee / hanchul@kribb.re.kr

- Operation of IRB, IACUC, and IBC

Minho An / minho@kribb.re.kr

- Operation of ABS help-desk of MSIT
- Research on laws, regulations, and current international trends regarding the Nagoya protocol and ABS agenda

Taeho Kang / thkang@kribb.re.kr

- Operation of Biological Research Resources Information Center of MSIT
- Operation of Advanced bioResource Information System (ARIS) of MSIT

A Rum Cheon / arum415@kribb.re.kr

- Operation of institutional bio-safety and bio-security

Jayoung Paek / hahahoho@kribb.re.kr

- Taxonomic study and development of probiotic anaerobic bacteria to cope with ABS



RESEARCH AREAS

Project on comprehensive services for ABS agenda

- Research on laws, regulations and current international trends about ABS
- Capacity building and raising awareness through seminars and presentations
- Consult on the access to domestic and foreign genetic resources and their utilization
- Taxonomic study and development of probiotic anaerobic bacteria to cope with ABS

ACHIEVEMENTS

Capacity building and raising public awareness for ABS

- Monthly online publication and distribution of ABS Brief (domestic and international news briefs on the Nagoya Protocol)
- Publication of *Agreement on Access and Benefit-sharing for Academic Research* (ABS Guide for Researchers Series Vol. 6, '18.2)
- Publication of *National ABS Regulatory Frameworks in Central America and Viet Nam* (ABS Guide for Researchers Series Vol. 7, '18.2)
- Publication of *BioTrade and Access and Benefit Sharing: From Concept to Practice* (ABS Guide for Researchers Series Vol. 8, '18.12)
- Holding ABS-related seminars

Management of institutional IRB, IACUC, and IBC

- Publication of *Ethics Guidelines for Researchers* ('18.9)

SELECTED PUBLICATIONS

Capnocytophaga endodontalis sp. nov., isolated from a human refractory periapical abscess

Curr Microbiol. 75(4):420-5.
Young Hyo Chang

Clostridium composti sp. nov., a new anaerobic bacteria isolated from compost

Int J Syst Evol Microbiol. 68(12):3869-73.
Young Hyo Chang



**JEONBUK
BRANCH INSTITUTE**

94-103

Jeonbuk Branch Institute was established in 2006 to develop advanced bio-materials from microorganisms and plants through the application of biotechnology techniques (e.g. biochemical engineering, genetic engineering, metabolic engineering, bioprocess engineering, etc.). The institute mainly focuses on green technologies. The goal is to promote the industrialization of high value-added bio-materials for the applications in bio-based industries such as food, feed, agriculture, health, energy, and environment.

- Functional Biomaterial Research Center
- Microbial Biotechnology Research Center
- Immunoregulatory Materials Research Center
- Biological Resource Center
- Primate Resources Center

Functional Biomaterial Research Center

The center's goal is to develop natural biomaterials with a broad range of biological activities against human or livestock diseases caused by infectious/contagious pathogens, aging, inflammatory, and immune-mediated responses from natural resources (plants, microorganisms, and marine sources).

INVESTIGATORS

Young Bae Ryu / ybryu@kribb.re.kr

- Isolation and structural identification of bioactive compounds from natural products
- Performance of metabolite profiling and analysis
- Disease target enzyme inhibition and kinetic studies

Woo Song Lee / wslee@kribb.re.kr

- Identification of infection-related target molecules and the establishment of screening systems for infectious diseases
- Isolation and structure elucidation of bioactive compounds

Su-Jin Park / sjpark@kribb.re.kr

- Development of active biomaterials by studies of *in vitro* and *in vivo* anti-viral activity and their mechanisms of action
- Molecular genetic analysis and pathogenesis of viruses causing enteritis & pneumonia (coronavirus, rotavirus, influenza virus, etc.) in cows, pigs, and poultry
- Histopathologic, immunohistochemical, and electro-microscopic studies

Hyung-Jun Kwon / hjkwon@kribb.re.kr

- Animal model establishment and research using animal disease models
- Development of an anti-viral drug to cure veterinary viral infectious diseases and its study
- Development of active biomaterials via studies on *in vitro* and *in vivo* antiviral activity and study of their mechanisms of action

Ji Young Park / loveme@kribb.re.kr

- Establishment of a library and securing of bio-materials through the establishment of an effective search system for bioactive substances
- Purification of bioactive substances from natural materials

In-Chul Lee / leeic@kribb.re.kr

- Development of animal models for viral/bacterial diseases and evaluation of their efficacy *in vivo* using infectious models
- Evaluation of general toxicity of natural biomaterials or bioactive substances
- Evaluation of efficacy of active biomaterials using animal models for studying human diseases (metabolic syndrome and inflammatory diseases)

Kyungsook Jung / jungks@kribb.re.kr

- Studying the therapeutic mechanism of active materials and compounds in experimental animal models for immune diseases



Associate Director Young Bae Ryu / Tel. +82-63-570-5171 / E-mail ybryu@kribb.re.kr

RESEARCH AREAS

Construction of a natural product fraction library

- Construction and utilization of both fractions from plant and microbial culture extracts and a natural compound library
- Isolation and identification of bioactive compounds from natural resource extracts
- Quantitative and qualitative analysis of components from natural resources
- The role of LC-MS in metabolism and pharmacokinetic studies of natural products

Development of bioresource related to neutraceuticals and cosmeceuticals

- Establishment of bioassay and system for screening such biologically active extracts/compounds in target items
- Target items include individuals exhibiting metabolic disease, anti-inflammation, immune regulation, andropause, menopause, benign prostatic hyperplasia, dysmenorrhea, anti-wrinkle, whitening, atopic dermatitis, etc

Construction of bioassay system related to infectious and immune diseases

- Establishment of bioassay and screening system to search for biomaterials or compounds that have a therapeutic effect against pathogen-mediated inflammatory and immune diseases
- Development of active compounds or materials inhibiting inflammatory- or immune-mediated responses and improving the disturbance of immune functions
- Development of active compounds or materials with a therapeutic effect against aging- and metabolism-related diseases

Development of mass-production technologies for useful biological compounds and research into practical technologies via field applications

- Development of mass-production technologies for generating useful biological compounds using pilot plants
- Development of technologies for field applications and the commercialization of useful compounds

ACHIEVEMENTS

Evaluation of natural products for use thereof

Natural products are chemical compounds or substances isolated from living organisms. A study of the chemistry of natural products in-

cludes the investigation of their biosynthesis, extraction, identification, quantification, structural elucidation, physical and chemical properties, and reactivity. They are produced via pathway for primary or secondary metabolism. Plant secondary metabolites can be found in leaves, stem, root, or bark of plant, depending on the type of secondary metabolite that is being produced. The most bioactive secondary metabolites include alkaloids, tannins, flavonoids, and phenolic compounds. The study of these natural products has played a major part in development of medicinal chemistry and functional foods/cosmetics, and the center is now starting to understand the important role of these compounds/extracts.

