Korea
Research
Institute of
Bioscience and
Biotechnology

KRIBB

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Korea Research Institute of Bioscience and Biotechnology Annual Report 2011

KRIBB

2011 ANNUAL REPORT

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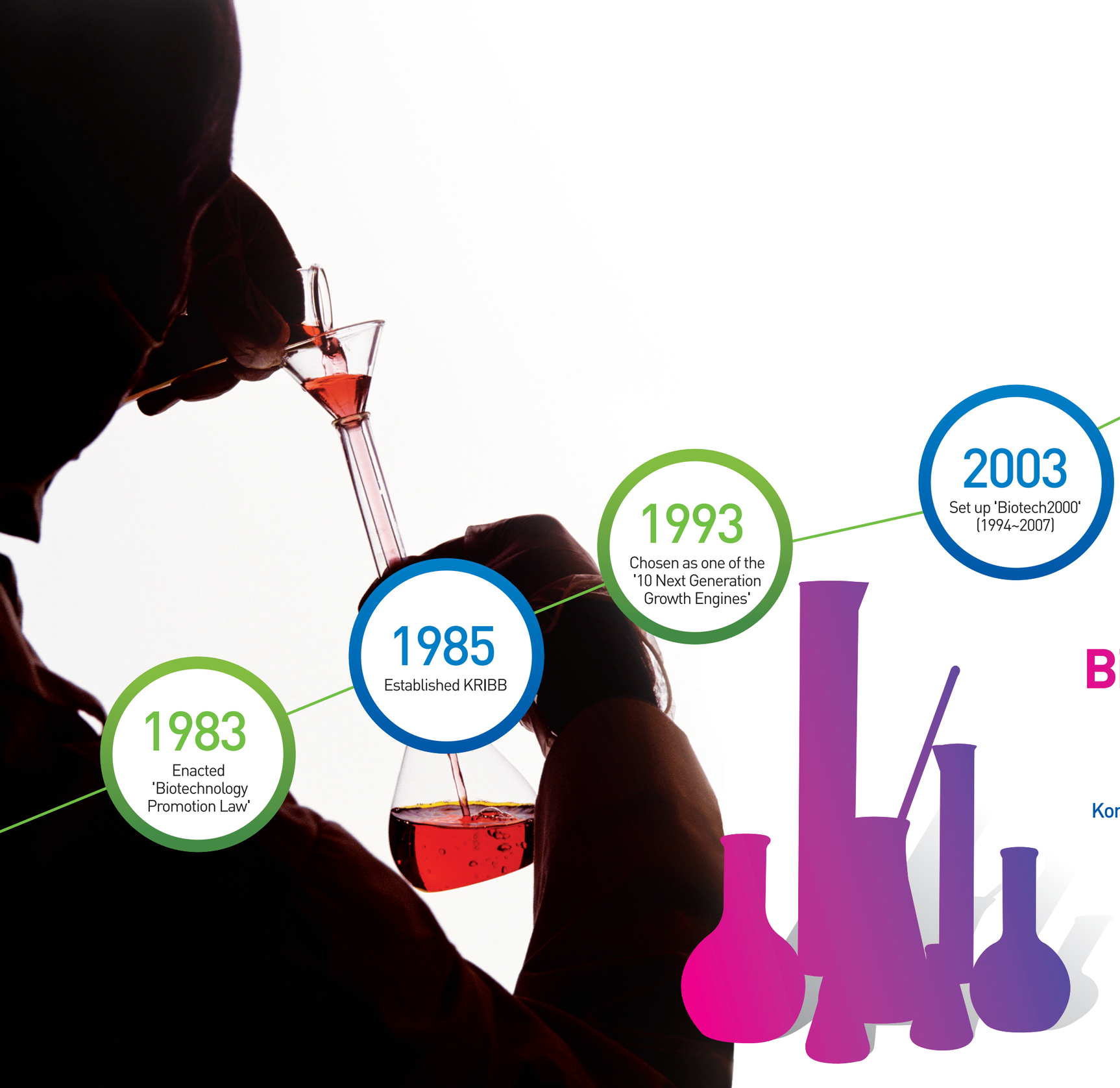
A Message from the President

Biotechnology plays an important role in human welfare, in the living environment and economic growth. The Korea Research Institute of Bioscience and Biotechnology (KRIBB) has provided cutting-edge technologies in the areas of public health, agriculture, bio-nanotechnology and bio-energy, over the 27 years since its establishment in 1985.

Specifically in 2011, KRIBB achieved outstanding research and technology commercialization, including five publications in prestigious international journals such as 'Nature' and 'Science', and initiated a KRIBB joint venture, the 'Institute Company'. In order to further advance innovation, we are now open to global leading research entities for international cooperation. Through our efforts and achievements, KRIBB continues to be a competitive global research organization.

Under our vision of being "A Global Research Institute, Leading Biotechnology Innovations for Humankind", KRIBB will continue to pursue innovative new ways of adding value to bioindustry and improving our living environment through biotechnology.

Dr. Hyouk JOUNG
President



1983
Enacted 'Biotechnology Promotion Law'

1985
Established KRIBB

1993
Chosen as one of the '10 Next Generation Growth Engines'

2003
Set up 'Biotech2000' (1994~2007)

2006
Set up 'Phase 1 of Bio-Vision 2016' (2007~2016)

2011
Set up 'Phase 2 of Bio-Vision 2016' (2012~2016)

Biotechnology Policy in Korea

Korea is now hedging its bet on biotechnology with the highest priority as a next growth engine.

KRIBB

nature immunology

Thioredoxin-interacting protein links oxidative stress to inflammasome activation

The orphan nuclear receptor SHP acts as a negative regulator in inflammatory signaling triggered by Toll-like receptors

Science

Innate immune homeostasis by the homeobox gene Caudal and commensal-gut mutualism in *Drosophila*

Conservation and rewiring of functional modules revealed by an epistasis map in fission yeast

Mapping human genetic diversity in asia

nature genetics

Comparative analysis of chimpanzee and human Y chromosomes unveils complex evolutionary pathway

nature cell biology

Drosophila short neuropeptide F signalling regulates growth by ERK-mediated insulin signalling

Cell

Substrate-specific translocational attenuation during ER stress defines a pre-emptive quality control pathway

Stc1: a critical link between RNAi and chromatin modification required for heterochromatin integrity

Inactivation of peroxiredoxin I by phosphorylation allows localized H_2O_2 accumulation for cell signaling

nature biotechnology

Analysis of a genome-wide set of gene deletions in the fission yeast *Schizosaccharomyces pombe*

nature

Human chromosome 11 DNA sequence and analysis including novel gene identification

Genome evolution and adaptation in a long-term experiment with *Escherichia coli*

nature REVIEWS MOLECULAR CELL BIOLOGY

The N-end rule pathway: emerging functions and molecular principles of substrate recognition responses

nature structural & molecular biology

A metazoan ortholog of SpoT hydrolyzes ppGpp and functions in starvation responses

Bilateral inhibition of HAUSP deubiquitinase by a viral interferon regulatory factor protein

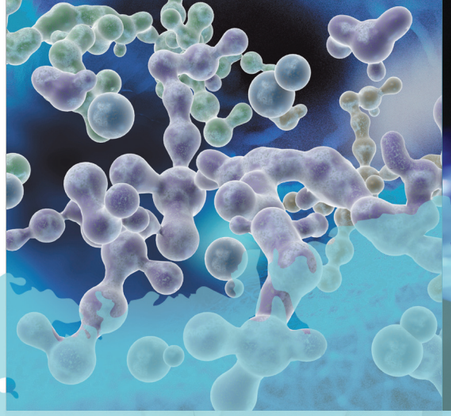
nature medicine

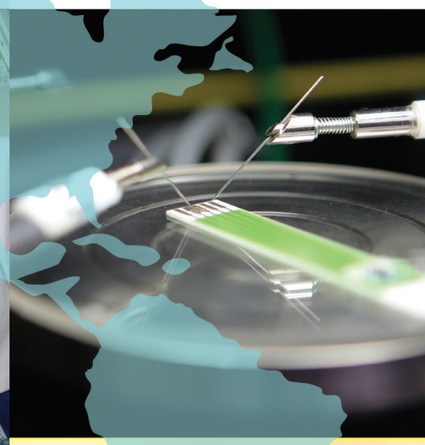
E2-EPF UCP targets pVHL for degradation and associates with tumor growth and metastasis

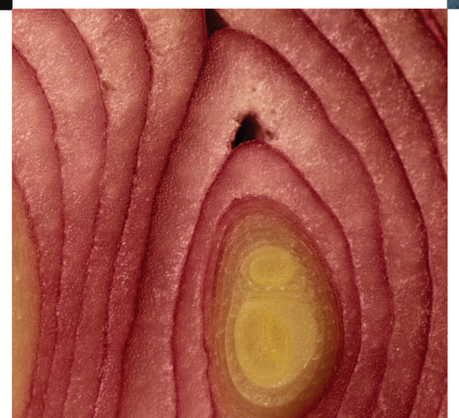
A novel prognostic subtype of human hepatocellular carcinoma derived from hepatic progenitor cells

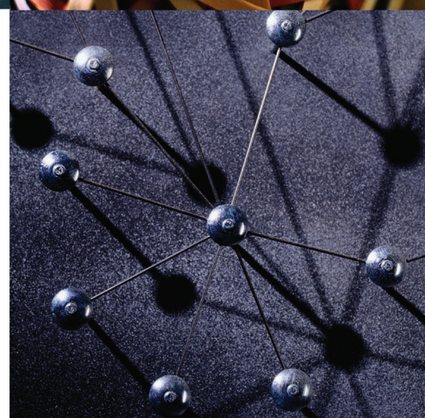
Biotech for Economic Growth and Better Living Standards

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 for Koreans all over. Our goal is to shape a brighter, better and healthier future for all, in Korea and around the world.





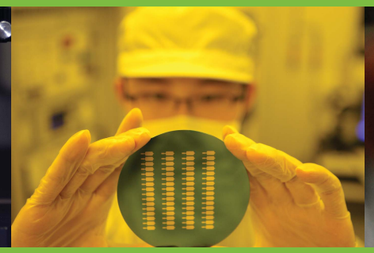




MISSION & VISION

MISSION

- To carry out R&D activities and related projects in the field of bioscience and biotechnology in joint effort with other research institutes, academic, and businesses at home and abroad
- To disseminate the results of its scientific research and technological development



VISION

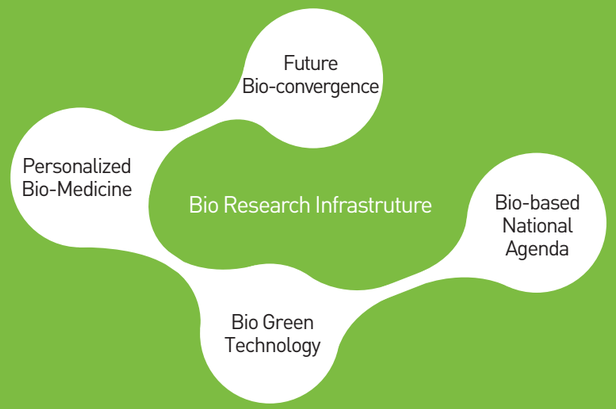
2018 GLOBAL BEST KRIBB

Global Research Institute Leading Bio-Innovation for the Humankind

Generating New Economic Growth Engine
: Five World-class Generic Technologies

Providing Solutions to National Agenda
: Three Internationally Competitive R&D Bases

Establishing World-class Research Infrastructure
: World's Top Five Biotechnology Research Infrastructure



MAJOR OBJECTIVE

CORE DIRECTIONS FOR RESEARCH & BUSINESS PROJECTS

Biotechnology to Create New Economic Growth Engines
- Development of BINT (BT, IT, NT) convergence technology
- Development of disease controlling technologies using stem cells and antibodies
- Identification of targets and development of candidate materials for the diagnosis and treatment of five major diseases
- Development of the generic technology for cell factories and biomaterials

Biotechnology to Address the National Agenda
- Technology Development for infection control
- Fostering R&D on cranial nerves and the aging society
- Development of biomass and bioenergy technology

National Infrastructure to Enhance National Biotechnology Competitiveness
- Improvement of the infrastructure for compiling, managing and utilizing bio resources and data
- Consolidation of the infrastructure for biological assessment and GMO risk assessment

CORE DIRECTIONS FOR ORGANIZATIONAL MANAGEMENT

Improvement of the Framework to Facilitate R&D
- Introduction of an open R&D system and acquisition of competitive human resources
- Strategical selection and concentration
- Expansion of global cooperation

Contributions to the Society and the Country
- Improvement of the ability to respond to future biotechnology demands
- Promotion of demand-based R&D and commercialization of technologies
- Raising public awareness of biotechnology and public interest in science

Improvement of the Management Efficiency
- Promotion of result and objective-oriented management
- Augmentation and efficient allocation of the R&D budget
- Maintenance of an up-to-date and facility infrastructure

GENERAL INFORMATION

FOUNDATION BASIS

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

KEY FUNCTIONS

Advanced R&D and development & distribution of generic technologies in bioscience and biotechnology

- Future bio-convergence, personalized bio-medicine, bio green technology, bio-based national agenda

Public infrastructure development support for research on bioscience at home and abroad

- Public infrastructure development support, national policy think-tank, specialized education and training

HISTORY

- **Feb. 1985 -** Established as a Genetic Engineering Research Center (Seoul)
- **Jul. 1990 -** Moved to Daejeon, Current Location
- **Mar. 1995 -** Changed its name to the Korea Research Institute of Bioscience and Biotechnology (KRIBB)
- **May. 1999 -** Became an independent legal entity under the Korea Research Council of Fundamental Science & Technology (KRCF)
- **Sep. 2005 -** Established Ochang Campus (Bio-Therapeutics Research Institute)
- **Nov. 2006 -** Established Jeonbuk Campus (Bio-Materials Research Institute)

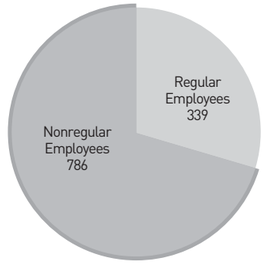
FACILITY

- **Headquarters : 100,978 m²**
  - Human Gene Bank, Plant Extract Bank, KCTC
- **Bio-Theraputic Research Institute (Ochang Campus) : 212,258 m²**
  - National Primate Research Center, Bio-Evaluation Center
- **Bio-Materials Research Institute (Jeonbuk Campus) : 43,559 m²**
  - Applied Microbiology Research Center, Infection Control Material Research Center

YEARLY PROGRESS

PERSONNEL

1,125

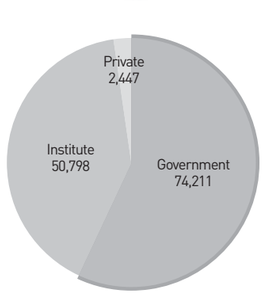


BUDGET (million won)

141,700

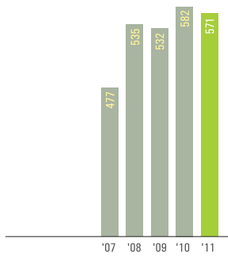
RESEARCH EXPENSES (million won)

127,456



PUBLICATIONS (items)

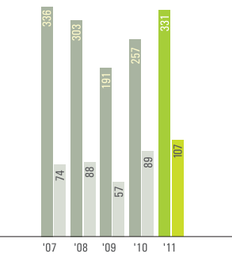
571



- Domestic _ 99
- Overseas _ 472

PATENTS (items)

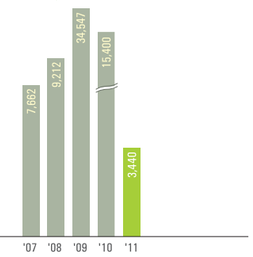
331/107



- Domestic & Overseas Application _ 331
- Domestic & Overseas Registration _ 107

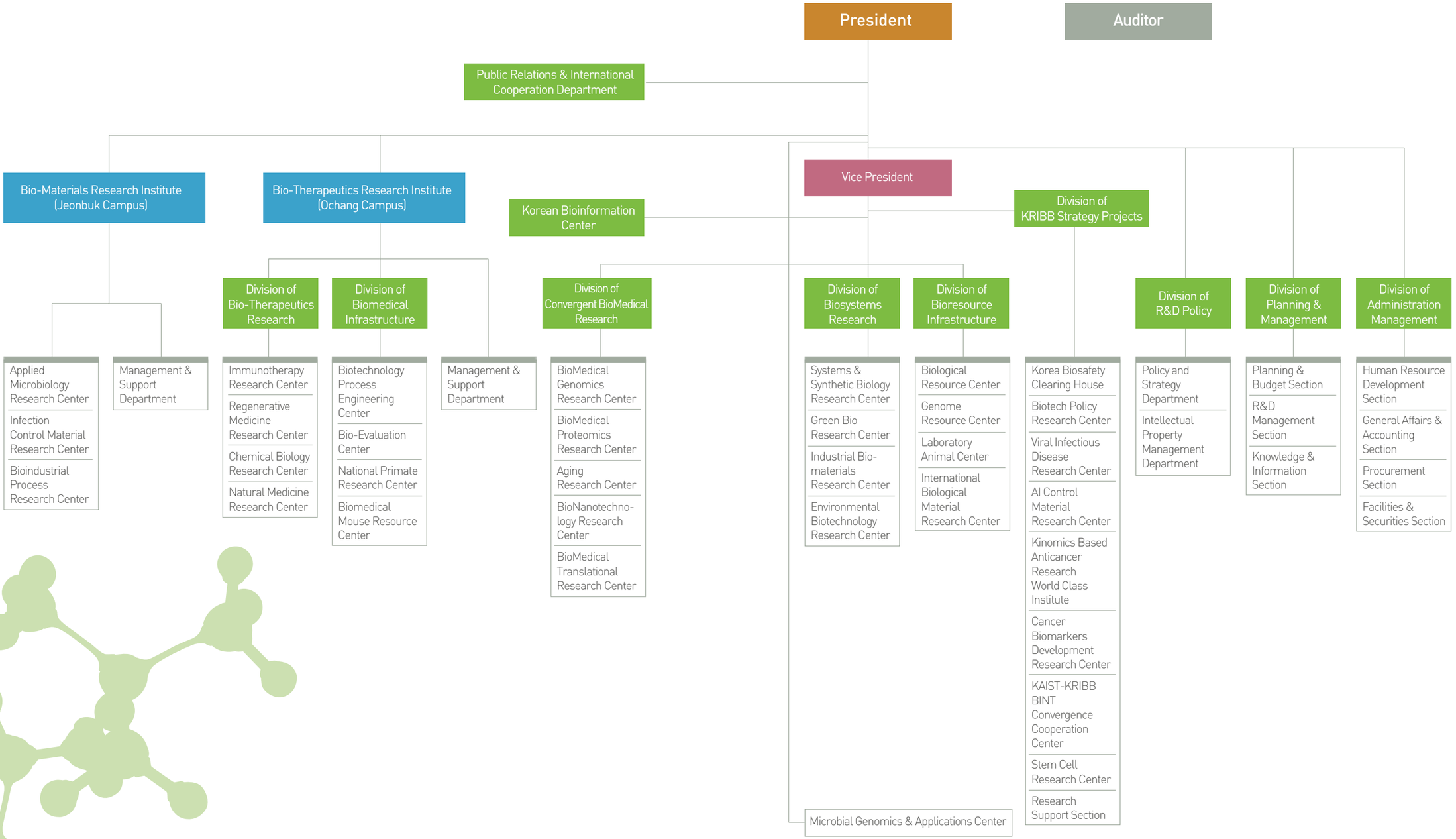
TECHNOLOGY TRANSFERS (million won)

3,440



- Domestic _ 3,395 (19 items)
- Overseas _ 45 (1 item)

ORGANIZATION



RESEARCH INFRASTRUCTURE

1985
Biological Resource Center

1995
Natural Product Plant Extract Bank

2001
Biotechnology Process Engineering Center

2003
Korean Bioinformation Center

2005
Human Gene Bank

2006
National Primate Research Center

2007
Bio-Evaluation Center
Genome Resource Center

2010
International Biological Material Research Center

2012
Miniature Pig Resource Center

RESEARCH DIRECTION

Emerging Technology

Commercialization
Industrialization
Local-based Cooperation

National Bio Agendas
Bio Infrastructures

Ochang Campus

Drug Discovery
Oriental Medicine
Bioinfrastructure
: Toxicology

Daejeon HQ

Genomics
Proteomics
BioNanotech
Neurobiology
Bioinformatics

Oncology
Plant Biotech
Industrial Biotech
Microbiology

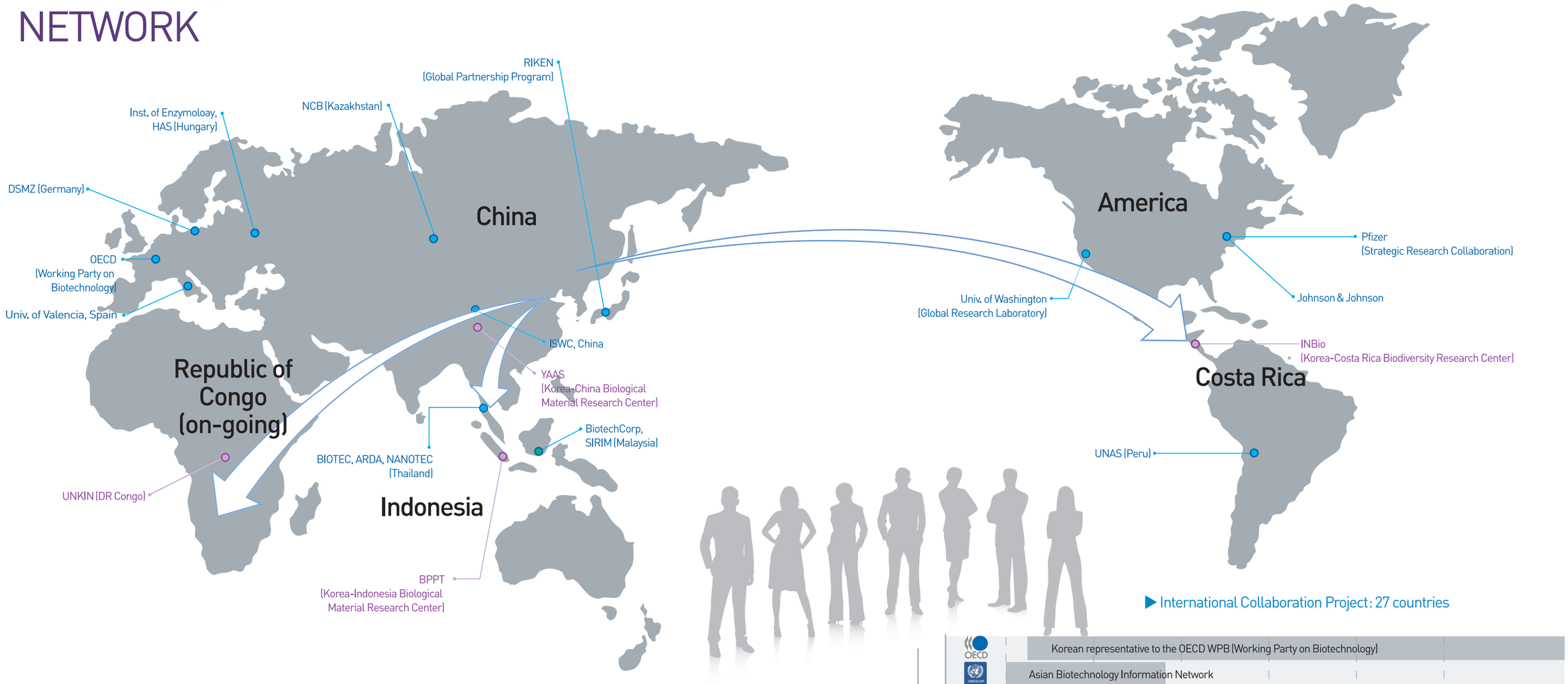
* GT : Green Technology

Ochang
Daejeon
Jeonbuk

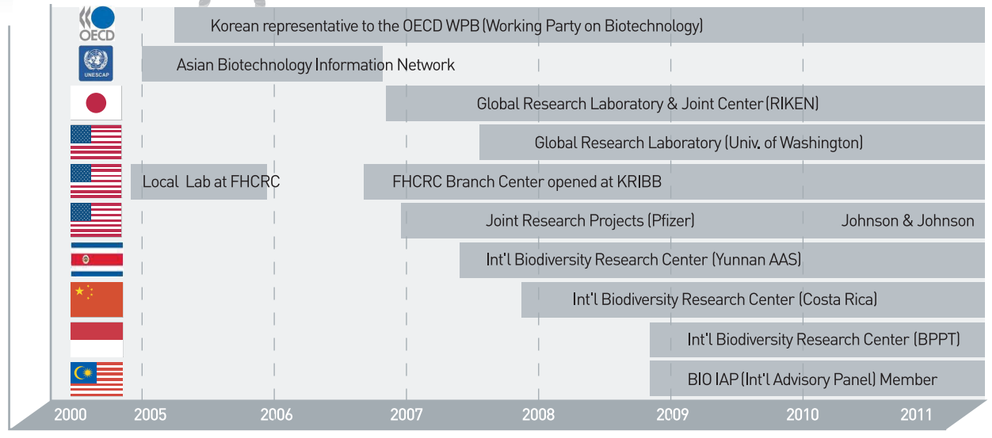
Jeonbuk Campus

Microbial Tech
Bio-Materials

INTERNATIONAL NETWORK



▶ International Collaboration Project: 27 countries



To strengthen its global cooperation in mutually beneficial relationships

▶ Globalization business from Ministry of Education, Science & Technology, Korea
- World Class Institute (WCI) Program, Global Research Laboratory (GRL)

▶ Research collaboration with Pfizer, J&J and RIKEN

▶ Established a network for the preservation and utilization of biological material with China, Costa Rica, Indonesia, and Africa region.

