

2013

Fall Symposium

Nov. 15 (Friday) - **16** (Saturday)

Sheraton Edison Hotel-Raritan Center
125 Raritan Center Pkwy, Edison,
New Jersey, USA

Hosted by
KASBP Daewoong Green Cross

Invitation Letter from KASBP Symposium

Korean American Society in Biotech and Pharmaceuticals (KASBP) cordially invites all members and friends to the 2013 KASBP Fall Symposium, hosted by KASBP, Daewoong Pharmaceutical Co. Ltd. and Green Cross Corp., and sponsored by KHIDI, KSEA and KUSCO following the success of previous symposiums. Topics of the symposium are focused on general issues in drug discovery and development with the following formats to share experiences and expertise of the speakers with the attendees.

a. Forum A

Recent trend in oncology drug discovery and development presented by the scientists working in pharmaceutical companies and nonprofit research organizations

b. Forum B

New topics and trends in other areas than oncology, such as new technologies and antifungal

c. Round Table Discussion

Small group discussion between researchers in academia and industry to understand the drug discovery and development process in the pharmaceutical industry and to share career development experience

d. Job Fair

An open job fair for attendees to have a chance to meet the hiring managers and representatives from pharmaceutical companies or life science research institutes in Korea.

This symposium will focus on current trends in drug discovery and highlighting young professionals in biotech and pharmaceutical industries. This year, the symposium has successfully recruited outstanding speakers and panels to cover the sections described above. Additionally, Joseph Kim, Ph.D. as a biotech business entrepreneur and recipient of 2013 KASBP-Daewoong Achievement Award will give a keynote speech with a title, “Revolutionizing DNA Vaccines for treating and preventing cancers and infectious diseases”. The symposium also offers a round table discussion with pharmaceutical industry and academia professionals to provide career development tips to students. Another meaningful event is presenting the KASBP-Daewoong and KASBP-Green Cross fellowship awards to young scholars such as graduate students and post-docs who exhibit excellence in their research areas. This symposium will provide an opportunity for members to establish professional networks, and share information and experiences amongst members in pursuit of excellence in research and development.

2013 KASBP Fall Symposium Organizing Committee

Symposium Schedule at a Glance

November 15, 2013, Friday

02:00 pm –	Job Fair
05:30 pm – 09:30 pm	Registration
05:30 pm – 06:30 pm	Reception
06:30 pm – 06:50 pm	Opening and Congratulatory Remarks
06:50 pm – 07:30 pm	Dinner
07:30 pm – 07:40 pm	Award Ceremony
07:40 pm – 08:40 pm	Keynote Speech
08:40 pm – 09:00 pm	Sponsor Talk 1: Daewoong
09:00 pm – 09:20 pm	Sponsor Talk 2: KHIDI
09:20 pm – 10:20 pm	Round Table Discussion A (Pharma industry - Academia)

November 16, 2013, Saturday

07:30 am – 09:00 am	Round Table Discussion B (US Regulatory Guidelines)
08:30 am – 09:00 am	Registration & Light Breakfast
09:00 am – 09:10 am	Opening Remarks
09:10 am – 10:20 am	Forum A1 Presentation
10:20 am – 10:40 am	Coffee Break
10:40 am – 11:50 am	Forum A2 Presentation
11:50 am – 12:30 pm	Award Presentation – Seven Oral Presentations by Fellowship winners
12:30 pm – 02:00 pm	Lunch & Poster Viewing
02:00 pm – 02:20 pm	Sponsor Talk 3: Ildong
02:20 pm – 02:40 pm	Sponsor Talk 4: KSEA
02:40 pm – 03:50 pm	Forum B1 Presentation
03:50 pm – 04:10 pm	Coffee Break
04:10 pm – 05:20 pm	Forum B2 Presentation
05:20 pm – 05:40 pm	Closing Remarks & Picture Taking
06:00 pm – 08:30 pm	Dinner & Networking