- Isolation of secondary metabolites in natural products.
- Chemical and spectroscopic strategies for structure elucidation (UV, IR, and NMR)
- Performing quantitative/qualitative analysis using HPLC and an ultra high-performance liquid chromatography-high-resolution tandem mass spectrometric method (UPLC-HRMS-MS/MS), which was developed for the standardization of secondary metabolites in extracts
- In addition, the center has built a natural product fraction library, and collecting plant resources, and utilizing both plant extracts through open column chromatography in addition to natural product library.

Animal model establishment and research using animal disease model

- Development of animal models for efficaciously generating neutraceutical biomaterials *in vivo*
- Development of animal models for studying viral/bacterial diseases and the evaluation of *in vivo* efficacy using infectious models

Identification of biomaterials against inflammatory diseases

Development and utilization of cell-based screening system for new active substrates with anti-inflammatory activity:

- Screening system for inhibitors of NF- κ B signaling
- Screening system for inhibitors of JNK/AP-1 signaling
- Screening system for inhibitors of COX-2/PGE2

Identification of biological targets and pharmacological properties:

- Development of active compounds showing anti-inflammatory activity through the inhibition of NF- κ B signaling, JNK/AP-1 signaling, and TLRs
- Development of active compounds showing

inhibitory effects on human disease-related enzymes (such as alpha-glucosidase, tyrosinase, etc.)

- Development of active compounds showing anti-oxidative activity because of scavenging of highly reactive oxygen radicals and elevating the levels of intrinsic anti-oxidants
- Development of active compounds showing inhibitory effects on pathogen-related enzymes related to internalization, replication, and release (such as3CLSP, etc.)

SELECTED PUBLICATIONS

Design, synthesis, and evaluation of curcumin analogues as potential inhibitors of bacterial sialidase

J Enzyme Inhib Med Chem. 33(1):1256-65.
Woo Song Lee and Young Bae Ryu

Copper nanoparticles induce early fibrotic changes in the liver via TGF- β /Smad signaling and cause immunosuppressive effects in rats

Nanotoxicology. 12(6):637-51,
In-Chul Lee

Preventive effect of garlic oil and its organo-sulfur component diallyl-disulfide on cigarette smoke-induced airway inflammation in mice

Nutrients. 10(11):e1659.
Hyung-Jun Kwon

Microbial Biotechnology Research Center

The goal is to develop biotechnologies and bioprocesses for the production of microbial metabolites, proteins, industrial enzymes, and bioenergy, all of which are useful for pharmaceutical, nutraceutical, dietetic, cosmetic, feed, fine chemical, and other industries.

INVESTIGATORS

Jeong-Woo Seo / jwseo@kribb.re.kr

- Development of microbial strains and bioprocesses for integrated biorefinery
- Development of biotechnological process for bio-oil production and its utilization using microorganisms

Jae Jun Song / jjsong@kribb.re.kr

- Development of platform technologies for performing screening on a large-scale and the commercialization of industrially valuable enzymes using the HTS system
- Development of technology used to prepare a genomic library from single unculturable microorganisms sorted out from natural sources

Chul Ho Kim / kim3641@kribb.re.kr

- Biorefinery and bioenergy, functional biomaterials, bioprocess

Min Soo Kim / ms5732@kribb.re.kr

- Development of functional food ingredients using microbial strains

Jong Hyun Choi / jhchoi@kribb.re.kr

- Development of platform technologies for screening useful enzymes/metabolic pathways using high throughput technology
- Development of the tool box applicable to white biotechnology based on synthetic biotechnology

Seonghun Kim / seonghun@kribb.re.kr

- Glycoengineering and glyco (bio)technology
- Development of sugar platform technologies using renewable bioresources

Baek Rock Oh / baerock.oh@kribb.re.kr

- Development of bioprocess engineering
- Biofuels and biochemical production

Ji Young Kang / jiyoka@kribb.re.kr

- Development of microbial materials for prebiotics
- Development of functional materials using microorganisms

Sun Yeon Heo / heosy@kribb.re.kr

- Microbial genomic engineering for the production of value-added products

Yunjon Han / gugin@kribb.re.kr

- High-throughput screening (HTS) system operator
- HTS protocol development
- Microbiome taxonomic profile (MTF) analysis of environmental sample

Binna Lee / skanwodd@kribb.re.kr

- Development of a high-throughput system based on FACS for novel enzyme screening and enzyme engineering
- Bacterial metabolic profiling using LC-MS/MS and CE-MS/MS for synthetic biological processes



Associate Director Jeong-Woo Seo / Tel. +82-63-570-5160 / E-mail jwseo@kribb.re.kr

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
- Production of useful biomaterials by bioconversion

Animal microbiome

- Microbiome taxonomic profile (MTF) analysis of animals
- Development of pre/probiotic materials for industrial animals

Molecular bioprocess engineering

- Production of therapeutic recombinant proteins
- Development of bio-refinery technologies

ACHIEVEMENTS

Microbial strains and processes to produce chemicals

Microbial strains and processes that are optimized to produce valuable chemicals (1,3-propanediol, 2,3-butanediol, 3-hydroxypropionic acid, etc.) were developed via genetic and metabolic engineering, using crude glycerol derived from the biodiesel industry. These can be used as platform chemicals for ecofriendly biochemical industries, producing substances such as bio-plastics, textiles, etc.

Production and utilization of microbial oil

Oleaginous heterotrophic microalgal strains were isolated to enable them to produce lipids containing functional substances, such as polyunsaturated fatty acids and an optimal process was developed. The microbial oil can be valuable as a source of feedstock for the production of biofuels, chemicals, and active substances (drugs, food, and feed ingredients).

Bioenergy

Lignocellulosic biomass is a renewable bioresource for second-generation bioethanol production. These potential sugar resources, derived from various agricultural residuals, contain cellulose, hemicellulose, and lignin. These can be hydrolyzed or enzymatically degraded to sugars, and then be fermented to produce bioethanol. In addition, these sugar platform technologies might be used in various biorefinery processes, to create an environmentally friendly process.

High-Throughput Screening System and Biotechnological Applications

The center developed mass screening methods for various enzymes from metagenomic libraries, using an HTS system based on robots. The center was able to screen new enzymes, such as cellobiohydrolases, glycosyltransferases, BVMO, cold-adapted esterase, and deoxyribose 5-phosphate aldolase (DERA) based on the fluorescence intensity. These new strategies, combined with the HTS system, were able to achieve the screening of various new enzymes faster, and with greater sensitivity and ease than previously reported screening methods. This approach may be applied to other useful enzymes and to the screening for metabolic pathways from metagenomic resources.

Screening enzyme from single cell based polymerase Fosmid cloning

A new method was developed for the enrichment of minor bacteria from environmental samples, and single cell based fosmid libraries were generated from these minor bacterial pools. This method is based on fluorescence in situ hybridization (FISH), fluorescence associated cell sorter (FACS), and multiple displacement amplification (MDA). The center has demonstrated the enrichment of minor bacteria from an artificial microbial community and single cell-based MDA, followed by the construction of a fosmid library for screening the activity.