Cutting-Edge Biotechnology Research and Creation of Bioindustry

At KRIBB, we conduct cutting-edge research of biotechnology for our society and economic growth in the field of medical healthcare, foods and agriculture, and bioenergy. We are also fostering the creation of new bioindustry in Korea.

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Division of Convergent BioMedical Research

BioMedical Genomics Research Center

BioMedical Proteomics Research Center

Aging Research Center

BioNanotechnology Research Center

BioMedical Translational Research Center

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Improving the Quality of Life Technology Innovations for Unmet Medical Needs

KRIBB is developing platform technologies for therapeutics for cancer and aging treatment. Based on bionanotechnology, we also providing new innovations in disease diagnostics.

Division of Convergent BioMedical Research

BioMedical Genomics Research Center

Our goal is to establish world-class genomics-based technology platforms and to apply them to biomedical research programs. This will achieve high-throughput identification and global function analysis of the genes associated with diseases most prevalent in the Korean population, such as colon, stomach and liver cancers. We also conduct functional and chemical genomics research to discover validated targets and biomarkers for the development of effective diagnostics and therapeutics.

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RESEARCHERS

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‣ Identification and functional study of therapeutic novel targets related to cancers and large-scale collection of full-length human cDNAs

Young Il Yeom yeomyi@kribb.re.kr
‣ Genomic analysis of cancers and identification and functional validation of therapeutic targets

Dong-Soo Im imdongsu@kribb.re.kr
‣ Identification and validation of target for cancer therapy

Yong Sung Kim yongsung@kribb.re.kr
‣ Epigenomics in gastric and colon cancers

Mi Sun Won misun@kribb.re.kr
‣ Functional validation of candidate target genes and development of anticancer drugs by chemical screening and study of modes of action

Hee Gu Lee hglee@kribbre.kr
‣ Production and application of antibodies for functional analysis of cancer related genes

Dong Cho Han dchan@kribb.re.kr
‣ Study of cancer cell migration and metastasis using chemical biology

Kyung-Sook Chung kschung@kribb.re.kr
‣ Development of anticancer drugs by chemical screening and study of modes of action

Jae Wha Kim wjkim@kribb.re.kr
‣ Isolation and characterization of tumor related molecules

Eun Young Song eysong@kribb.re.kr
‣ Investigation of cancer diagnostic markers

Seon-Young Kim kimsy@kribb.re.kr
‣ Functional genomics approach to understand human cancers

Kyung Chan Park kpark@kribb.re.kr
‣ Large-scale screening and identification of cancer related genes

Cho-Rok Jung crjung@kribb.re.kr
‣ Functional analysis of genes associated with cancer

Seon-Jin Lee sjlee@kribb.re.kr
‣ Functional study of novel targeting molecule in cancer and microenvrionment

Bo Kyung Kim kimbk@kribb.re.kr
‣ Study of regulation mechanism and validation of therapeutic target

RESEARCH AREAS

‣ Establishment of a functional and chemical genomics research infrastructure and technology platforms
‣ Large-scale screening and identification of disease related genes
‣ Functional validation of candidate target genes and biomarkers for therapeutics and diagnostics development
‣ Development of tools and strategies for modulating therapeutic targets and monitoring biomarkers / Development of a diagnostic assay system
‣ Production and application of antibodies for functional analysis of novel genes

ACHIEVEMENTS

Development of therapeutic target genes for liver cancer

We analyzed human HCC tissues using a combination of transcriptome profiling and cell chip technologies and identified 682 genes that show frequent expression changes in HCC and bear functional relevance to the development of liver cancer. We have collaborated with Pfizer to define top-priority therapeutic targets for HCC from this candidate gene pool, and identified a limited number of promising targets, some of which are being advanced to an early stage of drug development.

Identification of DNA methylation markers for lineage commitment of *in vitro* hepatogenesis

We profiled gene expression and DNA methylation of three cell states of *in vitro* hepatogenesis-hESC, definitive endoderm and hepatocyte-using microarray analysis. Among 525 state-specific expressed genes, 67 showed significant negative correlation between gene expression and DNA methylation. State-specific expression and methylation of target genes were validated by quantitative reverse transcription-polymerase chain reaction and pyrosequencing, respectively. To elucidate genome-scale methylation changes beyond the promoter, we also performed high-throughput sequencing of methylated DNA captured by the MBD2 protein. We found dynamic methylation changes in intergenic regions of the human genome during differentiation.

ADGO 2.0: interpreting microarray data and list of genes using composite annotations

ADGO 2.0 is a web-based tool that provides composite interpretations for microarray data comparing two sample groups as well as lists of genes from diverse sources of biological information. This new version has the following additional features: first, it provides multiple gene set analysis methods for microarray inputs as well as enrichment analyses for lists of genes. Second, it screens redundant composite annotations when generating and prioritizing them. Third, it incorporates union and subtracted sets as well as intersection sets. Lastly, users can upload their own gene sets (e.g. predicted miRNA targets) to generate and analyze new composite sets. The new ADGO is available at http://www.btool.org/ADGO2.

Development of anti-cancer drug: Technology transfer of anticancer compound, HIF-1 inhibitor

We developed a novel anti-cancer drug candidate "LW7" showing strong tumor-inhibiting ability by regulating HIF-1 expression, and transferred a technology to Ildong Pharmaceutical Co. Ltd. The development was made in collaboration with Dongkuk University. "LW7", an organic compound, has proved effective in suppressing tumor growth, formation of new blood vessels and metastasis when orally administered to animal models of solid tumor with colon, lung, prostate, renal, pancreatic cancer and etc. From these data, it seems to have potential to be developed into a broad-spectrum anticancer drug.

SELECTED PUBLICATIONS

Byoung-Mog Kwon & Dong Cho Han (Co-Corresponding)
J Biol Chem. 286(3):1737-47.
KRIBB11 inhibits HSP70 synthesis through inhibition of heat shock factor 1 function by impairing the recruitment of positive transcription elongation factor b to the *hsp70* promoter.

Hee Gu Lee (Corresponding)
Cancer. 117(12):2608-19.
Up-regulation and clinical significance of serine protease kallikrein 6 in colon cancer

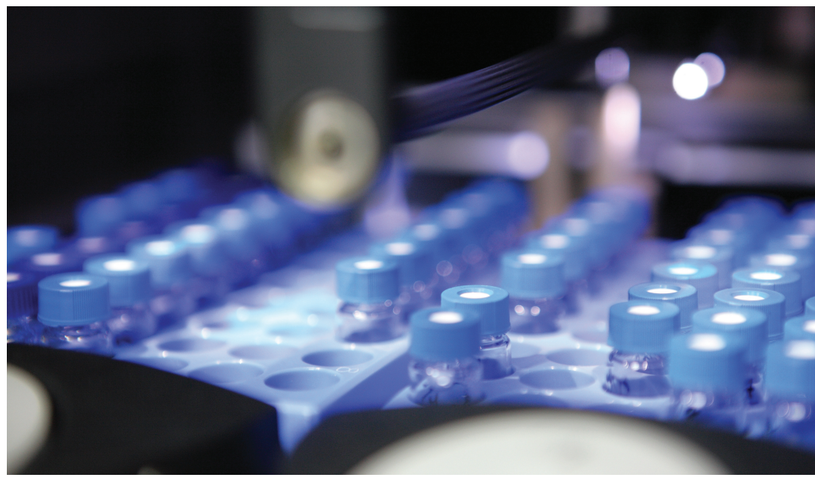
Nam-Soon Kim (Corresponding)
Int J Cancer. 129(9):2124-33.
Human ZNF312b oncogene is regulated by Sp1 binding to its promoter region through DNA demethylation and histone acetylation in gastric cancer

Mi Sun Won (Corresponding)
Carcinogenesis. 32(3):254-61.
Upregulation of RhoB via c-Jun N-terminal kinase signaling induces apoptosis of the human gastric carcinoma NUGC-3 cells treated with NSC12618

Seon-Young Kim (Co-Corresponding)
Nucleic Acids Res. 39(W):W302-6.
ADGO 2.0: interpreting microarray data and list of genes using composite annotations

Yong Sung Kim (Co-Corresponding)
Clin Cancer Res. 17(5):1200-9.
Novel chemosensitive single-nucleotide polymorphism markers to targeted regimens in metastatic colorectal cancer

Yong Sung Kim (Corresponding)
Hum Mol Genet. 20(14):2722-33.
Identification of DNA methylation markers for lineage commitment of *in vitro* hepatogenesis



Division of Convergent BioMedical Research

BioMedical Proteomics Research Center

We will become the R&D hub of nationwide PTPome research in Korea using functional and structural proteomics as a research tool. We are establishing close collaborations with many partner groups in basic research and clinical medicine. Our major research interests include autoimmune disorders, apoptosis, neurodegenerative diseases, stem cell differentiation, and cell signaling.

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RESEARCHERS

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

Byoung Chul Park parkbc@kribb.re.kr
‣ Target mining and validation using proteomics, Signal transduction

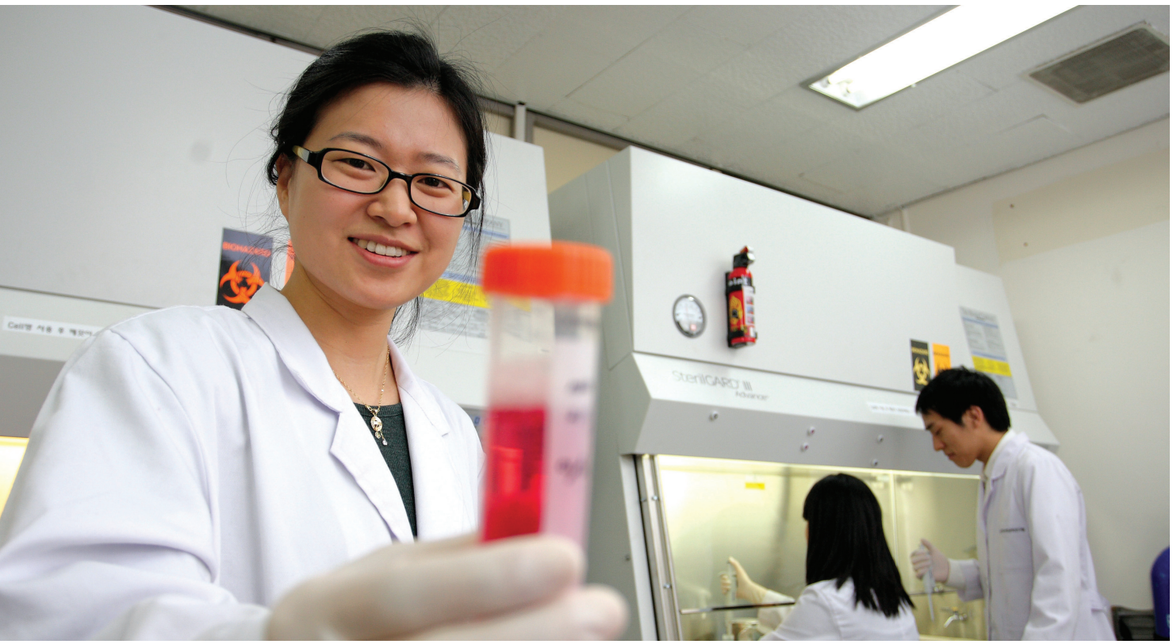
Sang Chul Lee lesach@kribb.re.kr
‣ Discovery of novel biomarkers using proteomic analysis, Stem cell differentiation

Seung Jun Kim ksj@kribb.re.kr
‣ Structural studies on anti-oxidant proteins and protein tyrosine phosphatases, Drug development using 3-D structural information

Seung-Wook Chi swchi@kribb.re.kr
‣ Antiapoptotic drug development using NMR studies
‣ Functional studies on apoptosis-related proteins

Kwang-Hee Bae khbae@kribb.re.kr
‣ Target mining and validation using proteomics and reverse genetics tools
‣ Studies on proteins involved in stem cell differentiation and neurodegenerative diseases

Eui-Jeon Woo ejwoo@kribb.re.kr
‣ Structural and functional studies on DNase and proteins in apoptosis
‣ Hormone nuclear receptors and their application



Sunghyun Kang skang@kribb.re.kr
‣ Aptamers
‣ Proteomics and Mass spectrometry

Dae Gwin Jeong dgjeong@kribb.re.kr
‣ Structural proteomics, Virtual screening for lead compounds

Jeong Hee Moon jhdal@kribb.re.kr
‣ Mass spectrometry

Tae-Sung Yoon yoonts@kribb.re.kr
‣ Structural proteomics, X-ray crystallography

Jeong Hoon Kim jhoonkim@kribb.re.kr
‣ Epigenetics, Transcription regulation

Yun Kyung Kim ykim@kribb.re.kr
‣ Bioconjugate chemistry

Baek Su Han bshan@kribb.re.kr
‣ Stem cell biology

Won Kon Kim wkkim@kribb.re.kr
‣ Stem cell biology

RESEARCH AREAS

Autoimmune disorders
‣ Discovery and functional verifications of biomarkers from patients suffering from immune diseases, e.g. atopic dermatitis, asthma, and rheumatoid arthritis

Apoptosis
‣ Identification and functional studies on new substrates of caspases, key regulators of apoptosis

Neuroscience and neurodegenerative diseases
‣ Proteomic research on neuronal cell functions and neurodegenerative diseases
‣ Differentiation of stem cells
‣ Discovery and functional verification of genes and marker proteins, which are involved in the differentiation of stem cells into various lineages including adipocytes and osteoblasts

Cell signaling
‣ Research on the mechanisms of key cell signaling pathways, e.g. MAPK and NF-κB pathways

Research on structures and functions
‣ Ascertainment of structures, based on X-ray crystallography and NMR, which will lead to findings concerning the unique functions and mechanisms of various proteins (such as protein tyrosine phosphatases and hormone receptors) with medical and industrial importance

ACHIEVEMENTS

Proteomic research on neuronal cell death
Proteomic research led to the discovery of key proteins involved in the apoptosis of neuronal cells. Functional studies of these proteins were conducted.

Research on apoptosis and cell signaling
Proteomic research led to the discovery of regulators of cellular apoptosis and cell signaling. The results were published in major scientific journals.

Structural studies on human protein tyrosine phosphatases (PTPs)
Efforts to determine the complete PTP structure and broadening our understanding of the functions of human PTPs.

SELECTED PUBLICATIONS

Baek Soo Han (Co-First)
Apoptosis. 16(11):1087-100.
Translocation and oligomerization of Bax is regulated independently by activation of p38 MAPK and caspase-2 during MN9D dopaminergic neurodegeneration

Kwang-Hee Bae & Sang Chul Lee (Co-Corresponding)
Mol Biol Cell. 22(24):4883-91.
RPTPμ tyrosine phosphatase promotes adipogenic differentiation via modulation of p120 catenin phosphorylation

Seung Jun Kim (Co-Corresponding)
Acta Crystallogr D Biol Crystallogr. 67(1):25-31.
Exploring binding sites other than the catalytic core in the crystal structure of the catalytic domain of MKP-4

Seung-Wook Chi (Co-Corresponding)
J Am Chem Soc. 133(5):1244-7.
Molecular mimicry-based repositioning of nutlin-3 to anti-apoptotic Bcl-2 family proteins

Tae-Sung Yoon (Co-Corresponding)
J Appl Crystallogr. 44(1):252-3.
A simple technique for consistently obtaining large single crystals of hen egg-white lysozyme in a concentration gradient of $NiCl_2$

Division of Convergent BioMedical Research

Aging Research Center

We investigate the molecular mechanisms of aging process in the aspect of cellular changes and organism degeneration. We are going to develop the fundamental technologies in the prevention and therapeutics for healthy aging.

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RESEARCHERS

Ki-Sun Kwon kwonks@kribb.re.kr
- Characterizing the function of age-associated genes in human muscular aging
- Understanding molecular mechanisms of muscle cell differentiation

Dae-Yeul Yu dyyu10@kribb.re.kr
- Studies on cellular senescence regulated by antioxidant enzymes and aging-associated molecules using MEF cells

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

Jeong Soo Lee jeongsoo@kribb.re.kr
- Developing zebrafish as a model system for studying human genetic disorders related to neural development, angiogenesis, and cancer

Kweon Yu kweonyu@kribb.re.kr
- Molecular genetic studies on aging using the *Drosophila* model system
- Neurophysiological studies of neuropeptides using the *Drosophila* model system

Sung Sup Park ssparkl@kribb.re.kr
- Understanding the pathogenesis of muscle dysfunction (sarcopenia)
- Studies on the molecular mechanisms of neuronal cell death

Kyu-Sun Lee ekuse74@kribb.re.kr
- Development of *Drosophila* model systems for studying age-related diseases including diabetes and neurodegenerative diseases

Kwang Pyo Lee kplee@kribb.re.kr
- Molecular mechanisms of myoblast (satellite cell) differentiation, dysfunction and diseases (aging and sarcopenia)

Young Woo Park ywpark@kribb.re.kr
- Development of biological pre-clinical candidates (such as human monoclonal antibody and soluble receptor-Fc fusion protein) for cancer, autoimmune and muscle diseases

RESEARCH AREAS

- Discovery of new genes involved in the aging process, and studies on signaling pathways therein
- Roles of insulin signaling pathway and stress pathway in the aging process
- Functional identification of aging-related genes using model flies and mice
- Development of drug candidates and biologics for the control of aging-associated diseases

ACHIEVEMENTS

- Identification of aging-related genes in human muscles: We identified up-regulated genes which are involved in the RNA maturation and splicing and various transcriptional regulators, and also discovered down-regulated genes involved in the activities of cell surface receptors and enzymes in mitochondrial electron transport chain.
- We are analysing the broad-range anti-aging mechanisms using animal models, after development of transgenic flies with mutation in energy metabolism and transgenic mice with mutation in antioxidant genes.
- We are developing the biologics on the basis of a new ligand interacting with a receptor related with muscular aging (ACVRII) (under patent registration and technology transfer).

SELECTED PUBLICATIONS

Dae Yeul Yu (Co-Corresponding)
J Biol Chem. 286(34):29872-81.
Hepatitis B virus X protein regulates hepatic glucose homeostasis via activation of inducible nitric oxide synthase

Dae Yeul Yu (Co-Corresponding)
Neurobiol Aging. 32(6):1054-68.
Peroxiredoxin II preserves cognitive function against age-linked hippocampal oxidative damage

Ki Sun Kwon (Corresponding)
J Biol Chem. 286(29):25729-38.
TRIM32 protein sensitizes cells to tumor necrosis factor (TNFα)-induced apoptosis via its RING domain-dependent E3 ligase activity against X-linked inhibitor of apoptosis (XIAP)

Kweon Yu (Co-Corresponding)
BMC Mol Biol. 12:25.
Functional characterization of the ER stress induced X-box-binding protein-1 (Xbp-1) in the porcine system

Division of Convergent BioMedical Research

BioNanotechnology Research Center

Our research center is involved in the development of nano-biochips, nano-biosensors and nano-biomaterials based on the exploitation and utilization of bio-content. By conducting integrated research in the fields of biotechnology (BT), nanotechnology (NT) and information technology (IT), our goal is to develop tools to facilitate new drug discovery as well as new technologies for the diagnosis and treatment of diseases, which will contribute to the creation of new businesses and realize our dream of prolonging human life.

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RESEARCHERS

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▸ Smart biochips & biomolecular process engineering

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▸ Nanotechnology, molecular self-assembly

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▸ Molecular biology, bioelectronics

Yongwon Jung ywjung@kribb.re.kr
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▸ Antibody engineering, biological chemistry

Jin Young Jeong jyjeong@kribb.re.kr
▸ Nanomaterials, Bionanomedicine

RESEARCH AREAS

Protein chips
▸ Development of platform technologies to construct a new generation of protein chips, whose detection systems are free of fluorescence and radioisotopes
▸ Creation of protein chips with bio-content that can be employed in disease diagnosis and in high throughput screening of potential pharmaceuticals

Nanomaterials and bioimaging
▸ Conjugation of inorganic materials, such as metals and magnetic nano-particles, to various organic molecules in order to investigate the characteristics of proteins and to develop new drugs

Nanobiosensors
Development of platform technologies to establish and to economically implement biosensors in early disease diagnosis
▸ Label-free, ultrasensitive nanobiosensing
▸ Bio-content and hardware interfacing
▸ Disease diagnosis biomarker design and production

Mobile life care system
▸ Development of technology for Mobile Life Care Systems, enabling portable healthcare, by combining IT with biochips and biosensor technology

ACHIEVEMENTS

Developed source nanomaterial for multiple-image imaging technology
The team has successfully developed a source nanomaterial for new-concept, multiple-image bio-imaging technology, which is useful for a wide variety of applications ranging from new drug development, disease diagnosis to verification of bio-phenomena.
The development was achieved through synthesis technology of organic and inorganic nanomaterial and interfacing technology between biomaterial and nanomaterial.

The team invented a hybrid nano-imaging probe capable of optical imaging and magnetic resonance imaging. The invention was made through the development of perfluorocarbon having a unique nuclear magnetic resonance spectrum and a quantum dot with high fluorescence ratio and little cell toxicity.

These nano-probes are made of highly sensitive, bio-compatible nanomaterial, which are capable of monitoring *in-vivo* cell movement. They support real-time monitoring of *in-vivo* images including the movement of immune cells within the body and the process of cancer cell treatment, which is particularly useful for cancer treatment.

Furthermore, the team independently developed a next-generation bio-imaging system whereby it is possible to monitor *in-vivo* cell movement using smart phones and smart pads. The system allows researchers to check various image data in real-time, mobile environment without any geographical constraint. The technology is particularly promising for remote diagnosis and medical equipment.

Developed source technology for null micro RNA analysis
Recently, the team successfully developed a series of array analysis methods for null micro RNA multiple analysis. The methods utilize structure-specific RNA-binding protein or hexane plasmodium.
It is particularly noteworthy that the null micro RNA analysis method using hexane plasmodium demonstrates 10 fM sensitivity and higher specificity than any other existing methods, which presents promising opportunity for standardization of micro RNA analysis method. Furthermore, the technology is suitable for a variety of solid-surface applications, which opens up positive prospects for device application of nano-structured material or microfluidics.

SELECTED PUBLICATIONS

Bong Hyun Chung (Corresponding)
Adv Funct Mater. 21(19):3681-9.
Nonstick, modulus-tunable and gas-permeable replicas for mold-based, high-resolution nanolithography

Bong Hyun Chung (Co-Corresponding)
Biomaterials. 32(26):6254-63.
Simultaneous *in vivo* tracking of dendritic cells and priming of an antigen-specific immune response

Bong Hyun Chung (Corresponding)
Biosens Bioelectron. 26(5):2125-9.
Improving Pb^{2+} detection using DNAzyme-ased fluorescence sensors by pairing fluorescence donors with gold nanoparticles

Bong Hyun Chung (Corresponding)
Biosens Bioelectron. 26(5):2805-9.
Naked eye detection of mutagenic DNA photodimers using gold nanoparticles

Bong Hyun Chung (Corresponding)
Biosens Bioelectron. 28(1):454-8.
Label-free electrochemical detection of human-thrombin in blood serum using ferrocene-coated gold nanoparticles

Bong Hyun Chung (Corresponding)
Chem Commun. 47(20):5756-8.
Electric detection of target DNA by fabricating gold nanowire bridges on planar nanogap electrodes

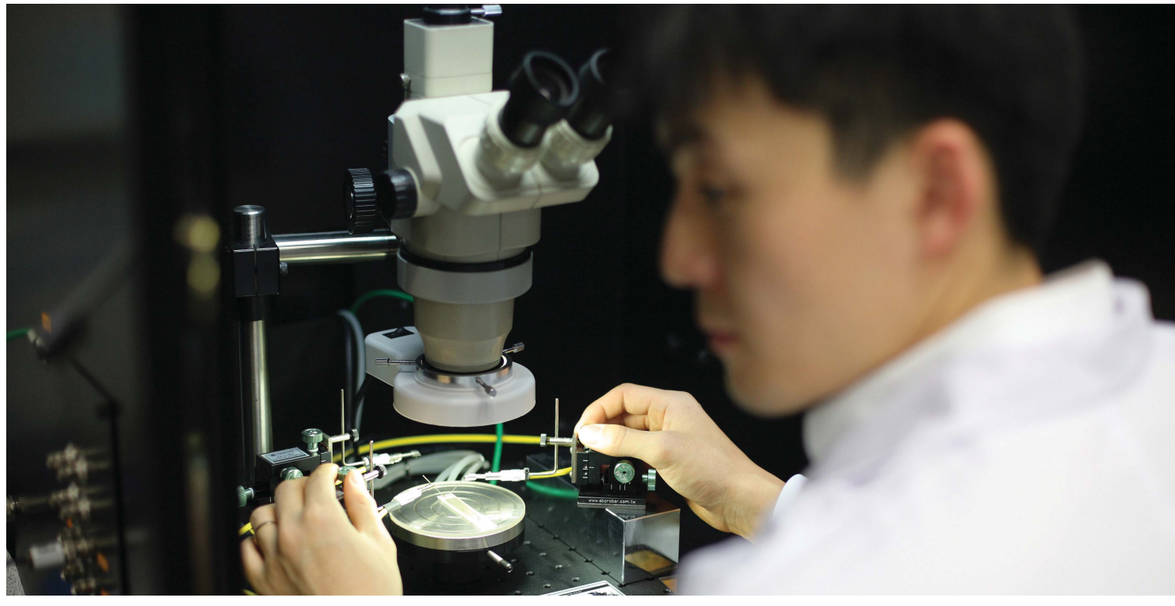
Bong Hyun Chung (Corresponding)
Chem Commun. 47(38):10668-70.