Symposium Schedule in Detail

November 15, 2013, Friday

Job Fair 2:00 pm ~

Coordinator: *Nakyen Choy, Dow AgroSciences*

Registration & Reception Cocktail

5:30 pm ~ 6:30 pm

Coordinators: *Chris Lee (BMS), Jun Hyuk Heo (Merck), Alex Kim (Merck)*

Opening & Congratulatory Remarks and Dinner

6:30 pm ~ 7:40 pm

Coordinator: *KASBP President-Designated: Yun H. Choe, Lucas & Mercanti, LLP*

Opening Remarks

KASBP, President: *Jae-Hun Kim, Merck*

Congratulatory Remarks

Daewoong Pharmaceutical Co.: *President, Jong-Wook Lee*

Green Cross Corp.: *CSO, Doo-Hong Park*

KSEA: *Vice President, Youngsoo Kim, North Carolina State University*

Award Ceremony

7:30 pm ~ 7:40 pm

KASBP-Daewoong Achievement Award

Keynote Speech

7:40 pm ~ 8:40 pm

Award Lecture (KASBP-Daewoong Achievement Awardee 2013)

“Revolutionizing DNA Vaccines for treating and preventing cancers and infectious diseases”

Joseph Kim, President & CEO, Inovio Pharmaceuticals

Sponsor Talk

8:40 pm ~ 9:20 pm

Daewoong: “Introduction to Daewoong R&D”

Sang Ho Lee, Head of New Drug Development Lab., Daewoong Pharmaceutical Co

KHIDI: “Introduction to KHIDI”

Jung-hoon Woo, General Director of KHIDI USA

Round Table Discussion A

9:20 pm ~ 10:20 pm

Pharma Industry - Academy -----Chair: *Jae Uk Jung, GSK*

“Career Development in Drug Discovery and Development”

Chongwoo Yu, Silver Spring, MD

Networking

9:20 pm ~ 11:20 pm

November 16, 2013, Saturday**Round Table Discussion B**

7:30 am ~ 9:00 am

“US Regulatory guidelines for drug substance manufacturing process”

Chair: Yong-Hae Han, Bristol-Meyers Squibb

Registration & Breakfast

8:30 am ~ 9:00 am

Coordinators: Chris Lee (BMS), Jun Hyuk Heo (Merck), Alex Kim (Merck)

Opening Remarks

9:00 am ~ 9:10 am

Program Chair: Chang-Sun Lee, PTC Therapeutics

Forum A1-----Chair: Suktae Choi, Celgene

9:10 am ~ 10:20 am

“Translating genomic instability to clinical applications”

Kyungjae Myung, NIH

“How to gain a competitive advantage in the flood of antibodies and small molecules intercepting EGFR signal pathway?”

Kyuhyun Lee, Green Cross Corp./ MBRI (Mogam Biotech Research Institute)

Coffee Break *10:20 am ~ 10:40 am*

Forum A2-----Chair: Young-Choon Jung, Vertex

10:40 am ~ 11:50 am

“Structure-Based Design of Novel Inhibitors of the MDM2-p53 Protein-Protein Interaction”

Yosup Rew, Amgen

“Targeting Cancer using Fragment-Based Drug Discovery”

Hai-Young Kim, Merck

Award Presentation-----Chair: Eunsung Junn, Rutgers University

11:50 am ~ 12:30 pm

KASBP-Green Cross and KASBP-Daewoong Fellowship Award Ceremony
Oral Presentations by Fellowship Awardees

Lunch & Poster Presentation-----Chair: Eunsung Junn, Rutgers University

12:30 pm ~ 2:00 pm *Lunch & Poster Viewing*

Sponsor Talk-----Chair: Chang-Sun Lee, PTC Therapeutics

2:00 pm ~ 2:40 pm

Ildong; Introduction to Ildong R&D

Soo Bong Park, Director of Pharmacology, Ildong Pharmaceuticals Co. Ltd.

KSEA: Introduction to KSEA

Youngsoo Kim, KSEA Vice President, North Carolina State University

Forum B1-----Chair: Ik-Hyeon Paik, Melinta Therapeutics

2:40 pm ~ 3:50 pm

“A different journey to a lead; Proposing a new antibody discovery platform”

Yuncheol Kim, Pfizer

“PET (Positron Emission Tomography) modality and its potential application to pharmaceutical industry”

Keunpoong Lim, Yale University

Coffee Break 3:50 pm ~ 4:10 pm

Forum B2 -----Chair: Youngsun Kim, VaxInnate

4:10 pm ~ 5:20 pm

“Can agricultural fungicides be used as potential human antifungal drugs?”

