

Biocon's Report II 2010-2015

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The Target Factory

Biocon's Report II 2010-2015

Integrated Research Platform for Novel Target and Lead Discovery

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Greeting

Medicinal Bioconvergence Research Center (Biocon) was initiated in 2010 as one of the Global Frontier Projects that are by Ministry of Science, ICT and Future Planning. Our goal is to build an integrated research platform namely "The Target Factory" to develop well-validated packages of targets and leads that can be used in biotech and pharmaceutical industry.

Biocon consists of the experts in target identification, drug design, drug screening and disease modeling. The results from these four specialist groups are converged into integration core group. The matured packages of target and lead are then relayed to the group for translation and

development (named TRADE).

"Biocon's Report II" is prepared to introduce our target and lead pipeline, and research articles and patents that have been produced for past 5 years. We will do our best to establish Biocon the world's first and best target factory that systematically translate original science and technology to new therapy and diagnosis for future medicine.

I appreciate the Korean governments, members and collaborating partners for the support of Biocon for last five years.

Sunghoon Kim Ph.D.

Director, Biocon / Profes Director, Biocon / Professor, Seoul National University

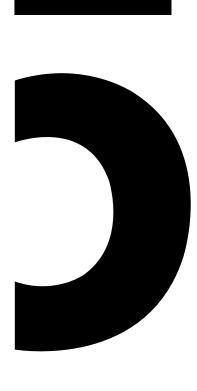


Vision: The Target Factory

An Integrated Research Platform for Novel Target and Lead Discovery

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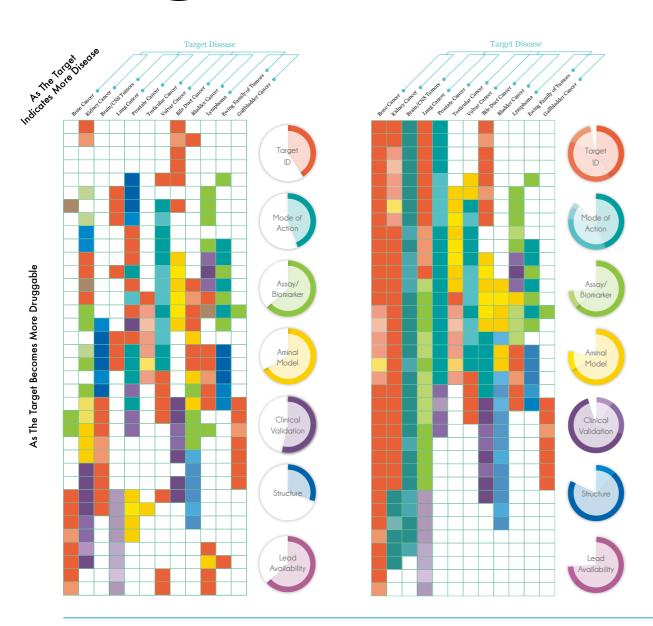
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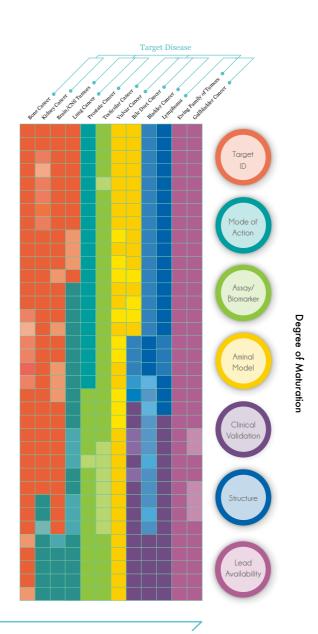
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National University to Research Platform for druggable targets the success Probreduce the Establish and cost while established and cost while established establis



Atlas Of Targetome





Biocon's integrated target discovery team involves genomics, proteomics, molecular and cell biology, biochemistry, animal modeling and pathology to fill out the criteria that are required for druggable targets. The processes include; "understanding the mode of action"; "creating assays for drug screening"; "clinical validation"; "biomarker discovery"; "understanding target structure"; "generation of disease models" and "development of early drug leads". With this set of data, Biocon seeks deliver targets to industry at an early stage, so that the drugs can be developed seamlessly with a higher probability of success. Ultimately, Biocon aims to build a 3D atlas (with the axis of target identification, disease indication, data attributes) of druggable targets (3D targetome) that provides a groundwork from which new drug discovery initiatives can be launched.

As More Targets are Collected over Time

<u>02.</u>

Initiation

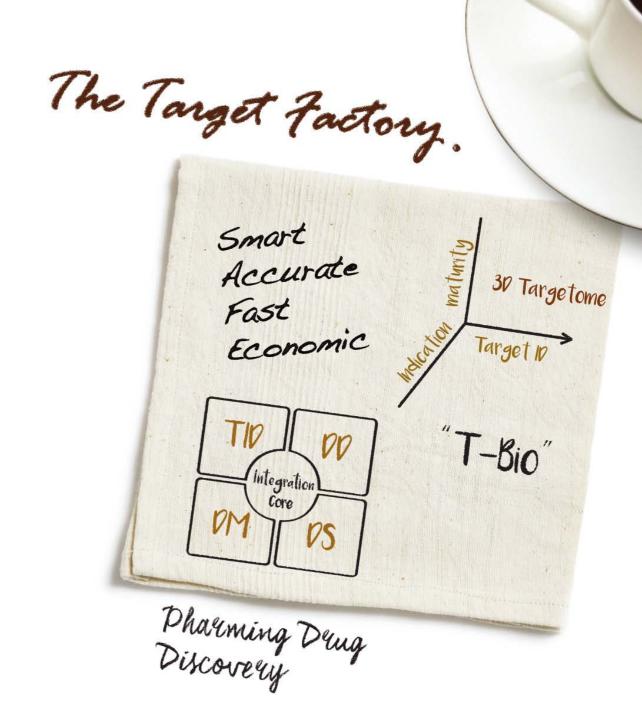
Searching for Novel Targets

The need for new drugs is ever increasing due to the surge in diseases such as cancer, diabetes and dementia that are mainly caused by extended life span. However, the number of newly approved drugs is continuously decreasing, giving a crisis not only for drug industry but also eventually for human health.

In 2010, the Korean Ministry of Education, Science and Technology (MEST) launched the Global Frontier Project, targeted at solving global challenges in major R&D areas. The Medicinal Bioconvergence Research Center (Biocon) was initiated as one of the three projects with the aim of resolving difficulties during the development of novel drug discovery. This project will proceed for an initial nine years from 2010 to 2019, and is divided into three stages (1st: 2 years, 2nd: 3 years, 3rd: 4 years). With the financial support of about 140 million dollars and a projected time-line of 9 years, Biocon has leveraged a unique capability to discover and validate molecular pathways and targets at a level that is possible at few commercial enterprises.

For the last five years, Biocon has achieved outstanding progress in basic and applied researches. On the academic side, it produced more than 179 research articles including high impact journals such as Cell, Molecular Cell, Cell Reports, Nature Structure and Molecular Biology, Nature Chemical Biology, Nature Materials, Nature Rev Cancer and PNAS.

On the application side, Biocon has filed more than 152 patents from the related research and has established research alliance with ten pharma and biotech companies.





The **Target Factory PRS GRS LRS** KRS **MRS** AIMP2-DX2 **TRS** bi CON

03.

Strategy

4 specialist groups + I integration core group

Biocon seeks innovation across all of its activities including research, technology and strategy. At its core, Biocon is remodeling the R&D process itself. In the current global drug development process, target discovery, drug design, drug screening and disease model are generally addressed in a linear fashion, much like a factory product assembly line. In this system, the downstream processes totally depend on the upstream, and any errors occurring upstream can be cumulative since there is little communication between the different research functions. This situation can be one of the attributes to the high failure rate of drug discovery. To avoid this problem, Biocon has built a unique "4+1" matrix system.

Specifically, four specialist groups have been established for target identification, drug design, drug screening and disease modeling. The discoveries and inventions generated from these four units are integrated, validated and matured in the integration core unit (ICU). This way, the time and cost for target validation and discovery can be significantly reduced. The team also includes the specialists from clinical and pharma industry to orient target development according to the clinical and industry unmet needs.

In addition, Biocon actively seeks and nurtures technical innovation by adopting cutting-edge technologies into bioscience. To achieve this goal, each project is driven by a under the technical framework that we call S.A.F.E. (standing for Smart, Accurate, Fast, Economic). Through these integrated biology and convergence technologies, Biocon seeks to build up world's most efficient operational research system for target and lead discovery.



04.

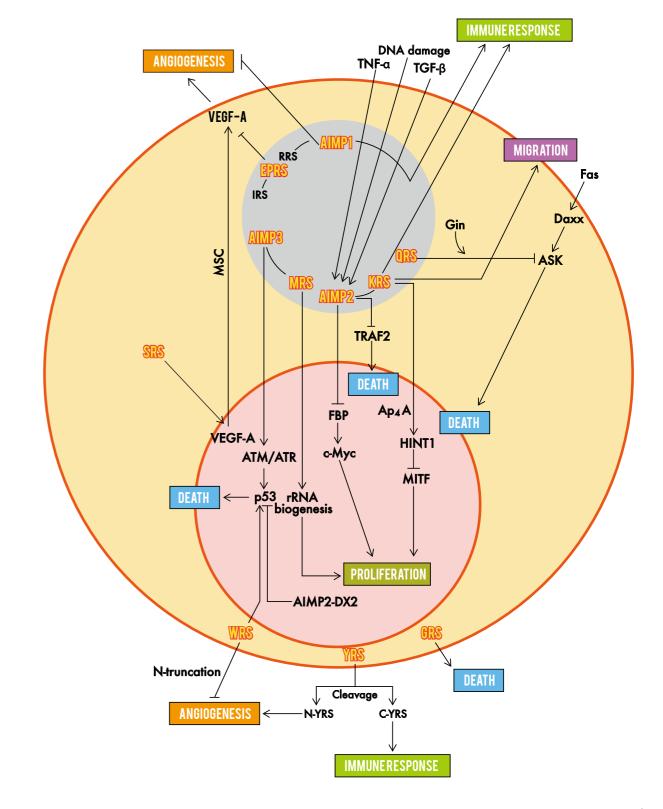
Focused Subject & Pipeline

Oncology and other complex diseases

Biocon focuses on human aminoacyl-tRNA synthetases (ARSs) and their interacting proteins as our primary target space of interest, and explores their potential to address diverse human diseases. These enzymes emerged early in evolution and catalytically link their cognate amino acids to tRNAs for protein synthesis.