Bong Hyun Chung (Corresponding)
Chem Commun. 47(38):10668-70.
Photoreversible cellular imaging using photochrome-conjugated fullerene silica nanoparticles

Joong Hyun Kim (Co-First)
Biosens Bioelectron. 26(10):4058-63.
The affinity ratio--its pivotal role in gold nanoparticle-based competitive colorimetric aptasensor

Yongwon Jung (Corresponding)
Angew Chem. 50(52):12487-90.
Two-temperature hybridization for microarray detection of label-free microRNAs with attomole detection and superior specificity

Yongwon Jung & Bong Hyun Chung (Co-Corresponding)
Biomaterials. 32(34):9051-8.
Splitting and self-assembling of far-red fluorescent protein with an engineered beta strand peptide: application for alpha-synuclein imaging in mammalian cells



Division of Convergent BioMedical Research

BioMedical Translational Research Center

Translational research refers to the "bench-to-bedside" enterprise of harnessing knowledge from basic sciences to produce new drugs, devices, and treatment options for patients. Biomedical Translational Research Center was established to develop core technologies and infra-structures required for the effective translation of new knowledge from basic science into new approaches for prevention, diagnosis, and treatment of disease.

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RESEARCHERS

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▸ Chemical genomic study using cell- or phenotype-based assay, gene and protein expression profiling for identification of the genes and proteins involved in tumor progression and metastasis

Seung-Ho Kim shkim@kribb.re.kr
▸ Studies on development of pharmaceuticals against thrombosis and haemostsis from plant and food.
· Target discovery and development for fibrinolytic enzymes.

Kyou Hoon Han khhan600@kribb.re.kr
▸ Studies on intrinsically unfolded / unstructured proteins (IUPs). Information derived from the studies on IUP-protein interactions should lead to a novel paradigm for designing peptide pharmaceuticals against many diseases such as cancer, fatal viral diseases, Parkinson's disease, and Alzheimer's disease.

Jang-Seong Kim jangskim@kribb.re.kr
▸ Development of core *in vivo* technologies required for the development of anti-cancer drugs
· Development of orthotopic animal models and monitoring system for testing biological efficacy of anti-cancer drugs.
▸ Target discovery and development for innovative anti-cancer therapeutics
- Establishment of metastasis animal models and organ-specific metastatic variants of gastrointestinal tumors.
- Selection of potential targets and the development of therapeutics against them in the tumor cells and stroma through a biological analysis of tumor cells and tissues.

Kee Nyung Lee knlee@kribb.re.kr
▸ Screening of novel Th17 differentiation factors in Mouse and Human system.
▸ TLR (Toll Like Receptors) signal studies in inflammation.
▸ Innate Immunity

RESEARCH AREAS

▸ Translational research for the development of innovative anti-cancer drugs: Establishment of animal models and monitoring systems for testing biological efficacy of anti-cancer drugs.
▸ Discovery of novel targets to control cancer metastasis.
▸ Characterization of the novel intrinsically unfolded / unstructured proteins (IUPs).
▸ Immunology: screening of Th17 differentiation factors, TLR signaling in inflammation, and innate immunity.

ACHIEVEMENTS

Translational research for the anti-cancer therapeutics
We have established several orthotopic animal models for cancer and experimental metastasis animal models to be used for the preclinical evaluation of anti-tumor efficacy of anti-cancer drugs in accordance with the global standards.

Studies on intrinsically unfolded / unstructured proteins (IUPs)
▸ Dr. Han is one of the world pioneer in the IUP area and discovered the first Pre-Structured Motifs (PreSMos) in the trans-activation domain of tumor suppressor p53 in 1995. The results were published in the *Journal of Biological Chemistry* in 2000 [cited more than 120 times].
▸ He wrote an invited review that summarizes the novel concept of PreSMos which was published in the Current Protein and Peptide Science in 2012.
▸ Two patents have been filed on the anti-cancer peptide derivatives of PreSMos.

SELECTED PUBLICATIONS

Byoung-Mog Kwon (Corresponding)
Bioorg Med Chem. 19(24):7582-9.
Cosmomycin C inhibits signal transducer and activator of transcription 3 (STAT3) pathways in MDA-MB-468 breast cancer cell

Byoung-Mog Kwon (Co-Corresponding)
Cancer Sci. 102(1):212-8.
Differential antiproliferation effect of 2'-benzoyloxycinnamaldehyde in K-ras-transformed cells via downregulation of thiol antioxidants

Dong Cho Han & Byoung-Mog Kwon (Co-Corresponding)
Bioorg Med Chem Lett. 21(2):747-51.
2-Hydroxycurcuminoid induces apoptosis of human tumor cells through the reactive oxygen species-mitochondria pathway

Division of Biosystems Research

Systems & Synthetic Biology Research Center

Green Bio Research Center

Industrial Bio-materials Research Center

Environmental Biotechnology Research Center

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More Prosperous Future with Biotechnology

Solving critical problems facing our planet and maximizing our natural resources for a sustainable future is an important area of activity at KRIBB. Unveiling the hidden secrets of plants, microorganisms and insects and using them to brew new technologies for biomaterials and bioenergy. These are some examples of our endeavors in this applied biotechnology.

Division of Biosystems Research

Systems & Synthetic Biology Research Center

Our goal is to become a world-class research and development center specializing in microbial biotechnology by developing the core technologies required for endowing microbial cell factories with novel functions through omics/systems analyses and synthetic biology. The center has established a solid foundation for genomic sciences and biotechnological applications. We have established many international collaborations, and we are actively cooperating with many academic and industrial R&D groups.

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▸ Bacteria-plant interactions, plant immunity

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Haeyoung Jeong hyjeong@kribb.re.kr
▸ Analysis of microbial genome structure

Soo-Keun Choi sookeun@kribb.re.kr
▸ Bacillus genetics, Bacillus cell factory

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▸ Microbial physiology, systems metabolic engineering

Dong-Woo Lee leehicam@kribb.re.kr
▸ Bioenergetics, protein biochemistry and biophysics

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▸ Metabolic engineering, systems biology

Kwang-sun Kim sunny06@kribb.re.kr
▸ Microbial RNomics of small noncoding RNAs, RNA biogenesis / decay

Bong Hyun Sung bhsung@kribb.re.kr
▸ Microbial genome engineering, bioenergy production

Dae-Hee Lee dhlee@kribb.re.kr
▸ Evolutionary engineering, *E. coli* cell factory

RESEARCH AREAS

Microbial genome analysis
Genome sequencing and functional genomics of industrial microorganisms; deciphering microbial diversity on a metagenomic scale

Microbial cell / protein factory
Developing novel expression systems with yeast and bacteria, metabolic pathways engineering, and molecular bacteria-plant interactions

Systems / synthetic biology
Systems analysis and synthesis of novel biological functions, systems, and life forms by utilizing bio-parts, genetic circuitries, and metabolic pathways

Biocatalyst innovation
Custom-made enzymes, biomolecular engineering, and innovative biocatalysis processes

ACHIEVEMENTS

Genome analysis of microbes and integrative omics-based cell factory engineering
Genome sequencing and analysis of prokaryotic or eukaryotic microbes of environmental, biotechnological or scientific importance; Genome dynamics, the evolution of bacteria, functional genomic studies, remodeling of signal transduction networks and protein glycosylation pathways

Structural basis and mechanism of microbe-host interaction
Understanding the molecular basis of interaction between microbe and host, and the mechanism of microbial pathogenesis

Dissecting probiotic *Paenibacillus*-plant interactions and their genome analysis
Understanding and applying *Paenibacillus*-elicited plant growth promotion and induced resistance, as well as polymyxin and fusaricidin biosynthesis

Construction of a yeast protein factory for the efficient production of recombinant proteins for therapeutics and bio-based industry
Genome-wide screening of the TFP library and efficient secretion of difficult-to-express proteins and enzymes

FRET-based biosensors exhibiting increased signal output and novel specificity
Development of a highly-responsive FRET signal in living cells by combinatorial engineering of the domain linker and binding moiety of CFP-bp-YFP proteins

Development of bioenergy production processes
Bioethanol fermentation using consolidated bioprocessing and enzymatic production of biodiesel with an immobilized lipase

SELECTED PUBLICATIONS

Choong-Min Ryu (Corresponding)
J Ecol. 99(1):46-56.
Whitefly infestation on pepper plants elicits defence responses against bacterial pathogens in leaves and roots and changes the below-ground microflora

Eui Sung Choi (Co-Corresponding)
Metab Eng. 13(6):648-55.
Metabolic engineering of *Escherichia coli* for α-farnesene production

Haeyoung Jeong (Co-First)
J Bacteriol. 193(16):4292-3.
Complete genome sequence of the polycyclic aromatic hydrocarbon-degrading bacterium *Alteromonas* sp. strain SN2

Jae Wha Kim & Myung Hee Kim (Co-Corresponding)
J Biol Chem. 286(14):12450-60.
Crystal structure of the human N-Myc downstream-regulated gene 2 protein provides insight into its role as a tumor suppressor

Tae Kwang Oh & Myung Hee Kim (Co-Corresponding)
Nat Struct Mol Biol. 18(12):1336-44.
Bilateral inhibition of HAUSP deubiquitinase by a viral interferon regulatory factor protein

Division of Biosystems Research

Green Bio Research Center

The research of the center focuses on the development of green and platform technologies for the use in plant science and the improvement of industrially important crop plants. These include identifying functionally important genes as well as establishing a novel transformation system and new transgenic plants with useful traits. We have established platform technologies for structural and functional genomics of important crops by actively participating in International Solanaceae Genome Project. We are currently expanding our genomics platform technology for improving useful crops and developing breeding tools.

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Hye Ran Kim kimhr@kribb.re.kr
‣ Comparative, functional and structural genomics of major crops
‣ Genomics for molecular breeding of Brassica crops and evolutionary genomics

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Sung Ran Min srmin@kribb.re.kr
‣ Development of "CyanoCrops" by introducing cyanobacterial genes into the chloroplast genome of crops
‣ Cloning of salt resistant genes from marine cyanobacteria via a functional genomics approach and the development of salt-tolerant crops
‣ Algal biotechnology for biofuel and biomass

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Hyun Soon Kim hyuns@kribb.re.kr
‣ Mass production of the seeds or seedling of useful vegetative-propagation crops
‣ Development of useful transgenic crops
‣ Establishment of the optimal system (eg, glycosylation pattern, RNAi knockdown) for molecular farming

Hye Sun Cho hscho@kribb.re.kr
‣ Photosynthesis regulation and mechanism
‣ Functions of chloroplast immunophilins
‣ Identification of rice immunophilins

Jeong Mee Park jmpark@kribb.re.kr
‣ Molecular mechanisms of pathogen-induced cell death
‣ Plant immunity to viruses

Jae Sun Moon jsmoon@kribb.re.kr
‣ Molecular plant-microbe interactions
‣ Development of oligo chips for the pathogen diagnosis
‣ Identification of the genes involved in the development by virus-induced gene silencing

RESEARCH AREAS

‣ Structural, funtional and evolutionary genomics of plants
‣ Functional genomics of plant-microbe interactions
‣ Development of an environmentally-friendly binary vector system
‣ Signal transduction network of plant cell death
‣ CyanoCrop using cyanobacterial genes
‣ Post-translational regulation for environmental stress

ACHIEVEMENTS

International collaboration on the analysis of the Solanaceae genome
Launched in 2004, this ten-year project involves twenty nations, ten of which are participating in the primary operations to decode the genomic sequence. Korea is responsible for the 2nd chromosome, which consists of 12% of the entire genome. So far, we have accomplished approximately 90% of our designated task.

Large-scale isolation of pepper genes and public release
We have undertaken the task of gene identification in peppers, the most important vegetable crop in Korea, and have finished analyzing about 120,000 expressed sequence tags. A database containing this information has been built and opened to the public. We believe that we have secured more than two-thirds of the pepper genome, which consists of 30,000 uni-genes, and expect information of varieties to be helpful in the development of new strains. (http://sol.pdrc.re.kr)

Development of platform technology for research on functional genomics
Virus-induced gene silencing technology, developed for the large-scale screening of genes is currently being used in the screening of many types of Solanaceae plants including *Nicotiana benthamiana*, peppers, and tomatoes.

Development of transplastomic technology
We have succeeded in developing transformation technology for foreign gene expression in plastids. These genes can only be inherited from the maternal line, which cannot be spread through pollen, thereby ensuring a low environmental risk.

Development of an edible plant-derived vaccine for Alzheimer's disease
Antigens for mutant b-amyloid proteins, which are known to be a cause of Alzheimer's disease, were overexpressed in potatoes as an edible vaccine. We have developed the transgenic potato, and have confirmed through experiments with mice that the potato vaccine does produce specific antibodies for b-amyloids.

Development of genomics assisted breeding tools
We have embarked on an ambitious genomics program entitled the 'Cabbage genomics assisted breeding support project'. The long-term objective of the project is to create a genome-level closed breeding system for the Brassica oleracea that can be used as a research platform to study evolution, development, genome organization, polyploidy, domestication, gene regulatory networks and crop improvement

Development of algal biotechnology
We have been developing algal biotechnology using *Chlamydomonas*, *Chlorellar*, and *Porphyra*. Our research projects are (1) understanding of gene expression using transcriptome / epigenetics / functional genomics studies and (2) genetic engineering using overexpression or knock down technology.

Immunopphilin functions in *Arabidopsis* and rice
We have identified and classified rice immunophilin (29 FKBPs and 27 CYPs) firstly. Classification of the putative FKBPs and CYPs in rice provides the information about their evolution / functional significance when comparisons are drawn with the relatively well studied genera *Arabidopsis* and *Chlamydomonas*.
In addition, many of the genes upregulated by water stress offer the possibility of manipulating the stress responses in rices.

SELECTED PUBLICATIONS

Cheol-Goo Hur (Corresponding)
BMB Rep. 44(4):250-5.
Predicting tissue-specific expressions based on sequence characteristics

Jae Sun Moon (Co-Corresponding)
Plant Biotechnol J. 9(3):348-58.
A novel light-dependent selection marker system in plants

Jang Ryol Liu (Corresponding)
Plant Methods. 7:14.
A rapid, simple method for the genetic discrimination of intact *Arabidopsis thaliana* mutant seeds using metabolic profiling by direct analysis in real-time mass spectrometry

Won Joong Jeong (Corresponding)
Planta. 234(5):1065-72.
Host-dependent suppression of RNA silencing mediated by the viral suppressor p19 in potato

Division of Biosystems Research

Industrial Bio-materials Research Center

Based on bio-diversity of insects, microorganisms, plants and marine organisms, our group is trying to figure out and build-up new platform technologies that can make new biomaterials, diverse enzymes (including feed enzymes and saccharification enzymes), functional foods, nutraceuticals and biopesticides.

- New industrial enzymes from insects and related microflora
- Nutraceuticals and functional foods for metabolic disorders and liver diseases
- Bio-pesticide ingredients from natural sources
- Business development and bio-plant know-how in biodiversity field

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RESEARCHERS

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- Microbial biotechnology
- Bio-diversity based enzymes for industrial uses
- Microbial natural products for pharmaceutical uses

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- Search, *in vivo* efficacy test, mechanism study, and development of bioactive materials for prevention and treatment of metabolic syndroms (including diabetes, obesity, hyperlipidemia, atherosclerosis)

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- Molecular biology, Hepatology
- Development of antiviral, anti-cirrhosis and anti-liver cancer agents using recombinant DNA techniques and identifying active compounds from natural resources

Sung Uk Kim kimsu@kribb.re.kr
- Search and development of bio-materials for agriculture including biological control agents, fungicides, and TTSS inhibitors from natural resources

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- Highly active enzymes and bio-materials from invertebrates & microbes for industrial application, Development of bio-insecticides for the control of agricultural insects by insect pathogens

Hyun-Woo Oh hwoh@kribb.re.kr
- Search and development of bio-materials for agriculture including biological control agents, insecticides and insect repellents from natural resources. Provide imaging and analytical services, including scanning and transmission EM for bio-research

RESEARCH AREAS

Development of bio-materials based on biodiversity and FT (Fusion Technology)
- Unique enzymes from insect and related (symbiotic etc.) microorgnaisms.
- Bio-catalysts to resolve recalcitrance of biomass
- Environment-friendly bio-pesticides using entomopathogenic microorganisms

Development of anti-virus drugs to cure virus originated hepatitis B
- Isolation of 3 new materials from plant natural products in Korea (Alleviate drug resistance caused by mutation)

Development of platform technology for metabolic disease control
- Study of drug mechanism and target identification
- Development of nutraceuticals or lead compound from plant and edible sources

Development of antibiotic biomaterials from natural sources
- Search for the inhibitors of type III secretion system in plant-pathogenic Gram(-) bacteria
- Screening of antifungals for plant pathogenic fungi

ACHIEVEMENTS

Protein degrading enzyme, Arazyme
From the gut-bacteria pool of Korean golden web spider,multi-conditional enzyme, Arazyme was developed. Core technology with the protein producing strain was transferred to the bio-company and resulted in various industrial materials, biocosmetics and feed enzymes.

SELECTED PUBLICATIONS

Ho-Yong Park (Corresponding)
Bioresour Technol. 107(1):25-32
Novel modular endo-β-1,4-xylanase with transglycosylation activity from Cellulosimicrobium sp. strain HY-13 that is homologous to inverting GH family 6 enzymes

Hyun Woo Oh (Corresponding)
Bull Entomol Res. 101(4):429-34.
DNA barcodes for two scale insect families, mealybugs (Hemiptera: Pseudococcidae) and armored scales (Hemiptera: Diaspididae)

Kwang Hee Son & Ho-Yong Park (Co-Corresponding)
Bioresour Technol. 102(19):9185-92.
Cloning and characterization of a modular GH5 β-1,4-mannanase with high specific activity from the fibrolytic bacterium *Cellulosimicrobium* sp. strain HY-13

Tae Sook Jeong (Co-Corresponding)
Food Chem. 126(3):1057-63.
The most abundant polyphenol of soy leaves, coumestrol, displays potent α-glucosidase inhibitory activity

Environmental Biotechnology Research Center

We aim to develop industrial platform technologies using high-tech ecogenomics and biological resources in response to three United Nations Environmental Conventions on Biodiversity, Climate Change and Combating Desertification. To achieve these goals, we focus on the development of integrated fusion technologies combined with plant science, microbial science (including microalgae), and environmentally-friendly materials science. In addition, we are operating the Korea-China Biotechnology Joint Research Center to Combat Desertification.

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RESEARCHERS

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▸ Molecular analysis of microbial diversity and functions in contaminated environments / Production and harvest of microalgae

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▸ Ecophysiological study of microalgae and biological CO_2 fixation using microalgae

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▸ Transgenic plants with enhanced tolerance to multiple stresses on marginal lands

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▸ Molecular breeding of crops for bioenergy and functional feed on marginal lands

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▸ Enhancement of multi-resistances of plants using natural lipids and plant green biotechnology on natural rubber

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▸ Characterization of bioactive substances from microorganisms and environmental sources

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▸ Ecophysiology, ecogenomics and ecoinformatics of microalgae and cyanobacterial bloom

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▸ Transgenic plants with enhanced tolerance to drought stress for combating desertification

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▸ Molecular breeding of sweetpotato and potato plants for sustainable agriculture

RESEARCH AREAS

Plant antioxidation research
Developing industrial transgenic plants with enhanced tolerance to multiple environmental stresses for sustainable agriculture on global marginal lands including desertification areas

Microalgae research
Using diverse microalgae in carbon dioxide sequestration and developing environmentally-friendly production technologies for useful materials

Microbial community research
Development of functional microbial communities for bioremediation of contaminated soil and analysis of their microbial diversity and functions

Biomaterials research
Screening, characterization, and mode-of-action studies of bioactive substances from microorganisms, plants, and other environmental sources

ACHIEVEMENTS

Development of eco-friendly industrial plants with enhanced tolerance to oxidative stress
SN Transgenic poplar plants expressing AtNDPK2 gene under the oxidative-stress inducible *SWPA2* promoter were generated and characterized in LMO fields. SN poplar plants showed enhanced growth as well as oxidative stress tolerance. In addition, *IbOr* gene responsible for accumulation of carotenoids was isolated from the orange-fleshed tuberous roots of sweetpotato and characterized. As expected, transgenic sweetpotato expressing *IbOr* gene showed increased contents of carotenoids as well as oxidative stress tolerance.

Increased lipid productivity in microalgae for biofuel production
Domestic microalgae strains were collected from Korean freshwaters and screened for high lipid production. Diverse molecular techniques have been applied to increase lipid productivity by manipulating lipid production pathways. To find out optimal cultivation system, a lot of strains, environmental conditions, and culturing methods are being compared.

Development of functional microbial communities for bioremediation
The functional microbial communities (FMCs), capable of highly dechlorinating PCE/TCE, were obtained from contaminated sediments. We analyzed the bacterial structure of the FMC and their dynamics during dechlorination of PCE/TCE.

New bioactive metabolites from microorganisms
Microorganisms, including microalgae and cyanobacteria, are rich in secondary metabolites with diverse chemical structures and various biological functions. New inhibitors of bacterial fatty acid synthase (FabI, K, G) and peptide deformylase were found in microorganisms for the first time in this study and have potential for new antibacterials.

Environmentally safe natural bioactive substances from plants
Bioactive lipid compounds that enhance multi-resistances in plants to abiotic and biotic stresses were found and are being applied to agricultural fields.

SELECTED PUBLICATIONS

Chi-Yong Ahn (Corresponding)
Harmful Algae. 10(2):188-93.
Correlations between environmental factors and toxic and non-toxic Microcystis dynamics during bloom in Daechung Reservoir, Korea

Hee-Mock Oh (Corresponding)
Bioresour Technol. 102(3):3163-8.
Harvest of *Scenedesmus* sp. with bioflocculant and reuse of culture medium for subsequent high-density cultures

Sang-Soo Kwak (Corresponding)
Plant Biotechnol J. 9(3):334-47.
Transgenic poplar expressing *Arabidopsis NDPK2* enhances growth as well as oxidative stress tolerance

Sang-Soo Kwak (Corresponding)
Planta. 233(3):621-34.
Sweetpotato late embryogenesis abundant 14 (*IbLEA14*) gene influences lignification and increases osmotic- and salt stress-tolerance of transgenic calli

Division of Bioresource Infrastructure

Biological Resource Center

Genome Resource Center

Laboratory Animal Center

International Biological Material Research Center

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Building Infrastructure of Biological Resources

As a national supporting system for biotechnology, the Korea Biological Resource Center (KBRC) has been strengthening to manage biological resources and information, and providing the basis of research support. Also, it has helped to foster the bioindustry for providing biological resources to research institutes, academia and industries.

Division of Bioresource Infrastructure

Biological Resource Center

Biological Resources Centers (BRC) are essential infrastructures for the life sciences, biotechnology and bio-industry. The main goal of the BRC is to collect, preserve and distribute of biological resources, thereby encouraging the development of bioscience and biotechnologies. We are a think-tank of biological resources and perform national research and developments related to biological resources.

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RESEARCH AREAS

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 valuable biological resources
▸ Developing platform technologies for the management, preservation and taxonomy of useful biological resources

Construction of an information network and support of various services related with biological resources
▸ Construction of local and global networks for biological resources
▸ Support the related information and providing workshops, conferences, consultations, etc

ACHIEVEMENTS

Collection, preservation and distribution of biological resources
We acquired 1,940 strains, including bacteria, actinobacteria, yeasts, filamentous fungi, anaerobes, archaea, animal and plant cell lines, microalgae and patent strains, and preserved 66,436 cases for long-term preservation in this year. KCTC was the third ranked culture collection in the world in acquiring new bacterial resources. Also, we distributed 5,131 strains to academia, industries, and researchers.

Research activities
We published 32 papers related to biological resources and described 25 new species. We also registered 6 patents, including one international patent. Recently, we have developed novel knock-in overexpression system for *G. sulfurreducens* and now we are constructing novel *Geobacter* mutant bank. The developed technology will help us to expand the new microbial resources of the model organisms. In addition, The several new species of *Methanobrevibacter* from the rumen of a Korean native cattle (Hanwoo) were isolated and this is the first example for isolation of pure methanogens in Korea. The molecular mechanisms for bio-control of methane emission from ruminants will be able to be investigated by the new isolates.

Construction of an information network and support of various services
We constructed local and global networks of biological resource centers. We also connected biological resource information through national and international database systems because one of our main services is to provide biological resource information to public. We held four workshops and two conferences, and offered consultation and technical support for 7,053 cases in this year.