Kyung Myung, Dow AgroSciences

“ICH Q11 Development and Manufacture of Drug Substances”

Chong-Ho Kim, Silver Spring, MD

Closing Remarks 5:20 pm ~ 5:40 pm

KASBP President: Jae-Hun Kim, Merck

Dinner & Networking 6:00 pm ~ 8:30 pm

Ichiumi Restaurant (Tel. 732-906-2370)

352 Menlo Park Dr. at Menlo Park Mall, Edison, NJ 08837

Abstract

Revolutionizing DNA Vaccines for treating and preventing cancers and infectious diseases

Joseph Kim, Ph.D.

Inovio Pharmaceuticals, 1787 Sentry Parkway West Building 18, Blue Bell, PA 19422

Dr. Jong Joseph Kim will discuss how he built his business and his technology from an idea shared between him and his University of Pennsylvania professor into a publically traded biotech company pioneering DNA vaccines to treat and prevent challenging cancers and infectious diseases. In human studies, Dr. Kim's synthetic vaccine technology platform has demonstrated best-in-class T-cell immune responses and, for the first time by any non-live platform, the killing effect of those T-cells. Inovio has also achieved evidence of universal protection against multiple unmatched virus strains. Inovio's platform is applicable to cancers and infectious diseases with vaccine product candidates for cervical dysplasia/cancer, prostate cancer, hepatitis C virus, HIV, influenza, malaria and other tropical diseases. Its lead program targeting cervical dysplasia is in a Phase II clinical study; the Gates Foundation is funding Inovio's malaria vaccine development; and, the NIH has provided a \$25 million grant to speed the development of Inovio's HIV synthetic vaccine.

Translating genomic instability to clinical applications

Kyungjae Myung, Ph.D.

National Human Genome Research Institute, National Institutes of Health, Bethesda, MD 20892

One distinctive characteristic of cancer cells is persistent cell division that requires DNA replication. This feature is often exploited to develop chemotherapeutic drugs since cancer cells are exquisitely sensitive to the inhibition of DNA replication by the introduction of DNA damage by radiation or genotoxic chemicals. DNA lesions resulting from exposure to genotoxic agents stall DNA replication, collapse replication forks, and produce DNA double-strand breaks (DSBs), resulting in cell death. Thus, cancer treatment may greatly benefit from the identification of genotoxic agents that kill rapidly dividing cells with minimal mutagenic side effects. ATAD5 makes a heteropentameric alternative replication factor C complex and suppresses genomic instability and tumorigenesis. ATAD5 is stabilized and forms nuclear foci at the site of stalled replication forks in response to DNA damage. We screened over 300,000 compounds with a novel, cell-based quantitative high-throughput ATAD5-luciferase assay detecting genotoxic compounds. In the initial effort, we reported 22 antioxidants, including resveratrol, genistein, and baicalein, that are currently used or investigated for the treatment of cardiovascular disease, type 2 diabetes, osteopenia, osteoporosis, and chronic hepatitis, and for anti-aging. In continuing effort, we narrowed potential ~200 compounds as targeted putative cancer treatment.

How to gain a competitive advantage in the flood of antibodies and small molecules intercepting EGFR signal pathway?

Kyuhyun Lee, Ph.D.

Green Cross Corp./ MBRI (Mogam Biotechnology Research Institute), Korea

Since the first discovery of EGFR by Dr. Stanley Cohen in 1984, a wide variety of EGFR-targeted therapeutics such as Erbitux®, Vectibix™, and Iressa® has been developed and is currently used for the treatment of non-small cell lung cancer, head and neck cancer and colorectal cancer in clinic. For that reason, EGFR targeting market is not blue-ocean in economics any more. Moreover, EGFR is now

considered as a kind of old-fashioned target in the field of single-targeted therapies unless it is armed with next generation technology such as bispecific or two-in-one antibody. Nevertheless, unmet needs have been continuously raised by the accumulating clinical data of marketed therapeutics. One of major drawbacks in EGFR-targeted therapeutics is poor efficacy in colorectal cancer patients with KRAS mutation. GC1118A, a novel anti-EGFR-targeted antibody developed under collaborative work of Green Cross Corp. and MOGAM Biotechnology Research Institute, showed distinct character in binding mode and efficacy compared with currently-marketed antibodies. We observed tumor inhibitory activity of GC1118A in a subset of CRC xenografts with KRAS mutation and are investigating the mode of action. In this talk, I suggest that the GC1118A antibody will have different clinical implication and patient pool, and provide another therapeutic option for cancer patients.

Structure-Based Design of Novel Inhibitors of the MDM2-p53 Protein-Protein Interaction

Yosup Rew, Ph.D.