For this reason, ARSs have been traditionally considered as housekeeping proteins solely dedicated to protein synthesis. However, recent new findings from Biocon and other groups world-wide on the novel functions of ARSs are rapidly changing the classical view of these enzymes. Indeed ARSs are emerging as central coordinators linking cell fate determination processes with protein synthesis.

Many ARSs are involved in the regulation of diverse signaling pathways beyond their catalytic roles in protein synthesis. Some representative functions of different ARSs (red letters) are shown schematically. Many ARSs change their cellular locations for their new roles outside protein synthesis. The pink circle indicates the nucleus of the cell and the grey circle indicates the macromolecular protein complex consisting of the indicated ARS. In the period from initiation of the program until the mid-point in 2015, Biocon has rapidly advanced the science in several key areas of ARS technology. A depiction of the key programs is shown below, together with the key high impact paper published for that program. In addition, several new targets with different indications are currently under active validation although they are not included in the table.



Glycyl-tRNA synthetase (GRS)

We have demonstrated that secreted human GRS is implicated in immune surveillance against cancer. Specifically, we have shown that GRS is secreted by macrophages and acts against certain tumor types via an interaction with K-cadherin. Injection of purified GRS has shown potent anti-tumor activity in vivo. This pathway is likely to have important implications in various cancers, including colon and lung cancer, and suggests GRS and its peptides as a novel resource for cancer immunotherapy.

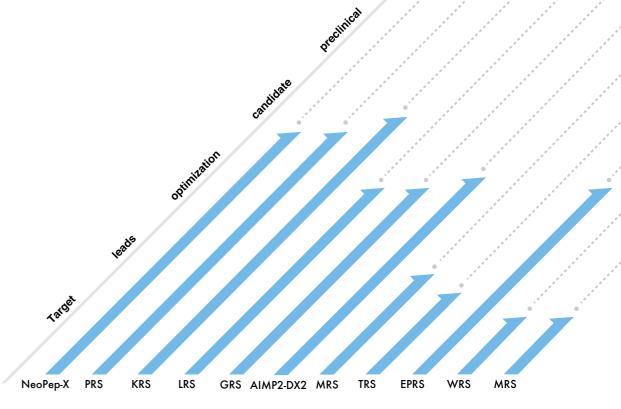
Lysyl-tRNA synthetase (KRS)

relocates to the plasma membrane after a laminin signal and enhances the cancer metastatic properties of cancer cells. We have discovered a class of small molecules that specifically binds to a unique cleft of KRS to inhibit its pro-metastatic activity. We believe that this set of observations offers an interesting new pathway to the development of novel drugs against metastasis and some other relevant diseases.

We found that human KRS

AIMP2-DX2

AIMP2 (ARS-interacting multifunctional protein 2) was previously found as an auxiliary factor associated with many different ARSs. We found that AIMP2 can also serve as a potent tumor suppressor with multiple mechanisms, including the activation of p53, a well-studied tumor suppressive protein. While establishing the important role of AIMP2 in tumor suppression over the past decade, we identified AIMP2-DX2, an exon-2 deleted splice variant of AIMP2 that trumps the tumor suppressive nature of AIMP2, and importantly, is upregulated in specific cancers. Thus, this variant may represent a promising target for many refractory cancers. We have identified potent small molecule candidates that inhibit AIMP2-DX2 with excellent selectivity over the wild type full-length AIMP2.



Biocon's Current Pipeline

| Targets | Potential indications | Status | Key references | | |
|---------------------------------------|----------------------------------|-------------------------|---|--|--|
| NeoPep-X | Tissue Regenerationi Alopecia | Pre-candidate | Unpublished | | |
| PRS (prolyl-tRNA synthetase) | Fibrosis Immune Diseases | Pre-candidate | Son et al, Acta Cryst D 2013 Unpublished | | |
| KRS (lysyl-tRNA synthetase) | Metastasis | Pre-candidate | Kim et al, Nat Chem Biol 2014 Unpublished | | |
| LRS (leucyl-tRNA synthetase) | Cancer Metabolic Diseases | Lead optimization | Han et al, Cell 2012 In preparation, 2016 | | |
| GRS (glycyl-tRNA synthetase) | Cancer | Lead optimization | Park et al, PNAS 2012 | | |
| AIMP2-DX2 | Cancer Neural Disease | Lead optimization | Choi et al, Plos Genet 2011 | | |
| MRS (methionyl-tRNA synthetase) | Cancer | Hit identified | Kwon et al, PNAS 2011 Nat Comm 2016, review | | |
| TRS (threonyl-tRNA synthetase) | Angiogenesis | Hit discovery | Fang et al, Nat Comm 2015 | | |
| EPRS (glu-prolyl-tRNA synthetase) | Anti-viral | Lead optimization | Nat Immunol 2016, under review | | |
| WRS (tryptophanyl-tRNA synthetase) | Sepsis | Therapeutics & Biomaker | In preparation | | |
| MRS | Pancreatic cancer | Biomarker | In preparation | | |

<u>05.</u>

Translation & Drug Development

Well-matured Leads are Linked to Industry



With excellent research achievements during last five years of Biocon, it is time to put in place a flexible and professional management group that can assess, decide and implement decisions for downstream development that are independent of, but in co-operation with, the underlying scientific mission of Biocon. The action of this group needs to be focused and operated at the standard of global Pharmas since Biocon's assets in the pipeline are all "first-in-class". In light of the imperative to move programs from the academic to a translational setting, Biocon has established a TRAnslation and DEvelopment Group (TRADE), comprised of experienced professionals from the global drug development industry. The TRADE group, led by the Biocon's Chief Business Officer, has a mandate to take Biocon's inventions and capabilities to global drug development partners. Currently, the TRADE group carries out rigorous assessment of internal Biocon programs with a particular emphasis on matching the target discovery and validation progress of Biocon with unmet market needs or opportunities.



biccon

Target & Lead Packages

The TRADE group is unique in having the capability to advance certain projects further downfield than most academic institutions. This capability is again derived from the internal structure of Biocon wherein access can be sought in a collaborative way with research groups specializing in chemistry, pre-clinical development or toxicology. Wherever necessary, Biocon has the financial capability to contract with well-recognized commercial laboratories to confirm data at a level that is appropriate to initiate formal discussion with pharma partners. Additionally, the TRADE group is working to establish relationships with both Known Opinion Leaders (or KOLs) in many of the target diseases that Biocon is seeking to address. Since the Biocon model is to develop first-in-class approaches to many if not all of our disease targets, we recognize the need to get early "buy-in" from the key clinical leaders addressing these disease targets.

We expect that this strategy will pay dividends as our programs advance to the clinic, and to interactions with regulatory bodies such as the FDA and EMEA. We also recognize the value of interacting with experienced US and global drug development experts. In this case, we have a specific aim to hire, consult with and bring to Korea, development experts who have previously taken other drugs to the market in indications of interest to us such as oncology or fibrosis. By finding the right people we believe that we will both save time and money by being efficient in our down-stream activities but also have the benefit of avoiding development mistakes. There is additional benefit in the "cross fertilization" of these experts with the internal Biocon professional team members. It is not the expectation that Biocon team members become drug development experts themselves but it is vital that their activities are integrated and assimilated into downstream clinically focused efforts to ensure true sustain-

ability for the Biocon efforts.

· IND: Investigational New Drug



Well-matured leads are linked to industry

Spinoff & License

Partnering

The Biocon's downstream strategy is flexible and pragmatic. We recognize that our academic network is best suited to basic research and to the development of students and future science professionals. However, we constantly seek ways to coordinate our work with the demand and the capabilities of the global pharma industry. We have identified three possible pathways as part of our translational and development strategy:

- Direct partnering of assets to global pharma or biotech partners.
- Spinning off start-up companies that will seek funding for further development.
- Internal development of assets to the IND stage, followed by either of the two pathways above.

At this moment, several different pharmaceutical and biotech companies and venture capital groups are working with Biocon on the early assessment of Biocon's original research outcome.

While commercialization efforts are still at an early stage, there is a continuing appetite among global pharma and venture capital companies to exploit novel targets and approaches. The role of the TRADE group is to continue to bridge the gap between Biocon and these down-stream customers.



Innovative Tech Products

Smart, Accurate, Fast, Economic (S.A.F.E.) technologies



Micropillar/microwell chip platform

- · High-throughput screening platform for 3D human cell cultures
- Cost effectiveness: Minimal volume < 1 uL (beneficial for valuable human cells)
- · Higher predictability: Spanning a gap between gene sequencing and xenografted animal
- · Social responsibility: Minimizing need for animal testing for drug development



Microarray Spotter

- · Liquid handling system designed for high speed, non-contact dispensing
- Dispensing volume of sample can be measured by a camera inspection
- · Flexible dispensing volume between 20 nL and 1000 nL by solenoid valves
- · Ultra small dispensing volume such as 0.1 nL by piezoelectric pipettes



Scanner

- High-throughput fluorescence scanning system designed for cell-based biochemical assay
 - Mercury lamp or a high-power LED illuminator is accommodated as a light
 - · Real-time autofocus that enables uniform image quality across the whole scan area

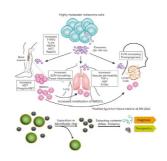




IntraVital Microscopy (IVM)

- · Full custom-built system providing flexible system design for future modification and update
- · Highly optimized for in vivo observation of mouse model for human disease
- Video-rate imaging (max. 100 fps - 512x512 pixels)
- · 4-Color simultaneous imaging acquisition & recording
- · Sub-pm in vivo imaging resolution
- · In vivo visualization of molecular, cellular mechanism for novel target identification
- In vivo efficacy monitoring of various novel drug compound
- In vivo 4D cell tracking and monitoring
- · In vivo monitoring of material delivery to target tissue
- · In vivo real-time monitoring of microcirculation

Biotechnology is to support drug to be commercialized and increase the productivity of drug use high technology, kit, and equipment in new drug discovery and to develop actual drug. For outstanding product, we have machine that can analyze the protein interaction, antibody develop technology, live image of disease detection, 3D culture analysis and also new biochip products are in process of development or have been developed.



Nanobio Platform for Ultrafine Separation

- Exosome separation by Pseudo-PFF
- Chip function
- Pseudo-PFF principle is adopted for minimal damage during exosome separation
- Various resolution improving techniques (ex. drain channel) were introduced
- · PS particle separation
- PS particles were separated using Pseudo-PFF chip
- · Exosome separation
- Size sorting of exosome confirmed through NTA and WB



Drug Library

- · Multi project data management : Efficient and simple data storage
- · Storing chemical compounds, bioactivity data: MOL file format, Batch import support
- · Robust security policy for CDA(Confidential Disclosure Agreement)
- · Low solution price (Opensource framework/toolkit a RDKit and JSME Editor)



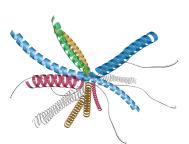
Project Landscaping System

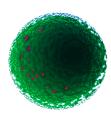
- · All Knowledge in One Place : Project definition and planning, data
- WBS(Work Breakdown Structure) based project management
- · Human Resource and Project process map management
- · Improve for Project Management Office(PMO)

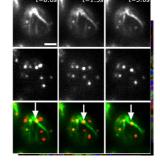
Infra-structure and Services

Providing cutting-edge technology to research community

Biocon builds up the infrastructure that is not easily accessible to individual labs and even invents new instruments if necessary. Although these instruments are primarily established for Biocon's own research purpose, they are also open for the researchers outside of Biocon. For last five years, Biocon provided about 5 thousands of service activities to the research community and this activity will be further encouraged and expanded. Some of the Biocon's analytical services are listed below.