SELECTED PUBLICATIONS

Jung-Sook Lee (Corresponding)
Int J Syst Evol Microbiol. 61(9):2101-6.
Reclassification of *Paenibacillus ginsengisoli* as a later heterotypic synonym of *Paenibacillus anaericanus*

Jung-Sook Lee (Corresponding)
Syst Appl Microbiol. 34(8):576-80.
Halogranum salarium sp. nov., a halophilic archaeon isolated from sea salt

Kee-Sun Shin (Corresponding)
Int J Syst Evol Microbiol. 61(10):2543-6.
Wickerhamomyces ochangensis sp. nov., an ascomycetous yeast isolated from the soil of a potato field

Young Hyo Chang (Corresponding)
Am J Rhinol Allergy. 25(1):e18-22.
Detection of bacteria in normal adult nasal cavity based on polymerase chain reaction-denaturing gradient gel electrophoresis

Genome Resource Center

Our goal is to understand the biological phenomena of life through genomic science, which is a systematic and comprehensive technology of the genomes of various organisms. The Genome Resource Center (GRC) established a solid platform for genomic sciences, and archived many world-leading research products through international cooperation. We are actively collaborating with many academic and industry research groups to contribute to genome technology advancement in Korea.

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▸ Discovery and characterization of chimpanzee specific fusion genes by next generation sequencing platform

ACHIEVEMENTS

Major chimpanzee specific structural changes in sperm development-associated genes

A comprehensive analysis of transcriptional structures of chimpanzee sperm development-associated genes is of significant interest for deeply understanding sperm development and male reproductive process. In this study, we sequenced 7,680 clones from a chimpanzee testis full-length cDNA library and obtained 1,933 nonredundant high-quality full-length cDNA sequences.

Comparative analysis between human and chimpanzee showed that 78 sperm development associated genes, most of which were yet uncharacterized, had undergone severe structural changes (mutations at the start / stop codons, INDELs, alternative splicing variations and fusion forms) on genomic and transcript levels throughout chimpanzee evolution. Specifically, among the 78 sperm development-associated genes, 39 including ODF2, UBC, and CD59 showed markedly chimpanzee-specific structural changes.

Through dN/dS analysis, we found that 56 transcripts (including seven sperm development-associated genes) had values of greater than one when comparing human and chimpanzee DNA sequences, whereas the values were less than one when comparing humans and orangutans. Gene ontology annotation and expression profiling showed that the chimpanzee testis transcriptome was enriched with genes that are associated with chimpanzee male germ cell development.

Taken together, our study provides the first comprehensive molecular evidence that many chimpanzee sperm development-associated genes had ex-perienced severe structural changes over the course of evolution on genomic and transcript levels.

Draft genome sequencing and construction of portal DB for Kimchi

Kimchi is any one of numerous traditional Korean pickled dishes made of vegetables with varied seasonings. We constructed web site that will introduce all about Kimchi. Have been consisted of page that supply history and kind introduction of Kimchi, sequencing status associated microbial organism, Blast search, Pubmed search, Genome browser, annotation report etc... in the Web site. This is KIMI, provide all the genetic information about kimchi related bacteria and Looking for new genetic resources and service microbial genetic information. Currently about 16 bacteria species related kimchi have been completed genome sequencing and published in the journal of bacteriolgy.

Developmental Transcriptomic Features of the Carcinogenic Liver Fluke, *Clonorchis sinensis*

In this study, we generated gene expression profiles of three developmental stages of *C. sinensis* by analyzing expressed sequence tags (ESTs). Complementary DNA libraries were constructed from the adult, metacercaria, and egg developmental stages of *C. sinensis*. A total of 52,745 ESTs were generated and assembled into 12,830 *C. sinensis* assembled EST sequences, and then these assemblies were further categorized into groups according to biological functions and developmental stages.

Most of the genes that were differentially expressed in the different stages were consistent with the biological and physical features of the parti-cular developmental stage; high energy metabolism, motility and reproduction genes were differentially expressed in adults, minimal metabolism and final host adaptation genes were differentially expre-ssed in metacercariae, and embryonic genes were differentially expressed in eggs. The higher expression of glucose transporters, proteases, and antioxidant enzymes in the adults accounts for active uptake of nutrients and defense against host immune attacks. The types of ion cha-nnels present in *C. sinensis* are consistent with its parasitic nature and phylogenetic placement in the tree of life.

We anticipate that the transcriptomic information on essential regulators of development, bile chemotaxis, and physicometabolic pathways in *C. sinensis* that presented in this study will guide further studies to ident-ify novel drug targets and diagnostic antigens.

SELECTED PUBLICATIONS

Hong-Seog Park (Co-Corresponding)
PLoS Negl Trop Dis. 5(6):e1208.
Developmental transcriptomic features of the carcinogenic liver fluke, *Clonorchis sinensis*

Hong-Seog Park (Corresponding)
Funct Integr Genomic. 11(3):507-517.
Major chimpanzee specific structural changes in sperm development-associated genes

Hong-Seog Park (Corresponding)
J Bacteriol. 193(3):799-800.
Genome sequence of *Leuconostoc gelidum* KCTC 3527, isolated from Kimchi

Hong-Seog Park (Corresponding)
J Bacteriol. 193(18):5023.
Draft genome sequence of *Lactobacillus zeae* KCTC 3804

Hong-Seog Park (Corresponding)
J Bacteriol. 193(21):6100-1.
Genome sequence of *Leuconostoc carnosum* KCTC 3525

Young Joo Kim (Co-Corresponding)
BMC System Biol. 5(S2):S10.
SigCS base: an integrated genetic information resource for human cerebral stroke

Division of Bioresource Infrastructure

Laboratory Animal Center

The goal of our center is to establish an infrastructure for animal experiments and to generate animal models for human diseases by mutagenesis (such as transgenic, gene targeting and natural breeding) for *in vivo* validation of genes associated with human diseases.

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- Research supports for animal experiments, veterinary care, and pathological, hematological and biochemical analyses using animal model resources
- Functional validation of the genes associated with human diseases Technical supports for the disease model production and maintenance

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- Development of laboratory animal models of non-human primates

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- Discovery of bioactive materials for human brain-neurological diseases

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- Phenotyoing of functional genes associated with metabolic diseases

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- Supports for veterinary care and histopathological analysis
- Microbiological quality control of laboratory animals

RESEARCH AREAS

- Development and establishment of animal models for human diseases by using transgenic, knock-out and selective breeding techniques

ACHIEVEMENTS

Animal model establishment and research supports for animal experiments

We have established 3 mouse models for human disease research as transgenic and knockout strains, and supported 78 cases of IACUC-approved animal experiment, 56 cases of pathological experiment, and 50 cases of hematological and biochemical analyses. Also, we have performed (4 times) educational service associated with animal ethics and appropriate animal experiments for animal experimenters and periodical health monitorings (4 times) of animals being maintained for the prevention of disease transmission.

RESEARCH ACTIVITIES

In 2011, we published 15 papers concerning metabolic diseases (arising from our research using disease animal model resources) and submitted 2 patents. Also, we contributed 33 papers for publications resulting from KRIBB research into animal experiment support; including animal husbandry and pathological, hematological and biochemical analyses.

SELECTED PUBLICATIONS

Chul-Ho Lee (Corresponding)
Cardiovasc Res. 91(3):519-27.
Activation of NAD(P)H:quinone oxidoreductase ameliorates spontaneous hypertension in an animal model via modulation of eNOS activity

Chul-Ho Lee (Corresponding)
Food Chem Toxicol. 49(7):1537-43.
Hepatoprotective effects of chestnut (*Castanea crenata*) inner shell extract against chronic ethanol-induced oxidative stress in C57 BL/6 mice

Kyoung-Shim Kim (First)
Psychopharmacology. 215(2):391-8.
Mice lacking adenylyl cyclase type 5 (AC5) show increased ethanol consumption and reduced ethanol sensitivity

Division of Bioresource Infrastructure

International Biological Material Research Center

We are aiming at procuring indigenous biological materials from four overseas regional centers and their neighboring countries through legal routes within the scope of international collaborative research projects. Our mission is to provide researchers with a biodiversity of materials and ethno-botanical information, including indigenous medicinal knowledge and also to establish the nation's core infrastructure for developing new natural drugs and nutraceutical products, along with other commercially important natural products.

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RESEARCH AREAS

‣ Establishment of four collaborative biological material research centers for collection and preparation of biological materials worldwide
‣ Establishment and operation of a comprehensive system and database to manage biological materials and related traditional medicinal knowledge procured from four regional centers and their neighboring countries
‣ Establishment and operation of a supply system for efficiently providing biological materials to leading research groups within the scope of the assigned project
‣ Development of new natural drugs, nutraceuticals and other commercially important natural products

ACHIEVEMENTS

Establishment of the International Biological Material Research Center
Center organization has been completed. Equipment and facilities have been set up: highly-sensitive equipment (LC/MS and electric microscopes) and an expanded herbarium (storage capacity over 100,000 voucher specimens). In addition, nearly 200,000 plant extracts have been distributed to date.

Procurement of Foreign Biological Materials
China and neighboring countries
‣ Establishment of the Korea-China Biological Material Research Center in Kumming, Yunnan
‣ Personnel (2 experts from Korea) and research equipment set up
‣ Biological materials: 10,623 dried plant species and extracts with ethnobotanical information

Central and South America
‣ Establishment of the Korea-Costa Rica Biological Material Research Center in Santo Domingo de Heredia, Costa Rica
‣ Personnel (1 experts from Korea) and research equipment set up
‣ Biological materials: 2,559 dried plant species and extracts with ethnobotanical information

South-East Asia
‣ Establishment of the Korea-Indonesia Biological Material Research Center
‣ Personnel (2 experts from Korea) and research equipment set up
‣ Biological materials: 2,351 dried plant species and extracts, including oceanic biological materials from Micronesia

Africa
‣ Signed an MOU with UNIKIN on "Establishment of KOREA-D.R. CONGO Biological Material Research Center (2010 August)
‣ Biological materials: 2,406 dried plant species and extracts with ethnobotanical information

SELECTED PUBLICATIONS

Joongku Lee (Corresponding)
J Med Plant Res. 5(10): 2095-103.
An ethnomedicinal inventory of Knotweeds of Indian Himalaya

Joongku Lee (Corresponding)
Saudi J Biol Sci. 18(2):123-7.
Studies on genetic diversity among populations of *Persicaria barbata* (L.) H. Hara from India based on internal transcribed spacer sequences of nuclear ribosomal DNA

Division of KRIBB Strategy Projects

Korea Biosafety Clearing House

Biotech Policy Research Center

Viral Infectious Disease Research Center

AI Control Material Research Center

Kinomics Based Anticancer Research World Class Institute

Cancer Biomarkers Development Research Center

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Sharing Biotech Values by Expanding Infrastructure and Providing Information Support

The Division of KRIBB Strategy Projects, responsible for national agenda programs, conducts important researches at the national level, which include researches on viral infectious disease, stem cell and drugs for cancer. The Division also extends policy support for biotechnology by providing biosafety information and undertaking biotechnology policy research.

Division of KRIBB Strategy Projects

Korea Biosafety Clearing House

The Korea Biosafety Clearing House (KBCH) is dedicated to the promotion of public awareness and exchange of information, survey and research, and international cooperation on issues regarding Living Modified Organisms (LMOs), as well as monitoring adherence to the requirements as per the "Cartagena Protocol on Biosafety" and the "Act on Transboundary Movements, etc. of LMOs".

Biosafety Protocol Article 20 (Information Sharing and the BCH)
A Biosafety Clearing House (BCH) is hereby established as part of the "clearing house mechanism" under Article 18, Paragraph 3 of the Convention.
LMO Act Article 32 (Korea Biosafety Clearing House)
The head of the Competent National Authority (CNA) may designate the Korea Biosafety Clearing House to be responsible for performing matters concerning the management and exchange of information on Living Modified Organisms (LMOs).

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RESEARCH AREAS

Implementation of the Biosafety Protocol & LMO Act
▸ Performance of information-related duties such as collection and dissemination
▸ Implementation of administrative matters (preparation of Country Reports, analysis of major issues in COP-MOP, management of Expert Forum for discussion of major issues, etc.)
▸ Support developing countries' capacity-building efforts
▸ Implementation of the LMO Act (operation of Biosafety Committee, support for implementation of LMO Act to attain purpose and achieve further improvements)

Improvement of Public Awareness & Communication
▸ Management of Korean and English Biosafety Portals and family sites
▸ Publications such as the Biosafety Whitepaper, the Biosafety Journal, etc.
▸ Hosting of communication activities (LMO forums, international seminars, essays on biosafety, debate competitions, etc.)

Survey & Research
▸ Survey of public perceptions
▸ Establishment of database consisting of LMO and BIO related statistics
▸ LMO and bioindustry trend analysis
▸ Analysis of the industrial impact of the ABS Protocol

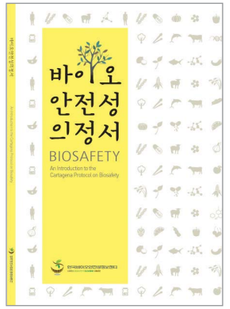
ACHIEVEMENTS

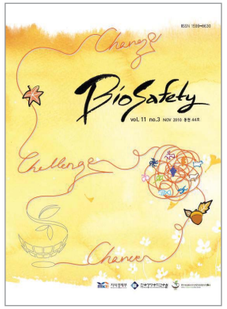
Compliance with the LMO Act and the Biosafety Protocol
Although its actual work in the management of LMO information and issues began six years before, the role of KBCH as an official organization began in January 2008. KBCH's primary mission is to undertake those duties mandated by the LMO Act and the Biosafety Protocol, which mostly involve information regarding the transfer, handling and use of LMOs.

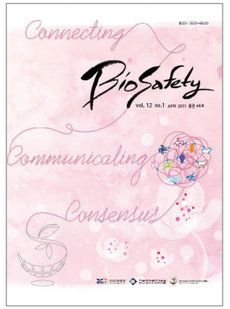
Its mission consists of the collection and distribution of accurate information on LMOs, the promotion of public awareness on LMOs, and participation in various related activities. Over the past four years, KBCH has handled approximately 15,000 domestic cases regarding LMOs, such as import approvals for LMOs-FFP (food and feed, and for processing), facilities registration, etc. KBCH has fulfilled its duty to disclose all collected information to the public by various means, such as the Internet, media and in printed form.

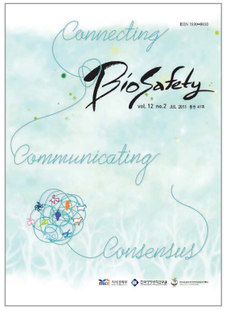
Promotion of Public Awareness and Participation
To promote awareness and participation, especially with the public, KBCH does its utmost to play an indispensable role in assuring biosafety, as stipulated in the Protocol. Above all, KBCH conveys to the public both the positive and negative aspects of LMOs, in order to allow public discussion concerning LMOs to be conducted based on facts. To this end, it operates the Korean "Biosafety Portal", participates in discussions on high-profile Internet sites, such as "Agora" on Daum and "Knowledge IN" on Naver, and distributes printed materials published by the KBCH, such as the quarterly "Biosafety", the "White Paper on Biosafety", and various booklets and pamphlets.

Its other activities include hosting of seminars (LMO forum, etc.), which anyone can attend to share their opinions, and the "Biosafety Essay Competition" and "Biosafety Debate Competition" for elementary, middle and high school students, which attracted many applicants this year.









Division of KRIBB Strategy Projects

Biotech Policy Research Center

Nominated and established by the Ministry of Science and Technology in 2004, the Biotech Policy Research Center aims to assist the government in establishing biotechnology policies. To do so, the center investigates domestic and international biotechnology policy information and runs a portal site to enhance the public understanding of biotechnology and biotechnology policies. The center also develops and provides biotechnology statistics, patents, bibliometrics, and market analysis. Additionally, the center organizes and supports various networks among expert groups related to biotechnology.

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RESEARCH AREAS

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

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

Information Gathering / Disseminating
To provide systematic information regarding biotechnology and biotechnology policy at large through portal sites (www.bioin.or.kr)

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

ACHIEVEMENTS

Policy Planning
‣ Planning for reaching the second stage of the development goal set in Bio-Vision 2016
‣ Action plan for 2011 Bio-Vision
‣ Strategy for studying on Stem cell research capability and technology development
‣ Planning for the creation of a government-wide New Type Influenza Response Team, etc

Bibliometric Analysis and Statistical Development
‣ Patent maps and article analysis systems are devised to assist the government in planning national R&D project strategies and to set the direction for biotechnology research projects.
‣ The center has published annual reports on domestic and overseas statistical data on biotechnologies categorized by investment, human resources, industry, and technology.

Policy Website
‣ A one-stop website was created with regard to BT policies, assisting policymakers understand detailed data on domestic and overseas BT policies.
‣ The site currently has 100,000 pieces of informational data.

Expert Network
‣ To operate the Korean Association of Biotechnology Research

International Collaboration
‣ To participate in the 28th Session of the OECD Working Party on Biotechology
‣ To participate in BAKAS-KOLIS-KASBP-NEBS-RTP-KRIBB Symposium

Division of KRIBB Strategy Projects

Viral Infectious Disease Research Center

Influenza pandemics generally occur following the emergence of new strains of influenza viruses that can be transmitted to humans from other animal species and spread easily within the human population on a worldwide scale. An influenza pandemic of this nature is regarded as a global disaster, threatening public health with high morbidity and mortality. Therefore, it is necessary to formulate plans to counter current and future influenza pandemics. The overall objective of our center is to develop new vaccine technologies and antiviral strategies to broadly address protective immune responses against various sub-types of influenza viruses, especially the current pandemic influenza virus (novel 2009 influenza A [H1N1]) and the highly pathogenic avian influenza virus, which are potential candidate viruses of future influenza pandemics.

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RESEARCHERS

Haryoung Poo haryoung@kribb.re.kr
▸ Development of a new vaccine adjuvant and study of its mechanism, Development of new candidates for universal vaccines

Jeong-Ki Kim jkim@kribb.re.kr
▸ Evaluation of the efficacy of newly developed vaccines in animal models
▸ Evaluation of the efficacy of the vaccine adjuvant in animal models, Surveillance and genetic characterization of influenza viruses circulating in our circumstance

Daesub Song sds1@kribb.re.kr
▸ Application of adjuvant candidate to large animal models, Study of interspecies transmission of influenza viruses, Surveillance of mammalian derived influenza viruses in Korea

Doo-Jin Kim joongsu@kribb.re.kr
▸ Development of universial influenza vaccines, Study on mucosal immune system and development of mucosal vaccines

RESEARCH AREAS

▸ Development of new vaccine technologies including subunit, genetic, and live attenuated vaccines capable of inducing cross-protective immunity
▸ Development of a new vaccine adjuvant using polymer (poly-γ-glutamic acid) and investigation of its immune mechanism,
Basic research on influenza viruses, including surveillance and genetic characterization

ACHIEVEMENTS

Development of new vaccine technologies, including subunit, genetic, and live attenuated vaccines against influenza viruses

Several candidates of subunit vaccines have been developed via prokaryotic and eukaryotic protein expression systems, using the HA, M2, and NP antigens (Shim *et al., PLoS ONE,* 2011). We have succeeded in the design and mass production of novel vaccine candidates, and have currently evaluated their efficacies as vaccine candidates in animal models (Kim *et al., J Infect Dis,* 2012).

Development of a new vaccine adjuvant using poly-γ-glutamic acid and the investigation of its immune mechanism

As an efficacious vaccine adjuvant candidate, we have developed poly-γ-glutamic acid nanogel, which was previously reported to activate NK cells (Kim *et al., J Immunol,* 2007). Study of the immune mechanism of the adjuvant has revealed that it strongly induces both humoral and cellular immune responses (Lim *et al., Small,* 2011). The efficacy of the nanogel adjuvant has been evaluated in various animal models using a pandemic influenza A (H1N1) vaccine; the nanogel adjuvant significantly increased the vaccine efficacy compared with conventional adjuvants such as alum or squalene emulsion.

Basic research on pandemic influenza, including surveillance and genetic characterization

We have isolated influenza viruses from fecal samples of wild migratory birds and ducks in Korea. We have completely identified the positive isolates and have genetically and pathogenically characterized them (Nam *et al., J. Virol* 2011). In addition, we have evaluated *in vitro* and *in vivo* activities of some candidates of antiviral agents.

SELECTED PUBLICATIONS

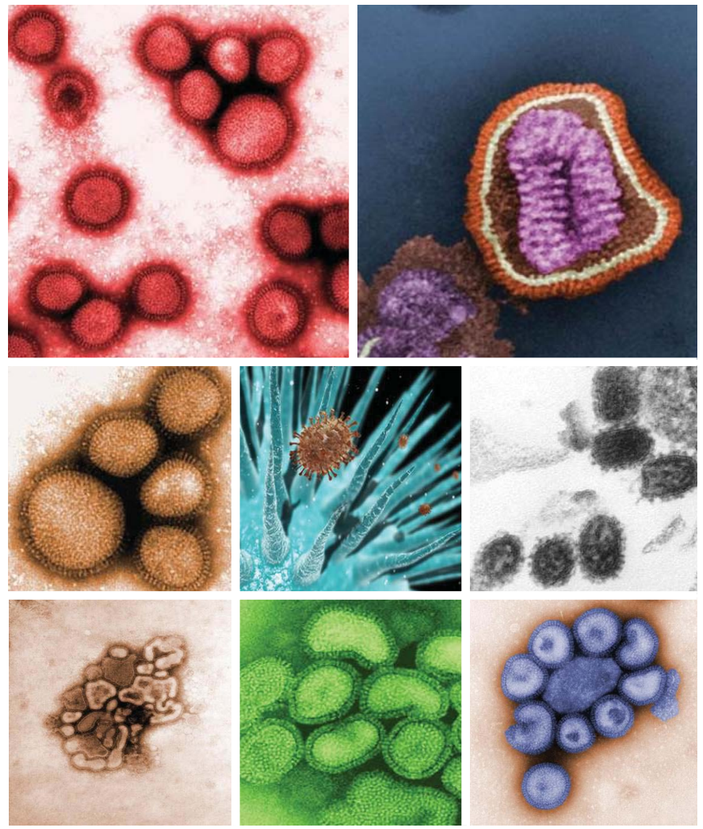
Daesub Song (Co-First)
J Gen Virol. 92(10):2350-5.
Interspecies transmission of the canine influenza H3N2 virus to domestic cats in South Korea, 2010

Haryoung Poo (Co-Corresponding)
ACS Nano. 5(10):8230-40.
Synthesis and high performance of magnetofluorescent polyelectrolyte nanocomposites as MR/near-infrared multimodal cellular imaging nanoprobes

Haryoung Poo (Co-Corresponding)
Small. 7(23):3281-6.
Bioderived polyelectrolyte nanogels for robust antigen loading and vaccine adjuvant effects

Haryoung Poo (Co-Corresponding)
Chem Commun. 47(31):8889-91.
Electrostatically assembled biocompatible polymer nanoparticles for MR/optical dual-modality imaging nanoprobes

Jeong-Ki Kim & Haryoung Poo (Co-Corresponding)
J Virol. 85(24):13271-7.
Emergence of mammalian species-infectious and -pathogenic avian influenza H6N5 virus with no evidence of adaptation



Division of KRIBB Strategy Projects

AI Control Material Research Center

Our aim is to develop functional foods, natural feeds and therapeutic materials against infectious diseases (virus, et al.) from the natural product library starting with traditional medicines.