Amgen, South San Francisco, CA

p53 is a short-lived transcription factor which plays a central role in preventing tumor development. It is stabilized by cellular stress and accumulates in the nucleus. Activated p53 binds to DNA and increases transcription of numerous genes involved in cell cycle arrest and apoptosis. The MDM2 oncogene is a key cellular negative regulator of p53. Inhibition of the MDM2-p53 interaction with small-molecule MDM2 inhibitors has been shown to be a tractable strategy for the reactivation of the endogenous p53 pathway, and the treatment of a variety of wild-type p53 tumors. This presentation will describe the structure-based de novo design of novel small molecule MDM2 inhibitors, which led to the discovery of a series of novel 1,3,5,6-tetrasubstituted piperidinone derivatives. The affinity of these molecules for MDM2 was significantly improved through conformational control of both the piperidinone ring and the appended N-alkyl substituent. Further systematic optimization afforded AM-8553, a potent and selective MDM2 inhibitor with excellent PK properties and in vivo efficacy.

Targeting Cancer using Fragment-Based Drug Discovery

Hai-Young Kim, Ph.D.

Merck Research Laboratories, Kenilworth, NJ

Currently, there are around 30 fragment-derived leads having progressed to clinical development along with ZELBORAF (Vemurafenib) that was approved by FDA in 2011. After the initial success with kinase targets, fragment-based approaches for finding potential new medical therapies are now a part of many drug discovery programs. Herein, we will discuss about the role of Fragment-Based Drug Discovery (FBDD), the fragment screening process, and the subsequent fragment hit elaboration; exemplified by successful cases targeting cancer from Fesik group (i) Fragment Linking: Discovery of Bcl-XL inhibitor, ABT-263 & ABT-737 (ii) Fragment Merging: Discovery of Potent Myeloid Cell Leukemia 1 (Mcl-1) Inhibitors.

A different journey to a lead; Proposing a new antibody discovery platform

Yuncheol Kim, Ph.D.

Pfizer, San Francisco, CA

For the past 20 years, chemical-based therapeutic approaches have been rapidly switched toward bio-therapeutics due to the unprecedented growth of molecular biology and antibody engineering technology as

well as bio-molecular medicine. Recently many Korean pharmaceutical companies in developing stage have been enthusiastically acquiring the high-end technologies and strategies by which big pharmaceutical companies currently produce and develop bio-therapeutics. These valuable assets will provide work-process improvement resulting in being competitive in R/D/P (Research / Development / Production) and achieving an imminent goal. However, the simply acquired technologies and strategies would never be enough for overtaking the leading big pharmaceutical companies. Therefore, developing highly innovative technologies and systematic and synergistic R/D/P processes should be the utmost long-term goal for sustainable growth and overcoming current barriers set by leading pharmaceutical companies. This presentation will briefly discuss general and basic antibody discovery processes and propose a novel antibody discovery platform, which can transform the current paradigm of discovery strategies.

PET (Positron Emission Tomography) modality and its potential application to pharmaceutical industry

Keunpoong Lim, Ph.D.

Yale University School of Medicine, New Haven, CT

PET (Positron Emission Tomography) is one of a nuclear medical imaging modality used to produce a 3D image or picture of biological functional processes in a living body. This technique is very much comprehensive and complicated in its nature. PET requires a lot diverse expertise from the areas of chemistry, physics, engineering, pharmacology and medicine to achieve its final goal of detecting tissue malignancy non-invasively. Upon the usage of a near right radiotracer which will interact with target(s) of interest(s), researchers will have ample information about the research or practice subject from the images generated. Its application to diagnosis and prognosis of disease as well as in the drug development process in the pharmaceutical industry will be introduced and briefly discussed.

Can agricultural fungicides be used as potential human antifungal drugs?

Kyung Myung, Ph.D.

Dow AgroSciences LLC, Indianapolis, IN

Currently twelve drugs from four different classes are commercially available for treatment of invasive fungal infections in human. In contrast, more than 100 chemistries from more than 30 different classes have been developed as agricultural fungicides, and these fungicides have been shown to control many plant fungal pathogens by targeting multiple sites in fungi. The diverse modes of action of agricultural fungicides raise a question whether agricultural fungicides can be served as useful sources to find new chemistries for the management of the human fungal infections. In this presentation, agricultural fungicides will be introduced and the utility of the agricultural fungicides as potential human antifungal drugs will be discussed.