SELECTED PUBLICATIONS

Cloning, expression, and production of xylo-oligosaccharides by using a newly screened xylanase isolated from bovine rumen

Appl Biochem Biotechnol. 184(4):1347-57.
Jong Hyun Choi

A novel core 1 O-linked glycan-specific binding lectin from the fruiting body of *Herichium erinaceus*

Int J Biol Macromol. 107(B):1528-37.
Seonghun Kim

Herichium erinaceus isolectins recognize mucin-type O-glycans as tumor-associated carbohydrate antigens on the surface of K562 human leukemia cells

Int J Biol Macromol. 120(A):1093-102.
Seonghun Kim

Tabrizicola fusiformis sp. nov., isolated from an industrial wastewater treatment plant

Int J Syst Evol Microbiol. 68(5):1800-5.
Baek Rock Oh

Efficient production of 1,3-propanediol from crude glycerol by repeated fed-batch fermentation strategy of a lactate and 2,3-butanediol deficient mutant of *Klebsiella pneumoniae*

Microb Cell Fact. 17(1):92.

Chul Ho Kim and Jeong-Woo Seo

Immunoregulatory Materials Research Center

The goal of the center is to develop natural biomaterials that possess a broad range of biological elements that combat inflammatory and immune-mediated diseases in human beings or livestock, as well as infectious inflammatory responses and immunological synapses. These biomaterials will be derived from natural resources (plants, microorganisms, and marine sources).

INVESTIGATORS

Young Bae Ryu / ybryu@kribb.re.kr

- Isolation and structural identification of bioactive compounds from natural products
- Metabolite profiling and analysis
- Disease target enzyme inhibition and kinetic study

Mun-Chual Rho / rho-m@kribb.re.kr

- Isolation of active fractions or compounds from natural products, such as plants and microbes, and the identification of structures for active compounds
- Identification of new target molecules related to several immune diseases and establishment of a screening system to develop biomaterials or compounds that combat inflammation and immune diseases

Seung Woong Lee / lswdoc@kribb.re.kr

- Activity-guided isolation of bioactive constituents from natural products
- Chemical structure determination of natural products

Soyoung Lee / sylee@kribb.re.kr

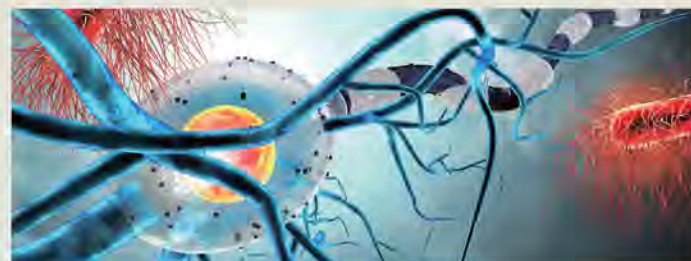
- Evaluation of efficacy and immunotoxicity of natural products and underlying mechanisms
- Development of animal models for immune diseases (Inflammatory Bowel Disease, hypersensitivity, allergic inflammation)

Seung-Jae Lee / seung99@kribb.re.kr

- Development of functional materials including animals and plants from natural products
- Evaluation of inflammatory diseases using the *in vitro* screening system

Chan Sun Park / chansun@kribb.re.kr

- Microorganism screening, sequencing and application



RESEARCH AREAS

Construction of bioassay system related to immune diseases

- Establishment of bioassay and screening system to determine the presence of biomaterials or compounds that have a therapeutic effect against immune diseases, including infectious and inflammatory diseases
- Development of active compounds such as inhibitors of cell adhesion molecules, inflammatory cytokines, and chemokines
- Development of active materials or compounds regulating the innate immune system, such as the Toll-like receptor family
- Development of active materials or compounds that boost immunity, such as the Type I interferon family

Development of mass-production technologies for useful biological compounds and research into practical technologies via field applications

- Development of mass-production technologies for useful biological compounds using pilot plants
- Development of technologies for field applications and the commercialization of useful compounds

Construction of natural product fraction library

- Construction and utilization of both fractions from plant and microbial culture extracts and natural compound library

ACHIEVEMENTS

Identification of biomaterials for modulating immune responses using *in vitro* and *in vivo* system

Development and utilization of cell-based screening system for new active substrates with anti-inflammatory activity:

- Screening system for inhibitors of cell adhesion molecules such as VCAM-1/VLA-4 and sialic glycosaminoglycan/P-selectin
- Screening system for inhibitor of IL-6 signaling
- Screening system for inhibitors of Toll-like receptors

Purification of active compounds from natural resources and determination of the structure

- Development of active compounds showing anti-inflammatory activity through inhibition of cell adhesion molecules, TLRs, and IL-6 signaling

Identification of biological targets and pharmacological properties:

- Norkurarinol showed anti-viral activity through the activation of IRF-3, followed by IFN-beta induction
- The anti-viral effect of KR-200 was demonstrated after coxsackievirus A21 infection: KR-200 inhibited the activation and inflammatory cytokine production of NF-kB and AP-1, which was induced by coxsackievirus A21 infection

- The presence of KR-300 and the active compounds resulted in an inhibition of IL-6 signaling

Verification of *in vivo* anti-inflammatory activity:

- KR-200 and KR-300 inhibited the expression of proinflammatory cytokines (IL-1beta, IL-6, and TNF-α) and mRNAs of inflammatory genes in mice after inflammation.

Evaluation of therapeutic effect on several animal models for immune diseases

- KR-300 ameliorated atopic dermatitis, osteoarthritis, rheumatic arthritis, and inflammatory bowel disease (IBD).
- KR-600 inhibited bone loss in the ovariectomized osteoporosis mice model.

Natural product fraction library

The center has built natural product fraction library, collecting plant resources and utilizing both plant extracts through open column chromatography and natural product library.

SELECTED PUBLICATIONS

Inhibitory effects of compounds and extracts from *Ampelopsis brevipedunculata* on IL-6-induced STAT3 activation

Biomed Res Int. 2018;3684845.

Mun-Chual Rho and Seung Woong Lee

***Portulaca oleracea* extracts and their active compounds ameliorate inflammatory bowel diseases *in vitro* and *in vivo* by modulating TNF-α, IL-6 and IL-1β signalling**

Food Res Int. 106:335-43.

Mun-Chual Rho and Seung-Jae Lee

Biological Resource Center

Biological Resource Center or Korean Collection for Type Cultures (KCTC) is very well known both domestically and internationally. KCTC joined the World Federation of Culture Collections (WFCC) in 1985 and the World Data Center for Microorganisms (WDCM) in 1986. It also gained the status of an International Depository Authority (IDA) from the World Intellectual Property Organization (WIPO) in 1990, under the Budapest Treaty. KCTC currently collects, preserves, and distributes biological resources, including archaea, aerobic, or anaerobic bacteria, molds, yeasts, plant cell lines, animal/human cell lines, and patent strains. All biological resources are extensively quality-controlled. KCTC also endeavors to construct collaborative networks with other BRCs to support both scientific and industrial communities.