Protein

Protein Expression & Purfication Service

Unlike other suppliers of purified proteins, we promise quik and accurate delivery of the proteins, though 1-to-1 consultation with ARS protein and

16 Aminoacyl-tRNA synthetase(16 ARSs)

Optimization for Protein Expression &

Protein Expression and Solubility Tests available in various E. Coli host strains

Bacterial Expression & Purification

- Customized Target Protein Purification Service (>87%) Guaranteed
- Affinity (6xHis, TRX-6xHis, GST-tagged protein), Ion-Exchange, gel filtration chromatography available

3D Cell Culture

Research with the Closest Cancer

UP-Grade your Cancer Research Level with 3D Cell Culture. Closet Properties to Cancer in vivo system.

Why? What is 3D Cell Culture?

- 3D Cell culture strongly resemble cells in a living organism.

- In Vitro potency of anti-cancer drugs
- Test protein-protein interations in tumor

Applications of 3D Cell Culture

- Screen cancer stem cell inhibitors

Cell Imaging

Choose images you want, Visualize them without distortion

Cell image Analysis Service

- 2D & 3D Imaging FRET (Fluorescene Resonant Energe
- FRAP (Fluorescene Loss in Photobleaching)
- Three-Dimensional Time-Lapse Imaging Multi-Point Time-Lapse Imaging
- Ultra High-Speed Imaging

SPR:Biacore T200

Broad Coverage

- LMW compounds
- Nucleic acid
- Carbohydrates
- Lipids
- Whole cells

- Yes/No Binding

- Viruses & bacteria

Detection System Biacore T200

- Real-Time Internation Analysis

Biacore T200 Service from basic to various

- Binding kinetics

Surface Plasmon Resonance

With Biacore T200, do the standard

- analysis for inter-molecular interactions
- Easy for Everyone
- Label-Free
- High Quality Service Provided by

- - Active concentration
- Reliable DATA Output

 - Thermodynamics
 - Binding affinity

Bead Based Bio-Plex 200 in center

Validated, Short Term, Human Antibody Delvelopment

Antibody Production Service from

Antibody

- Mammalian cells - Ab Production and Purification from mammalian cells after transient
- transfection of provided Ab DNA
- Production Scale: 500mg 2g Other customized service can be offered

ELISA Kit Development Service

- Sandwich ELISA development from
- purified Antibodies Report validation data: LoD, LoQ Precision, Accurary and Specificity

Multiplex Bread Assay Service

- Multiplex Assay: We have the Luminex

Antigen & Antibody Quality Check

- Check the Purity and Electrophoresis pattern of Antigen of Antibody based on the Lab-on-a-chip using Bioanalyzer



Proteomics

Proteomics Premium Service

Global Proteome Profiling Service

- Protein identification
- Quantitative proteomics
- (SILAC, mTRAQ, and Label-Free) - Interactome analysis (Binding partners

discovery of target protein) Post-translation modification (PTM) Analysis Service

- Protein PTM identification (Phosphorylation, acetylation,

ubiquitination..) Drug-Target Profiling Service

- Target protein discovery for drug selected from phenotype screening

Consulting for proteome analysis

- Sample preparation
- Analysis process - Data interpretation



In Vivo

Validate Your Research in Mouse

Animal models for ARS research on shelf

- ARS reporter mouse
- ARS transgenic mouse
- ARS conditional KO mouse Inducible Cre mouse

Animal models for Cancer research or

- shelf - MMTV-neu mouse
- MMTV-pyVT mouse - p53 KO mouse
- Standardized material for mouse research

- MEF cells from GEM mouse - Frozen or FFPE tissue from GEM mouse

- Frozen of FFPE cancer/normal tissue

- Tissue analysis service for mouse research
- Tissue selctioning/histology/IHC - Expression analysis from reporter mouse



Biobank

Contamination Free Research Meterial Infra

Danation - Cell line banking system We welcome any cell lines for donation to help build a biobank to help other laboratories. Before any cell lines are accepted, they should checked for contamination by STR

analysis.

- Management Processing Preservation
- Organization and documentation - Storage and stock
- QA/QC monitoring - A list of all standard operation procedures

Service - Make an order mycroplasm test-Orderina

- You can purchase any cell line cultured of frozen stock. - For delivery, you sent the agreement (MTA)
- and order, we can out the shipment.

Mycoplasma Testing Service - Please fill out the application form on our service page before sending sample. If you need more information, Please contact our Biobank Service Department.

- 1. Downregulation of lamin A by tumor suppressor AIMP3/p18 leads to a progeroid phenotype in mice. Aging Cell. 2010 Oct;9(5):810-22
- 2. Cancer-associated splicing variant of tumor suppressor AIMP2/p38: pathological implication in tumorigenesis.

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Nat Rev Cancer. 2011 Sep 23;11(10):708-18

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Nat Mater 2011 Oct;10(10):747-52

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complex.

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Nat Chem Biol. 2014 Jan; 10(1):29-34

11. Ageneral strategy for generating intact, full-length IgG antibodies that penetrate into the cytosol of living cells.

MAbs. 2014;6(6):1402-14

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- 13. The crystal structure of arginyl-tRNA synthetase from Homo sapiens.

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- 15. Structural basis for full-spectrum inhibition of translational functions on a tRNA synthetase.

Nat Commun. 2015 Mar 31;6:6402

16. Liposome-based engineering of cells to package hydrophobic compounds in membrane vesicles for tumor penetration.

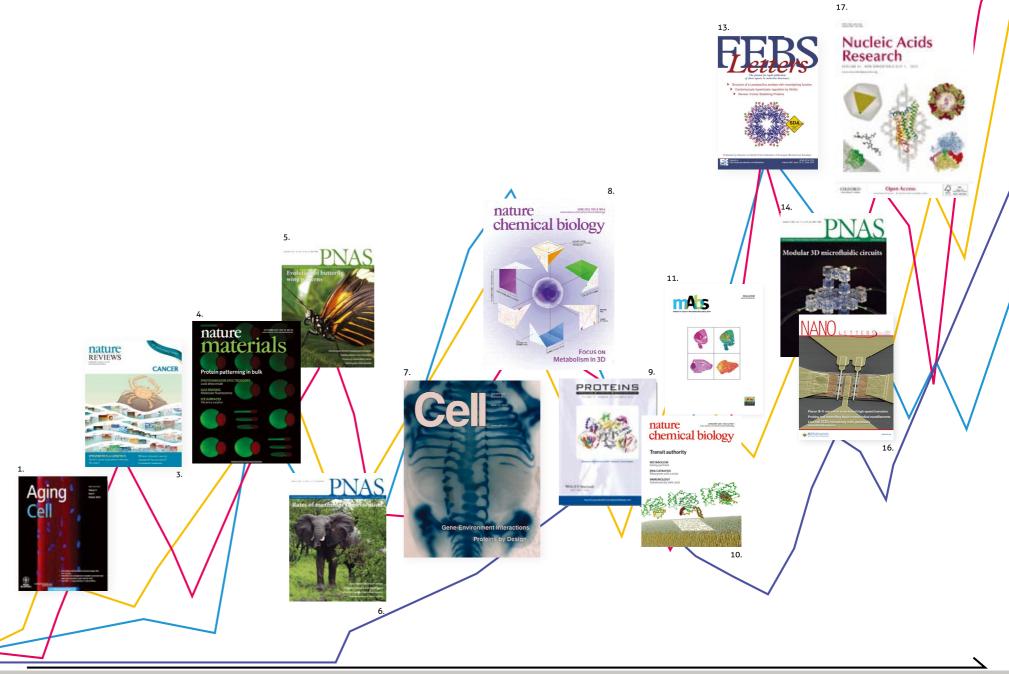
Nano Lett. 2015 May 13;15(5):2938-44

17. The BioMart community portal: an innovative alternative to large, centralized data repositories.

Nucleic Acids Res. 2015 Jul 1;43(W1):W589-98

Achievements

Total 179 research articles and 152 patents



FEATURE

Asia Pacific **Biotech News** 2012

Medicinal Bioconvergence Research Center:

Innovation of Drug Discovery through Novel Target Discovery and Convergence Technology

» Prof Sunghoon Kim

Seoul National University, Gwanak-ro, Gwanak-gu, Seoul 151-742, Korea Email: sungkim@snu.ac.kr, Tel: 82-2-880-8180, Fax: 82-2-875-2621

he extension of life expectancy dramatically increases chronic diseases such as cancer, dementia, diabetes, and ardiovascular diseases. Besides, a pandemic s considered as one of the four major risks at global level based on the recent OECD reports. Nonetheless, new drug discovery stays stagnant during last decade and ironically, pharmaceutical industry suffers from low eturn of investment in R&D. In 2010, only 21 new drugs were approved by FDA, USA.

Since 2009, the Korean Ministry of Education, Science and Technology (MEST) nas initiated the new program named Global Frontier Project' that can provide solutions to the challenges in major R&D area. Medicinal Bioconvergence Research Center (Biocon) was selected as one of the :hree projects to solve current difficulties in new drug discovery. As medicine becomes nore personal and stratified, Biocon foresees :hat the biggest bottleneck in drug discovery would be to secure novel therapeutic argets and biomarkers that can accurately address various human diseases. With this prediction, Biocon is initially focusing on novel therapeutic target discovery and ralidation that can be used by industry with high probability of success.

With the financial support of about 140 nillion dollars, this project will continue for a total 9-year period that is divided in three phases. By the end of the project, Biocon is aiming to establish '3D Atlas of Target-Drug nteractome' that shows the total map of the fully validated therapeutic targets with all the necessary attributes that are required or drug screening. (Fig. 2).

R&D productivity has dropped significantly from its peak

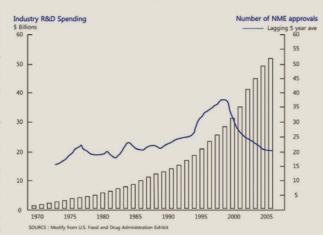


Fig. 1: Decreasing return of investment (ROI) in new drug discovery. Adapted from

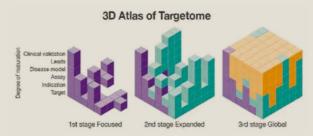


Fig. 2: Generation of fully validated target atlas that can be use for new drug discovery.