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RESEARCHERS

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‣ Identification of infection related target molecules and establishment of screening systems for infection related diseases
‣ Isolation and structure elucidation of active compounds
‣ Synthesis of active compounds

Mun-Chual Rho rho-m@kribb.re.kr
‣ Development of the active materials or compounds with anti-viral and/or anti-inflammatory activity by using the screening system for the infectious and inflammatory diseases
‣ Isolation of active compounds from biomaterials and elucidation of their structure

Cha Young Kim kimcy@kribb.re.kr
‣ Molecular metabolic engineering for production of secondary metabolites in microbe and plant systems
‣ Molecular farming for production of valuable proteins such as vaccines in plant systems
‣ Understanding of molecular mechanisms for the biosynthesis of plant pigments

Young Min Kim u9897854@kribb.re.kr
‣ Development of solubilized process of target compounds and mass production
‣ Enzymatic modification of infection and inflammation related target molecules

Su-Jin Park sjpark@kribb.re.kr
‣ Isolation and bulk culture of viruses (coronavirus, rotavirus, influenza virus) and genetic and phylogenetic analysis of isolated viruses
‣ Pathologic, immuno-histochemical, and electron microscopic studies using animals

Young Bae Ryu ybryu@kribb.re.kr
‣ Isolation and identification of secondary metabolites from natural resources
‣ Identification of infection related target molecules and establishment of screening systems for infection related diseases

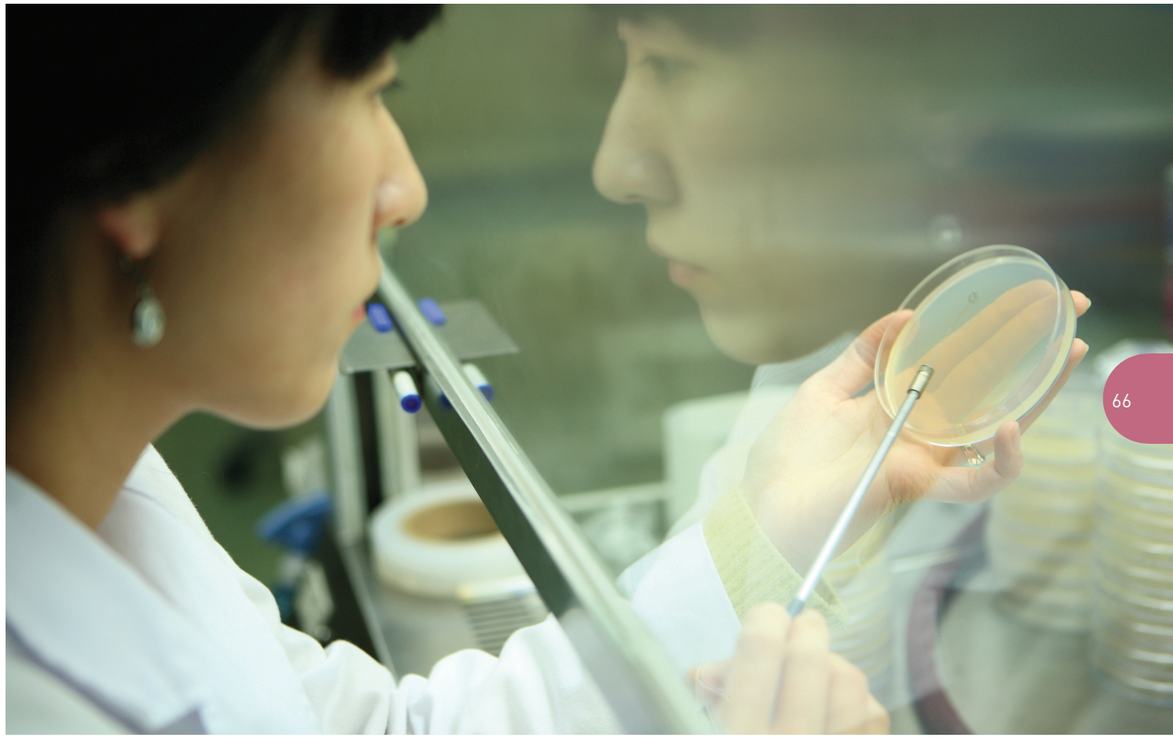
Hyun-Mee Oh ohhm@kribb.re.kr
‣ Development and utilization of the cell-ased and *in vivo* animal system to study of the biological activity of the active materials or compounds and identify the protective mechanism of the active materials against infectious diseases

RESEARCH AREAS

‣ Construction of bioassay systems related to infectious and inflammatory diseases
‣ Establish bioassay and screening systems for compounds against infectious diseases (virus, bacteria, and malaria)
‣ Establish bioassay and screening systems for compounds against inflammatory diseases (pneumonia, asthma, and arthritis)
‣ Developing specifically active compounds such as inhibitors of neuraminidase to combat the avian influenza virus (Neuraminidase inhibitors are a class of antiviral drugs targeted at the influenza virus, which work by blocking the function of the viral neuraminidase protein, thus preventing the virus from reproducing by budding from the host cell)
‣ Developing active compounds with the potential inhibitory activity for the production of inflammatory cytokines and chemokines and the activation of cell adhesion molecules
‣ Construction of a natural product fraction library
‣ Constructing and utilizing both a fraction from plant and microbial culture extracts and a natural compound library

ACHIEVEMENTS

Development of active materials or compounds against infectious and inflammatory diseases
‣ Development of several neuraminidase inhibitors including 10 bio-materials and 30 compounds
‣ Development of the preventive or therapeutic drug against AI viral infection including KW-100
‣ Establishment of bulk production and isolation system for neuraminidase
‣ Demonstrate the anti-AI viral effect of neraminidase inhibitors by using virus-infected animal model
‣ Identify the inhibition mechanism of neuraminidase by active materials or compounds
‣ Development of several M2 channel blockers
‣ Development of active materials or compounds with anti-inflammatory activity including KR-300 or KR-301
‣ Demonstrate the anti-inflammatory effect of KR-300 and KR-301 by using atopic dermatitis and arthritis animal model
‣ Found the novel compound, Norkurarinol, showing the anti-viral activity



Identification of new molecular targets related to infectious and inflammatory diseases
Through research of molecular targets such as proteomics and genomics, new target candidates of inflammatory and viral infectious diseases have been identified. We established assay / screening systems for inflammation and virus related diseases.

***In vitro* and *in vivo* antiviral evaluations**
We established the identification of cultures and quantitative titration methods for several viruses including the influenza virus, rotavirus, coronavirus, rhinovirus and enterovirus, and developed new active biomaterials and immunotherapies against viruses, utilizing virology, mechanisms of action, *in-vitro* activity and animal models.

Commercialization of technology and application research regarding "development of virus control material, KW-100"
In order to develope of virus control material (extract, graduates and KW-100) using hemagglutinin and neuramindase inhibitor of avian influenza virus
‣ Development of sub-ingredient material for increasing absorption rate of main ingredient material for virus control
‣ Development of privately made goods of antiseptic, drinking injector, and feed additives through cocktail medication with main ingredient or sub-ingredient
‣ Through studies on site application (livestock: henhouse, pigsty, and cowshed, fish culture: shrimp, king crab, and fish) using main ingredient or cocktail medication
‣ The final goal is to industrialize material for virus infection control.

SELECTED PUBLICATIONS

Woo Song Lee (Corresponding)
Bioorg Med Chem Lett. 21(18):5602-4.
Characteristic of alkylated chalcones from *Angelica keiskei* on influenza virus neuraminidase inhibition

Woo Song Lee (First)
J Agric Food Chem. 59(9):4589-96.
Isolation of cholinesterase-inhibiting flavonoids from *Morus lhou*

Woo Song Lee (Corresponding)
J Agric Food Chem. 59(12):6467-73.
Influenza virus neuraminidase inhibitory activity of phlorotannins from the edible brown alga *Ecklonia cava*

Division of KRIBB Strategy Projects

Kinomics Based Anticancer Research World Class Institute

Kinomics Based Anticancer Research Center (World Class Institute) aims at achieving outstanding result through open innovation and global network. Based upon the 13 billion won grant in total for 5 yrs until 2014 (2.5 bil/yr), WCI is focusing on identification of cancer-specific proteins and discovery of anticancer therapeutics candidates from microbial secondary metabolites or medicinal plants without side effect of most drugs so far developed.
WCI is composed of 8 non-Koreans including WCI director, Raymond Leo Erikson from Harvard University, as well as 8 Koreans as the main members. Global collaboration is now being actively conducted with 8 renowned foreign scientists from institutes including Harvard Medical School, MIT, Univ. Minnesota, Univ. Michigan, NIH, Univ. Torronto, and Univ. Pittsburgh.

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RESEARCH AREAS

Kinomics-based discovery and functional mining of anticancer targets
▸ Research on cancer cell division and its regulatory proteins, Polo-like kinase (PLK), mTOR and Cep131
▸ Exploitation of anticancer drug candidates extracted from traditional medicinal plants

Anticancer drug candidate discovery and its functional study using RANi, computer modeling, proteomics, and so on
▸ Polo box domain (PBD) of PLK1 and its synthetic substrate peptide are utilized for candidate discovery and its functional exploitation
▸ Study on one of the key cancer regulator mTOR complex2 and cell division modulator Check kinse 1 (Chk1)
▸ Identification of centrosomal protein Cep-131, a key molecule for cancer cell division

Research on the protein degradation based on N-end rule pathway
▸ N-end rule pathway linked with cancer therapy
▸ Redox modulated protein degradation in cancer cells

ACHIEVEMENTS

▸ Inhibitory effect of ERK1/2 and AP-1 by hyperoside isolated from *Acarithopanax sessiliflorus*
▸ The N-end rule pathway: emerging functions and molecular principles of substrate recognition
▸ Regulation of microtubule-based microtubule nucleation by mammalian polo-like kinase1
▸ Asperlin induces G_2/M arrest through ROS generation and ATM pathway in human cervical carcinoma cells
▸ Fusarikribsin A, An acinar morphogenesis inhibitor from a soil fungus, *Fusarium* sp.
▸ Mammalian polo-like kinase1-dependent regulation of the PBIP1-CENP-Q complex at kinetochores
▸ 6,7,4'-Trihydroxyisoflavone inhibits HCT-116 human colon cancer cell proliferation by targeting CDK1 and CDK2
▸ 7,3',4'-Trihydroxyisoflavone, a metabolite of the soy isoflavone daidzein, suppresses ultraviolet B-induced skin cancer by targeting cotand MKK4
▸ Structures of iron-dependent alcohol dehydrogenase 2 from *Zymomonas mobilis* ZM 4 with and without NAD+ Cofactor
▸ Crystal structure of constitutively monomeric *E. coli* Hsp33 mutant with chaperone activity
▸ Proteasome inhibitor-I enhances Tunicamycin-induced chemosensitization of prostate cancer cells through regulation of NF-κB and CHOP expression

SELECTED PUBLICATIONS

Jong Seog Ahn & Bo Yeon Kim (Co-Corresponding)
Biochem Biophys Res Commun. 409(3):489-93.
Asperlin induces G_2/M arrest through ROS generation and ATM pathway in human cervical carcinoma cells

Jong Seog Ahn & Bo Yeon Kim (Co-Corresponding)
Cell Signal. 23(5):857-65.
Proteasome inhibitor-I enhances tunicamycin-induced chemosensitization of prostate cancer cells through regulation of NF-κB and CHOP expression

Division of KRIBB Strategy Projects

Cancer Biomarkers Development Research Center

Our goal is to discover cancer biomarkers of high sensitivity and specificity that are useful for diagnosing and predicting cancers at the earliest possible stage and for monitoring the effects of drugs. In collaboration with the Fred Hutchinson Cancer Research Center in the USA and RIKEN in Japan, we focus on aberrant glycosylation and autoantibodies for cancer biomarker development in several cancers. This study aims to help treat cancer patients more effectively and efficiently, and ultimately raise the survival rate of cancer patients.

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RESEARCHERS

Jeong-Heon Ko jhko@kribb.re.kr
- Discovery of cancer biomarkers that show changes both in quantity and quality, with highly positive prediction values.
- Functional studies that relate the candidate biomarker proteins to the biology of a cancer

Eun Wie Cho ewcho@kribb.re.kr
- Discovery of auto-antibody-based biomarkers that show changes in the serum of cancer patients

Yong-Sam Kim omsys1@kribb.re.kr
- Discovery of biomarkers that show changes in terms of both quantity (amount of protein in serum level) and quality (aberrant glycosylation), with highly positive prediction values
- Development of a biomarker validation method and validation of biomarker candidates
- Mechanistic study of cancer progression focused on glycooncoproteins

Jeong-Gu Kang kang@kribb.re.kr
- Discovery of biomarkers that show changes in terms of both quantity (amount of protein in serum level) and quality (aberrant glycosylation), with highly positive prediction values
- Mechanistic study on the epithelial-mesenchymal transition in cancer

RESEARCH AREAS

- Development of *in vitro* cancer diagnostics through development of cancer biomarkers with clinical utility.
- Development of cancer biomarker based on aberrant glycosylation and autoantibodies.
- The molecular events during epithelial-mesenchymal transition in cancer and anoikis stress.
- Development of a highly efficient molecular scissor for gene editing

ACHIEVEMENTS

Mechanistic study on the effect of the aberrant glycosylation on cancer progression

Protein tyrosine phosphatase kappa (PTPk) is attacked by GnT-V, thereby experiencing the change in glycosylation. The aberrantly glycosylated PTPk is vulnerable to the attack by an extracellular protease, giving rise to the cleavage of extracellular domain of the adhesion molecule. The high cleavage is associated with a loosed cell-cell interaction and ultimately with an elevated cancer cell migration.

Development of *in vitro* diagnostics for liver cancer

We have reported the production of anti-ATIC and anti-cytokeratin 8/18 autoantibodies in hepatocellular carcinoma (HCC) using the HCC mouse model and suggested a novel method for the detection of those auto-antibodies in patient sera, which is very effective for the diagnosis of HCC.

SELECTED PUBLICATIONS

Eun Wie Cho (Corresponding)
Biotechnol Lett. 33(4):655-61.
Optimization of phage-immobilized ELISA for autoantibody profiling in human sera

Hyang Sook Yoo & Seungwoo Hwang (Co-Corresponding)
BMC Genomics. 12:S3.
Liverome: a curated database of liver cancer-related gene signatures with self-contained context information

Jeong-Heon Ko (Corresponding)
Biochem Biophys Res Commun. 404(1):96-102.
Galectin-3 binding protein promotes cell motility in colon cancer by stimulating the shedding of protein tyrosine phosphatase kappa by proprotein convertase 5

Jeong-Heon Ko & Sang Jick Kim (Co-Corresponding)
J Biotechnol. 151(2):225-30.
Generation of antibodies recognizing an aberrant glycoform of human tissue inhibitor of metalloproteinase-1 (TIMP-1) using decoy immunization and phage display

Bio-Therapeutics Research Institute

Division of Bio-Therapeutics Research

Immunotherapy Research Center
Regenerative Medicine Research Center
Chemical Biology Research Center
Natural Medicine Research Center

Division of Biomedical Infrastructure

Biotechnology Process Engineering Center
Bio-Evaluation Center
National Primate Research Center
Biomedical Mouse Resource Center

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Biotherapeutics, the New Economic Growth Engine

KRIBB builds a pipeline for biologics at the national level through the development of diagnostics, drug candidates for difficult-to-cure diseases such as cancer. In particular, the Division of Biomedical Infrastructure functions as public biotechnology infrastructure, both nationally and internationally.

As parts of the Division, the National Primate Research Center provides primate disease models by establishing research foundations. The Bio-Evaluation Center evaluates drug efficiency and toxicological factors for the development of drug candidates.

Bio-Therapeutics Research Institute

Immunotherapy Research Center

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

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RESEARCH AREAS

NK cell therapy
▸ Developing platform technology for the differentiation of stem cells
▸ Developing platform technology for the regulation of NK cell differentiation
▸ Developing NK cell therapy for cancer treatment
▸ Developing customized NK cell therapy through preclinical study

Antibody therapy
▸ Development of therapeutic target antigens
▸ Development of human and humanized antibodies for cancer treatment
▸ Evaluation of therapeutic antibodies

High efficient diagnosis
▸ Construction of molecular diagnostic devices
▸ Nano-particle for molecular diagnosis
▸ Analysis of diagnostic technology

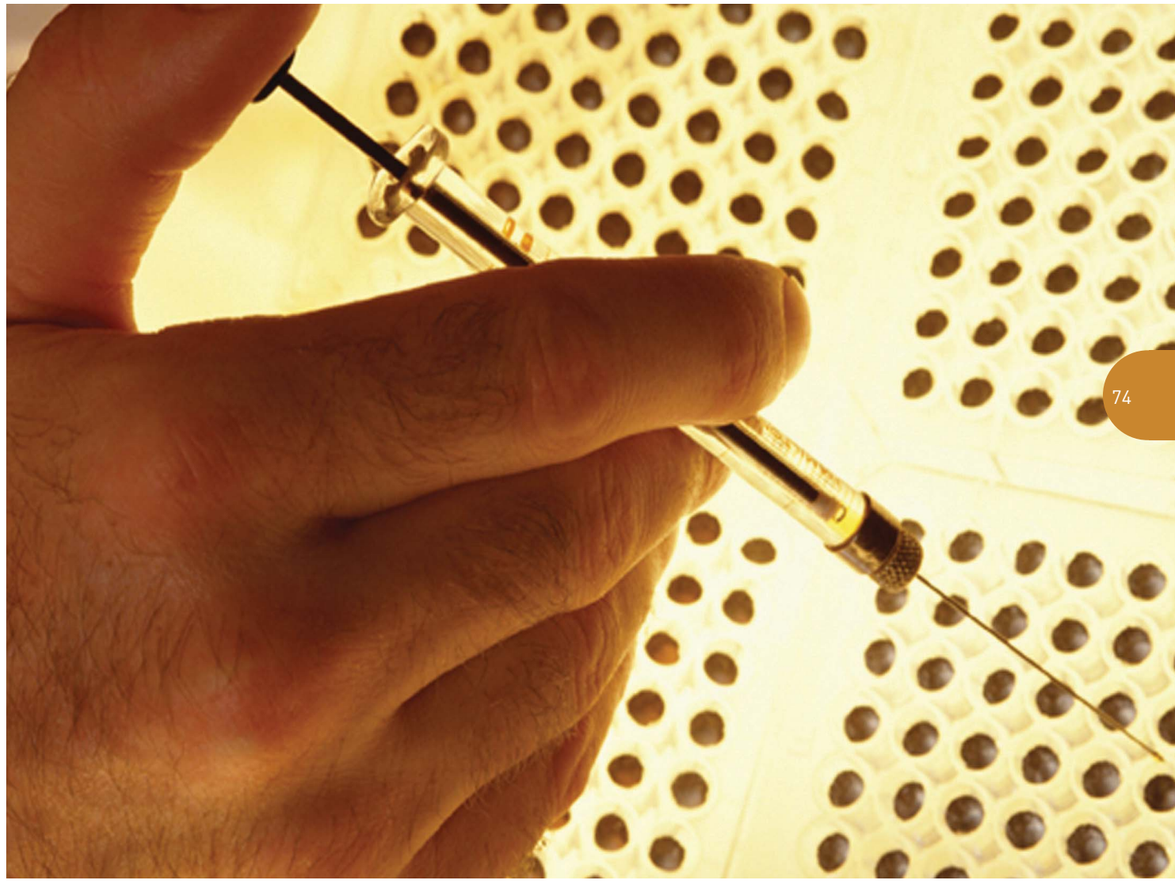
ACHIEVEMENTS

Molecular profiling for NK cell differentiation from stem cells
NK cells develop from hematopoietic stem cells (HSCs) in the bone marrow. To understand the molecular regulation of NK cell development, serial analysis of gene expression (SAGE) was applied to HSCs, pNK, mature NK cells cultured without (-OP9) or with (+OP9) stromal cells, OP9. From 170, 464 total individual tags from four SAGE libraries, 35,385 unique genes were identified. The Identification of genome-wide profiles of gene expression in different stages of NK cell development affords us a fundamental basis for defining the molecular network during NK cell development.

Development of immune therapy techniques utilizing NK cells
Based on the observations in NK differentiation, immunotherapy for cancer has been designed. Platform technology for drug development of cancer immune therapy was established and has been used in the treatment of incurable diseases involving immune cells.

Identification of PAUF and anti-PAUF antibody development
Based on DNA microarray, it was found that PAUF is highly expressed in patients with pancreatic cancer and that the factor roles in pancreatic cancer metastasis. Anti-PAUF antibody blocked the tumor growth *in vivo* successfully.

Development of nano-biosensor for tumor diagnosis
The Au elliptical nanoarrays fabricated on glass have designed and fabricated. For application to clinical PSA diagnostics, the peak shift of the LSPR band has been amplified by the enzyme-catalyzed BCIP/NBT precipitation, resulting in a remarkable enhancement of the detection limit that is far under the diagnostic level of 4-10 ng mL-1 PSA. The enzymecatalyzed precipitation method in the LSPR sensor could be extended to detect analytes with low molecular weight and other clinical biomarkers at low concentrations in actual clinical samples.



SELECTED PUBLICATIONS

Im Sik Chung (Co-Corresponding)
Chemistry. 17(30):8466-71.
Coordination power adjustment of surface-regulating polymers for shaping gold polyhedral nanocrystals

Inpyo Choi (Corresponding)
Blood. 118(20):5476-86.
Human microRNA-27a* targets Prf1 and GzmB expression to regulate NK-cell cytotoxicity

Jeong-Ki Min (First)
J Clin Invest. 121(5):1882-93.
The WNT antagonist Dickkopf2 promotes angiogenesis in rodent and human endothelial cells

Jeong Ki Min (Co-Corresponding)
Stem Cells. 29(12):2094-9.
L1 cell adhesion molecule, a novel surface molecule of human embryonic stem cells, is essential for self-renewal and pluripotency

Sang Seok Koh (Co-Corresponding)
Oncogene. 30(2):201-11.
Pancreatic adenocarcinoma upregulated factor promotes metastasis by regulating TLR/CXCR4 activation

Tae-Don Kim (Co-First)
FASEB J. 25(8):2757-69.
Modulation of exosome-mediated mRNA turnover by interaction of GTP-binding protein 1 (GTPBP1) with its target mRNAs

Yong Beom Shin (Co-Corresponding)
ACS Nano. 5(2):897-904.
Highly sensitive biosensing using arrays of plasmonic Au nanodisks realized by nanoimprint lithography

Yong Beom Shin (Co-Corresponding)
Biosens Bioelectron. 26(12):4690-6.
Electrical immunosensor based on a submicron-gap interdigitated electrode and gold enhancement

Bio-Therapeutics Research Institute

Regenerative Medicine Research Center

Our research goal is understanding mechanisms of animal development and stem cell functions to develop regenerative therapies to treat human diseases. We focus on early animal embryos and human stem cells both of which have potential to differentiate into a wide range of cell types. We take molecular, cellular and epigenetic approaches to identify critical factors and to investigate fundamental regulatory mechanisms in early embryogenesis, self-renewal and differentiation of stem cells and reprogramming of adult cells.

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RESEARCHERS

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- Epigenetic regulation of early mammalian development
- Molecular genetics on cell de-differentiation and reprogramming

Jeong-Woong Lee jwlee@kribb.re.kr
- Production of knock-out clone pigs
- Functional genomics in disease model animals

Janghwan Kim negapos@kribb.re.kr
- Neural differentiation of pluripotent stem cells
- Reprogramming of somatic cells

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- Molecular mechanisms underlying the reprogramming process

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- hESC self-renewal and differentiation
- Generation of induced iPSCs

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- Molecular mechanisms of stemness factors
- Small RNA pathways in hESCs/hiPSCs

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- Molecular mechanisms underlying reprogramming for hiPSC pluripotency

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- Somatic cell nuclear transfer
- Micromanipulation of mouse, porcine and bovine

RESEARCH AREAS

- Molecular studies on early embryogenesis
- Animal model development for organ transplatation
- Self-renewal and differentiation of pluripotent stem cells
- Molecular mechanism of cellular reprogramming
- Generation of reprogrammed cells
- Human disease modeling with reprogrammed cells

ACHIEVEMENTS

Dual functions of histone-lysine N-methyltransferase Setdb1 protein at promyelocytic leukemia-nuclear body (PML-NB): maintaining PML-NB structure and regulating the expression of its associated genes

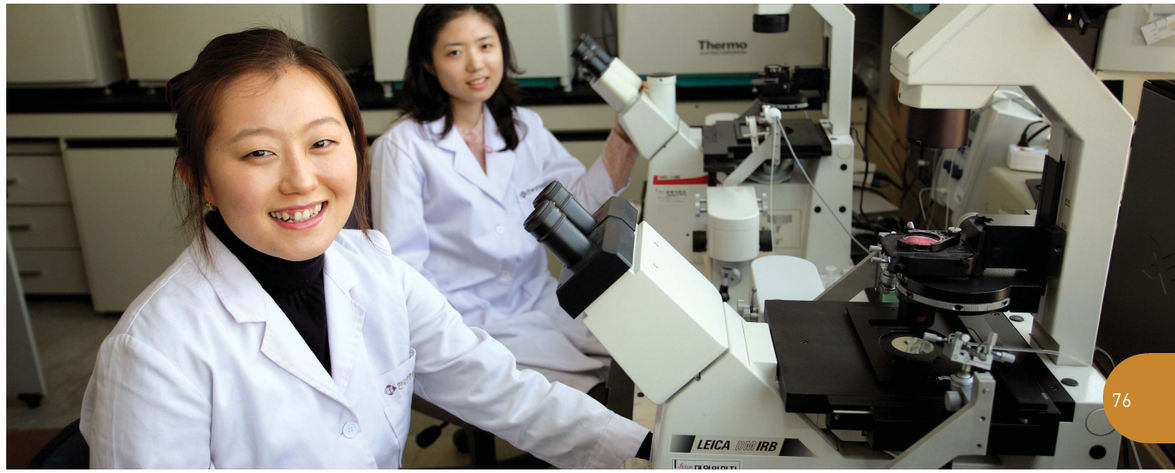
Setdb1/Eset is a histone H3 lysine 9 (H3K9)-specific methyltransferase that associates with various transcription factors to regulate gene expression via chromatin remodeling. We showed that Setdb1 associates with promyelocytic leukemia (Pml) protein from the early stage of mouse development and is a constitutive member of promyelocytic leukemia (PML)-nuclear bodies (PML-NBs) that have been linked to many cellular processes such as apoptosis, DNA damage responses, and transcriptional regulation.

Involvement of neuropeptide Y and its Y1 and Y5 receptors in maintaining self-renewal and proliferation of human embryonic stem cells

We showed that neuropeptide Y (NPY) and its Y1 and Y5 receptors have a role in maintaining human embryonic stem cell (hESC) self-renewal and pluripotency through AKT/protein kinase B and extracellular signal-regulated kinase 1/2 (ERK1/2) pathways. We demonstrated that addition of NPY improved a defined and xeno-free culture for the large-scale propagation of undifferentiated hESCs.

Physical passaging of embryoid bodies generated from human pluripotent stem cells

Embryoid bodies (EBs), have been widely used in *in vitro* differentiation protocols for human pluripotent stem cells. We provided evidence that a simple periodic passaging markedly improved hEB culture condition and thus allowed the size-controlled, mass production of human EBs. The passaging culture method of hEBs, which is simple, readily expandable, and reproducible, could be a powerful tool for improving a robust and scalable *in vitro* differentiation system of human pluripotent stem cells.