Major functions of KCTC:

- Collection, preservation, and distribution of biological resources
- Development of core technologies to foster valuable biological resources
- Construction of collaborative networks and support of services and education associated with biological resources

INVESTIGATORS

Song-Gun KIM / sgkim@kribb.re.kr

- Curator of Gram-negative bacteria
- Taxonomy and characterization of novel bacteria from oxic and anoxic conditions
- Biotransformation and production of natural products using microbial enzymes
- Microbial diversity in environment and human related ecosystems

Cha Young KIM / kimcy@kribb.re.kr

- Metabolic engineering and molecular farming for high-level production of valuable metabolites and proteins (vaccines etc.) in microbes and plant systems
- Development of plant cell and organ culture systems for production of valuable metabolites using bioreactors

Suk Weon KIM / kimsw@kribb.re.kr

- General curator for plant cell resources
- Development and commercialization of plant cell resources (calluses, adventitious roots, shoots, and micro-tubers)

Jung-Sook LEE / jslee@kribb.re.kr

- General curator for microbial resources
- Microbial diversity, taxonomy, and ecology
- Research regarding the human gut microbiome

Doo-Sang PARK / dspark@kribb.re.kr

- Development of lactic acid bacteria resources
- Host-microbe interaction research

Jae Cheol JEONG / jcjeong@kribb.re.kr

- Management of patent resources
- Understanding the epigenetic regulatory mecha-

nisms involved in modulating embryogenesis process in plant cultured cells

- Comparative transcriptomic analysis of plants in response to abiotic and biotic stimuli

Ju Huck LEE / juhuck@kribb.re.kr

- General curator for animal cell resources
- Isolation and identification of gut microbiota in humans and animals
- Development of gut microbiota resources
- Molecular study of bacterial pathogenesis

Seung-Hwan PARK / biopark@kribb.re.kr

- Curation of actinobacteria
- Isolation and identification of gut microbiota in humans and animals
- Study of bacteria-mediated cancer therapy
- Imaging analysis and application development for theranostics

Jiyoung LEE / jiyoung1@kribb.re.kr

- Isolation and characterization of plant growth promoting endophytes
- Exploration of the potential of endophytes from medicinal plants as sources of natural compounds
- Understanding plant-pathogen interactions

Se Won KANG / bioksw@kribb.re.kr

- Bioinformatic analysis of genome and transcriptome in animals, plants, and microbiota
- Metagenomic analysis of the gut microbiome in humans and animals
- Phylogenetic study of biological resources

Mi-Kyung LEE / miklee1010@kribb.re.kr

- Curation of fungal and yeast strain resources
- Collection and commercialization of fungal and yeast strain resources for research activities
- Research for regulation of fungal development

Keun Chul LEE / kcleee@kribb.re.kr

- Preservation and management of archaea, extremophiles, and gram-positive bacterial resources

Moon Soo RHEE / msrhee@kribb.re.kr

- Preservation and management of actinobacterial resources

Kang Hyun LEE / khlee@kribb.re.kr

- Preservation and management of gram-negative bacterial resources

Yong-Jae LEE / tmx@kribb.re.kr

- Development and management of biosystems for database and websites, to support internal and external users of biological resources

Min Ok JUN / ksmimo@kribb.re.kr

- Arrangement of training program for Asian Consortium for the Conservation and Sustainable Use of Microbial Resources (ACM)
- Support for gram-negative α - and β -bacterial resources

Mi Kyung EOM / mkeom@kribb.re.kr

- Preservation and management of gram-negative and anaerobic bacterial resources

Eun Yee JIE / jeannie@kribb.re.kr

- Management of plant cell line development: acquisition, preservation, sale, quality control, and building utilization system

Sang-Mi LEE / sm1219@kribb.re.kr

- Administrative affairs related to general deposit, patent deposit, security deposit, research result deposit

Jun-Mo YEON / jmyeon@kribb.re.kr

- KCTC Biological Resources Management program development work.
- Development of KCTC homepage.

Han Na CHOE / hanna86@kribb.re.kr

- Preservation and management of fungal resources

So-Yeon KIM / yeon9851@kribb.re.kr

- General distribution of biological resources and organizing workshops

Chan Seok YUN / godddung@kribb.re.kr

- Preservation and management of microbial resources produced after performing research projects supported by government funds

Won-Jeong CHOI / yori0902@kribb.re.kr

- Preservation and management of animal cell lines, animal viruses, and bacteriophages
- Preservation Associate Director

Yu Jeong JEONG / yjjeong@kribb.re.kr

- Large-scale plant cell cultivation and plant culture cell library construction
- Metabolic engineering and metabolite farming for high-level production of valuable metabolites from plant cell culture

RESEARCH AREAS

Acquisition and Management of biological resources

- Collection and preservation of core biological resources for research activities
- Distribution of biological resources to academia, research institutes, and industries

Development of core technologies for biological resources

- Development of platform technologies for isolation, long-term preservation, and application of useful biological resources

Construction of infrastructure networks and support for services and education related to biological resources

- Construction of local and global networks for biological resources
- Support training workshops, conferences, and consultations

Construction and application technology development of the infra-system for Korean gut microbiome

- Establishment of the Korean gut microbiome bank
- Support Korean gut microbiome research and industry

Development and management of valuable plant cell resources

- Development, collection, preservation, and distribution of plant cell resources (calluses, adventitious roots, shoots, and micro-tubers)
- Mass production of valuable plant cell resources using bioreactors
- High-level production of useful metabolites by eliciting responses from plant cells

Development of core technologies for plant cell differentiation and plant regeneration

- Development of core technologies for cell differentiation and regeneration of useful plant resources
- Establishment of a national platform for the genome editing of useful plant resources

Biotechnological application of plant-associated microbes

- Collection, isolation, and identification of plant associated microbes
- Application of useful natural products from plant associated microbes

ACHIEVEMENTS

- KCTC has collected 34,626 biological resources nationally and internationally, and distributed 6,453 strains to research organizations, such as universities, research institutes, and private companies in 2018.

- Biological resources of KCTC include 6,544 patent strains, 5,797 proteobacteria, 4,875 molds, 4,604 actinobacteria, 4,009 firmicutes, 2,672 yeasts, 1,658 microalgae, 262 archaea, 703 plant cell lines, 185 animal/human cell lines, and 3,317 other resources.

- KCTC provides workshops and training courses on the cultivation, preservation, and management of biological resources for domestic users of bioresearches as well as international researchers who are ACM members. Last year, 11 domestic workshops were provided and the 8th international training course on microbial taxonomy was held for 6 weeks in KCTC, in conjunction with 7 international ACM members from Malaysia, Thailand, Iran, Indonesia, Mongolia, Vietnam, and Philippines.

- KCTC is conducting "The Korean Gut Microbiome Bank (KGMB) Project," which includes the metagenomic analysis of the human gut microbiome and the isolation of real bacterial resources such as anaerobic bacteria, from Korean people.

- KCTC is currently developing database for rapid identification of fungal species by matrix-assisted laser desorption/ionization time of flight mass spectrometry (MALDI-TOF MS).

- Researchers at KCTC have published 25 scientific papers, including descriptions of 20 microbial

taxa in 2018.

- KCTC acquired 342 novel type strains that were reported in international taxonomy journals in 2018.

- In addition, biological resources of KCTC have been cited by over 421 research papers in 2018 (based on Scopus).

- KCTC and WDCM are collaborating on the project GCM* 2.0 to determine the whole genome sequence of microbial type strains. KCTC also takes an active part in ACM proceedings for discussing collaborative plans for the conservation and sustainable use of biological resources with BRC in Asian countries.