"Published total 179 research articles in top-notched journals and filed 152 patents."

BioCentury, the Bernstein Report on BioBusiness

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Product Discovery & Development

Neomics' new tricks

By Emily Cukier-Meisner

tRNA synthetases and their interacting require this process, human ARSs were proteins to build a pipeline of therapeutics generally not considered useful therapeuand diagnostics for cancer. The most advanced program focuses on detecting and targeting an oncogenic splice variant of target bacterial ARSs with antibiotics, but

have been known for almost four decades cess. Investigational compounds targeting as essential housekeeping enzymes that attach the correct amino acid to tRNA due to resistance or pipeline reprioritizaously unknown functions of aminoacyl during protein synthesis. Since all cells tion

AlfMP2 that may be overexpressed in lung, colon and ovarian cancers.

Aminoacyl tRNA synthetases (ARSs) these efforts have met with limited such the pathway in human disease was opened.

Sequester Arithmetic PLAN B FOR FDA, NIH

Sequestration is under way, which means FDA is facing a \$209 million budget cut this year, and NIH is looking at losing \$1.6 billion.

If they can't avoid the knife, what happens next?

The newest edition of BioCentury This Week television asks if there are ways to keep budget austerity from eroding the oversight of the nation's food and drugs, or from sacrificing America's biomedical research engine.

- Rep. Sam Farr, the top Democrat and only California lawmaker on the
- Diane Dorman, President of the Alliance for a Stronger FDA and Vice President for Policy at the National Organization for Rare Disorders.
- Jeffrey Senger, Partner at Sidley Austin and former Acting Chief Counsel at FDA.
- Margaret Anderson, Executive Director of Faster Cures and immediate past President of the Alliance for a Stronger FDA.
- Lynn Marquis, Director of the Coalition for Life Sciences, the policy umbrella group for the American Society for Biochemistry and Molecular Biology; the American Society for Cell Biology; the American Society for Clinical Investigation; the Genetics Society of America; Howard Hughes Medical Institute; and the Society for Neuroscience.

Key opinion leaders; sophisticated questions Always on *BioCentury This Week* television

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later declared the target "simply not druggable" based on low hit rates and difficulty generating lead compounds (see

in the late 1990s when Sunghoon Kim of the **Seoul National University** College of Pharmacy and colleagues researched components of eukaryotic ARSs unrelated

"It's old research, but in this aspect it is completely new biology and new medi-cine," said Kim, who is a scientific advisor

Neomics spun out of Seoul National University in 2005 to develop therapeu-University in 2005 to develop therapeutics and diagnostics related to AIMP2 (aminoacyl tRNA synthetase complex-interacting multifunctional protein 2), which is a non-enzymatic component of the macromolecular protein complex that forms with a subset of the ARSs.

In 2002, Kim and colleagues published in the Proceedings of the National Academy of Sciences the finding that AIMP2-knock-out mice die neonatally. In a 2003 publication in Nature Genetics, the group deter-mined the deaths arose largely from severe overproliferation of epithelial cells in lung alveoli, suggesting that AIMP2 functioned beyond protein synthesis as a potent suppressor of cell proliferation

Further investigation conducted by Kim's lab and presented in publications over 2003-09 showed that AIMP2 exerts antiproliferative and pro-apoptotic effects through multiple potential mechanisms including promotion of transforming growth factor (TGF) beta-mediated growth arrest, mediation of tumor necrosis factor (TNF) pro-apoptotic signaling, and prevention of p53 ubiquitylation, as summarized in a 2011 review in *Nature Reviews*

Though the protein itself generally acts as a tumor suppressor, a splice variant of AIMP2 lacking exon 2 (AIMP2-DX2) is highly expressed in lung cancer and has been shown to compromise the tumor See next page



Nature Science Cafe Asia

Novel Cancer Therapeutics Derived from Aminoacyl-tRNA Synthetases Sunghoon Kim, Ph.D. Professor and Director



Medicinal Bioconvergence Research Center (BIOCON), Dept. Molecular Medicine & Biopharmaceutical Sciences, College of Pharmacy, Graduate School of Convergence Science and Technology, Seoul National University, Korea

Sunghoon Kim is a professor at Seoul National University College of Pharmacy and Graduate School of Convergence Science and Technology, and also a director of "Medicinal

Bioconvergence Research Center (Biocon, http://biocon.re.kr)" that is the biggest national project in Korea for novel target and lead discovery. In this project, he is building up the pipeline of druggable "target and lead" packages for industrial development.

In academic community, he is globally recognized as a pioneer in the new biology and translational research of human aminoacyltRNA synthetases and their signaling network. He published more than 150 research articles in top-notched journals and filed more than 70 patents. He was nominated as a distinguished university professor and received several prestigious awards in Korea such as the best scientist award (2012), the scientist of the year (2006) and Korea science award (2003)

For educational and professional background, he received bachelor's degree at Seoul National University College of Pharmacy, master's degree at Korea Advanced Institute of Science and Technology Department of Biological Sciences, Korea and PhD degree at Division of Biology and Medicine, Brown University, USA. He worked as post-doctoral fellow at MIT and also as a senior research scientist of Cubist Pharmaceuticals, USA. He also worked as visiting professor at Scripps Institute, and as a founding scientist of ATYR Pharma, USA. He is currently a visiting scientist of Institute of Cell and Material Sciences, Kyoto University, and an advisor of National Center for Drug Screening, China.

> Nature Science Cafe Asia 2015

Neomics in **Biocentury** 2013



Research Network & People

Serving as a hub to bridge basic science to drug discovery



Biocon's Network

Biocon is embracing many domestic and foreign institutions in order to keep up the quality of the research. Currently, 60 different institutions and universities are participating in Biocon. As foreign partners, researchers affiliated to 21 institutions in 10 countries work as science advisors as well as research collaborators. Biocon also mediates translational research in collaboration with major leading hospitals in Korea. Through this domestic and global collaborative network with academia, hospital and industry, Biocon will serve as a research hub to bridge basic science to drug discovery through translational research.

Biocon is multi-disciplinary and multi-organizational project while retaining the headquarter office and integration core unit in Seoul National University. Many researchers in diverse areas, who share the same vision, are participating in the Biocon project. Those include professors, medical doctors and principal investigators in national institutes and industries. The total number of the participating researchers and organizations would vary dynamically depending on the project goal and emerging needs.

Most of the participating PIs joined to Biocon while maintaining their own affiliated institutions. Since the integration core unit (ICU) consists of only full-time specialists in different areas in biology, chemistry and engineering, their roles are to integrate all the new discoveries and technologies into one package, and to facilitate the interactions and communications among the extramural research partners. Thus, the people in ICU functions like a heart to circulate energy among the Biocon researchers.

Advisory Board Members and Research Collaborators

| Name | Institution | Country | Nobel Prize |
|-------------------|--|-------------|--|
| Aaron Ciechanover | Technion | Israel | 2004 Nobel Prize in Chemistry |
| Ada Yonath | Weizmann Inst. | Israel | 2009 Nobel Prize in Chemistry |
| Alex Matter | Exp. Therapeutics Cntr. | Singapore | |
| Andy Yun | Mass General Hospital | USA | |
| Chales Lee | Yale Univ. Jackson Lab. | USA | |
| Ehud Razin | Hebrew Univ. | Israel | |
| Hiroaki Osada | Riken | Japan | |
| Hubert Becker | CNRS | France | |
| John Blenis | Harvard Medical School | USA | |
| Louis Ignarro | UCLA | USA | 1998 Nobel Prize in Physiology or Medicine |
| Marius Ueffing | University Medical Center, Tübingen | Germany | |
| Min Guo | Scripps, Florida | USA | |
| Ming Wei Wang | Shanghai Isnt. Materia Medica | China | |
| Minoru Yoshida | Riken | Japan | |
| Motonari Uesugi | Kyoto Univ. | Japan | |
| Nahum Sonenberg | McGill Univ. | Canada | |
| Paul Schimmel | Scripps, La Jolla | USA | |
| Peter Hodder | Scripps, Florida | USA | |
| Peter Shepherd | Auckland Univ. | New Zealand | |
| Richard Lerner | Scripps, La Jolla | USA | |
| Richard Simpson | La Trobe Univ. | Australia | |
| Robert Huber | Max Planck Inst. | Germany | 1988 Nobel Prize in Chemistry |
| Roger Kornberg | Stanford Univ. | USA | 2006 Nobel Prize in Chemistry |
| Susan Martinis | Univ. of Illinois | USA | |
| Young Tae Chang | NUS | Singapore | |

4 Specialist Groups

| Target Identification | | | | | |
|-----------------------|-------------------------|--|--|--|--|
| Beom Sik Kang | Kyungpook Natl. Univ. | | | | |
| Kyung Jin Kim | Postech | | | | |
| Key Sun Kim | KIST | | | | |
| Myung Hee Kim | KRIBB | | | | |
| Jaesang Kim | Ewha Univ. | | | | |
| Hyeong Gon Moon | Seoul Natl. Univ. Hosp. | | | | |
| Eun Ok Paek | Hanyang Univ. | | | | |
| Ji Joon Song | KAIST | | | | |
| YoungKee Shin | Seoul Natl. Univ. | | | | |
| Ki Won Lee | Seoul Natl. Univ. | | | | |
| Cheolju Lee | KIST | | | | |
| Young Ho Jeon | Korea Univ. | | | | |
| Hyun Suk Jung | Kangwon Univ. | | | | |
| Yunje Cho | Postech | | | | |
| Yoon La Choi | Sungkyunkwan Univ. | | | | |
| Byung Woo Han | Seoul Natl. Univ. | | | | |
| Won Shik Han | Seoul Natl. Univ. Hosp. | | | | |
| Kwang Yeon Hwang | Korea Univ. | | | | |
| Daehee Hwang | Postech | | | | |
| Murim Choi | Seoul Natl. Univ. | | | | |
| Mi Rim Jin | Daejeon Univ. | | | | |
| Jin Won Huh | Asan Med. Ctr. | | | | |