Generation of human induced pluripotent stem cells from osteoarthritis patient-derived synovial cells

We generated human induced pluripotent stem cells (iPSCs) from synovial cells of patients with osteoarthritis (OA) and showed that these iPSCs are differentiated into functional chondrocytes. Our findings indicate that patient-derived synovial cells are an attractive source of iPSCs and have the potential to advance cartilage tissue engineering and cell-based models of cartilage defects.

Transdifferentiation of fibroblasts to neural progenitor cells

We demonstrated that transient overexpression of the four Yamanaka factors (Oct4, Sox2, Klf4, and c-Myc) could be biased by specific signaling inputs toward generating functional and readily expandable neural stem/progenitor cells (NPCs) directly from fibroblasts in a surprisingly efficient manner. Our approach fundamentally changed the Yamanaka-factor-based reprogramming paradigm, and dramatically expanded its utilities into lineage-specific transdifferentiation.

SELECTED PUBLICATIONS

Janghwan Kim (First)
Proc Natl Acad Sci U S A. 108(19):7838-43.
Direct reprogramming of mouse fibroblasts to neural progenitors

Yee Sook Cho (Corresponding)
Arthritis Rheum. 63(10):3010-21.
Generation of human induced pluripotent stem cells from osteoarthritis patient-derived synovial cells

Yee Sook Cho (Corresponding)
J Cell Mol Med. 15(1):152-65.
Involvement of neuropeptide Y and its Y1 and Y5 receptors in maintaining self-renewal and proliferation of human embryonic stem cells

Yee Sook Cho (Corresponding)
PLoS One. 6(5):e19134.
Physical passaging of embryoid bodies generated from human pluripotent stem cells

Yee Sook Cho (Corresponding)
Stem Cells Dev. 20(9):1479-90.
Combinatorial activin receptor-like kinase/Smad and basic fibroblast growth factor signals stimulate the differentiation of human embryonic stem cells into the cardiac lineage

Yong-Kook Kang (Corresponding)
J Biol Chem. 286(6):4461-70.
JHDM3A module as an effector molecule in guide-directed modification of target chromatin

Yong-Kook Kang (Corresponding)
J Biol Chem. 286(47):41115-24.
Dual functions of histone-lysine N-methyltransferase Setdb1 protein at promyelocytic leukemia-nuclear body (PML-NB): maintaining PML-NB structure and regulating the expression of its associated genes

Bio-Therapeutics Research Institute

Chemical Biology Research Center

The goal of the research center is discovering bio-functional drug candidates from the metabolites of microorganisms and plants, and defining the function of their cellular targets for application to chemotherapeutics development. To accomplish this goal, we adopt chemical biology techniques based on biometabolites and cellulomics technology to develop medicinal and bio-functional compounds.

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‣ Development of botanical drugs for treatment of metabolic disorders

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‣ Oxidative stress / Antioxidants and functional cosmetics

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‣ Medicinal chemistry

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‣ Molecular microbiology
‣ Combinatorial biology of natural product biosynthetic genes

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‣ Target validation via pharmacologically active compounds

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Validation of drug target

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‣ Natural product chemistry

RESEARCH AREAS

Obesity / Diabetes
‣ Developing anti-obesity and anti-diabetic lead compounds with regulatory roles in metabolism and gene expression

Anti-osteoporosis
‣ Developing new bioactive compounds inhibiting osteoclast differentiation from oriental herbs and plant resources

Epigenomic modulators
‣ Developing bioactive compounds regulating DNA methyltransferase-mediated gene expression and carcinogenesis

Antioxidants / Cosmetics
‣ Discovering bioactive compounds for anti-aging, whitening and skin protection

Microbial metabolite biotechnology
‣ Discovering bioactive secondary metabolites and compiling a library of microbial secondary metabolites

Combinatorial and Synthetic Biology
‣ Create novel organic molecules through deliberate *in vivo* and *in vitro* engineering of these pathways for production of human and veterinary pharmaceuticals, specialty chemicals, and high value biomaterials.

ACHIEVEMENTS

Isolation of ER-stress inducers and inhibitors
An endoplasmic reticulum (ER)-stress inducer isolated from a plant extract strongly induced the expression of ER-stress-associated proteins, including GRP78 chaperone, and the splicing of XBP-1 mRNA, a hallmark of ER-stress-induced IRE-1a activation. Also, an ER-stress inhibitor was isolated to be used as an inhibitor of type II diabetes mellitus. Both of them are expected to challenge cancer therapeutics and anti-diabetes.

Isolation of osteoclast differentiation inhibitors
Osteoclast differentiation inhibitors isolated from oriental herbs are promising candidates for osteoporosis treatment.

Isolation of DNA methyltransferase inhibitors and new target tumor suppressors genes
Purified compounds from a fungus were found to have an inhibitory activity against human DNA methyltransferase-1 *in vitro* and cellular system. The compounds elevated tumor suppressor gene expression in HCT 116 cells. In addition, a few tumor suppressor genes were revealed to be regulated by DNA methylation in K-*ras* overexpressing prostate cancer cells. Hence the compounds and the targets are valuable for chemotherapeutics development.

Improved Hsp90 inhibitors via engineering of the geldanamycin biosynthetic genes
We developed a series of potent heat shock protein (Hsp) 90 inhibitors based on the polyketide natural product geldanamycin via the biosynthetic gene engineering techniques.

SELECTED PUBLICATIONS

Bo Yeon Kim & Jong-Seog Ahn (Co-Corresponding)
J Am Chem Soc. 133(18):6865-7.
Fusarisetin A, an acinar morphogenesis inhibitor from a soil fungus, *Fusarium* sp. FN080326

Jong-Seog Ahn (Co-Corresponding)
J Nat Prod. 74(5):1284-7.
Protuboxepins A and B and protubonines A and B from the marine-derived fungus *Aspergillus* sp. SF-5044

Sangku Lee (Co-Corresponding)
Bioorg Med Chem Lett. 21(3):977-9.
Biological evaluation of KRIBB3 analogs as a microtubule polymerization inhibitor

Young-Soo Hong (Corresponding)
J Ind Microbiol & Biotech. 38(10):1657-65.
Biosynthesis of plant-specific phenylpropanoids by construction of an artificial biosynthetic pathway in *Escherichia coli*

Young Shin Kwak (Co-Corresponding)
Org Biomol Chem. 9(20):7237-42.
Syntheses of sulfur and selenium analogues of pachastrissamine via double displacements of cyclic sulfate

Young Shin Kwak (Co-Corresponding)
Tetrahedron. 67(48):9401-4.
Expedient synthesis of 4-O-methylhonokiol via Suzuki-Miyaura cross-coupling

Bio-Therapeutics Research Institute

Natural Medicine Research Center

Our aim is to develop drug candidates for natural / synthetic drugs mainly from plant sources which are effective against chronic diseases such as asthma / COPD, virus, metabolic diseases and cancers.

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RESEARCHERS

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‣ Identification of biologically active compounds from natural resources
‣ Evaluation of natural products and/or extracts against chronic diseases
‣ Metabolomic research of medicinal plants for origin discrimination and standardization

Hyeong-Kyu Lee hykylee@kribb.re.kr
‣ Identification of new molecular targets related to immune diseases
‣ Development of active compounds for pharmaceuticals
‣ Construction of natural product library

Young Kook Kim kimyk@kribb.re.kr
‣ Establishment of screening systems for metabolic diseases
‣ Development of bioactive compounds specifically against obesity and diabetes

Kyung-Seop Ahn ksahn@kribb.re.kr
‣ Evaluation of anti-inflammatory and anti-asthmatic activity of natural products
‣ Identification of new bio-markers for asthma/COPD treatment

Hyun-Jun Lee hjlee@kribb.re.kr
‣ Regulation of immune cell differentiation and function
‣ Control of inflammation by innate and adaptive immune mechanisms

Dur Han Kwon dhkwon@kribb.re.kr
‣ Evaluation natural products for anti-viral activity *in vitro* & *in vivo*
‣ Development of new active compounds against viral diseases including influenza virus, rotavirus, corona virus, rhinovirus and enterovirus

Sung Chan Cho sungchan@kribb.re.kr
‣ Development of DGAT2 inhibitors for treatment of metabolic disorders
‣ Research on the molecular mechanism of Spinal Muscular Atrophy & its application for drug discovery

Su Ui Lee iamsuui@kribb.re.kr
‣ Development of cell-based assays using the molecular targets involved in metabolic diseases
‣ Identification and validation of bioactive small molecule through screening

RESEARCH AREAS

Molecular targets related to immune diseases
‣ Identification of major genes & proteins involved in asthma and their functional analysis
‣ Establishment of bioassay / screening systems using the molecular targets of asthma / COPD

Chronic disease modulation
‣ Screening of cellular response modulators involved in immune cell activation
‣ Researches of the inhibitory activity of respiratory viruses
‣ Research of molecular targets for metabolic diseases and cancers

Natural product Chemistry
‣ Isolation of bioactive materials from plant and microbial sources.
‣ Elucidation of natural product structure using analytical instruments (HPLC, LCMS, NMR)

Natural product library
‣ Production of medicinal plant extracts from domestic and foreign plant sources
‣ Management of plant extracts bank and natural compounds library

ACHIEVEMENTS

Identification of natural products effective against chronic diseases
We isolated active compounds as therapeutic candidates from natural resources and evaluated biological activities of them in inflammation, asthma, cancer and metabolic disorder.

Development of anti-viral materials
We discovered several kinds of natural compounds attenuating viral infection via NK cell activation or inhibiting viral reproduction. These actives are under investigation towards pre-clinical test for anti-viral pharmaceuticals.

Construction of biomaterial infra-structure
Plant materials were collected and their extracts were deposited in the Plant Extract Bank (over 5,000 domestic and 14,000 international extracts) and distributed to researchers.

Industrial research
We have licensed out two natural drug candidates for asthma (Han Kook Shin Yak pharmaceutical Co. Ltd. and Yungjin Pharm. Co. Ltd.), a neutraceutical for atherosclerosis (Unigen Ltd.) and a drug candidate for cholesterol lowering agents (Dong-Hwa Pharm. Ind. Co. Ltd.).

SELECTED PUBLICATIONS

Hyeong-Kyu Lee (Corresponding)
Chem Pharm Bull. 59(3):382-4.
Anti-inflammatory diterpene from *Thyrsanthera suborbicularis*

Kyung-Seop Ahn (Corresponding)
Int Immunopharmacol. 11(2):266-73.
Effects of astilbic acid on airway hyperresponsiveness and inflammation in a mouse model of allergic asthma

Kyung-Seop Ahn (Corresponding)
J Med Food. 14(10):1144-51.
Capsicum annuum L. methanolic extract inhibits ovalbumin-induced airway inflammation and oxidative stress in a mouse model of asthma

Young Kook Kim (Corresponding)
Arch Pharm Res. 34(5):727-31.
The conformation and CETP inhibitory activity of [10]-dehydrogingerdione isolated from *Zingiber officinale*

Bio-Therapeutics Research Institute

Biotechnology Process Engineering Center

Our goal is to develop industrial platform technology for biological products. In particular, we intensively carry out a process scale-up towards the optimization and commercialization for the production of biomaterials and biopharmaceuticals using pilot-plant facilities in order to expand research outcomes and to stimulate commercialization. Additionally, we systematically support the business activities of the bioindustry and cultivate human resources through academic-industrial collaborations.

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‣ Bioprocess engineering

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‣ Separation and purification

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‣ Biochemical engineering
‣ Molecular breeding of yeast and bacterial cells

Yeon-Gu Kim ygkim@kribb.re.kr
‣ Biochemical engineering
‣ Animal cell culture

RESEARCH AREAS

Microbial fermentation and scale-up research
‣ Development of novel expression system for recombinant proteins
‣ Development of industrial strain
‣ Process development
‣ Scale-up research for the production

Animal cell culture for biologics production
‣ Screening of stable cell line producing therapeutic antibody
‣ High-cell density 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 in separation and purification process

ACHIEVEMENTS

Development of biological process for the production of microbial metabolites
Pilot-scale processes for the production of microbial metabolites such as amino acids (ornithine, threonine, and proline), antibiotics, and shikimic acid have been pioneered. This technology includes not only process development but also strain development by traditional mutagenesis and genetic engineering.

Over-expression and purification of recombinant proteins
Here technology for the production of heterologous proteins of interest in both *E. coli* and *P. pastoris* have been developed.
It involves over-expression of a target protein, fusion tag selection, cleavage optimization, and serial chromatographic purification, which can be applied for manufacturing therapeutic proteins and functional enzymes.

Development of a novel Pichia expression system
Two strong methanol-free promoters in *P. pastoris:* translation elongation factor 1a promoter (PTEF1) with high growth-associated expression characteristics and phosphate-responsive promoter (PPH089) of a sodium phosphate symporter were developed. Also, a cost-effective and simple PTEF 1- and PPH089-based fermentation process was developed for industrial applications. Furthermore, we established an easy-to-use multicopy system in *P. pastoris* using autonomous replication sequences (ARS) and an episomal plasmid to maintain multiple genes of interest in *P. pastoris* and enhance heterologous expression compared with a single copy integration in *P. pastoris.*

Developement of recombinant vaccines for livestock
We established an integrated system for the expression of Apx toxins, which are essential proteins for protection against *A. pleuropneumoniae* infection, as subunit antigens against porcine pleuropneumonia that makes it possible to obtain soluble and biologically active Apx toxins in *E. coli* without additional refolding steps.
Additionally, the products from the developed expression vectors elicit immunological responses and protective immunity aginst *A. pleuropneumoniae* infection in an infected guinea pig model.

Production of therapeutic proteins in mammalian cell culture
Mammalian cell culture has become the dominant system for the production of recombinant proteins for clinical applications because of their proper protein folding and complete post-translational modification. We are currently developing rCHO cell culture technology for the manufacture of therapeutic proteins in a suspension bioreactor. Additionally, we are improving upon avaliable boosting technology for high-quality proteins by genetically engineered cells. Furthermore, we have developed chromatographic purification technologies and high-throughput precision analysis.

SELECTED PUBLICATIONS

Eun-Gyo Lee (First)
Anal Biochem. 408(2):206-11.
Carbon nanotube-assisted enhancement of surface plasmon resonance signal

Eun-Gyo Lee (Co-Corresponding)
Process Biochem. 46(11):2201-4.
Effect of Bcl-xL overexpression on erythropoietin production in recombinant Chinese hamster ovary cells treated with dimethyl sulfoxide

Hong-Weon Lee (Corresponding)
Vet Microbiol. 148(1):89-92.
Identification of novel immunogenic proteins in pathogenic *Haemophilus parasuis* based on genome sequence analysis

Jung-Oh Ahn (First)
FEMS Microbiol Lett. 324(1):10-6.
NADPH-dependent pgi-gene knockout *Escherichia coli* metabolism producing shikimate on different carbon sources

Bio-Therapeutics Research Institute

Bio-Evaluation Center

Our aim is to establish a collective and specific infrastructure of techniques, facilities, and manpower to support the effective and successful development of biotech products. For this purpose, we have not only constructed developmental and evaluational infrastructure for optimizing, analyzing, and standardizing living modified organisms and drug candidates; but also assessed the usefulness and risks of biotech research and development processes and the biotech products themselves, to facilitate commercialization.

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RESEARCHERS

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▸ Efficacy evaluation of anti-cancer agents

RESEARCH AREAS

Living modified organisms (LMOs)
▸ Conducting genetic analysis and assessing the risks of LMOs

New drugs
▸ Discovery and preclinical evaluation of new drug candidates

ACHIEVEMENTS

Living modified organisms
We have established and developed infrastructure for genetic analysis and risk assessments of living modified organisms.
In particular, we have been assessing the potential risks of domestically developed transgenic rices, chilli peppers, potatoes, poplars and watermelons. We also conduct national environmental monitoring on domestic soybeans, corns and oilseed rapes in order to the inspect the extent of genetic contamination by imported LMOs.

Drug discovery
We developed and implemented an integrated infrastructure for drug discovery encompassing preclinical efficacy, ADME and toxicity evaluations. We have applied this technology platform to the discovery and preclinical evaluation of drug candidates in the areas of cancer and immune-related diseases and supported drug discovery in the pharmaceutical industry, academia and research institutes.

SELECTED PUBLICATIONS

Chang-Gi Kim (Co-Corresponding)
Planta. 233(4):807-15.
Gene flow from herbicide-tolerant GM rice and the heterosis of GM rice-weed F2 progeny

Jong Soon Kang (First)
Food Chem Toxicol. 49(9):2453-58.
Improvement of high-fat diet-induced obesity by a mixture of red grape extract, soy isoflavone and L-carnitine: Implications in cardiovascular and non-alcoholic fatty liver diseases

Soon-Chun Jeong (Corresponding)
Theor Appl Genet. 122(5):865-74.
Fine genetic mapping of the genomic region controlling leaflet shape and number of seeds per pod in the soybean

Soon-Chun Jeong (Corresponding)
Theor Appl Genet. 122(5):875-84.
Glycine max non-nodulation locus rj1: a recombinogenic region encompassing a SNP in a lysine motif receptor-like kinase (GmNFR1α)

Bio-Therapeutics Research Institute

National Primate Research Center

The NPRC was established within KRIBB as a major national infrastructure component to support industrial, academic and research institutions in the development of xenotransplant organs, providing animal models for research in regenerative medicine and incurable diseases, and evaluating the preclinical trials of new drug candidates.

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RESEARCHERS

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▸ Developing cell and tissue resources derived from nonhuman primates and conducting research for their applications
▸ Developing new breeder miniature pigs for research and development of bio-organs

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▸ Microbiological monitoring of specific-pathogen free animals
▸ Structure / Function studies of outer membrane vesicles

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▸ Stem cell research in mammals
▸ Reproductive developmental biotechnology

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▸ Maintaining quality standards of primate resources by SPF health monitoring
▸ Development of neuronal disease models (Stroke, Dementia, Parkinson's disease) with non-human primates

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▸ Human and non-human primate comparative genomics / Primate molecular genetics / Primatology / Identification and molecular characterization of primate genes

RESEARCH AREAS

Acquisition, propagation and distribution of specific pathogen free (SPF) primate resources
▸ Acquiring and distributing SPF primate resources to industrial, academic and research institutions

Standardization in handling of and regulating lab requirements for primate research
▸ Maintaining quality standards of 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 primate resources at the international level

Xenotransplantation research
▸ Transplanting organs (e.g. pancreatic islet, heart) from transgenic germ-free pigs into SPF primates and analyzing the efficacy and safety of the organs transplanted

Regenerative medical research and applications
▸ Using primate disease models in cell therapy and gene therapy research, and evaluating their efficacy and safety for the treatment of incurable diseases

Preclinical efficacy assessments of newly-developed drug candidates
▸ Applying various biodrugs and biomaterials to SPF primates to evaluate efficacy

Evaluation of immunogenicity and safety of vaccine candidates
▸ Testing and assessing the immunogenicity, efficacy and safety of AIDS and various other vaccines

Development of disease models
▸ Constructing disease models for incurable primate diseases, which have metabolic pathways most similar to man, and thus developing new drugs and applications for organ and regenerative research
▸ Developmental biotechnologies and applications
▸ Establishing cell resources, including embryonic stem cells and a variety of tissue cells, and applying them to cell therapies, nuclear transfers, and the study of molecular mechanisms

Molecular identification and characterization of non-human primate genes
▸ Investigation of molecular mechanisms of gain and loss of genes in various primates

Collaboration and support for nationwide non-institutional research involving primates
▸ Providing specialized technologies and information about primate care and facilities to other researchers, and conducting collaborative research for the development of related technologies

ACHIEVEMENTS

Procurement of SPF primate resources, maintenance and breeding of healthy SPF animals, and preclinical evaluation of biomedical technologies
The NPRC currently houses six types of SPF primates: rhesus monkeys, cynomolgus monkeys, African green monkeys, Japanese monkeys, squirrel monkeys and common marmosets - a total of 240 animals.
And NPRC produced two IVF newborns.

Transfer of primate-related resources and techniques to national partners of industrial, academic and research institutions
The NPRC shares its primate-related expertise with researchers nationwide, in fields such as neuroscience, pharmacokinetics, etc. We provide services for the upkeep of SPF primates, including microbiological monitoring, quarantine and maintenance workshops, and train the personnel (e.g. veterinarians and breeders) who work with primates.

Establishment of disease model using primates
Establishment of production technology of IVF newborns and stem cell lines (13 case) and primary somatic cell line (3 case) for the production of transgenic and nuclear transferred primates. Establishment of primate brain disease model (Stroke and Alzeheimer's disease) and development of MRI-evaluation system

Collaboration with national and international research teams
We conducted collaborative studies in various fields, including xenotransplantation and the pharmacokinetic evaluation of therapeutic drugs against aplastic anemia. For the introduction of the baboon monkey, we cooperated with the Washington, Tulane, and Southwest National Primate Research Centers, and are currently collaborating with world-renown researchers in embryo implantation and development. We are also working with domestic companies for the development of mini-pigs useful in organ xenotransplantation.

SELECTED PUBLICATIONS

Kyu-Tae Chang (Corresponding)
BBA-Biomembranes. 1808(10):2359-65.
Instability of toxin A subunit of AB5 toxins in the bacterial periplasm caused by deficiency of their cognate B subunits

Kyu-Tae Chang (Corresponding)
Fertil Steril. 95(8):2582-4.
Supplementation with estradiol-17β improves porcine oocyte maturation and subsequent embryo development

Kyu-Tae Chang (Co-Corresponding)
J Alzheimers Dis. 25(3):517-23.
Spatial distribution of glucose hypometabolism induced by intracerebroventricular streptozotocin in monkeys

Kyu-Tae Chang (Co-Corresponding)
Vaccine. 29(46):8293-301.
Adjuvant effect of bacterial outer membrane vesicles with penta-acylated lipopolysaccharide on antigen-specific T cell priming

Bio-Therapeutics Research Institute

Biomedical Mouse Resource Center

Mice are an essential resources for functional genetics and biomedical drug development. Our aim, as a national infrastructure, is to establish a domestic representative infrastructure of resources, technologies, facilities and manpower to support national biomedical researches using mouse resources. For this purpose, we have been collecting, preserving and distributing laboratory animal resources since 1984. We are developing technologies for the quality control of the laboratory animals, especially microbiological and genetical monitoring, and for the development of genetically engineered mice. We also cooperate with several international organizations in mouse resources and primary mouse phenotyping.

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RESEARCHERS

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▸ Genetic monitoring of laboratory animals health safety of LMO

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▸ Bacteriology
▸ Health monitoring of laboratory animals

RESEARCH AREAS

Laboratory animal resources center
▸ Collection, maintenance, and allocation of laboratory animal resources
▸ Breeding and distribution of laboratory animal resources to research communities
▸ Permanent preservation of laboratory animal resources as frozen resources
▸ Establishment of a laboratory animal database
▸ Quality control of laboratory animals
▸ Phenotyping of mutant mice
▸ Development of animal disease models
▸ Training of laboratory animal techniques

ACHIEVEMENTS

A highly representative and the largest Korean laboratory animal resource bank
▸ Deposits of laboratory animal resources: 380 strains
▸ Distribution of laboratory animal resources: 6,105 animals

Quality control center for laboratory animals
▸ Health monitoring: 2,123 animals
▸ Mouse genotyping: 3,878 animals
▸ Animal clearing: 45 strains

Preservation of laboratory animal resources as frozen resources
▸ Embryo freezing: 105 strains

Training in laboratory animal techniques
▸ The 34th Laboratory Animal Workshop was held on December 6-7, 2011

Technical advice and animal testing support
▸ Blood chemical analysis: 1,897 animals
▸ Technical advice: 35 cases

International cooperation with ICLAS and AMMRA
▸ ICLAS: International Council for Laboratory Animal Science
▸ AMMRA: Asian Mouse Mutagenesis Resource Association
▸ AMPC: Asia Mouse Phenotyping Consortium

SELECTED PUBLICATIONS

Hyoung-Chin Kim (Co-Corresponding)
J Hepatol. 54(6):1168-76.
Vitamin D3 up-regulated protein 1 deficiency accelerates liver regeneration after partial hepatectomy in mice

Bio-Materials Research Institute

Applied Microbiology Research Center

Infection Control Material Research Center

Bioindustrial Process Research Center

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Enhancing Industrial Value of Biotechnology through Development of New Biomaterials Technologies

The Bio-Materials Research Institute was established with the core objective of developing functional materials through the application of biotechnology techniques, such as metabolic engineering, natural material engineering and bioprocess engineering. Our goal is to industrialize these biomaterials for applications in energy, food, agriculture and the environment.

Bio-Materials Research Institute

Applied Microbiology Research Center

Our goal is to develop biotechnologies and bioprocesses for the production of microbial metabolites, proteins, industrial enzymes and bioenergy, all of which are useful for the phamaceutic, nutraceutic, dietetic, cosmetic, feed, fine chemical and other industries.