*GCM: Global Catalogue of Microorganisms

SELECTED PUBLICATIONS

Jatrophihabitans telluris sp. nov., isolated from sediment soil of lava forest wetlands and the emended description of the genus *Jatrophihabitans*

Int J Syst Evol Microbiol. 68(4):1107-11.

Jung-Sook Lee

Sulfitobacter aestuarii sp. nov., a marine bacterium isolated from a tidal flat of the Yellow Sea

Int J Syst Evol Microbiol. 68(5):1771-5.

Song-Gun Kim

Methyl jasmonate increases isoflavone production in soybean cell cultures by activating structural genes involved in isoflavonoid biosynthesis

J Agric Food Chem. 66(16):4099-105.

Cha Young Kim and Jae Cheol Jeong

Plant synthetic GP4 and GP5 proteins from porcine reproductive and respiratory syndrome virus elicit immune responses in pigs

Planta. 247(4):973-85.

Cha Young Kim and Jae Cheol Jeong

Bacterial diversity of bat guano from Cabalorisa Cave, Mabini, Pangasinan, Philippines: a first report on the metagenome of Philippine bat guano

PLoS One. 13(7):e0200095.

Doo-Sang Park



Primate Resources Center

Primate Resource Center (PRC) is the largest non-human primate infrastructure in Korea. Non-human primates in PRC are extensively quality-controlled by means of health monitoring (e.g., infectious viruses and bacteria) in order to maintain specific pathogen free (SPF) non-human primate resources. In addition, PRC endeavors to construct collaborative networks to support industry, academia, institute for non-human primate research, including for neurodegenerative disease models, regenerative medicine, and new-drug discovery related to incurable diseases.

INVESTIGATORS

Ji-Su Kim / kimjs@kribb.re.kr

- Development of transgenic animal models in xenotransplantation research and support
- Establishment of developmental biotechnology and regenerative medicine in non-human primates
- Development and derivation of research resources from non-human primates

Seung-Bin Yoon / ellysbin@kribb.re.kr

- Production of early monkey embryos with a high developmental competence
- Research of molecular mechanism used for early embryogenesis in monkeys
- Support SPF monkey mass production system

Yeonghoon Son / sonyh@kribb.re.kr

- Veterinary clinical diagnosis for non-human primates
- Support veterinary care and histopathological diagnosis
- Behavioral analysis of group-housed primates

Dong-Ho Lee / luckyberry@kribb.re.kr

- Veterinary clinical diagnosis and care for non-human primates
- Establishment of environment enrichment strategies for non-human primates

Ja-Rang Lee / jrlee@kribb.re.kr

- Health monitoring of SPF non-human primate resources
- Comparative genomics of human and non-human primates
- Functional genomics of the non-human primate model

Sangil Lee / sangil0120@kribb.re.kr

- Reproduction and maintenance of SPF non-human primates
- Handling and training non-human laboratory primates
- Support experiments using non-human primates

Ki Jin Kim / kj0211@kribb.re.kr

- Reproduction and maintenance of SPF non-human primates
- Handling and training of laboratory primates

Sang-Yong Lee / active@kribb.re.kr

- Observation of non-human primate health conditions
- Development and construction of primate research infrastructure

Se-Yong Kim / seyong093@kribb.re.kr

- Reproduction and maintenance of SPF non-human primates
- Support experiments using non-human primates

Taeho Kwon / kwon@kribb.re.kr

- Development and functional validation of primate disease models
- Establishment of molecular phenotyping of primates
- Studies on regulation of cancer and cancer stem cells in primates

Min seong Kim / minseongkim@kribb.re.kr

- Establishment of standard operating procedure for primate group feeding
- Development of primate welfare programs for behavior enrichment

Byoung-Jin Park / parkbj@kribb.re.kr

- Reproduction and maintenance of SPF non-human primates
- Establishment of cell line and derivation of research resources from non-human primates

Jun-Ki Lee / junki@kribb.re.kr

- Development and management of facility for studying non-human primate behavioral-activity
- Construction of non-human primate group breeding SOP

Yu-Jin Jo / joyj@kribb.re.kr

- Support development of transgenic non-human primate models
- Breeding for standardization of non-human primates

RESEARCH AREAS

Maintenance, production, and distribution of non-human primate resources

- Establishment and preservation of laboratory nonhuman primate resources
- Construction of stable breeding colony for non-human primate 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, and environment enrichments
- Establishing 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 of non-human primate disease models

- Constructing disease models for incurable non-human primate diseases, which have metabolic pathways that are most similar to those of humans, and thus developing new drugs and applications for organ and regenerative research
- Establishing methods for analyzing behavioral patterns in non-human primate models

Collaboration and support for industry-academia- institute research groups using non-human primates

- Provision of external researchers with expertise and information on care methods and facilities for the large-scale reproduction of non-human primates, and conducting collaborative research to develop specific related technologies in industries, universities, institutes, and hospitals

ACHIEVEMENTS

Maintenance and breeding of healthy SPF animals, and preclinical evaluation of biomedical technologies

- PRC currently houses two types of macaques: *Macaca mulatta* (rhesus monkeys) and *Macaca fascicularis* (cynomolgus monkeys).

Distribution of non-human primate-related resources and techniques to national partners in industry, universities, institutes, and hospitals.

- PRC shares its non-human primate-related expertise with researchers nationwide. The center provides services for upkeep of SPF non-human primates, including microbiological monitoring, quarantine and maintenance workshops, and training of personnel (e.g., veterinarians and breeders), who work with non-human primates.

Collaboration with national and international research teams

- The center conducts collaborative studies in various fields, including xenotransplantation and the pharmacokinetic evaluation of therapeutic drugs against aplastic anemia. The center currently is collaborating with world renowned researchers to study embryo implantation and development.

SELECTED PUBLICATIONS

Impact of long-term RF-EMF on oxidative stress and neuroinflammation in aging brains of C57BL/6 mice

Int J Mol Sci. 19(7):e2103.
Yeonghoon Son

Long-term RF exposure on behavior and cerebral glucose metabolism in 5xFAD mice

Neurosci Lett. 666:64-9.
Yeonghoon Son





DIVISION OF
RESEARCH STRATEGY

106-113

Division of Research Strategy is responsible for creating national agenda programs. The division also extends policy support to biotechnological industries by providing biosafety information and undertaking biotechnology policy research.

- Korean Bioinformation Center
- Biotech Policy Research Center
- Korea Biosafety Clearing House
- National Research Safety Headquarter

Korean Bioinformation Center

Korean Bioinformation Center (KOBIC) has been designated as the National Information Center of Biological Research Resources by the act for the acquisition, management, and utilization of biological research resources. KOBIC plays the following major roles:

In the field of bio-resource information, it collects and integrates information about bio-resources and biodiversity observed nationwide, across institutions and ministries, to facilitate sharing and utilization of bio-resource data. To achieve this, Korean Bioresource Information System (KOBIS), the database for Korean bio-resource information, is also operated.