| Drug Design | | | | | | |
|----------------|-------------------|--|--|--|--|--|
| Taek Jin Kang | Dongguk Univ. | | | | | |
| Wan Kyu Kim | Ewha Univ. | | | | | |
| Yong Sung Kim | Ajou Univ. | | | | | |
| Sung Ho Ryu | Postech | | | | | |
| Byung Doo Song | SKAI | | | | | |
| Hyun Bo Shim | Ewha Univ. | | | | | |
| Bong Yong Lee | Kyung Hee Univ. | | | | | |
| Sunkyung Lee | KRICT | | | | | |
| Jeewoo Lee | Seoul Natl. Univ. | | | | | |
| Hae Ryun Lee | Postech | | | | | |
| Heeyeong Cho | KRICT | | | | | |
| Yun Heo | Yuhan Coporation | | | | | |
| Younghoon Kim | Crystal Genomics | | | | | |
| Ji Ho Park | KAIST | | | | | |
| Gyoonhee Han | Yonsei Univ. | | | | | |
| Kyeong Lee | Dongguk Univ. | | | | | |
| Young-Ger Suh | Seoul Natl. Univ. | | | | | |
| | | | | | | |

| Drug S | creening |
|------------------|-------------------|
| Sunghoon Kwon | Seoul Natl. Univ. |
| Philhan Kim | KAIST |
| Seung Bum Park | Seoul Natl. Univ. |
| Joon Myong Song | Seoul Natl. Univ. |
| Noo Li Jeon | Seoul Natl. Univ. |
| Honggu Chun | Korea Univ. |
| Jin Woo Choi | Wonkwang Univ. |
| Byung Joon Hwang | SKAI |
| Seong Keun Kim | Seoul Natl. Univ. |
| Hee-Sung Park | KAIST |
| Soo Hyun Kim | Konkuk Univ. |

| Disease Model | | | | | |
|----------------|-------------------|--|--|--|--|
| Kyung Sun Kang | Seoul Natl. Univ. | | | | |
| Young Yun Kong | Seoul Natl. Univ. | | | | |
| Bum Joon Park | Pusan Natl. Univ. | | | | |
| Ho Jun Seol | Samsung Med. Ctr. | | | | |
| Jung Weon Lee | Seoul Natl. Univ. | | | | |
| Ho Lee | Natl. Cancer Ctr. | | | | |
| Young Bum Huh | Kyung Hee Univ. | | | | |
| Yung-Jin Kim | Pusan Natl. Univ. | | | | |
| Youngil Koh | Seoul Natl. Univ. | | | | |
| Dong Ki Lee | Yonsei Univ. | | | | |
| Kang Young Lee | Yonsei Univ. | | | | |
| Kweon Yu | KRIBB | | | | |
| | | | | | |

⁻ KIST: Korea Institute of Science and Technology

⁻ KRIBB: Korea Research Institute of Bioscience and Biotechnology

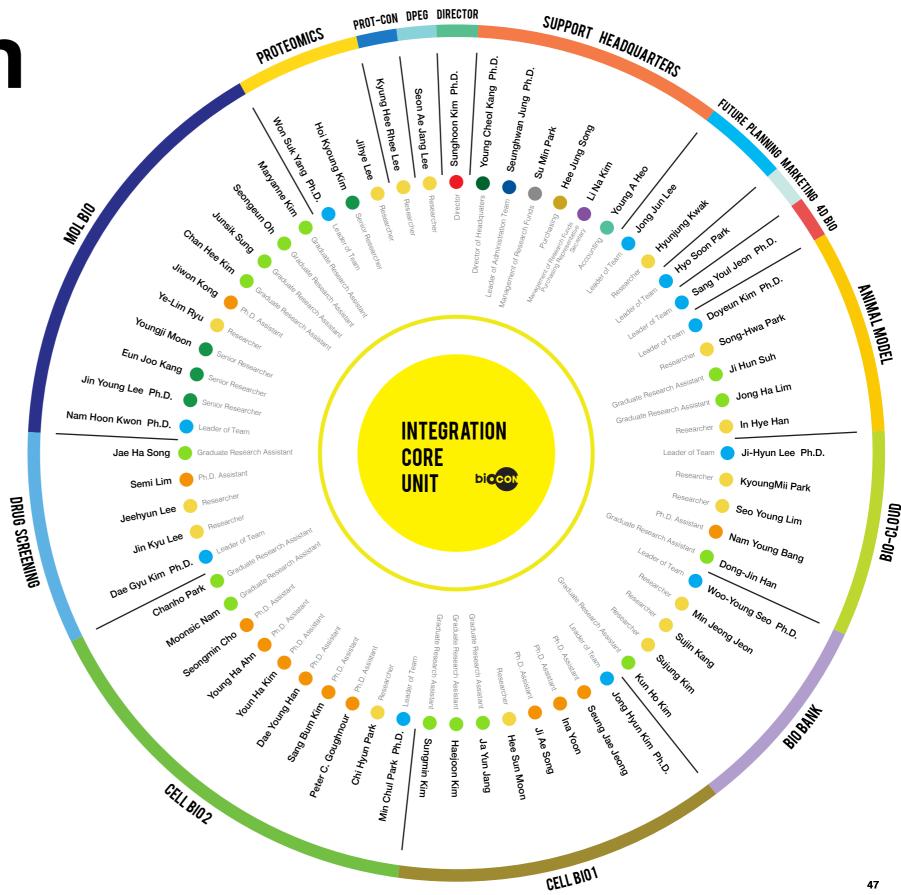
⁻ KAIST: Korea Advanced Institute of Science and Technology

⁻ POSTECH: Pohang University of Science and Technology

⁻ SKAI: Scripps Korea Antibody Institute

⁻ KRICT: Korea Research Institute of Chemical Technology

Integration Core Unit



Director of Headquaters

Leader of Administration Team

Management of Research Funds

Management of Research Funds Purchasing Representative Secretary

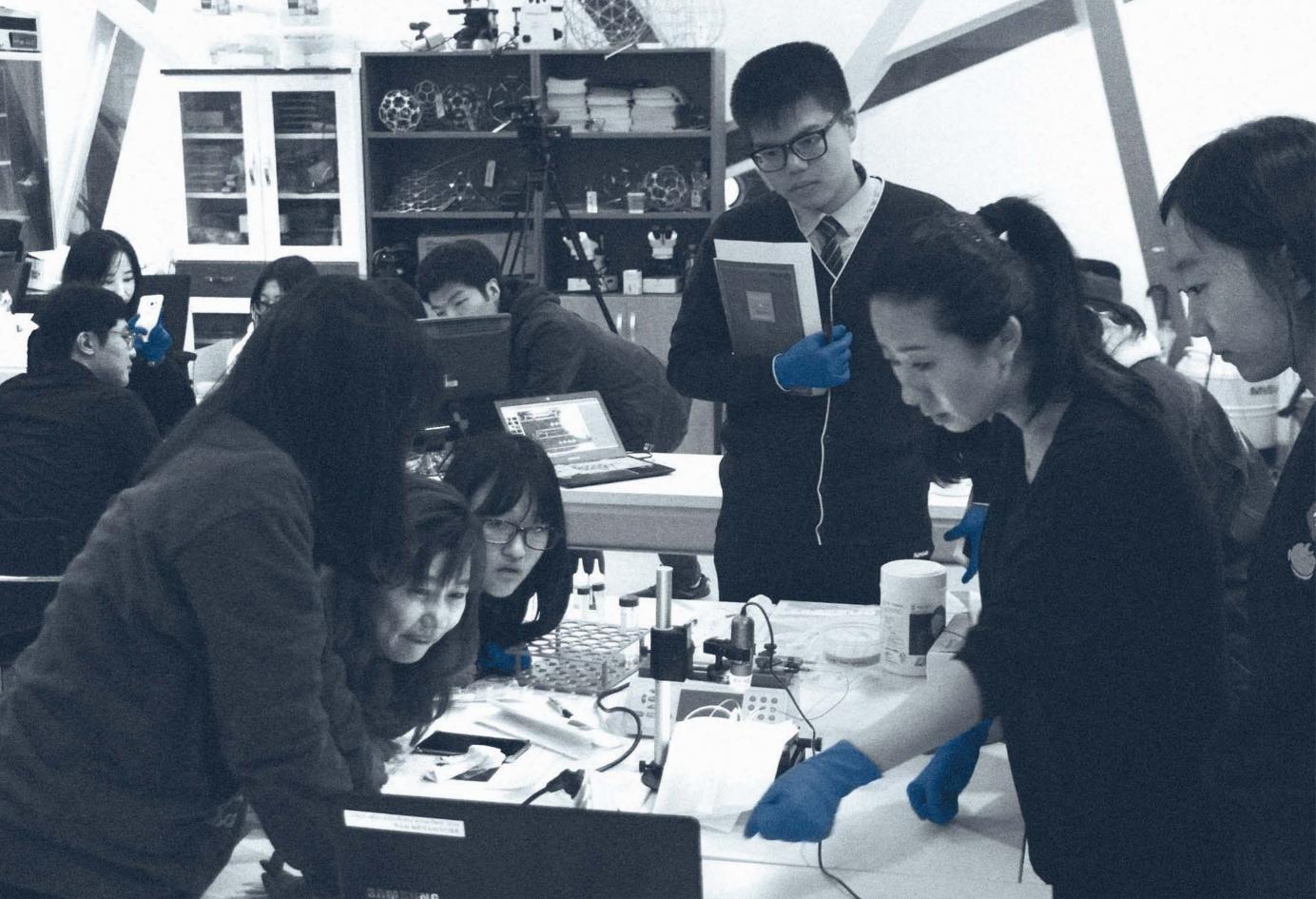
Leader of Team

Graduate Research Assistant

Ph.D. Assistant

Senior Researcher

BIO-CLOUD



10.

Cultural Activities

Delivering Biocon's vision to the public via art and culture

Since **Biocon** is supported by citizen's taxes, it is necessary to explain why Biocon was established and how Biocon's activities are connected to public. To facilitate the public relationship, Biocon initiated several different activities. First, some of the published research subjects are remade as animations or cartoons, and posted in the sites of social network. Second, Biocon hosted Bio-Art Contest so that anybody can show the beauty of life in their own eyes. Please visit the website for more information. bioart.biocon.re.kr Third, Biocon signed up "memorandum of understanding" with a several different centers (science museum, cultural center and gallery) to co-organize exhibitions, events, and the education of bioscience to public.