ICH Q11 Development and Manufacture of Drug Substances

Chong-Ho Kim, Ph.D.

Silver Spring, MD

The Agency had published ‘Guidance for Industry: Q11 Development and Manufacture of Drug Substances’ in November 2012. The guidance describes approaches to developing and understanding the manufacturing process of the drug substance, and also provides guidance on what information should be provided in Module 3 of the Common Technical Document (CTD) sections 3.2.S.2.2 – 3.2.S.2.6.

2013 Fall KASBP Fellowship Recipients

A Novel Strategy of Protein Bioconjugation to Prolong the Circulation Time In Vivo

Sung In Lim

Department of Chemical Engineering, University of Virginia

Therapeutic proteins are indispensable in treating numerous human diseases. However, therapeutic proteins often suffer short in vivo half-life, leading to frequent injections and poor patient compliance. In order to extend in vivo half-life, a natural albumin ligand, a fatty acid, has been conjugated to small therapeutic peptides resulting in a longer duration of action via binding to serum albumin upon injection. However, lack of site-specific chemistry for the fatty acid-conjugation inevitably causes severe heterogeneity and a significant loss in pharmaceutical activity, precluding a broader application to therapeutic proteins. In a quest to address these issues, we incorporated a non-natural amino acid, p-ethynylphenylalanine (pEthF), into a permissive site of a protein by using an engineered pair of yeast tRNA/aminoacyl tRNA synthetase, and then conjugated a fatty acid analog derivatized with an azide group to the pEthF-bearing protein through a bioorthogonal reaction called copper-catalyzed alkyne-azide cycloaddition. As a proof-of-concept, we show that a single palmitic acid site-specifically conjugated to superfolder green fluorescent protein (sfGFP) with high homogeneity enhanced the albumin-binding capability in vitro about 20 times and the in vivo half-life 5 times when compared to those of the unmodified sfGFP. Furthermore, the fatty acid conjugation did not cause a significant reduction in fluorescence of the sfGFP. Therefore, these results clearly indicate that the site-specific fatty acid-conjugation is a very promising strategy to prolong in vivo half-life of a therapeutic protein without compromising its folded structure and activity.

Regulator of fatty acid metabolism, acetyl CoA carboxylase 1 (ACC1), controls T cell activation and survival

JangEun Lee, Ph. D.

Department of Pathology and Laboratory Medicine, University of Pennsylvania

Fatty acids (FA) are essential constituents of cell membranes, signaling molecules, and bioenergetic substrates. As lymphocytes undergo both functional and metabolic changes during activation and differentiation, dynamic changes in FA metabolism also occur. However, the contributions of *de novo* lipogenesis to acquisition and maintenance of T cell function are unclear. Here, we demonstrate the role of FA synthesis on T cell immunity. T cell-specific deletion of ACC1 (ACC1DT), an enzyme that catalyzes production of malonyl CoA, a carbon donor for long chain FA synthesis, resulted in impaired peripheral persistence and homeostatic proliferation of T cells in naïve mice. Loss of ACC1 did not compromise effector CD8⁺ T cell differentiation upon listeria infection, but did result in a severe defect in Ag-specific CD8⁺ T cell accumulation due to increased death of proliferating cells. Furthermore, *in vitro* mitogenic stimulation demonstrated that defective ACC1DT cell growth and survival could be rescued by provision of exogenous FA. These results suggest an essential role for ACC1-mediated *de novo* lipogenesis as a regulator of CD8⁺ T cell blastogenesis and survival. Our study lays groundwork for understanding how this manipulation of T cell activation and survival may be applied to therapeutic interventions in cancer, autoimmune diseases, and chronic infections.

Anoxia-Reoxygenation Regulates Mitochondrial Dynamics Through The Hypoxia Response Pathway, SKN-1/Nrf, And Stomatin-Like Protein STL-1/SLP-2

Eun Chan Park, Ph. D.