In the field of bioinformatics, the center serves as the national center for omics data produced by studies funded with national R&D grants, and operate data repository known as BioData. From the Post-Genome Multi-Ministry Genome Project in Korea, the center also collects data and provides a cloud computing-based genome analysis system known as Bio-Express. The center carries out R&D to develop various bioinformatics databases and tools, and carries out scientific genomics studies. For conducting collaborative and outreach activities, various genomics projects in Korea are supported, bioinformatics data analysis services and bioinformatics education programs are provided by the center.

INVESTIGATORS

Yong-Kyung Choe / ykccoruk@kribb.re.kr
· Management of Korean Bioinformation Center

Byungwook Lee / bulee@kribb.re.kr
· Bioinformatics, software development

Seungwoo Hwang / swhwang@kribb.re.kr
· Bioinformatics

Tae-Eun Jin / tejin@kribb.re.kr
· Bio-resource policy, bio-resource information

Yong-Min Kim / ymkim@kribb.re.kr
· Bioinformatics

Pan-Gyu Kim / pgkim@kribb.re.kr
· Software development, bioinformatics

Seongjin Park / psj420@kribb.re.kr
· Bio-resource information

Jin Ok Yang / joy@kribb.re.kr
· Bioinformatics, bio-resource information

Iksu Byeon / isbyeon@kribb.re.kr
· Computer system administration

Kwang Hoon Cho / khcho@kribb.re.kr
· Bio-resource information

Gukhee Han / hgh87@kribb.re.kr
· Software development

Insu Jang / insoo078@kribb.re.kr
· Database, software, and bioinformatics tool development

Yong Jin Jeon / yjjeon@kribb.re.kr
· Bio-resource information

Gunwhan Ko / kogun82@kribb.re.kr
· Software development

Bang Hyuck Lee / lbh12@kribb.re.kr
· Computer system administration

Wangho Song / wangho84@kribb.re.kr
· Software development

Jong-Cheol Yoon / yescheol@kribb.re.kr
· Computer system administration

RESEARCH AREAS

Bio-resource Information Division

- Operation of Korean Bioresource Information System (KOBIS)
- Nationwide bioresource data integration across institutions and ministries
- Strategic planning of national management of bioresource information

Computing Infrastructure and Development Division

- Development of core software and systems (KOBIS, BioData, Bio-Express)
- Construction and management of computing hardware infrastructure

Bioinformatics Division

- Bioinformatics data analysis service
- Bioinformatics education service
- Development of various bioinformatics databases, tools, and pipelines

ACHIEVEMENTS

The national Biological Research Resource Information Center in Korea operates Korean Bioresource Information System (KOBIS), which integrates nationwide bioresources and biodiversity information across institutions and ministries. To ensure its role as the national bioresource hub for expanding the impact of data sharing and utilization is fulfilled, the center has been continuously improving the data quantity and content of KOBIS since 2011.

Genomics studies have continuously resulted in a huge amount of data, which is often more than the amount that can be analyzed by individual research labs. Therefore, it is necessary to have adequate infrastructure, to allow the analysis and sharing of biological big data, for maximizing their scientific potential and value. KOBIC as the national bioinformatics center, operates BioData, a repository of genomics data produced from research supported by national R&D funds.

KOBIC also assists both large- and small-scale genomics research activities in Korea. The most notable example of large-scale national genomics research activities is the Post-Genome Multi-Ministry Genome Project in Korea. For this project, the center developed and operated a cloud computing-based genome analysis system known as Bio-Express, to provide a comprehensive genomics data analysis environment. Through KOBIC research support program, the center also assists individual researchers, who are in need of expert bioinformatics support for their small-scale projects. In addition, the center offers bioinformatics education programs in the form of workshops and online programs.

Over last decade, KOBIC collaborated with the research community and pioneered the development of public resources for data-sharing, databases, analysis pipelines, and research, as evident in many published papers, including data regarding the first Korean human genome sequence in 2009. All the activities mentioned were made possible by the center's ever-expanding computing infrastructure, which is the largest among bioinformatics research centers in Korea.

SELECTED PUBLICATIONS

Closha: bioinformatics workflow system for the analysis of massive sequencing data

BMC Bioinformatics. 19(Sup 1):43.
Byungwook Lee

GEMicCL: mining genotype and expression data of cancer cell lines with elaborate visualization

Database. 2018:bay041.
Byungwook Lee

3DIV: a3D-genome Interaction Viewer and database

Nucleic Acids Res. 46:D52-7.
Byungwook Lee

Pan-cancer analysis of somatic mutations and transcriptomes reveals common functional gene clusters shared by multiple cancer types

Sci Rep. 8(1):6041.
Yong-Min Kim



Biotech Policy Research Center

Nominated and established by the Ministry of Science and ICT in 2004, Biotech Policy Research Center is a non-profit organization devoted to the research and development of biotech policy and policy alternatives. The mission of the center is the following:

- ① To provide government officers with accurate, relevant, and timely information on biotech trends.
- ② To act as a think tank, to develop biotech R&D strategy and help government officers.
- ③ To build networks with opinion leaders and act as a platform for the generation of ideas.

The center also operates a portal site (BioIN, www.bioin.or.kr) to enhance public knowledge of biotechnology and biotechnology policies.

INVESTIGATORS

Heoung-Yeol Kim / yeolhee@kribb.re.kr

- Research on biotech R&D activities and technological innovations

Seong Hoon Moon / shnb8@kribb.re.kr

- BT policy planning and policy research, biotechnology support act
- BT industrial trends research

Moo Woong Kim / moongkim@kribb.re.kr

- BT emerging technologies and statistics
- BT policy website (www.bioin.or.kr)
- Bio information system for lab to market acceleration

Young Cheol Kim / yckkr@kribb.re.kr

- Bio-infrastructure issue research and analysis
- BT R&D project planning

June Hyuck Yang / yangjh@kribb.re.kr

- BT industrial trend research
- BT R&D project planning

Min Jung Kim / bestkmj@kribb.re.kr

- BT policy planning and tech trend research
- BT R&D project planning

Hyeon Su Kim / lawghost@kribb.re.kr

- Bio regulation / legislation issue research
- BT R&D project planning

Sung Hoon Park / rock@kribb.re.kr

- BT policy website (www.bioin.or.kr)
- Bio information system for lab to market acceleration

Ju Yeon Park / juyeon@kribb.re.kr

- International cooperation (OECD), MD – PhD fostering program
- Establishment of international cooperation network and responding to issues

Ji Yeon Lee / jylee1@kribb.re.kr

- Bio-Infrastructure Issue monitoring & research
- Publication of BioINPro

Ji Hyun Lee / ljih@kribb.re.kr

- Biotechnology white paper / domestic and foreign public relations booklet
- Promotion of public issues (media, forum, etc.)

Yoon Jung Hong / hongyj79@kribb.re.kr

- BT information analysis
- BT statistics/industry



RESEARCH AREAS

Policy Planning

- To plan a comprehensive national policy and strategies to foster biotechnological research and development.

Policy Research

- To investigate technology, industry, infra, and institutional policy information, and conduct the relevant analysis of patent maps, and statistical and bibliometric analysis.

Information(Issue)Gathering/Disseminating

- To systematically provide information regarding biotechnology and biotechnology policy on portal sites (www.bioin.or.kr).

Public Relations

- To publish biotechnology white papers and organize public workshops to enhance public knowledge of biotechnology.