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▸ Technologies for sustainable microbial oil / refinery

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▸ Development of platform technologies for massive screening and the commercialization of industrially valuable enzymes using the HTS system
▸ Development of the technology to prepare genomic library from single unculturable microorganism sorted from nature

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▸ Development of platform technologies for screening useful enzymes / metaboic pathways using high thoughput technology
▸ Development of the tool box applicable to the white biotechnology based on synthetic biotechnology

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▸ Glycoengineering and glyco(bio)technology
▸ Development of sugar platform technologies for biorefinery using renewable bioresources

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

Molecular bioprocess engineering
▸ Production of therapeutic recombinant proteins
▸ Development of bio-refinery technologies

ACHIEVEMENTS

Microbial strains and processes to produce biochemicals
Microbial strains and processes optimized to produce valuable chemicals (1,3-propanediol, 2,3-butanediol, 3-hydroxypropionic acid and etc.) using crude glycerol derived from biodiesel industry were developed through genetic and metabolic engineering, which would be applicable for platform chemicals for eco-friendly biochemcal industries such as bio-plastics, textiles and so on.

Production and utilization of microbial oil
Oleaginous heterotrophic microalgal strains to produce lipid containing functional substances such as polyunsaturated fatty acids were isolated and the optimal process was developed. The microbial oil would be valuable as a feedstock source for biofuel, chemicals and active substance (for drug, food and feed ingredient).

Bioenergy
Lignocellulosic biomass is a renewable bioresource for second-generation bioethanol production. These potential sugar resources, derived from various agricultural residuals, containing cellulose, hemicellulose, and lignin can be hydrolyzed or enzymatically degraded to sugars, and then be fermented to produce bioethanol. Also these sugar flat form technology could be applied to various biorefinery process as an environmentally friendly process.

High-throughput screening system and its biotechnological applications
We developed mass screening methods for various enzymes from metagenomic libraries using HTS system based on robot. We could new enzymes such as cellobiohydrolases, glycosyltransferases, BVMO, cold-adapted esterase and deoxyribose 5-phosphate aldolase (DERA) based on fluorescence intensity. These new strategies combined with HTS system could screen various new enzyems more fast, sensitive mbineasy than previously reported screening methods. This approach would be applied for other useful enzyme and metabolic pathway screening from metagenomic resources.

Screening enzyme from single cell based polymerase Fosmid cloning
A new method was developed for enrichment minor bacteria from environmental samples. And single cell based fosmid libraries generated from this minor bacterial pools. This method is based on the Fluorescence in situ hybridization (FISH), Fluorescence associated cell sorter (FACS), and Multiple displacement amplification (MDA). We demonstrated enrichment minor bacteria from artificial microbial community and single cell based MDA followed by fosmid library construction for activity screening.

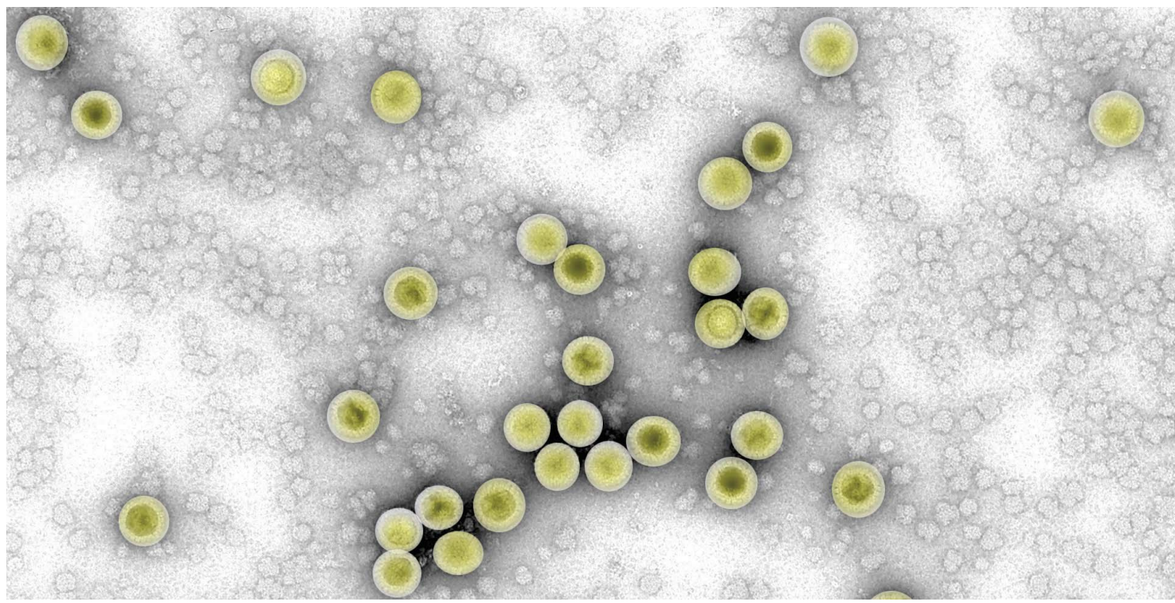
SELECTED PUBLICATIONS

Chul Ho Kim (Corresponding)
Appl Microbiol Biotechnol. 89(3):697-703.
Identification and characterization of the propanediol utilization protein PduP of *Lactobacillus reuteri* for 3-hydroxypropionic acid production from glycerol

Chul Ho Kim (Corresponding)
Bioresour Technol. 102(4):3918-22.
Efficient production of ethanol from crude glycerol by a *Klebsiella pneumoniae* mutant strain

Jae Jun Song (Corresponding)
Appl Microbiol Biotechnol. 89(5):1453-62.
A novel bifunctional endo-/exo-type cellulase from an anaerobic ruminal bacterium

Jeong-Woo Seo (Corresponding)
Bioprocess Biosyst Eng. 34(2):231-6.
1,3-Propandiol production by engineered *Hansenula polymorpha* expressing *dha* genes from *Klebsiella pneumoniae*



Bio-Materials Research Institute

Infection Control Material Research Center

Our aim is to develop functional foods, natural feeds and therapeutic materials against infectious (viruses, bacteria and malaria) diseases from the natural product library, starting with traditional medicines.

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RESEARCHERS

Hyo Kon Chun hkchun@kribb.re.kr
- Metabolomics studies of fermented products
- Fuctional studies of fermented food

Joong Su Kim joongsu@kribb.re.kr
- The biochemical studies for bioactive carbohydrate derivatives synthesis using bioconversion technologies.
- The development of foreign epitope expression technology in *Bacillus subtilis*

Cha Young Kim kimcy@kribb.re.kr
- Molecular metabolic engineering for production of secondary metabolites in microbe and plant systems
- Molecular farming for production of valuable proteins such as vaccines in plant systems

Su-Jin Park sjpark@kribb.re.kr
- *In vitro* and *in vivo* screening and mechanism studies of antiviral drugs
- Molecular genetic analysis and pathogenesis of viruses causing enteritis & *pneumonia* (Coronavirus, Rotavirus, Influenzavirus, etc.) in cows, pigs and poultry

Young Min Kim u9897854@kribb.re.kr
- Enzymatic modification of bio-active material
- Discovery of enzyme for carbohydrate engineering

Young Bae Ryu ybryu@kribb.re.kr
- Isolation and structural identification of bioactive compound from natural product
- Determination of enzyme inhibition and kinetic mode of bioactive compound

RESEARCH AREAS

Construction of a bioassay system related to infectious diseases
- Establishment of a bioassay and screening system for such compounds against infectious diseases (virus, bacteria and malaria)
- Development of specifically active compounds such as inhibitors of neuraminidase for the anti-avian influenza virus.

Construction of a natural product fraction library
- Construction and utilization of both fractions from plant and microbial culture extracts and a natural compound library

ACHIEVEMENTS

Identification of biomaterials against infectious diseases
Influenza viruses bind to sialic acid on the surface of the host cell to initiate infection. Since sialic acids are ubiquitous, this presents two problems for the virus: (1) the virus may bind to a wide variety of cells, regardless of whether or not the cell can support virus replication, and (2) the virus particles themselves have sialic acid incorporated into their surface glycoproteins, so potential virus particles will bind to each other.

Neuraminidase promotes the release of the influenza virus from infected cells and facilitates the spread of the virus within the respiratory tract.
Therefore, we have developed active biomaterials from natural resources with *in vitro* assay systems for infectious diseases, and have obtained bioactive compounds from selected biomaterials using chromatographic techniques.

Identification of new molecular targets related to infectious diseases
By conducting research into molecular targets such as proteomics and genomics, new target candidates of viral infection disease have been identified. We have established assay and screening systems for viral related diseases.

***In vitro* and *in vivo* antiviral evaluations**
We have identified methods of culture and quantitative titration for several viruses including influenza virus, rotavirus, coranvirus, rhinovirus and enterovirus; and we are developing new active biomaterials and immune-therapies against viruses, including virology, mechanism of action, *in vitro* activity and animal models.

Natural product fraction library
We have built a natural product fraction library, and are collecting plant resources and utilizing both plant extracts through open column chromatography and a natural products library.

SELECTED PUBLICATIONS

Cha Young Kim (Corresponding)
Biochim Biophys Acta. 1810(12):1317-22.
Rice *OsERG3* encodes an unusual small C2 -domain protein containing a Ca(2+)-binding module but lacking phospholipid-binding properties

Hyo Kon Chun (Corresponding)
Biotechnol Lett. 33(4):783-6.
Regioselective deglycosylation of onion quercetin glucosides by *Saccharomyces cerevisiae*

Hyo Kon Chun (Corresponding)
Phytother Res. 25(9):1415-7.
Hypouricemic effects of anthocyanin extracts of purple sweet potato on potassium oxonate-induced hyperuricemia in mice

Young Min Kim (Co-Corresponding)
Appl Microbiol Biotechnol. 91(2):329-39.
Truncation of N- and C-terminal regions of *Streptococcus mutans* dextranase enhances catalytic activity

Bio-Materials Research Institute

Bioindustrial Process Research Center

Our goal is development of functional foods and therapeutic materials with the immune regulatory activity from the natural product library (plant, microorganism, and their metabolites). To elicit candidates of feed additives, food, and medicine which have a potential therapeutic effects against systemic immune diseases including infectious and inflammatory diseases.

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RESEARCHERS

Mun-Chual Rho rho-m@kribb.re.kr
▸ Identification of inflammation related target molecules and establishment of screening systems for inflammation related diseases
▸ Isolation and structure elucidation of active compounds

Byung Dae Yoon bdyoon@kribb.re.kr
▸ Construction of a base for the development of the regional bio-industry based on research into microbial materials for agriculture and stockbreeding
▸ Development of mass production processes and analysis of immune activity of β-glucan purified from *Aureobasidium* sp.

Min Soo Kim ms5732@kribb.re.kr
▸ Development of functional foods using microorganisms derived from Korean traditional fermented foods and bio-process development for mass production

Hyun-Mee Oh ohhm@kribb.re.kr
▸ Development and utilization of the cell-based and *in vivo* animal system to study of the biological activity of the active materials or compounds and identify the protective mechanism of the active materials against immune diseases

RESEARCH AREAS

Construction of a natural product fraction library
▸ Construction and utilization of both fractions from plant and microbial culture extracts

Construction of a bioassay system related to immune diseases
▸ Establishment of a bioassay and screening system searching biomaterials or compounds which have a therapeutic effect against immune diseases including infectious and inflammatory diseases
▸ Development of active compounds such as inhibitors of cell adhesion molecules, inflammatory cytokine and chemokine
▸ Development of active materials or compounds regulating the innate immune system including Toll-like receptor family
▸ Development of active materials or compounds boosting immunity such as a 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

ACHIEVEMENTS

Identification of biomaterials against inflammatory diseases
Development and utilization of cell-based screening system for the new active substrates with anti-inflammatory activity:
▸ Screening system for the inhibitor of cell adhesion molecules like VCAM-1/VLA-4 and sialic glycosaminoglycan/P-selectin
▸ Screening system for the inhibitor of IL-6 signaling
▸ Screening system for the inhibitor of Toll-like receptors

Purify the active compounds from natural resources and determine the structure of the compounds:
▸ Development of active compounds showing anti-inflammatory activity through the inhibition of cell adhesion molecules, TLRs and IL-6 signaling

Identify the biological target and the pharmacological properties:
▸ Norkurarinol showed the anti-viral activity through the activation of IRF-3, followed by IFN-β induction
▸ Demonstrate the anti-viral effect of KR-200 after coxsackievirus A21 infection: KR-200 inhibit the NF-κB and AP-1 activation and inflammatory cytokine production induced by coxsackievirus A21 infection
▸ KR-300 and the active compounds showed inhibition of IL-6 signaling

Verify *in vivo* anti-inflammatory activity:
▸ KR-200 and KR-300 inhibited the expression of proinflammaory cytokine (IL-1β, IL-6, and TNF-α) and mRNA of inflammatory genes in mice with inflammation
▸ KR-300 also ameliorated osteoarthritis

Natural product fraction library
We have built a natural product fraction library, and are collecting plant resources and utilizing both plant extracts through open column chromatography and a natural products library.

SELECTED PUBLICATIONS

Min Soo Kim (Corresponding)
Biotechnol Lett. 33(8):1663-6.
Silver-stained fibrin zymography: separation of proteases and activity detection using a single substrate-containing gel

Mun-Chual Rho (Corresponding)
Food Chem. 128(3):778-82.
Phenolic compounds isolated from *Zingiber officinale* roots inhibit cell adhesion

Mun-Chual Rho (Corresponding)
J Pharmacol Sci. 115(1):84-8.
Manassantin A and B from *Saururus chinensis* inhibit interleukin-6-induced signal transducer and activator of transcription 3 activation in Hep3B cells

Korean Bioinformation Center

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The Korean Bioinformation Center (KOBIC) is the national research center for bioinformatics which plays a key role in various areas such as genomics, proteomics, systems biology, and personalized medicine. KOBIC is also responsible for the integration and management of bioresource and biodiversity information from various research labs and institutions across the country. KOBIC provides a centralized data access portal to promote data sharing and utilization among research groups.

RESEARCHERS

Sanghyuk Lee sanghyuk@kribb.re.kr
- Bioinformatics of genome and proteome
- Alternative splicing and microRNA

Byungwook Lee bulee@kribb.re.kr
- Processing NGS data gene expression analysis and epigenomic regulation

In-Sun Chu chu@kribb.re.kr
- Biomedical informatics
- Systems cancer biology

BoKyeng Hou bkher71@kribb.re.kr
- Development of Korean Bio-resource Information System (KOBIS)
- Systems biology and chemoinformatics

Namshin Kim deepreds@kribb.re.kr
- De novo assembly and integrative analysis of genomes

Seungwoo Hwang swhwang@kribb.re.kr
- Gene expression data analysis and knowledge discovery

Jinhyuk Lee jinhyuk@kribb.re.kr
- Protein structure modeling
- Chemo-informatics research

Kyung Mo Kim kmkim@kribb.re.kr
- Evolution of proteomes, functomes, and metabolomes
- Phylogenomics of transcriptomes for ontogenetic divergence

RESEARCH AREAS

Genome informatics team
- *De novo* genome assembly and their comparative genomics studies
- *De novo* transcriptome assembly and association with diseases
- Genome mutation analysis for rare disease and cancer genomes
- Genome variation analysis and population studies & genetics

Expression and regulation team
- Development of analysis pipelines and core algorithms for RNA-sequencing
- Construction of analysis pipelines for epigenome and small RNA data

Biomedical informatics team
- Development of databases and systems for microarray data analysis
- Development of integrated analysis systems for cancer genome data

Systems bioinformatics team
- Integration of biological networks and annotation of information
- Development of algorithms, tools, and DBs for systems bioinformatics
- Network pharmacology including drug repositioning and rational drug combination

Structural informatics team
- Protein structure modeling (homology modeling)
- Structure determination with experimental observables (NMR, X-ray)
- Development of algorithms, tools, and DBs for structural informatics

Metagenome team
- Development of algorithms and pipelines for metagenome analysis
- Finding genes related to microbial environmental changes
- Understanding microbial community and genome evolution
- Developing new algorithms for structural phylogenomics

Bioresource information team
- Construction of an integrated information system for national bioresources
- Development of national data standards
- Building national collaborations and liaison networks

Information service team
- Improvement and preservation of web-service system
- Development of service item

Computer system team
- Development and management of servers, clusters, and storage systems
- Support for developing web-based solutions
- Implementation of CLOUD computing infrastructure

ACHIEVEMENTS

In an effort to support bioinformatics and genomics research in Korea, we carry out multi-faceted tasks with emphases on (i) integrative system for national biomedical research information, (ii) analysis system for high-throughput genomic sequence data, (iii) collection and systematic organization of omics data, (iv) infrastructure for systems network bioinformatics, (v) KOBIC key project on lung cancer multi-omics data production and integrative analysis, and (vi) research & education support and collaborative network.

SELECTED PUBLICATIONS

Byungwook Lee & Sanghyuk Lee (Co-Corresponding)
Nucleic Acids Res. 39(D):D939-44.
VnD: a structure-centric database of disease-related SNPs and drugs

Jinhyuk Lee (Co-Corresponding)
J Biomol Struct Dyn. 29(3):463-70.
The effect of thiobarbituric acid on tyrosinase: inhibition kinetics and computational simulation

Namshin Kim (Co-First)
Am J Hum Genet. 89(6):760-6.
Whole-exome sequencing identifies mutations of KIF22 in spondyloepimetaphyseal dysplasia with joint laxity, leptodactylic type

Sanghyuk Lee (Co-Corresponding)
Nucleic Acids Res. 39(D):D158-62.
miRGator v2.0: an integrated system for functional investigation of microRNAs

Sanghyuk Lee (Corresponding)
Nucleic Acids Res. 39(2):e9
Accurate quantification of transcriptome from RNA-Seq data by effective length normalization

Microbial Genomics & Applications Center

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We aim to promote the discovery of novel genes, valuable biomolecules, engineered microbes and innovative bioprocesses. The Microbial Genomics and Applications Center focuses on developing technology platforms to utilize information about genome function obtained from analyses of microbial genomes isolated from diverse environments.

- Elevate Korea to one of the top countries in the world microbial industry
- Create a market exceeding a billion dollars
- Construct global knowledge infrastructure by acquiring key intellectual property rights

RESEARCHERS

Tae Kwang Oh otk@kribb.re.kr
- Microbial Enzymology
- Director of Microbial Genomics and Applications Center

JiHyun F Kim jfk@kribb.re.kr
- Microbial Genomics
- Bacteria-host interaction

Jung Hoon Yoon jhyoon@kribb.re.kr
- Biodiversity
- Metagenome

Myung Hee Kim mhk8n@kribb.re.kr
- Protein structure and function
- Macromolecular crystallography
- Mechanism of signaling by histidine kinase

RESEARCH AREAS

Microbial diversity and metagenomes
- Screening of extremophiles and interaction microbes
- Development of isolation and screening techniques for uncultivated microbes
- Screening of goal-directed and beneficial microbes
- Metagenome analysis and beneficial gene screening
- Analysis of viral metagenomes and development of beneficial genes

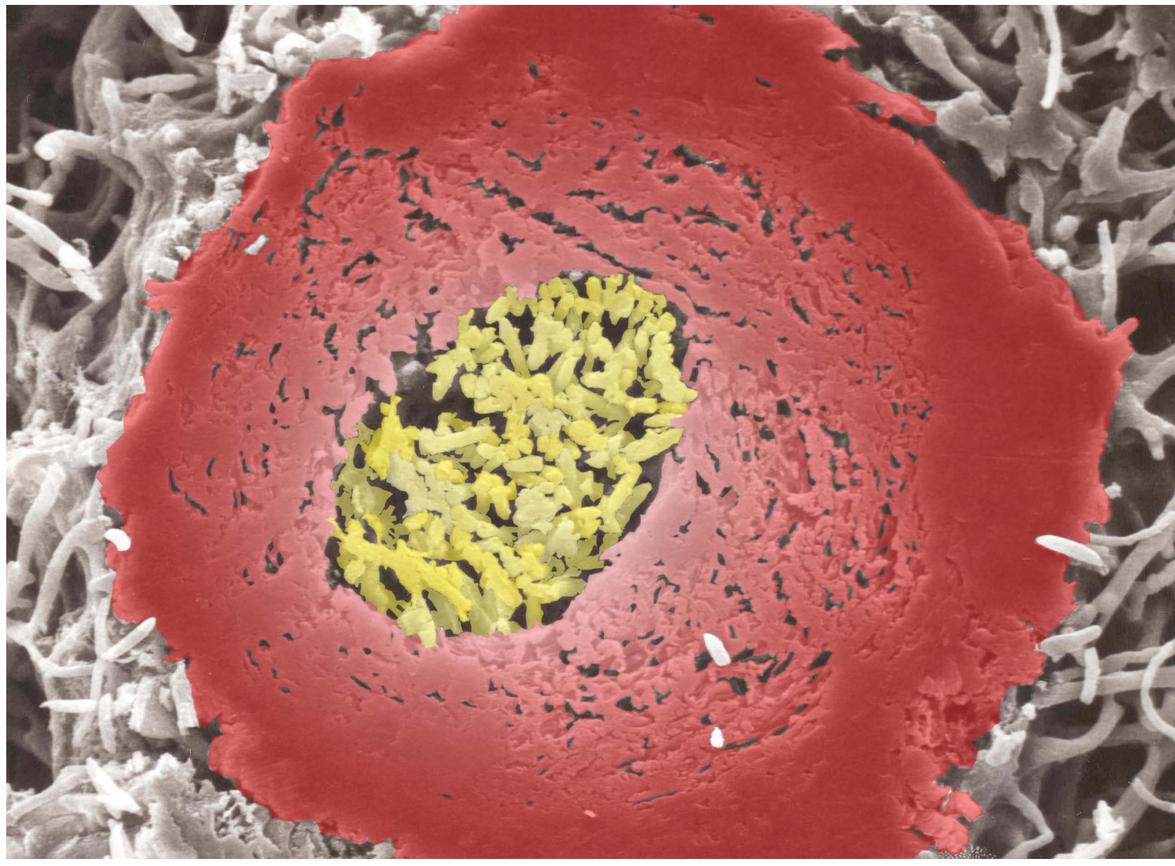
Integrated functional analysis of microbial genomes
- Genomic Network of Model Systems
- Regulatory Network of Interactive Microbes
- Applications of Microbial Interactions
- Redesign of Metabolic Circuits
- Microbial Technological Convergence
- Future Technologies for Bioenergy
- Microbial Protein Structure and Function

Industrial application of microbial genomes
- Development of fermentation and bioprocessing technologies based on cell reengineering
- Development of highly functional enzyme
- Investigation of novel physiological active materials
- Platform biomaterial development suitable for genome reengineering
- Synthetic biology-based novel biomaterial development
- Identification of novel enzyme and development of application technology

Infrastructure
- Microbial Genome InfoBase / www.gem.re.kr
- Microbial Resources Bank / www.microbank.re.kr
- Protein Bank / www.pbsb.re.kr

ACHIEVEMENTS

We developed of novel platform for designed glycoside synthesis and in silico pro-drug for various amylase family enzymes(Chonnam Univ.) and exhibited functional analysis of β-propeller phytase for the prevention of osteoporosis by increasing absorption rate of phosphate and Ca2+ in the intestine of animals.(Gachon Univ.)
Also we unveiled Cdc5-dependent Asymmetric Localization of Bfa1 Fine-tunes Timely Mitotic Exit(Yonsei Univ., publically available through PLOS Genetics) and Bilateral inhibition of HAUSP deubiquitinase by a viral interferon regulatory factor protein(KRIBB, publically available through Nature Structural & Molecular Biology)



International Cooperation Department

Technology Transfer Office

Support for Knowledge Information

International Cooperation Department

Mr. Moon Sun Kang / Director
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International Joint Reseach Project

Principal Investigator	Project Title	Period		Overseas Counterpart
		Start	End	
Dr. Bong Hyun Chung	Development of materialls for one-spot multiple bioanalysis	2008.7.1	2018.6.30	The University of Kitakyushu, Japan
Dr. Jihyun F. Kim	An Integrated Information Bank for Microbial Genome Research	2002.10.1	2012.3.31	Auburn University, USA
Dr. Haeyoung Jeong	Microbial Resources Bank	2002.10.1	2012.3.31	Yanbian University, China
Dr. Kyou Hoon Han	The role of pre-structured motifs (PreSMos) in the romiscuous interactions of intrinsically unfolded protein	2010. 9.1	2013.8.31	Hungarian Academy of Sciences, Hungary
Dr. Myung Hee Kim	Proteome Bank	2009. 4.1	2012.3.31	University of Southern California, USA
Dr. Inpyo Choi	Development of platform technology for cancer immunotherapy	2007. 6.1	2016.3.31	University of Washington, USA
Dr. Bo Yeon Kim	Global Research Center for Discovery of Cancer Targets and Chemotherapeutics Based on Kinomics	2009.12.1	2014.11.30	NIH, USA
		2009.12.1	2014.11.30	MIT, USA
		2009.12.1	2014.11.30	MPI, Germany
		2009.12.1	2014.11.30	Harvard University, USA
Dr. Jong Seog Ahn	KRIBB-RIKEN Collaboration Research Center for Chemical Biology	2006.12.1	2014. 8.31	RIKEN, Japan
Dr. Hyang Sook Yoo	Therapeutic Targets for Liver and Gastric Cancer	2009.3.20	2011. 9.30	Pfizer, USA
Dr. Joong ku Lee	The establishment and management of foreign biological resources center	2006. 8. 1	2016. 9.30	16 contries including YASS, China, INBio, Costa Rica, BPPT, Indonesia
Dr. Sang Soo Kwak	Development and application of the drought tolerant plants for combating desertification	2009.12.28	2012.12.27	Institute of Soil and Water Conservation, China
Dr. Sang Soo Kwak	Operation of the for Korea-China Biothchnology Collaboratioon Research Center on Combating Desertification	2009.12.28	2012.12.27	Institute of Soil and Water Conservation, China
Dr. Joon Ki Jung	Collaborative Program for Biotechnology between Malaysia-Korea	2010.1.1	2011.12.31	SIRIM, Malaysia
				BIOTECHCORP, Malaysia
Dr. Byoung Mog Kwon	Development of anti-metastatic agent through modulation of tumor cell migration	2011.4.1	2011.12.31	Johnson&Johnson, USA
Dr. Jeong Heon Ko	Development of hepatocellular cancer biomarkers on aberrant glycosylation	2011.4.1	2011.12.31	Johnson&Johnson, USA
Dr. Inpyo Choi	Development of anti-cancer/inflammation reagents by targeting VDUP1	2011.4.1	2011.12.31	Johnson&Johnson, USA
Dr. Sei Ryang Oh	Screening active extracts showing antibacterial and antifungal activities from plant sources	2011.4.1	2011.12.31	Johnson&Johnson, USA
Dr. Chul Ho Kim	International joint research project for biomass utilization	2011.11.1	2013.10.31	SIRIM, Malaysia
Dr. Inpyo Choi	Development of NK cell therapy using induced pluripotent stem cells	2011.11.1	2014.10.31	NCB, Kazakhstan
Dr. Won Gon Kim	Transcriptional regulatory mechanism of development and maintenance of Dopaminergic neurons : Anovel therapeutic target of Parkinson's Disease	2009.1.1	2011.12.31	Harvard University, USA
Dr. Jeong-Woo Seo	Development of platform technology for Bio-oil production using heterotrophic microalgae	2011.6.1	2014.5.31	Bhavans College, India
Dr. Young Il Yeom	Targeting the Wnt/β,-catenin cell signalling pathway in liver primary cancers	2011.12.1	2014.11.30	INSERM, France
Dr. Suk Weon Kim	Establishment of metabolite based high-throughput screening system for high functional african yam plants using FT-IR spectr	2011.10.1	2014.9.30	IITA, Kyana

