2011

Hanoi University of Science-KAIST SYMPOSIUM

Feb. 25, 2011, 9:30AM-3:30PM

KI Building 5th Fl, B501 Seminar Room

Hosted by the Department of Biological Sciences,

Supported by Brain Korea 21 (BK21) program, KAIST, Korea

BK21 Brain Korea21

Program & Abstract

Trường Đại học Khoa học Tự nhiên
Hanoi University of Science

KAIST
Korea Advanced Institute of Science and Technology

Program

Feb.25, 2011

9:30 – 9:40 AM	Welcoming Remarks, **Chair & Prof. CHOI Kwang-Wook**
9:40 – 9:50 AM	Opening Remarks, **Prof. SEO Yeon-Soo,** KAIST
9:50 – 10:00 AM	Opening Remarks, Prof. of HUS.
10:00 – 10:20 AM	**NGUYEN Thi Van Anh, Ph.D.**, HUS
10:20 – 10:40 AM	**David HELFMAN, Ph.D.**, KAIST
10:40 – 11:00 AM	Coffee Break
11:00 – 11:20 AM	**PHAM Xuan Hoi, Ph.D.**, Institute of Agricultural Genetics
11:20 – 11:40 AM	**CHOI Giltsu, Ph.D.**, KAIST
11:40 – 12:00 AM	**TRINH Hong Thai, Ph.D.**, HUS
12:00 – 2:00 PM	Lunch with Vietnamese students
2:00 – 2:20 PM	**LIM Dae-Sik, Ph.D.**, KAIST
2:20 – 2:40 PM	**HOANG Thi My Nhung, Ph.D.**, HUS
2:40 – 3:00 PM	**KIM Mi Young, Ph.D.**, KAIST
3:00 – 3:20 PM	**BUI Thi Viet Ha, Ph.D.**, HUS
3:30 – 5:00 PM	Individual Meeting / Campus Tour
	Prof. KIM Sun Chang and Dr. NGUYEN Thi Van Anh
	Prof. CHOI Giltsu and Dr. PHAM Xuan Hoi
	Prof. KANG Changwon and Dr. PHAM Xuan Hoi
	Prof. SONG Ji-Joon and Dr. TRINH Hong Thai
	Prof. KIM Mi Young and Dr. HOANG Thi My Nhung
	Prof. KANG Suk-Jo and Dr. BUI Thi Viet Ha
5:30 PM	Dinner with faculty of biological sciences

NGUYEN Thi Van Anh, Ph.D.

Nguyen Thi Van Anh holds a Pharmacist (Hanoi College of Pharmacy, 1997), M.S. in Life Sience (Tohoku University, Japan, 2001) and Ph.D. in Life Science (Tohoku University, Japan, 2004). During M.S. and Ph.D. study, she was trained to study mechanism of cooperative assembly of staphylococcal hemolysin on human erythrocyte membranes using single-molecule fluorescent imaging techniques. She has been a lecturer at HUS since 2005, and continued her research on fusion proteins of staphylococcal toxins with peptides that target breast cancer cells (2005-2007, TWAS grant). She then participates in several research projects, such as developing fluorescent based kit to count number of CD4+/CD8+T cells in blood of HIV infected patients (2007-2009, National MOST grant), conjugating antibodies to gold and magnetic nanoparticles for diagnostic purposes (2008-2010, VNU grant; 2010-2013, National MOST grant). She is now head of Nano-Biology unit of Key Laboratory of Enzymes and Protein Technology, and is collaborating with Prof. Simon Cutting at Holloway University of Science of London, UK, to manipulate Bacillus spores for diagnostics and drug delivery purposes (2010-2012, HUS grant, IFS grant, Loreal-Unesco fellowship, 2010-2013, National MOST grant).

PHAM Xuan Hoi, Ph.D.

Xuan Hoi Pham holds a B.S. (Hanoi University of Agriculture No. I, 1986), M.S. (Jawaharlal Nehru University New Delhi, India, 1998), and Ph.D. (International Centre for Genetic Engineering and Biotechnology New Delhi, 2001). He was trained with Dr. Narendra Tuteja for Molecular cloning and characterization of helicases from pea and study on its interactive proteins during Ph.D. study and was a post doctoral research fellow at Karolinska Institute, Stockholm-Sweden with Dr. Claes Gustafsson and at Japan International Research Centre for Agricultural Sciences with Prof. Kazuko Yamaguchi-Shinozaki. He has been a Head - Department of Plant Molecular Pathology and Abiotic stress – The Institute of Agricultural Genetics, Pham Van Dong road, Hanoi, Vietnam since 2009. His main research interest is to understand molecular mechanisms of Plant, Human transcription and DNA replication and apply genes, promoters for high salt and drought tolerance in plant.