ACHIEVEMENTS

Policy Planning

- Planning for the third Biotechnology Fostering Basic Plan-Science Technology-based Bioeconomy Innovation Strategy 2025.
- Planning of large-scale projects for survey and analysis of national R&D programs.
- Analysis of portfolio and positioning of national R&D projects.
- Establishing a strategy for innovation in the bioinfrastructure sector that forms the basis of bioresearch activities, such as life research resources, facilities, equipment, and research support services
- Research on BT regulatory issues and operation of "bio regulatory sinmungo (dealing with any complaints or inquiries)"

Emerging Technology Forecast and Statistical Development

- Discover promising and emerging BT technologies that would affect the industrial and technological fields in the next 5 to 10 years
- Publish annual reports on domestic and overseas statistical data for biotechnologies categorized by investment, human resources, industry, and technology.

Information system for bio discovery to market acceleration

- Establishment and provide service of information system for promoting national bio R&D industrialization, by supporting R&D and technological commercialization of small and medium-sized bio venture companies and researchers

Expert Network & International Collaboration

- Operate the Bio Innovation Growth Convention for conducting BT Seminars and BT expert discussions
- Participate in the annual session of OECD Working Party on biotechnology, nanotechnology and converging technology (BNCT).

Policy Website

- Operate website in regards to BT policies, to enhance the policy makers' understanding of detailed data on domestic and overseas BT policies.
- The site currently covers for at least 100,000 pieces of data.

Korea Biosafety Clearing House

Korea Biosafety Clearing House (KBCH) is dedicated to the promotion of public awareness and exchange of information regarding living modified organisms (LMOs). While implementing the legal duties associated with LMO related information, as per the “Cartagena Protocol on Biosafety” and the “Act for Transboundary Movements”, etc. of LMOs, KBCH also functions as the national focal point of the biosafety clearing-house, installed under the “Cartagena protocol on biosafety,” and is now expanding internationally to particularly promote sub-regional cooperation with regard to biosafety.

INVESTIGATORS

Doo-Byoung Oh / dboh@kribb.re.kr

· Management of Korea Biosafety Clearing House (KBCH)

Homin Jang / hmjang@kribb.re.kr

· Information management and risk communication about living modified organisms and other related topics, such as genome editing, white biotech, etc.

Gicheol Kim / kgccc@kribb.re.kr

· Establishment of KBCH strategies and monitoring of living modified organisms, biosafety and related topics

Byongchul Shin / bcshin@kribb.re.kr

· Management of adherence to CBD/ABS information, and Industrial genome information center

Wonhee Kim / whkim7@kribb.re.kr

· Sharing and management of information regarding biosafety and international cooperation for capacity building on biosafety

Jeongsuk Jo / chojs@kribb.re.kr

· Analysis of trends and promotion of public awareness and participation regarding LMOs and biosafety

Gookche Jeon / bobos302@kribb.re.kr

· Publication of trends in LMO related Industries(White Biotech) / collecting and sharing of post-genome data from MOTIE funded projects

Mihee Jeon / mhjeon@kribb.re.kr

· Management of budget and affairs

Dongho Won / wondh84@kribb.re.kr

· Education and promotion of the industrial LMO, and establishment of strategies for industrial biotechnology

Seongyun Kim / sykim@kribb.re.kr

· Improvement of the legal system related to Biosafety and mediation of work between government agencies under the jurisdiction of the LMO safety management

Geon-Ha, Moon / ghmoon@kribb.re.kr

· The risk assessments and Biosafety management measures for the industrial LMO

Hyosuk Lee / lhs9197@kribb.re.kr

· Publication of Whitepaper and Biosafety Journal, management of KBCH website, survey of public perceptions

Sunhee Park / sh1214@kribb.re.kr

· Communication activities to raise public awareness and participation in LMO and biosafety

RESEARCH AREAS

Implementation of the Biosafety Protocol & LMO Act

- Perform information-related duties such as collection and dissemination
- Implementation of administrative matters (preparation of country reports, analysis of major issues in CP-MOP management of expert forums for discussion of major issues, etc.)
- Support developing countries' capacity-building efforts
- Implementation of the LMO Act (for the operation of the Biosafety Committee, to provide support for the implementation of the LMO Act and achieve further improvements)
- Industrial LMO safety management (operation of Industrial LMO Risk Assessment Committee, as consigned by the Ministry of Trade, Industry, and Energy, according to government guidelines)

Improvement of Public Awareness & Communication

- Management of Biosafety portal, Asia BCH Family regional portal, and family sites
- Publications such as the 'Biosafety Whitepaper' (biennial), 'Biosafety' Journal (semiannual), etc.
- Hosting of communication activities (LMO forums, international seminars, debate competitions, KBCH reporters, etc.)

Survey & Research

- Survey of public perceptions
- Establishment of database exhibiting LMOs and BIO related statistics
- LMOs and bioindustry trend analysis
- Analysis of the industrial impact of the ABS Protocol

ACHIEVEMENTS

Compliance with the LMO Act and Biosafety Protocol

KBCH officially started its work in January 2008, when the LMO law and the Biosafety Protocol came into effect in Korea, even though its actual work in the management of LMO information began before. The primary mission of KBCH is to undertake the duties mandated by the LMO Act and Biosafety Protocol that are associated with information management, i.e. the transfer, handling, and use of LMOs. These duties include the collection and distribution of unbiased information about LMOs, as well as efforts to increase public awareness and participation in activities related to LMOs.

Promotion of public awareness and participation

To promote awareness and participation, KBCH puts efforts in order to ensure biosafety, as stipulated in the protocol. Above all, KBCH is trying to ensure that both positive and negative views on LMOs and find their ways to the public arena, through the promotion of open public discussions about all LMO-related issues. To this end, it operates the “Korean Biosafety Portal,” participates in discussions on websites, and distributes materials published by KBCH, such as the semiannual “Biosafety”, a biennial “White Paper on Biosafety”, and various booklets. The center also hosts seminars (LMO forums, etc.), which are public events for sharing opinions and “Biosafety Debate Competition” among high school students every year.

Implementation of Korea biosafety capacity-building initiative

At COP-MOP7 in 2014, Korea had proposed Korea Biosafety Capacity Building Initiative in order to contribute to BCH capacity building, along with parties of developing countries and economies in transition. Under the initiative, two main programs were implemented by KBCH. The first program aims to assist parties in Asia, to build capacities for their national BCH operations and achieve full compliance with the protocol. To achieve this, KBCH hosted the '4th Asia BCH Family-Informal Consultative Committee (ABF-ICC)' in 2018. The second program aims to explore collaborative areas with regard to biosafety, among Asian countries. In 2018, KBCH held the '2nd Asia Forum: Genome Editing' in Gangneung, in which 18 participants from 9 countries took part as either speakers or chair persons. This forum mainly focused on the development of genome editing technology and whether it should be regulated or not. Participants agreed to try to develop a regional cooperation system that could improve the level of safety management and follow-up on the world trends with regard to genome editing. With these activities, KBCH has been once again able to consolidate its status as the leader of the Asia BCH Family.