Expand Global Collaborative Network and Secure Overseas Hubs

▸ Develop strategic network for effective response to global R&D environment
- National Center for Biotechnology (NCB) of Kazakhstan in August 2011 - ❶, National Science and Technology Development Agency (NSTDA) of Thailand in March 2011

▸ Secure overseas hubs: Opening and operation of KRIBB-RIKEN Joint Research Center for Chemical Biology since June 2011, Ochang Campus - ❷

▸ Build and promote human networks with Korean scientists working overseas in the United State

Host International Academic Events

▸ Expand mutual cooperation and share research achievement through international academic exchanges
- The Korea–Thailand NanoBiotechnology Joint Symposium in March 2011 at the National Science and Technology Development Agency of Thailand
- The 3rd Bio-Asia Program organized by the French Ministry of Foreign & European Affairs and the French Regional Delegation for Cooperation in South-East Asia in April 2011, Ochang Campus - ❸
- The Korea - Kazakhstan International Joint Symposium in August 2011, NIF of Kazakhstan
- International Symposium on Agroforestry Biotechnology to Combat Desertification in October 2011 at the Changwon Exhibition Convention Center - ❹

Operate Human Resource Development Program to Support Developing Countries

▸ Biotechnology Training Program for Malaysian biotechnology majors from October to November 2011, 10 students recommended by Malaysian government

▸ Develop biotechnology experts with NANOTEC of Thailand from August 2011 to August 2012

Implement Foreign Scientists Support Program

▸ Publish handbook to guide KRIBB campus life

▸ Implement cultural program to raise understanding of Korean culture both in May and December

▸ Provide one-stop service for various supports for year-round

▸ Hold International Researchers' Day with President of KRIBB in December- ❺

Global Promotion

▸ Participate in the world's largest Bio event, 2012 Bio International Convention in June, Washington

▸ Participate in 2011 BioMalaysia in November at Kuala Lumpur

▸ Publish and circulate English Newsletter(12 issues)

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Technology Transfer Office (TTO)

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Bridging the Gap between the Bioscience Innovation and the Real World Applications

The business development based on the technologies of KRIBB has been doing by the Department of Intellectual Property Management which is plays a role as a technology transfer office (TTO). The idea or know-how as well as the technologies developed from the R&D centers are detected by the Technology Evaluation Committee of KRIBB run by the TTO, and their market and business values for creating new bioindustry are also assessed.

The selected technologies are actively licensed out to market leaders including domestic and global companies. Nurturing and incubating start-ups are another important function of the TTO of KRIBB. The joint venture with established partner company could be created by providing with highly valued technology.

MAIN FUNCTIONS

Knowledge (Intellectual) Property Management : Making a strong patent

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

Technology Transfer

- Technology valuation / marketing / negotiation for transfer
- Technology licensing-out

Business Incubation

- Creating new startups / joint ventures (Institute Enterprise)
- Arranging fund investment for spin-off KRIBB companies
- Incubating biotech start-ups at BioVenture Center (BVC)

Creating The Joint-Venture, BoGwang Resources, Co., Ltd. (Inc., Institute Enterprise)

- Company type : The Joint Venture (Institute Enterprise)
- Partner Company : BoGwang Resources, Co., Ltd.
- Technology base : Micro Tuber and Mini Tuber technology from Green Bio Center (Dr. Jeong Hyuk)
- Market area : Potato Seed Market
- Major Products: Potato Microtuber (Potato Seed)
- Technology advantages : Mass production, Disease-Free, Small-sized potato Seed.

Support for Knowledge Information 2011

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Information Collection and Current Status

The KRIBB Digital Library (http://library.kribb.re.kr) has made it a priority to collect electronic materials, such as electronic journals, electronic books, and web databases, for providing information more rapidly and improving user convenience. The library has subscribed to electronic journals since 1998 and has participated in the KESLI consortium. Currently, the library subscribes to 5,400 electronic journals, which is much more than its 40 printed journals. More than 400,000 articles are downloaded in PDF or HTML format each year.

Research Results and Information Databases

In an effort to facilitate the global promotion of its research accomplishments, KRIBB has been operating an open-access, standard repository system since July 2011 (http://repository.kribb.re.kr). Currently, 7,350 research papers, 1,621 research reports, 966 domestic patents and 12 other promotional materials are available for search and download full-text by outside system users. And by using the iLIPS program, users can search and gain access to all of data, including printed books, electronic journals, and electronic books within the library.

Document Delivery Service (DDS)

To solve the problems associated with the increasing amounts of information and the lack of collections in the library, the library has reached agreements with the Korean Medical Library Association (KMLA), the Korea Special Library Association (KSLA), the National Digital Science Library (NDSL), and the Korea Education and Research Information Service (KERIS) so that researchers can obtain copies of original materials.

The Document Delivery Service is making significant contributions to the nation-wide sharing of important materials by supplying KRIBB's materials, not only to internal users (1,781 documents in 2011), but also to external users (1,191 documents in 2011).

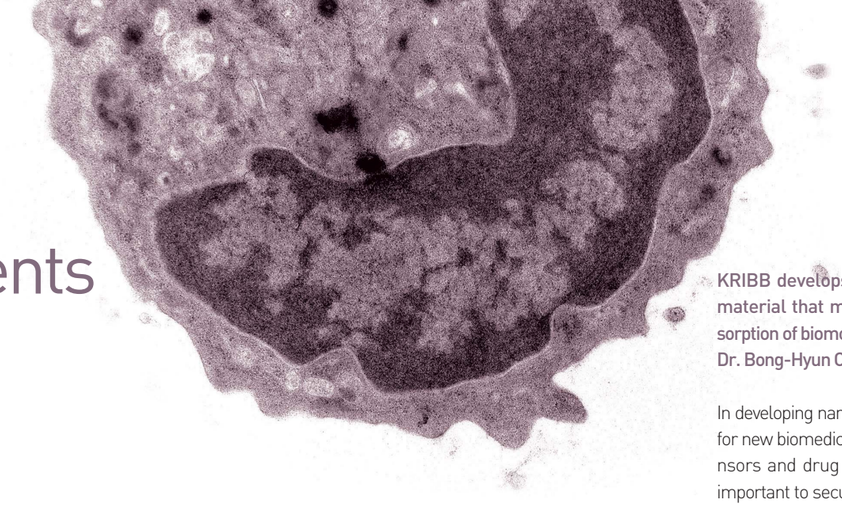
Management of Papers and Laboratory Notebooks

To assist with staff promotions and personnel performance evaluations, every paper published by researchers has been managed with a special program (MIS) according to the criteria for paper assessments. The program is used for registering and inputting papers, building a full-text database, checking SCI and IF, issuing statistical data, reporting the results in and out of the KRIBB Digital Library, providing a service for web users, and publishing references (SCI reference materials, vol. 9, in August 2011).

We manage the entire process related to laboratory notebooks tracking - from requests and issuances to taking over - by implementing the management program (825 notebooks were issued in 2011). We promote laboratory notebook recording, and assist in establishing a proper research culture by regularly running educational courses. In line with this policy, KRIBB has developed and has been operating the Electronic Laboratory Notebook (KRIBB-ELN) system since June 2011

APPENDIX

Outstanding Research Achievements



Proposed a molecular mimicry-based drug repositioning strategy
Dr. Seung-Wook Chi (Jan. 08. 2011)

"A shorter new drug development period, cost reduction and higher success rates" published in the Journal of the American Chemical Society.

Dr. Seung-Wook Chi's team at the Bio-Medical Proteomics Research Center in conjunction with Dr. Ho-Seop Yun at Nanyang Technolo-gical University in Singapore have explored a new molecular target for an existing anti-cancer drug, proposing a structure-based strategy to utilize existing drugs in new therapies.

This research was sponsored under a project to support experienced researchers (for core research) by the Ministry of Education and Science and the National Research Foundation. The research findings, titled "Molecular Mimicry-Based Repositioning of Nutlin-3 to Anti-Apoptotic Bcl-2 Family Proteins," were published in the January 7, 2011, online edition of the Journal of the *American Chemical Society*.

The research team, taking advantage of the structural similarity among disease-targeted proteins, made a first-of-its-kind discovery that previously developed anti-cancer drugs react upon binding with other disease-targeted proteins, and proposed a molecular mimicry-based drug repositioning strategy so that the existing drugs could be used to treat other diseases.

Dr. Ahn's team discovers a new anti-metastatic agent
Dr. Jong Seog Ahn (Apr. 26. 2011)

A team led by Dr. Jong Seog Ahn of the Chemical Biology Research Center succeeded in discovering Fusarisetin, a new anti-metastatic agent against cancer cells, from a fungus isolated from Korean soil.
Fusarisetin has a completely new chemical structure that is unknown in nature.

In the research, Dr. Ahn's team looked for anticancer active substance from microbial secondary metabolites by using a 3D cancer cell culture assay system, and successfully separated the new active substance from the cultured broth of Fusarium sp. FN080326 isolated from Korean soil.
Fusarisetin was identified as a novel compound with new carbon skeletal back bone structure that is fundamentally different from those found in nature. It has an anti-metastatic activity against cancer cells as it shows no cell toxicity. In addition, the new compound was found to have a different working mechanism from the known anti-metastatic agents, which suggests the possibilities of novel cancer drug targets.

Difference of sexual culture leads spermary function related gene mutation
Dr. Hong-Seog Park (Apr. 28. 2011)

This research conducted by Dr. Hong-Seog Park and his team at KRIBB with Japan Natio-nal Biomedical Research (Dr. Hashimoto) and Tokyo University (Dr. Sugano) was supported by the 'Original Technology Research Program' through the Ministry of Education, Science and Technology (MEST) and OASIS Project of KRIBB.

This research is posted on the online version of *"Functional & Integrative Genomics"* (Apr. 18th), one of the professional publications in genomics.
(Title: Major chimpanzee-specific structural changes in sperm development-associated genes)

Dr. Park's team concentrated on the physiological action that roles a distinctive mark between human and chimpanzee. Then, they conducted comparative analysis on the spermary function(production, persistence, fertilization) related genes of human and chimpanzee by extracting 1,933 kinds of genetic information from spermary of male chimpanzee.

In the result, he found out for the first time that genetic structure and information are different in the 50% (39 out of 78) of sperm production and function related genes of human and chimpanzee. Importantly, the research addressed that there is chimpanzee's own exclusive structure in the three genes (CD59, ODF2, UBC) that relate to number, movement speed and persistence of sperm. The research team interpreted that the reason of genetic mutation in the spermary of human and chimpanzee is that remarkable physiological differences, different sexual culture between human and chimpanzee influences on genes.

KRIBB develops nanostructured source material that minimizes nonspecific absorption of biomolecules
Dr. Bong-Hyun Chung (May. 13. 2011)

In developing nanostructured materials used for new biomedical devices, biochips / biosensors and drug delivery system, it is very important to secure technology that minimizes the nonspecific absorption of biomolecules such as cells, DNAs and protein.

To date, a variety of macromolecules have been studied as candidate materials for minimizing the nonspecific absorption of biomolecules. However, due to their instability in various thermal, chemical and biological environments, most of these materials present a host of practical challenges such as increase in nonspecific absorption, structural transformation and difficulty in manufacturing nanostructured materials.

Recently, a KRIBB research team led by Dr. Bong-Hyun Jung of the BioNanotechnology Research Center successfully developed an ideal source material for preventing nonspecific absorption, which could be effectively used for producing various biomedical devices, biochips/biosensors and labs-on-a-chip. The research was conducted with the support of the Growth Engine Development Program for New Technology Convergence extended under the auspices of the Ministry of Education, Science and Technology. The team also successfully produced a nanostructured material by using the newly developed material. The outcome of this study has been chosen as the cover paper for the May 2011 edition of Macromolecular Bioscience which is issued by Wiley-VCH of Germany.

KRIBB develops natural product having anti-inflammatory and anti-asthmatic effect
Dr. Hyeong-Kyu Lee & Dr. Sei-Ryang Oh (May. 16. 2011)

A team led by Dr. Hyeong-Kyu Lee and Dr. Sei-Ryang Oh of the National Medicine Research Center of KRIBB announced its plan to use extract of pseudolysimachion plants to get a active composition that has been proven effective in animal models for treating inflammatory asthma while having no toxicity, and to develop the composition into new drugs for inflammatory diseases, asthma and COPD (Chronic Obstructive Pulmonary Disease).

The team has filed up a domestic patent and overseas patent applications. For product development, a technology transfer and royalty contract (involving 500 million KRW for technology transfer and 6% of total revenue as running royalty based on the price as set in health insurance scheme) has been signed with Yungjin Pharmaceutical Co., Ltd (President : Sang-Dae Jeon) at 11:30 AM of May 16 (Mon) in the small meeting room of KRIBB.

Asthma is a chronic respiratory disease that accompanies wheezing and dyspnea caused by airway hyper-responsiveness and airway contraction. It is known as a complex airway dysfunction syndrome which is an encompassing term that includes genetic causes, chronic inflammation and airway remodeling.

Using smart phones to see immunocytes within human body
Dr. Bong-Hyun Chung (May. 26. 2011)

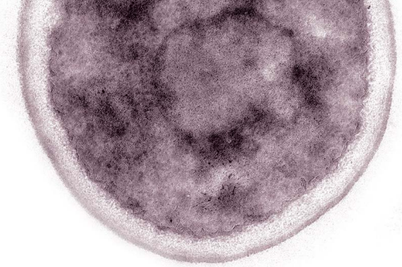
A team led by Dr. Bong-Hyun Chung developed a next-generation bio-imaging system which could monitor cell movement within the human body through the use of smart phones and smart pads. The team also successfully commercialized the technology by signing a technology transfer contract with U-BioMed Inc. The breakthrough research was conducted as part of the Pioneer Program for Future Convergence Technology supported by the Ministry of Education, Science and Technology (MEST) and National Research Foundation of Korea (NRF). The bio-imaging system, developed based on KRIBB's proprietary technology, has potential for a wide range of applications for life phenomena analysis, disease diagnosis and treatment, drug development and biopharmaceutical research such as stem cell research.

What the KRIBB team developed is a highly sensitive biocompatible nano-probe that is capable of monitoring cell movement within the human body. In the research, the team put the nano-probe into immunocytes, which could be used for cancer treatment, and was able to get images of the immunocytes approaching cancer cells. In addition, the same image data could be accessed simultaneously by smart phones and smart pads located far from the lab equipment.

The technology used for developing the nano-probe has been filed for Korean and international patents and published in highly authoritative journals in the field of chemistry and material science including the Journal of the *American Chemical Society and Biomaterials*.

A KRIBB team discovered key regulator of anti-cancer immune cells
Dr. In-Pyo Choi and Dr. Tae-Don Kim (Oct. 11. 2011)

A KRIBB team led by Dr. In-Pyo Choi and Dr. Tae-Don Kim of the Immunotherapy Research Center has successfully discovered a new RNA (micro RNA) and verified its functional mechanism. The newly discovered RNA (micro RNA) plays critical role for the activation of NK (Natural Killer) cells which are anti-cancer immune cells, which published in Blood Journal.



NK cells are natural immune cells within the human body that kill cancer cells. As such immune cells' activation is inhibited in cancer patients, a great deal of research is being undertaken for the development of immune cell-based cancer therapy.

The latest research conducted by the KRIBB team discovered miR-27a*, a new micro RNA that regulates Perforin (Prf1) and Granzyme B (GzmB), the two most essential effector molecules for NK cell activity.
Furthermore, the research successfully confirmed the critical role played by miR-27a* in the activation of NK cells.

For NK cells to inhibit the growth of tumors, the cancer patient's body needs to produce and secret Perforin (Prf1) and Granzyme B (GzmB) on its own, but the regulation mechanism of the micro RNA expression was unknown in the past. The KRIBB research is significant as it confirmed which micro RNA is regulated during the activation of NK cells, and further verified that the human microRNA (miR)-27a* is the most important regulator of Prf1 and GzmB expression.

It has been known that the small molecule, micro RNA, which is bound directly to the messenger RNA, regulates protein production and induces breakdown of messenger RNA. But its role in the activation of NK cells had not been uncovered until the KRIBB research.

The research observed that the activity of NK cells dropped by two times when injected with miR-27a* discovered in the research, while the NK cell activity increased by two times when injected with miR-27a* inhibitor. It also confirmed that tumor growth was inhibited by the same extent in animal models of colorectal cancer. This is how the research team verified that miR-27a* is the important negative regulator of NK cell activity.

KRIBB team successfully developed new cancer drug candidate
Dr. Mi Sun Won (Nov. 04. 2011)

KRIBB successfully developed a new anticancer drug candidate showing strong tumor-inhibiting ability by regulating HIF-1α expression, and signed a technology transfer contract with Ildong Pharmaceutical Co. Ltd. on October 18th. The development was made in collaboration with Dongkuk University.

For the development, the KRIBB team led by Dr. Mi Sun Won of the Biomedical Genomics Research Center took charge of drug candidate screening and mechanism research while the team at Dongkuk University led by Dr. Kyung Lee handled molecular design and therapeutic synthesis.
Efficacy evaluation was conducted by another team led by Hwan-Mook Kim at Gachon University of Medicine and Science. This project was carried out as "New Drug Candidate Discovery and Optimization Program" under the sponsorship of Ministry of Education, Science and Technology and National Research Foundation of Korea.

"LW7", the newly developed anti-cancer drug candidate, is an organic compound-based target cancer drug which targets HIF-1α. LW7 has proved effective in suppressing tumor growth, formation of new blood vessels and metastasis when orally administered to animal models of solid tumor with colon, lung, prostate, renal, pancreatic cancer and etc.

On top of the merit of oral administration, the new drug candidate demonstrated antitumor efficacy in renal and lung cancer, two of the conditions in which existing HIF-1α-inhibitor drugs have been less effective. Most HIF-1α-inhibitor drugs are recommended to be combined with other drugs.
However, LW7 shows potent antitumor efficacy even in case of stand-alone administration. When administered along with TKI (tyrosine kinase inhibitor) drug, LW7 delivers even greater antitumor efficacy thereby possessing potential to be developed into a broad-spectrum anticancer drug.

New material for cancer treatment derived from virus
Dr. Myung Hee Kim (Nov. 08. 2011)

A team of Korean researchers laid importance cornerstone for cancer drug development by discovering a material which stabilizes a protein (p53) with tumor-suppressing function.

In general, the therapeutic effect in the treatment of cancer patients can be maximized through expression of the p53 tumor suppressor protein. Thus, stabilization of p53 is crucial for its tumor suppressor function. The p53 tumor suppressor is a short-lived protein that is maintained at low levels in normal cells by MDM2-mediated ubiquitination and subsequent proteolysis.
Herpesvirus-associated ubiquitin-specific protease (HAUSP) regulates the stability of p53 and the p53-binding protein MDM2, implicating HAUSP as a therapeutic target for tuning p53-mediated antitumor activity.

The two teams, each led by Dr. Kim and Dr. Jung, performed the structural study of the Kaposi's sarcoma–associated herpesvirus (KSHV) vIRF4–HAUSP complex, and discovered two short viral peptides, vif1 and vif2, as potent, selective HAUSP antagonists. This study reveals a bilateral belt-type interaction that results in inhibition of HAUSP. The vif1 peptide binds the HAUSP TRAF domain, competitively blocking substrate binding, whereas the vif2 peptide binds both the HAUSP TRAF and catalytic domains, robustly suppressing its deubiquitination activity. The short vif1 and vif2 pep¬tides comprehensively suppressed HAUSP activity, effectively restoring p53-dependent apoptosis in wild-type p53-carrying cancer cells and suppressing tumor growth in a mouse xenograft model. Thus, these virus-derived short peptides represent biologically active HAUSP antagonists and potential new chemotherapeutic molecules for anticancer therapies.

The teams highlighted the significance of their research by saying "It has been a major accomplishment to discover the peptides, capable of controlling HAUSP, and its function since HAUSP has been a key therapeutic target in cancer. Our research opened up opportunities for a new kind of cancer drug, and is expected to accelerate the development of next generation cancer drugs.

Research of Dr. Young Il Yeom of KRIBB selected as "100 Best National R&D Projects 2011"
Dr. Young Il Yeom (Dec. 01. 2011)

The research outcome accomplished by Dr. Young Il Yeom of the BioMedical Genomics Research Center has been chosen as one of the "100 Best National R&D Projects 2011" by the National Science and Technology Commission.

The Commission recognized the noteworthiness of Dr. Yeom's research as it verified a previously unknown mechanism of TGFβ concerning its involvement in growth and metastasis of cancer cells. The research discovered that TGFβ, which is secreted in large amount among liver cancer patients, does, in fact, accelerate further progression and metastasis of cancer despite its well-known function as a physiological active substance against cancer.

The outcome is particularly valuable since it verified the mechanism of in which of the two directions TGFβ gets to become effective. With Dr. Yeom's research, technological groundwork has been laid to guide future cancer drug development efforts so that TGFβ will be made to suppress, not accelerate, cancer in new cancer drugs.
"100 Best National R&D Projects" is an annual award event where the National Science and Technology Commission selects and gives certification to commendable research projects which have been conducted by universities, government-invested research institutions and private research centers through the government's funding.

Single chip is enough for simple and precise cancer diagnosis
Dr. Yongwon Jung (Dec. 07. 2011)

The research, undertaken by Dr. Yongwon Jung and Jung-Min Lee, a doctoral student at UST, has been published in the November online early edition (November 9th) of *Angewandte Chemie*, one of the most authoritative journals in the field of chemistry.

A human cell typically contains extremely small micro RNAs which include hundreds of different genomic sequences. Lately, these micro RNAs are receiving a great deal of attention as a marker to diagnose and treat various diseases such as cancer, but their extremely small size has always made it very difficult to conduct highly reliable analysis using the existing, common gene chip.

The commonly used gene chips typically analyze genes using only one probe and one temperature, so they have been presenting limitations in equally label and specifically analyze hundreds of small micro RNAs.

The team led by Dr. Jung adopted a novel type of probe, which combines two probes into one, to be able to skip the very complicated RNA-labeling stage, and also invented a new analysis method where two different temperatures were applied. As a result, the team successfully developed a gene chip which is capable of specific but simple analysis of a wide variety of micro RNAs.

With the noteworthy development of a new analysis method boasting high reliability and sensitivity, the development of micro RNA-based diagnosis and treatment is expected to pick up the speed.

Obesity reduces effect of H1N1 vaccine
Dr. Haryoung Poo(Dec. 30. 2011)

A team of Korean researchers at KRIBB discovered that obesity dramatically lowers the effect of H1N1 vaccine.

As a joint research project, a KRIBB research team led by Dr. Haryoung Poo of the Viral Infectious Disease Research Center and Dr. Chul-Ho Lee of the Laboratory Animal Center announced their research results confirming the efficacy of H1N1 pandemic vaccine is significantly reduced by obesity.

In fact, many of the patients who have died of H1N1, which started becoming rampant from 2009, were obese. The Centers for Disease Control and Prevention of the U.S. reported that obese peoples showed high rate of morbidity and mortality in case of H1N1 virus infection.

This prompted the KRIBB teams to embark on the research in order to further verify the relationship between obesity and the effectiveness of H1N1 vaccination. After having normal and obese animal models vaccinated and infected with H1N1 virus, the researchers found out that the neutralizing antibodies in the blood of obese mice was dramatically lower than those in normal lean mice after vaccination. Furthermore, the survival rate also fell significantly among the obese models after H1N1 virus challenge.

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