Fungus Inhale Vaccination
Min Kyung Park



Life Force of Barnacle Ji Hyang Lim

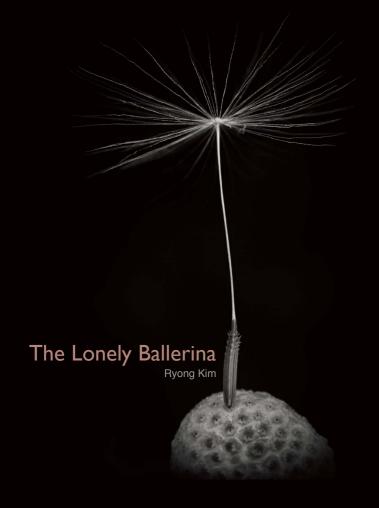


Bios Roberta Trentin

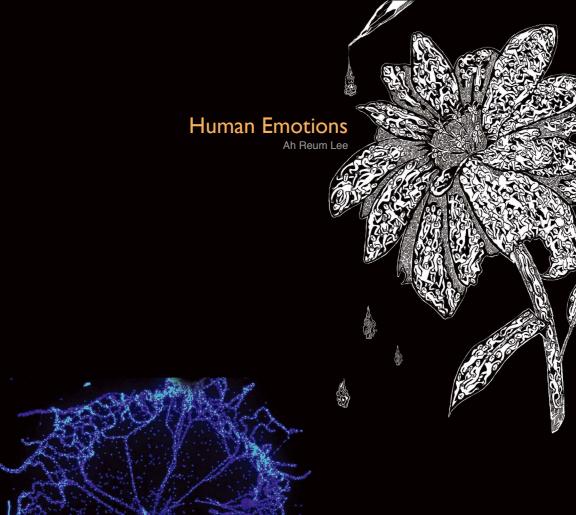
Creator of Abundance



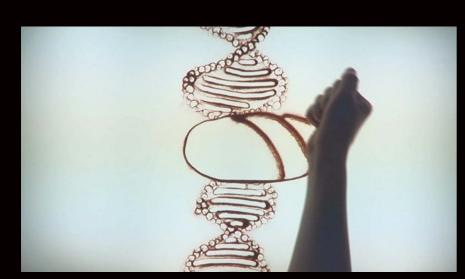
Cleared Fish Skeleton Adam P. Summers



Bio-Art Contest 2014 Winners







Find the Miracle
Mi Hyun Kim



365 Seo Youn Choi

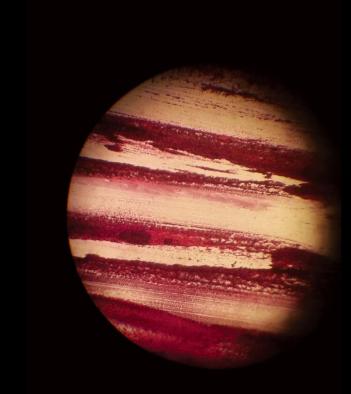




Nature and Human Eun Jung Kim



Beauty of Nature
Soo Youn Choi

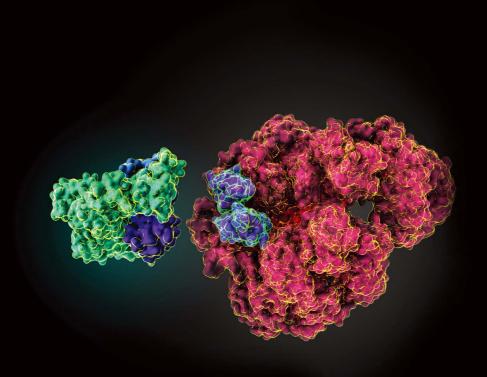


Jupiter
Woo Sang Hong

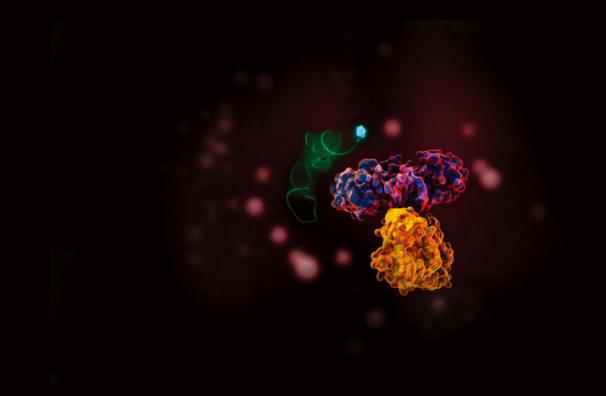
Bio-Art Contest 2013 Winners

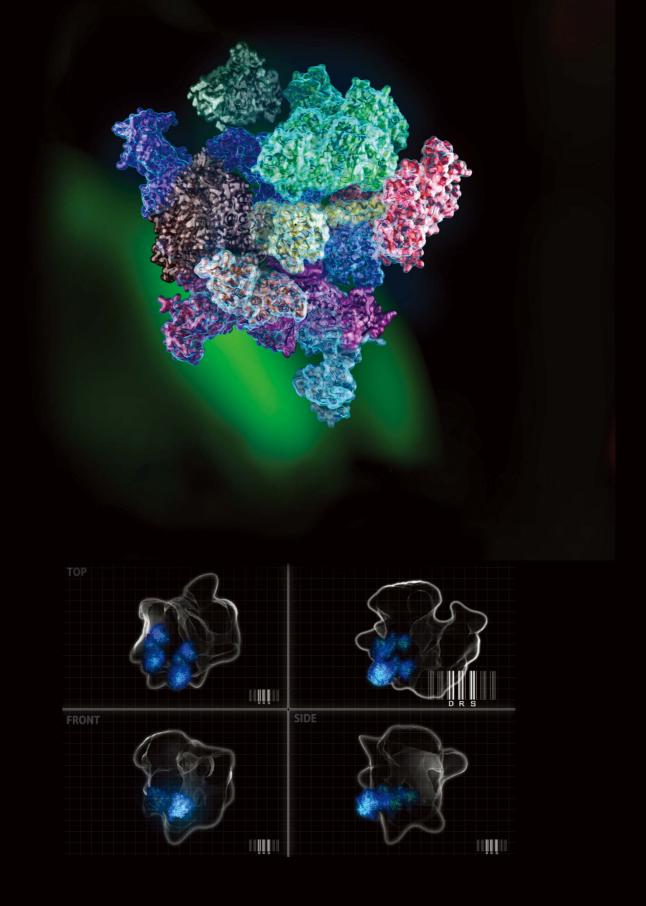


Life of Tree Sung Chul Ha



Biomedical Illustration

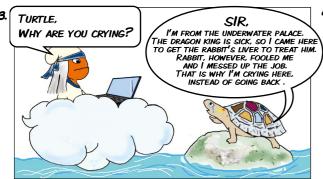


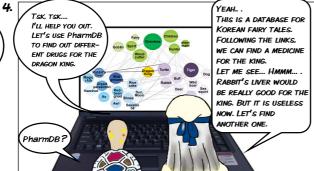


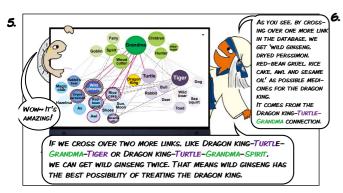
Cartoon

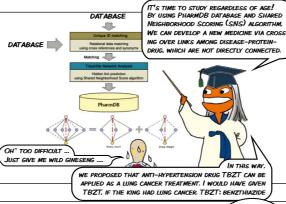












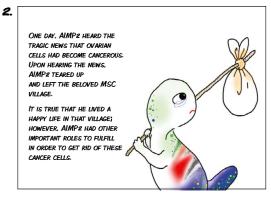
1. PharmDB

Rational drug repositioning guided by an integrated pharmacological network of protein, disease and drug.

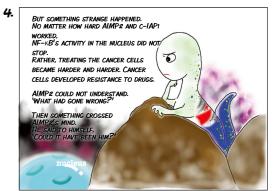
BMC Syst Biol. 2012 Jul 2;6:80



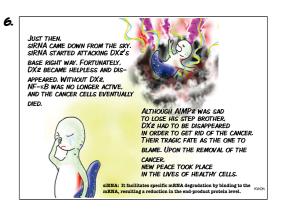








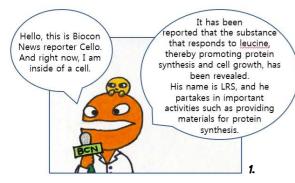


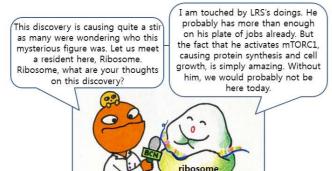


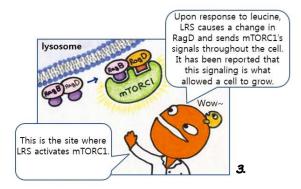
2. DX2 as an Effective Target against Chemoresist Ovarian Cancer

Splicing variant of AIMP2 as an effective target against chemoresistant ovarian cancer.

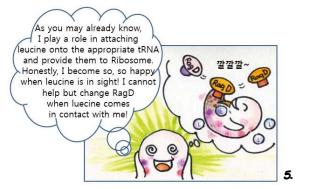
J Mol Cell Biol. 2012 Jun;4(3):164-73.

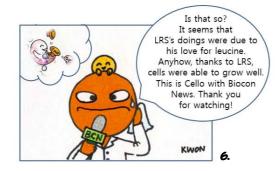








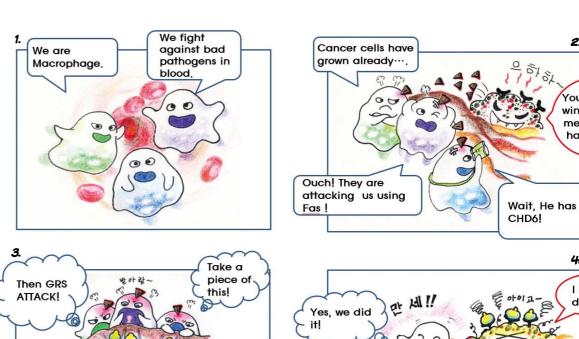




3. LRS as a Leucine Sensor

Leucyl-tRNA synthetase is an intracellular leucine sensor for the mTORC1-signaling pathway.

Cell. 2012 Apr 13;149(2):410-24



4. What's GRS?

Secreted human glycyl-tRNA synthetase implicated in defense against ERK-activated tumorigenesis

2.

You cannot win against me cause I have ERK!

dying-

GRS is best

for cancer

KWON

63

cells!

Proc Natl Acad Sci U S A. 2012 Mar 13;109(11):E640-7

Oh my,

what is

this?