Department of Genetics, Rutgers, The State University of New Jersey

Many aerobic organisms encounter oxygen-deprived environments and thus must have adaptive mechanisms to survive such stress. It is important to understand how mitochondria respond to oxygen deprivation given the critical role they play in using oxygen to generate cellular energy. Here we examine mitochondrial stress response in *C. elegans*, which adapt to extreme oxygen deprivation (anoxia, less than 0.1% oxygen) by entering into a reversible suspended animation state of locomotory arrest. We show that neuronal mitochondria undergo DRP-1-dependent fission in response to anoxia and undergo refusion upon reoxygenation. The hypoxia response pathway, including EGL-9 and HIF-1, is not required for anoxia-induced fission, but does regulate mitochondrial reconstitution during reoxygenation. Mutants for *egl-9* exhibit a rapid refusion of mitochondria and a rapid behavioral recovery from suspended animation during reoxygenation; both phenotypes require HIF-1. Mitochondria are significantly larger in *egl-9* mutants after reoxygenation, a phenotype similar to stress-induced mitochondria hyperfusion (SIMH). Anoxia results in mitochondrial oxidative stress, and the oxidative response factor SKN-1/Nrf is required for both rapid mitochondrial refusion and rapid behavioral recovery during reoxygenation. In response to anoxia, SKN-1 promotes the expression of the mitochondrial resident protein Stomatin-like 1 (STL-1), which helps facilitate mitochondrial dynamics following anoxia. Our results suggest the existence of a conserved anoxic stress response involving changes in mitochondrial fission and fusion.

Parthanatos mediates AIMP2-activated age-dependent dopaminergic neuronal loss

Yunjong Lee, Ph. D.

Institute for Cell Engineering, Johns Hopkins University

The defining pathogenic feature of Parkinson's disease is the age-dependent loss of dopaminergic neurons. Mutations and inactivation of parkin, an ubiquitin E3 ligase, induce Parkinson's disease through accumulation of pathogenic substrates. We found that transgenic overexpression of a parkin substrate, aminoacyl-tRNA synthetase complex interacting multifunctional protein-2 (AIMP2), led to a selective, age-dependent, progressive loss of dopaminergic neurons via activation of poly(ADP-ribose) polymerase-1 (PARP1). AIMP2 accumulation in vitro and in vivo resulted in PARP1 overactivation and dopaminergic cell toxicity via direct association of these proteins in the nucleus, providing a path to PARP1 activation other than DNA damage. Inhibition of PARP1 through gene deletion or drug inhibition reversed behavioral deficits and protected against dopamine neuron death in AIMP2 transgenic mice. These data indicate that brain-permeable PARP inhibitors could effectively delay or prevent disease progression in Parkinson's disease.

Essential Role of Apelin Signaling during Lymphatic Development in Zebrafish

Jun-Dae Kim, Ph. D.

Department of Internal Medicine, Yale University

Apelin and its cognate receptor Aplnr/Apj are essential for diverse biological processes. However, the function of Apelin signaling in lymphatic development remains to be identified, despite the preferential expression of Apelin and Aplnr within developing blood (BECs) and lymphatic endothelial cells (LECs) in vertebrates. Our data present compelling evidence suggesting that Apelin signaling regulates lymphatic development by promoting AKT activity in a VEGF-C/VEGFR3 independent manner during zebrafish embryogenesis.

Cellular self-defense: How cell-autonomous immunity by immune GTPase protects against pathogens

Bae-Hoon Kim, Ph. D.

Department of Microbial Pathogenesis, Yale University

Immune interferon gamma (IFN- γ) is essential for mammalian host defense against intracellular pathogens. IFN- γ induces nearly 2000 host genes, yet few have any assigned function. Here, we examined a complete mouse 65-kilodalton (kD) guanylate-binding protein (Gbp) gene family as part of a 43-member IFN- γ -inducible guanosine triphosphatase (GTPase) superfamily in mouse and human genomes. Family-wide loss-of-function analysis found that at least four Gbps-Gbp1, Gbp6, Gbp7, and Gbp10—conferred cell-autonomous immunity to listerial or mycobacterial infection within macrophages and gene-deficient animals. These Gbps solicited host defense proteins, including the phagocyte oxidase, antimicrobial peptides, and autophagy effectors, to kill intracellular bacteria. Thus, specific 65-kD Gbps coordinate a potent oxidative and vesicular trafficking program to protect the host from infection.

Metabolic Inflexibility Impairs Insulin Secretion and Results In MODY-like Diabetes In Triple FoxO-deficient Mice

Ja Young Kim-Muller, Ph. D.