TRINH Hong Thai, Ph.D.

Trinh Hong Thai holds a B.Sc. (Vietnam National Unviversity (VNU), 1979) and Ph.D. (VNU, 1996). He was trained with Prof. Dr. Pham Thi Tran Chau for study on proteinase and proteinous proteinase inhibitor during Ph.D. study, and was a post doctoral research fellow at University of Montpellier I, France (1996-1997), Institute of Structural Biology Jean-Pierre Ebel, Grenoble, France (1999-2000). He has been an associate professor at Department of Biology, College of Science, VNU since 2004. He has been a head of Proteomics and Structural Biology Unit, KLEPT since 2005. His main research interest is to investigate biomarkers for cancer by proteomics approaches.

HOANG Thi My Nhung, Ph.D.

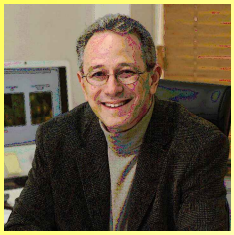
Hoang Thi My Nhung did her Master in Hanoi University of Science (HUS), Vietnam. She got a PhD fellowship from Vietnamese and French governments then done her PhD in Stefan DIMITROV's laboratory INSERM U823 (Albert Bonniot Institute, Grenoble, FRANCE) with Dr. Annie MOLLA as supervisor. During her Ph.D study, she received an ARC (Association for Research on Cancer) doctoral fellowship. She is now deputy Head of Cytology-Histology- Embryology and Biophysics Department, Faculty of Biology, and also a member of KLEPT (Key Laboratory of Enzyme and Protein Technology), HUS. Her main researches are on study of the Aurora kinases, a family of mitotic oncogenic kinases and characterize Aurora kinase inhibitors from synthesized and natural compounds in Vietnam. As a member of Nanobiology Units at KLEPT, she also works on applying nanotechnology to targeting/treating cancer.

BUI Thi Viet Ha, Ph.D.

Bui Thi Viet Ha holds a B.S. (Hanoi College of Science, Vietnam National University -VNU 1996), M.S. (Hanoi University of Science, VNU 1999), and Ph.D. (Vietnam National University, 2006). She was trained with Prof. Anant Patel in Germany for using biological control in plant protection during Ph.D. study. At present, she has been a lecturer at Department of Microbiology, Faculty of Biology, and HUS. She main research interest is to find out effective microorganisms against pathogenic fungi by biological control approaches.

Speakers

David HELFMAN, Ph.D.



David Helfman holds a B.S. (Northwestern University, 1976), M.S. (Emory University, 1979), and Ph.D. (Emory University, 1981). He was on the staff of Cold Spring Harbor Laboratory from 1981-2004. From 2004-2009 he was the Director of the Sheila and David Fuente Graduate Program in Cancer Biology and Professor of Cell Biology and Anatomy at the University of Miami School of Medicine. He has been a professor in the Department of Biological Sciences and Department of Nanoscience and Technology at KAIST since 2009. His main research interest is to understand molecular mechanisms of signaling in cancer cells.

LIM Dae-Sik, Ph.D.

Dae-Sik Lim received his B.S. in Microbiology from Seoul National University in 1988, his M.S. from SNU in 1990, and his Ph.D. from UT and M.D. Anderson Cancer Center in 1996. As a Postdoctral fellow, he was trained in the laboratory of with Dr. Michael Kastan at John Hopkins and St. Jude Children's Hospital from 1996 to 2000. He joined the faculty of KAIST in 2002. He is now Professor in the Department of Biological Science at KAIST. His main research interest is to understand molecular mechanism by which a new merging mammalian Hippo signaling regulates cell division and differentiation.

CHOI Giltsu, Ph.D.

Giltsu Choi holds a B.S. (KAIST, 1990) and Ph.D. (Brandeis University, 1997). He studied cellular differentiation processes of *Volvox carteri* during Ph.D. study, and investigated plant light signaling using *Arabidopsis thaliana* as a model system at Kumho Laboratory from 1997 to 2002. He has been an assistant professor, an associate professor, and a professor at Department of Biological Sciences, KAIST since 2002. His main research interest is to understand light signaling processes in germinating seeds by molecular genetic approaches.

KIM Mi Young, Ph.D.

Mi-Young Kim holds a B.S. (Yonsei Unviversity, 1999), and Ph.D. (Cornell University, 2004). She was trained with Dr. W. Lee Kraus for transcriptional regulation and chromatin modification during her Ph.D. study, and was a post doctoral research fellow at Memorial Sloan-Kettering with Dr. Joan Massague. She is a recipient of Era of hope postdoctoral fellowship from Department of Defense. She has been an assistant professor at Department of Biological Sciences, KAIST since 2010. Her main research interest is to understand the molecular mechanisms of metastasis.