National Research Safety Headquarter

National Research Safety Headquarter is responsible for the evaluation and management of biological safety under the act for the establishment of a safe laboratory environment and the transboundary movement, etc. of the Living Modified Organisms Act. Further, the center contributes to the prevention of accidents at laboratories and improvement of R&D productivity, by establishing a professional and systematic safety management system within domestic laboratories.

INVESTIGATORS

Young-Hee Roh / rohyh@kribb.re.kr
· National Research Safety Headquarter

Hwang-Won Lee / leehw@kribb.re.kr
· Safety Planning and Policy Department

Kyung-Hwa Choi / choi978@kribb.re.kr
· Safety Planning and Management Department

Seong-Pil Chung / chungsp4@kribb.re.kr
· Laboratory Policy Team

Ji-Eun Park / jumpje@kribb.re.kr
· Laboratory Education Team

Myung-Hwan Lee / lmh0884@kribb.re.kr
· Laboratory Safety Team

Sung Yun Yu / igpen@kribb.re.kr
· Planning and Management Team

Yeon-Ju Noh / safety@kribb.re.kr
· Culture and Information Team

In-Ja Song / injasong@kribb.re.kr
· LMO Policy Team

Sun-Hwa Lee / ssun@kribb.re.kr
· LMO Education Team

RESEARCH AREAS

Field inspection of laboratory safety management

- Strengthen safety management through field inspection, including inspection of the current state of safety management.
- Analyze accident statistics, conduct an online fact-finding survey, and manage reports on designation of managers of safe laboratory environments, etc.

Develop safety management policies and operate support policies

- Support enactment and revision of laboratory safety law, plan and develop policies for systematic laboratory safety management
- Develop detailed technological standards and guidelines for laboratory safety, etc.
- Operate 'a system for certifying exemplary laboratories in safety management', 'projects to create and improve safe laboratory environments', and 'establishment of dedicated organization for safety management'

Conduct laboratory safety training

- Develop policies and institutions on laboratory safety training
- Develop and operate customized laboratory safety training

National Research Safety Information System

- Provide information on laws and institutions related to the act for the establishment of a safe laboratory environment
- Report the compliance with the act and appointment and change of managers of safe laboratory environments
- Provide information about training and events related to laboratory safety management

Field guidance and inspection in LMO research facilities

- Conduct field guidance and inspection in LMO research facilities, after taking the characteristics of the LMO and organizational structure into account.

Improve LMO laws and institutions and develop policies

- Improve LMO laws and institutions to reflect changes in the research environment
- Establish a reasonable LMO safety management system for conducting experiments and research
- Establish safety management plan for new LMO research facilities.

Provide training on LMO safety

- Develop LMO safety training policies for conducting experiments and research
- Develop, reinforce, and operate LMO safety training programs, including compulsory training and customized training
- Develop and utilize the online LMO training course in Korean and English

Establishment and operation of online training system

- Provide on/offline training on laboratory and LMO safety.
- Inquire about the status of training completion and issue certificates.

Information system for LMO that was developed for test and research purpose

- Provide information about laws and institutions associated with a safe laboratory environment and the transboundary movement, etc. of the living modified organisms act.
- Receive online registrations, including LMO research facility registration and LMO import registration.
- Provide information about training and events related to LMO safety management

ACHIEVEMENTS

Laboratory policy

- Revision of Act on the Establishment of Safe Laboratory Environment and decrees under the act for field-centered safety management(Oct. 2018)
- Operation of a system for certifying exemplary laboratories in safety management(150 laboratories applied and 114 of them obtained certification)
- Promotion of projects to create and improve safe laboratory environments(800 million Korean won for 27 organizations)

Laboratory training

- Conducted laboratory safety training for those who demanded it to be carried out (classroom training: 116 times for 9,805 audiences, online training for 373,532 people)
- Established and conducted the training program for the laboratory safety management committee, to reinforce the awareness regarding safety of upper-level managers in research organizations (Apr. and Oct. '18)
- Developed and utilized customized laboratory safety training modules (provided 32 standard textbooks and lesson plans, 114 e-learning classes, 4 VR materials, and 12 safety training video materials) (Dec. 2018)

Laboratory inspection

- Conducted a survey on the status of laboratory safety management (on 4,178 organizations)
- Conducted field inspection to assess laboratory safety management (470 organizations/2,779 sample laboratories) (Mar. to Oct. 2018)
- Managed laboratory accident statistics (309 cases, as of '18), conducted 16 accident investigations (7 field inspections, 9 document investigations), and disseminated information about cases of accidents (7 times)

LMO policy

- Implemented a self-report campaign for reinforcement of the efficiency of the LMO act (Oct. to Dec. 2018)
- Revised the integrated notification for the LMO Act, to reflect changes in the recent research environment (Nov. 2018)
- Published Experiment/Research LMO FAQ for Field Researchers Vol I (Korean) and guidelines for laboratory response to earthquakes(Dec. 2018)

LMO training

- Implemented LMO safety training for experiments/research (132 training sessions completed by 19,759 people, including online course sessions)
- Developed and utilized LMO online training contents ('18) developed 4 online classes both in Korean and English)

LMO inspection

- Conducted field guidance and inspection of LMO research organizations (161 organizations, 408 facilities) and safety management status inspections (139 organizations, 444 facilities), and inspections on LMO research institutes (512 organizations)

- Published a self-inspection manual for LMO research institutes (Korean/English) and IBC review guidelines (Dec. 2018)
- Published a guidebook on the IBC report and approval procedures for LMO researchers (Dec. 2018)

Information system

Developed a new user-centered function in the national research safety information system

- Included the operation of online harmful factor management register, laboratory safety standard model for each field, etc.

Established and operated the LMO-specialized system

- Used an all-number inspection system to check the implementation of the LMO Act, LMO expert review system, LMO research facility, online inspection system, and field inspection application

Presentation at symposiums

- "Spring Conference of the Korean Society of Safety 2018" A Study on the need and direction for a laboratory safety expert certification system (May 2018)
- "Spring Conference of the Korean Society of Safety 2018" The establishment of measures to ease regulations for low-risk laboratories (May 2018)
- "Spring Conference of the Korean Society of Safety 2018" Investigation on the status of personal protective equipment usage in laboratory and study on improvement direction (May 2018)
- "Fall Conference of the Korean Society of Safety 2018" The study of the ways to improve field inspection of laboratory based on accident analysis (Nov. 2018)
- "Fall Conference of the Korean Society of Safety 2018" Development of new research safety technologies to create safe laboratory environments(Nov. 2018)
- "Fall Conference of the Korean Society of Safety 2018" The study of the current status and further development of e-learning training for laboratory safety (Nov. 2018)
- "ACSEL 2018" A study on improvement of safety education in laboratory in preparation for the changes in research environment(Nov. 2018)
- "ACSEL 2018" Investigation on the status of personal protective equipment usage in laboratory and study on improvement direction (Nov. 2018)

- "ACSEL 2018" Study on accident management improvement through analysis of research lab accidents in Korea (Nov. 2018)



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www.kribb.re.kr

125 Gwahak-ro, Yuseong-gu, Daejeon 34141, Korea
Tel. +82-42-860-4114 Fax. +82-42-861-1759