Publications

Patents

A. Publications

| Number | Title | Journal | Year | No, | Issue | Page | Author |
|--------|---|-----------------------|------|-----|-------|-------------|--|
| 1 | Fluocinolone Acetonide Is a Potent Synergistic Factor of TGF-β3-Associated Chondrogenesis of Bone Marrow-Derived Mesenchymal Stem Cells for Articular Surface Regeneration. | J Bone Miner Res | 2015 | 30 | 9 | 1585-1596 | Hara ES, Ono M, Pham HT, Sonoyama W, Kubota S, Takigawa M, Matsumoto T, Young MF, Olsen BR, Kuboki T |
| 2 | Crystal structures of immunoglobulin Fc heterodimers reveal the molecular basis for heterodimer formation. | Mol Immunol | 2015 | 65 | 2 | 377-383 | Choi HJ, Seok SH, Kim YJ, Seo MD, Kim YS |
| 3 | In vivo RNAi screen identifies NLK as a negative regulator of mesenchymal activity in glioblastoma. | Oncotarget | 2015 | 6 | 24 | 20145-20159 | Sa JK, Yoon Y, Kim M, Kim Y, Cho HJ, Lee JK, Kim GS, Han S, Kim WJ, Shin YJ, Joo KM, Paddison PJ, Ishitani T, Lee J, Nam DH |
| 4 | Tpl2 induces castration resistant prostate cancer progression and metastasis. | Int J Cancer | 2015 | 136 | 9 | 2065-2077 | Lee HW, Cho HJ, Lee SJ, Song HJ, Cho HJ, Park MC, Seol HJ, Lee JI, Kim S, Lee HM, Choi HY, Nam DH, Joo KM |
| 5 | In vivo quantitation of injected circulating tumor cells from great saphenous vein based on video-rate confocal microscopy. | Biomed Opt Express | 2015 | 6 | 6 | 2158-2167 | Seo H, Hwang Y, Choe K, Kim P |
| 6 | (1)H, (13)C and (15)N resonance assignment of WHEP domains of human glutamyl-prolyl tRNA synthetase. | Biomol NMR Assign | 2015 | 9 | 1 | 25-30 | Shin C, Hwang GS, Ahn HC, Kim S, Kim KS |
| 7 | Longitudinal tracing of spontaneous regression and anti-angiogenic response in individual microadenomas during colon tumorigenesis. | Theranostics | 2015 | 5 | 7 | 724-732 | Choi JW, Kim P, Kim JK, Kim YR, Fukumura D, Yun SH |
| 8 | Noncanonical roles of membranous lysyl-tRNA synthetase in transducing cell- substrate signaling for invasive dissemination of colon cancer spheroids in 3D collagen I gels. | Oncotarget | 2015 | 6 | 25 | 21655-21674 | Nam SH, Kim D, Lee MS, Lee D, Kwak TK, Kang M, Ryu J, Kim HJ, Song HE, Choi J, Lee GH, Kim SY, Park SH, Kim DG, Kwon NH, Kim TY, Thiery JP, Kim S, Lee JW |
| 9 | Transmembrane 4 L six family member 5 (TM4SF5)-mediated epithelial-mesenchymal transition in liver diseases. | Int Rev Cell Mol Biol | 2015 | 319 | - | 141-163 | Lee JW |
| 10 | The BioMart community portal: an innovative alternative to large, centralized data repositories. | Nucleic Acids Res | 2015 | 43 | W1 | W589-598 | Smedley D, Haider S, Durinck S, Pandini L, Provero P, Allen J, Arnaiz O, Awedh MH, Baldock R, Barbiera G, Bardou P, Beck T, Blake A, Bonierbale M, Brookes AJ, Bucci G, Buetti I, Burge S, Cabau C, Carlson JW, Chelala C, Chrysostomou C, Cittaro D, Collin O, Cordova R, Cutts RJ, Dassi E, Di Genova A, Djari A,Esposito A, Estrella H, Eyras E, Fernandez-Banet J, Forbes S, Free RC, Fujisawa T, Gadaleta E, Garcia-Manteiga JM, Goodstein D, Gray K, Guerra-Assunção JA, Haggarty B, Han DJ, Han BW, Harris T, Harshbarger J, Hastings RK, Hayes RD, Hoede C, Hu S, Hu ZL, Hutchins L, Kan Z, Kawaji H, Keliet A, Kerhornou A,Kim S, Kinsella R, Klopp C, Kong L, Lawson D, Lazarevic D, Lee JH, Letellier T, Li CY, Lio P, Liu CJ, Luo J, Maass A, Mariette J, Maurel T, Merella S, Mohamed AM, Moreews F, Nabihoudine I, Ndegwa N, Noirot C, Perez-Llamas C, Primig M, Quattrone A, Quesneville H, Rambaldi D, Reecy J, Riba M, Rosanoff S, Saddiq AA, Salas E, Sallou O, Shepherd R, Simon R, Sperling L, Spooner W, Staines DM, Steinbach D, Stone K, Stupka E, Teague JW, Dayem Ullah AZ, Wang J, Ware D, Wong-Erasmus M, Youens-Clark K, Zadissa A, Zhang SJ, Kasprzyk A |
| 11 | Crystal structure of the protein At3g01520, a eukaryotic universal stress protein-like protein from Arabidopsis thaliana in complex with AMP. | Proteins | 2015 | | - | | Kim DJ, Bitto E, Bingman CA, Kim HJ, Han BW, Phillips GN Jr |
| 12 | Discovery of orally available runt-related transcription factor 3 (RUNX3) modulators for anticancer chemotherapy by epigenetic activation and protein stabilization. | J Med Chem | 2015 | 58 | 8 | 3512-3521 | Yang JS, Lee C, Cho M, Kim H, Kim JH, Choi S, Oh SJ, Kang JS, Jeong JH, Kim HJ, Han G |
| 13 | Liposome-based engineering of cells to package hydrophobic compounds in membrane vesicles for tumor penetration. | Nano Lett | 2015 | 15 | 5 | 2938-2944 | Lee J, Kim J, Jeong M, Lee H, Goh U, Kim H, Kim B, Park JH |

| 14 | Self-renewal and circulating capacities of metastatic hepatocarcinoma cells required for collaboration between TM4SF5 and CD44. | BMB Rep | 2015 | 48 | 3 | 127-127 | Lee D, Lee JW |
|----|---|---------------------------|------|--------------|-------|-------------|--|
| 15 | Structural basis for full-spectrum inhibition of translational functions on a tRNA synthetase. | Nat Commun | 2015 | 6 | - | 6402 | Fang P, Yu X, Jeong SJ, Mirando A, Chen K, Chen X, Kim S, Francklyn CS, Guo M |
| 16 | Comprehensive data resources and analytical tools for pathological association of aminoacyl tRNA synthetases with cancer. | Database | 2015 | in- press | - | - | Lee JH, You S, Hyeon do Y, Kang B, Kim H, Park KM, Han B, Hwang D, Kim S |
| 17 | Interaction of tetraspan(in) TM4SF5 with CD44 promotes self-renewal and circulating capacities of hepatocarcinoma cells. | Hepatology | 2015 | 61 | 6 | 1978-1997 | Lee D, Na J, Ryu J, Kim HJ, Nam SH, Kang M, Jung JW, Lee MS, Song HE, Choi J, Lee GH, Kim TY, Chung JK, Park KH, Kim SH, Kim H, Seo H, Kim P, Youn H, Lee JW |
| 18 | Twist1 and AP-1 cooperatively upregulate integrin α5 expression to induce invasion and the epithelial-mesenchymal transition. | Carcinogenesis | 2015 | 36 | 3 | 327-337 | Nam EH, Lee Y, Moon B, Lee JW, Kim S |
| 19 | High-throughput, miniaturized clonogenic analysis of a limiting dilution assay on a micropillar/microwell chipwith brain tumor cells. | Small | 2014 | 10 | 24 | 5098-5105 | Lee DW, Choi YS, Seo YJ, Lee MY, Jeon SY, Ku B, Nam DH |
| 20 | miR-543 and miR-590-3p regulate human mesenchymal stem cell aging via direct targeting of AIMP3/p18. | Age | 2014 | 36 | 6 | 9724 | Lee S, Yu KR, Ryu YS, Oh YS, Hong IS, Kim HS, Lee JY, Kim S, Seo KW, Kang KS |
| 21 | A novel in vitro permeability assay using three-dimensional cell culture system. | J Biotechnol | 2014 | 205 | - | 93-105 | Lee JB, Son SH, Park MC, Kim TH, Kim MG, Yoo SD, Kim S |
| 22 | A general strategy for generating intact, full-length IgG antibodies that penetrate into the cytosol of living cells. | MAbs | 2014 | 6 | 6 | 1402-1414 | Choi DK, Bae J, Shin SM, Shin JY, Kim S, Kim YS |
| 23 | DNA end recognition by the Mre11 nuclease dimer : Insights into resection and repair of damaged DNA. | ЕМВО Ј | 2014 | 33 | 20 | 2422-2435 | Sung S, Li F, Park YB, Kim JS, Kim AK, Song OK, Kim J, Che J, Lee SE, Cho Y |
| 24 | Selective photosensitizer delivery into plasma membrane for effective photo- dynamic therapy. | J Control Release | 2014 | 191 | - | 98-104 | Kim J, Santos OA, Park JH |
| 25 | Promiscuous methionyl-tRNA synthetase mediates adaptive mistranslation to protect cells against oxidative stress. | J Cell Sci | 2014 | 127 | Pt 19 | 4234-4245 | Lee JY, Kim DG, Kim BG, Yang WS, Hong J, Kang T, Oh YS, Kim KR, Han BW, Hwang BJ, Kang BS, Kang M, Kim MH, Kwon NH, Kim S |
| 26 | Structure of the ArgRS–GInRS–AIMP1 complex and its implications for mammalian translation. | Proc Natl Acad Sci USA | 2014 | 111 | 42 | 15084-15089 | Fu Y, Kim Y, Jin KS, Kim HS, Kim JH, Wang D, Park M, Jo CH, Kwon NH, Kim D, Kim MH, Jeon YH, Hwang KY, Kim S, Cho Y |
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B. Patents