Departments of Medicine, Columbia University

Pancreatic beta cell failure is a critical factor in the pathogenesis of diabetes. Defects of beta cell function in diabetes have complex repercussions. Therefore, prevention of beta cell dysfunction is a major goal of diabetes treatment. The forkhead box O-family transcription factors (FoxOs) regulate diverse cellular and physiological processes, such as energy metabolism and development in various tissues. In pancreatic beta cells, we have previously shown that FoxO1 affects beta cell responses to oxidative stress and modulates beta cell replication in response to peripheral insulin resistance. To understand the molecular mechanisms underlying the progression of beta cell failure, we have investigated the function of FoxO proteins in beta cells. Here we show that ablation of the three FoxO genes (1, 3, and 4) in mature β -cells results in MODY-like diabetes, with signature abnormalities of the MODY gene networks of Hnf4 α , Hnf1 α , and Pdx1. Transcriptome and functional analyses reveal that FoxO-deficient β -cells are metabolically inflexible, i.e., utilize preferentially lipids rather than carbohydrates as source of acetyl-CoA for mitochondrial oxidative phosphorylation. This results in impaired ATP generation, and reduced Ca-dependent insulin secretion. When viewed in the context of prior data illustrating a role of FoxO1 in β -cell dedifferentiation, the present findings outline a unified FoxO-dependent mechanism linking the twin abnormalities of β -cell function in diabetes.

Awardees

2013 AWARDEES (FALL)

KASBP-DAEWOONG ACHIEVEMENT

Joseph Kim, Ph. D. Inovio Pharmaceuticals

KASBP-DAEWOONG FELLOWSHIP

Dr. JangEun Lee, University of Pennsylvania

Dr. Eun Chan Park, Rutgers

KASBP-GREENCROSS FELLOWSHIP

Dr. Yunjong Lee, Johns Hopkins University

Dr. Jun-Dae Kim, Yale University

Dr. Bae-Hoon Kim, Yale University

Dr. Ja Young Kim-Muller, Columbia University

KASBP-KSEA FELLOWSHIP

Mr. Sung In Lim, University of Virginia

PAST AWARDEES

KASBP-DAEWOONG ACHIEVEMENT

2009 김정은 Gilead Sciences, Inc. (Kainos Medicine Inc, Korea, Current)

2010 주중광 University of Georgia

2011 김성호 University of California, Berkeley

2012 Dennis Choi (MD, PhD) Stony Brook Medicine and Stony Brook University

KASBP-DAEWOONG SCHOLARSHIP

2006 배진건 Schering-Plough (Handok Pharmaceuticals, Korea, Current)

2007 박영환 Merck (National Cancer Center, Korea, Current)

2008 문영춘 PTC Therapeutics

2009 김홍용 Novartis

KASBP-DAEWOONG FELLOWSHIP

- 2006** 민재기 New York University, 김 한 Princeton University, 박혜진 Rutgers University
2007 문지숙 Harvard University, 박성연 Rutgers University, 이석근 Columbia University
2008 이흥규 Yale University, 김정환 Rutgers University, 강민식 Columbia University
2009 박진아 Harvard University, 최재민 Yale University, 김덕호 Johns Hopkins University
2010 기정민 Rockefeller University 김형욱 NIH, 안세진 Harvard University
2011 한무리 University of California, LA, 장환중 Boston College
2012 장정호 Columbia University, 최재우 Oregon State University

KASBP-HANMI FELLOWSHIP

- 2011** 안형진 Rockefeller University, 조창훈 Abramson Research Center
2012 김유나 University of North Carolina, 태현섭 Yale University, 이인혜 NIH

KASBP-YUHAN FELLOWSHIP

- 2011** 김기영 Boston University, 심중섭 Johns Hopkins University
2012 허예민 University of Michigan, 방숙희 University of Pennsylvania, 백정호 Columbia University

KASBP-GREEN CROSS FELLOWSHIP

- 2011** 조한상 Harvard Medical School, 강성웅 Johns Hopkins University,
김미연 Columbia University, 소재영 Rutgers University, 황성용 NIEHS/NIH
2012 조원진 Drexel University, 강효정 Yale University, 이정현 Columbia University
이용재 Yale University, 윤재현 NIH

KASBP FELLOWSHIP

- 2009** 최상호 NIH
2010 김상령 Columbia University, 윤태숙 Rutgers University, 허은미 Cal. Tech.