| No. Patent No. Country Title Date 1 101551696 Rep. of Korea A novel TM4SF5 specific monoclonal antibody and use thereof 2015-09-03 2 101551299 Rep. of Korea Neuropilin specific tumor penetrating peptide and fusion protein fused with the same 2015-09-02 3 101522954 Rep. of Korea CH3 domain mutant pairs for the high yield formation of heterodimeric Fc of antibody, method of production and use thereof 2015-04-16 4 101514320 Rep. of Korea Novel pharmaceutical composition for preventing or treating cancer 2015-04-16 5 02497471 Europe Use of benzo-heterocycle derivatives for preventing and treating cancer or for inhibiting cancer metastasis 2015-04-15 6 101491108 Rep. of Korea Direct preparation of functional insulin producing cell from human dermal fibroblasts 2015-02-02 7 05628807 Japan Method for controlling cancer metastasis or cancer cell migration by modulating the cellular level of lysyl-IRNA synthetase 2014-09-11 8 101441503 Rep. of Korea Zinc finger library and engineered zinc finger protein screening using the same 2014-07-31 9 101427328 | | Registration | | | | | | | | | | | |
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| thereof thereof 2015-09-02 101551299 Rep. of Korea protein fused with the same CH3 domain mutant pairs for the high yield formation of heterodimeric Fc of antibody, method of production and use thereof 101514320 Rep. of Korea Protein fused with the same CH3 domain mutant pairs for the high yield formation of heterodimeric Fc of antibody, method of production and use thereof Novel pharmaceutical composition for preventing or treating cancer Use of benzo-heterocycle derivatives for preventing and treating cancer or for inhibiting cancer metastasis 101491108 Rep. of Korea Direct preparation of functional insulin producing cell from human dermal fibroblasts Method for controlling cancer metastasis or cancer cell migration by modulating the cellular level of lysyl-tRNA synthetase Method for controlling cancer metastasis or cancer cell migration by modulating the cellular level of lysyl-tRNA synthetase 101441503 Rep. of Korea Zinc finger library and engineered zinc finger protein screening using the same 9 101427328 Rep. of Korea Method for Identification of proteins 2014-07-31 10 101426056 Rep. of Korea Device for in vitro blood vessel formation and vascular permeability assay using the same 11 101425032 Rep. of Korea Novel use of leucyl-tRNA synthetase 2014-07-28 12 101419836 Rep. of Korea Composition comprising Δ5-2-oxopiperazine derivative for inducing differentiation of mesenchymal stem cells into chondrocytes 13 08771611 U.S.A. System and methods of log-scale concentration gradients Method for screening anticancer substance inhibiting function of TM4SF5 and anticancer composition containing chalcone-based compound Method for screening anticancer composition containing chalcone-based compounds Method for screening anti-cancer compounds inhibiting function of TM4SF5 and anticancer compounds containing chalcone compounds Method for screening anti-cancer compounds containing behaviour of JM4SF5 and anticancer compounds containing chalcone compounds Method for screening anti-cancer compounds cont | No. | Patent No. | Country | Title | Date | | | | | | | | |
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| 101522954 Rep. of Korea heterodimeric Fc of antibody, method of production and use thereof was thereof Novel pharmaceutical composition for preventing or treating cancer Novel pharmaceutical composition for preventing or treating cancer Direct preparation of functional insulin producing cell from human dermal fibroblasts Rep. of Korea Direct preparation of functional insulin producing cell from human dermal fibroblasts Rep. of Korea Direct preparation of functional insulin producing cell migration by modulating the cellular level of lysyl-tRNA synthetase Rep. of Korea Zinc finger library and engineered zinc finger protein screening using the same 101427328 Rep. of Korea Method for Identification of proteins Device for in vitro blood vessel formation and vascular permeability assay using the same 10 101426056 Rep. of Korea Novel use of leucyl-tRNA synthetase 11 101425032 Rep. of Korea Novel use of leucyl-tRNA synthetase 12 101419836 Rep. of Korea Novel use of leucyl-tRNA synthetase Composition comprising Δ5-2-oxopiperazine derivative for inducing differentiation of mesenchymal stem cells into chondrocytes Nethod for screening anticancer substance inhibiting function of TMASF5 and anticancer composition containing chalcone-based compound Method for screening of anti-cancer agent and inflammatory disease agent Method for screening anticancer compounds inhibiting function of TMASF5 and anticancer compounds inhibiting function of TMASF5 and anticancer compounds containing chalcone-based compounds Method for screening anti-cancer compounds inhibiting function of TMASF5 and anti-cancer compounds containing chalcone-oppounds Method for screening anti-cancer compounds containing chalcone compounds Method for screening anti-cancer compounds containing function of TMASF5 and anti-cancer compounds containing function of TMASF5 and anti-cancer compounds containing brain tumor or glioblastoma having resistance of 2014-08-03 | 2 | 101551299 | Rep. of Korea | | 2015-09-02 | | | | | | | | |
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| 4 | 1020150066835 | Rep. of Korea | Apparatus comprising nanoporous membrane□for separating organic molecule | 2015-05-13 | | | | | | | | |
| 5 | 1020150066864 | Rep. of Korea | Apparatus for separating fine endoplasmic reticulum by electrophoresis sample pH adjustment | 2015-05-13 | | | | | | | | |
| 6 | 1020150058333 | Rep. of Korea | Vectors for measuring multiple protein-protein interactions simultaneously | 2015-04-24 | | | | | | | | |
| 7 | 1020150058335 | Rep. of Korea | Yeast strain with dual reporter system for barcode transfer assay | 2015-04-24 | | | | | | | | |
| 8 | 10-2015-0054577 | Rep. of Korea | A composition for specifically degrading nuclear proteins and a method using the same | 2015-04-17 | | | | | | | | |
| 9 | PCT/ KR2015/003807 | PCT | Pharmaceuticalcompositionfortreatingandpreventingleu- kemia, containing thie nopyrimidine derivative or pharmaceu tically acceptables alt there of | 2015-04-15 | | | | | | | | |
| 10 | 14670390 | U.S.A. | Method for screening EMT inhibitor | 2015-03-26 | | | | | | | | |
| 11 | 1020150037979 | Rep. of Korea | Method for measuring multiple protein-protein interac- tions simultaneously between two yeast library | 2015-03-19 | | | | | | | | |
| 12 | 13824875.2 | Europe | Novel monoclonal antibody which is specifically bound to TM4SF5 protein and use thereof | 2015-03-03 | | | | | | | | |
| 13 | 1020150027617 | Rep. of Korea | Compositions comprising tryptophanyl-tRNA synthetase for treating or preventing diseases caused by bacterial infections and for enhancing immune responses | 2015-02-26 | | | | | | | | |
| 14 | 14613014 | U.S.A. | Novel monoclonal antibody which is specifically bound to TM4SF5 protein and use thereof | 2015-02-13 | | | | | | | | |
| 15 | 13816643.4 | Europe | Pharmaceutical composition comprising azathioprine as active ingredient for preventing or treating brain tumors or temodal-resistant glioblastomas | 2015-02-10 | | | | | | | | |
| 16 | 1020150014616 | Rep. of Korea | Anti-EPRS monoclonal antibody and uses thereof | 2015-01-29 | | | | | | | | |
| 17 | 1020150014617 | Rep. of Korea | Anti-CRS monoclonal antibody and uses thereof | 2015-01-29 | | | | | | | | |
| 18 | 1020150008668 | Rep. of Korea | Crystal of FAN1-5' FLAP DNA complex and method of manufacturing the same | 2015-01-19 | | | | | | | | |
| 19 | 1020150008537 | Rep. of Korea | Crystal structure of human Mus81-Eme1-DNA complex and preparing method thereof | 2015-01-19 | | | | | | | | |

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| 22 | 1020140194204 | Rep. of Korea | Anti-KRS monoclonal antibody and uses thereof | 2014-12-30 |
| 23 | PCT/ KR2014/012980 | PCT | Anti-KRS monoclonal antibody and uses thereof | 2014-12-29 |
| 24 | 1020140160710 | Rep. of Korea | Production methods of functional cell-derived membrane vesicles using membrane fusogenic liposomes including functionalized phospholipids and functional cell-derived membrane vesicles producing thereto | 2014-11-08 |
| 25 | 13778232.2 | Europe | Use of novel aminopyridine derivative to prevent or treat cancer | 2014-11-03 |
| 26 | 14518753 | U.S.A. | Use of novel aminopyridine derivative to prevent or treat cancer | 2014-10-20 |
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| 31 | 2015506906 | Japan | Use of a novel aminopyridine derivative to prevent or treat cancer | 2014-10-15 |
| 32 | 1020140135813 | Rep. of Korea | The composition for the prevention and treatment of cancers, or inhibition of metastasis containing binding inhibitor of TM4SF5 protein and c-Src protein | 2014-10-08 |
| 33 | 1020140114142 | Rep. of Korea | Production methods of functional cell-derived membrane vesicles using membrane fusogenic liposomes including functionalized phospholipids and functional cell-derived membrane vesicles producing thereto | 2014-08-29 |
| 34 | 1020140100605 | Rep. of Korea | Method and apparatus for separating microvesicle | 2014-08-05 |
| 35 | PCT/ KR2014/006627 | PCT | Method for screening cancer therapeutic agent using modified arginyl-tRNA synthetase | 2014-07-22 |
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| 37 | 1020140077075 | Rep. of Korea | The composition against abnormal cell migration through reduced methionine level | 2014-06-24 |
| 38 | 1020140076674 | Rep. of Korea | Novel heterocyclic compounds | 2014-06-23 |

| 39 | 1020140076763 | Rep. of Korea | The crystal structure of the NanR and ManNAc-6P complex, and uses thereof | 2014-06-23 |
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| 41 | 1020140072240 | Rep. of Korea | Neuropilin-1 specific binding and tumor-penetrating peptide and its fusion protein | 2014-06-13 |
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| 43 | PCT/ KR2014/004933 | PCT | Novel maleic acid derivative, production method for same and anti-cancer composition comprising same | 2014-06-03 |
| 44 | 1020140067225 | Rep. of Korea | Novel Maleic acid derivatives, preparation method thereof, and anti-cancer compositions containing them | 2014-06-02 |
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| 47 | 201280056503.X | China | Novel use of leucyl tRNA synthetase | 2014-05-16 |
| 48 | 1020140058634 | Rep. of Korea | AIMP2-DX2-34S protein and method for manufacturing the same | 2014-05-15 |
| 49 | 1020140056973 | Rep. of Korea | Screening method for metastasis inhibitor of cancer using cell or spheroid cell mass regulated expression of lysyl-tRNA synthetase in 3-dimensional collagen gels environments | 2014-05-13 |
| 50 | PCT/ KR2014/004276 | PCT | Method for screening cancer metastasis inhibitor using culture of cells or spheroidically aggregated cells in which lysyl-tRNA synthetase is regulated to be expressed or unexpressed | 2014-05-13 |
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| 63 | 1020130167032 | Rep. of Korea | Anti-YRS monoclonal antibody and uses thereof | 2013-12-30 |
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| 65 | 1020130167854 | Rep. of Korea | Anti-TRS monoclonal antibody and uses thereof | 2013-12-30 |
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| 67 | 1020130167851 | Rep. of Korea | Anti-AIMP1/p43 monoclonal antibody and uses thereof | 2013-12-30 |
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| 70 | PCT/ KR2013/010861 | PCT | CH3 domain variant pair inducing formation of heterodimer of heavy chain constant region of antibody at high efficiency, method for preparing same, and use thereof | 2013-11-27 |
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| 85 | 1020130054262 | Rep. of Korea | Method for monitoring metastasis of cancer cells using cells cultured in three-dimensional collagen environment | 2013-05-14 | - | 109 |
| 86 | 13778232.2 | Europe | Use of a novel amiopyridine derivative to prevent or treat cancer | 2013-04-19 | | 110 |
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| 90 | 1020120148212 | Rep. of Korea | Crystal structure and crystallization of modified EPRS protein | 2012-12-18 | _ | 113 |
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