KASBP-KUSCO FELLOWSHIP

- 2008** 김현호 National Institutes of Health, 온택범 Harvard Medical School, 주원아 Wistar Institute

KASBP-KRICT FELLOWSHIP

- 2009** 신승식 Rutgers University, 정은주 Columbia University, 백규원 University of Pennsylvania

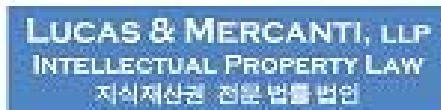
KASBP-KHIDI FELLOWSHIP

- 2010** 배재현 Yale University, 조희연 Boston College

2013-2014 KASBP Officers

Title	Name	Affiliation
President	KIM, Jae-Hun	Merck
President Designated	CHOE, Yun H	Lucas & Mercanti
1st Vice President	KIM, Youngsun	VaxInnate
2nd Vice President	JUNG, Jae Uk	GSK
Executive Director	CHUNG, Cheol K.	Merck
General Director	CHOI, Suktae	Celgene
Science Director	JUNN, Eunsung	Rutgers University
Program Director	LEE, Chang-Sun	PTC Therapeutics
Financial Director	HWANG, Seongwoo	PTC Therapeutics
Web Director	KIM, Alex	Merck
Public Relations Director	SHIN, Hunwoo	KHIDI
YG Director	CHOI, Christopher	Colgate-Palmolive
1st Membership Director	LEE, Chris	Bristol-Myers Squibb
2nd Membership Director	HEO, Jun Hyuk	Merck
Auditor	LEE, Hak-Myung	Shionogi Inc.
Legal Director	LEE, Elizabeth	Lucas & Mercanti
Boston Regional Director	JUNG, Young Chun	Vertex
Philadelphia Regional Director	LEE, James	Merck
Connecticut Regional Director	PAIK, Ik-Hyeon	Melinta
Councilor	HAN, Yong-Hae	Bristol-Myers Squibb
Councilor	LEE, Hak-Myung	Shionogi Inc.
Councilor	MOON, Young-Choon	PTC Therapeutics
Councilor	RYOO, Je-Phil	NAL
Advisor	KANG, Shinhong	Purdue Pharma
Advisor	LIM, Hanjo	TPI
Advisor	CHOY, Nakyeon	Dow AgroScience
Advisor	SUNG, Moo Je	Novartis

Sponsors for KASBP





Korea-U.S. Science Cooperation Center

한미과학협력센터

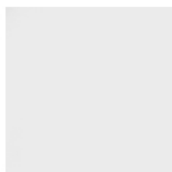
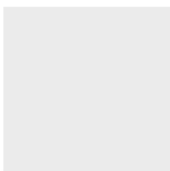


S&T Program Portfolio

- ✚ U.S.-Korea Joint Meetings
- ✚ KSEA Chapter Meetings
- ✚ Washington S&T Forum
- ✚ S&T Information Exchange
- ✚ S&T Professional Association Meetings

Professional Exchanges & Networking

- ✚ WEST Program
- ✚ Graduate Scholarship
- ✚ Korea Summer Institutes (KSI)
- ✚ Scholarship for Descendants of Korean War Veterans
- ✚ National Mathematics & Science Competition (NMSC)
- ✚ Young Generation Technical and Leadership Conference (YGTLC)



Established in 1997 as a non-profit organization in the U.S.A, KUSCO has promoted and supported various programs to become a premier center for S&T cooperation and exchanges between the U.S. and Korea.

www.kusco.org

대한민국 녹색자, 지금 세계로 가야합니다 세계 곳곳의 아픈 이들이 우리에게 새로운 희망을 걸고 있기 때문입니다

독감백신

아시아 최초 세계 4번째 WHO PQ 승인

면역글로불린제제

국내 최초 미국 임상 3상 진행

3세대 유전자 재조합 혈우병 치료제

세계 세 번째 개발

수두백신

세계 두 번째 개발, 범미보건기구 남미지역 전향 수주

헌터증후군 치료제

세계 두 번째 개발

지금보다 더 건강하고 행복하려면 누군가는 새 길을 열어가야 합니다

1967년 설립 이래, 모두가 가고 싶어 하는 편한 길을 선택하기보다 힘들지만
누군가 반드시 가야할 길을 외면하지 않고 묵묵히 걸어온 녹색자가 이제
대한민국을 넘어 세계인의 건강을 지키는 새로운 희망으로 도약하고 있습니다.
이미 세계적으로 인정받은 백신과 혈액제제 등을 개발한 탁월한 R&D 역량을 바탕으로 세포배양,
유전자재조합 등의 차원 높은 솔루션을 더해 세계로 나아가는 녹색자, 만들기는 힘들지만
꼭 필요한 의약품으로 세계인의 건강과 행복을 지키는 믿음직한 이름이 되겠습니다.