NGUYEN Thi Van Anh, Ph.D.

"Development of streptavidin-expressing *Bacillus subtilis* spores as bio-microparticles for drug delivery and diagnostics purposes"

Baccilus subtilis spores have been widely used as pharmaceutical probiotics to balance bacterial environment in human intestinal tract. With certain advantages including extreme heat-stability and non-toxicity, the spores are potential biomaterials which are easily to be manipulated for expression of bioactive proteins for application in drug delivery and diagnostics.

By genetic engineering, monovalent streptavidin was successfully expressed on the outer coat of *Baccilus subtilis* spores to carry biotinylated antibodies. Here, the streptavidin-spores were bound to biotinylated anti-EGFR IgG (cetuximab/ erbitux), a chimeric IgG1 monoclonal antibody that targets the extracellular domain of EGFR superexpressed on the surface of colon cancer cells. The created ***-EGFR IgG-spores*** were used as carrier for specific delivery of anti-cancer chemical named paclitaxel. Paclitaxel conjugated with fluorescent dye Oregon Green (excitation/emmision: 488 nm/520 nm) at 0.25 M when being adsorbed on the ***-EGFR IgG-spores*** showed a binding intensity on microtubules of the colon cancer cells almost at the same level as ororpaclitaxel-Oregon Green only (without spore) at 1 M, indicating that the binding was enhanced about four-fold. In addition, a dose of four-fold lower paclitaxel adsorbed on the ***-EGFR IgG-spores*** was shown to give similar real-time inhibition curves of the colon cancer cell growth as paclitaxel alone. Moreover, the streptavidin-spores were also found to bind to biotinylated anti-VP28 IgG for detection of the VP28 antigen of white spot syndrom virus (WSSV) which causes diseases in shrimps, suggesting the application of the created ***-VP28 IgG-spores*** for WSSV detection.

PHAM Xuan Hoi, Ph.D.

"A novel transcription factor OsRap 2.4 A expressed in salinity and drought stresses bind to DRE localized on downstream of TATA box and repress expression of the target genes in rice"

Plants are not mobile and environmental stress is an inescapable and persistent condition. Since, drought and salinity are among the most important abiotic stress factors limiting food production word-wide. Plant sense and respond to these stresses by means of complex systems of signalling pathways. DRE (dehydration responsive element)/CRT (C-repeat) is a *cis*-acting element that is involved in gene expression responsive to abiotic stress in higher plants. To date, all well known DREBP transcription factors like DREB1/CBFs and DREB2s in *Arabidopsis*, rice, maize and other plants regulate gene expression in response to drought, high-salt and cold stresses by binding specifically to the DRE/CRT. Using a target sequence of 50 nucleotides on Glutamate dehydrogenase-like protein (JRC2606) promoter containing DRE *cis*-acting element for yeast one hybrid screening, we identified two transcription factors belong to A6 subgroup of DREB subfamily named *OsRAP2.4A* and *OsRap2.4B*. Sequence alignment of *OsRap2.4A and OsRap2.4B* with homolog DREB subfamily transcription factors from different species shown that they had homology with *ZmDBF*, a maize transcription factor increases drought tolerance in plant.

OsRap2.4A was drought, high-salt and tempreture stresses and bound very specifically to DRE sequence localization on the downstream miniTATA box of JRC2606 promoter both *invivo* and *invitro*. However, transactivation assay of OsRap2.4A did not show transactivation activity both in yeast and rice protoplast. Coding sequence of OsRap2.4A was transformed in to rice and *arabidopsis* using over express, repression domain, DEX systems for functional analysis. Both in rice and *arabidopsis* transgenic overexpressing OsRap2.4A at high level resulted in retardation growth while overexpressing OsRap2.4A at low or medium level did not show any retardation growth. Transgenic *arabidopsis* over expressing OsRap2.4A at medium level increase high-salt and drought tolerances but high level expression of OsRap2.4A resulted in reducing stresses tolerances. These data indicates that OsRap2.4A is a transcription factor bound to DRE on downstream promoter and function as represor.

TRINH Hong Thai, Ph.D.

"Proteomic analysis of bone marrow cells from leukemia patients"

Acute Myeloid Leukemia (AML) is a malignant disorder which affects myeloid development or myelopoiesis. Based on morphology, cytochemistry, and immunology, it was classified in to eight major groups that were from Mo to M7. Applying the combination of two-dimensional electrophoresis (2-DE) and the MALDI-TOF mass spectrometry, our study was conducted to analyse protein expression of bone marrow cells of AML. Using 2-DE, the differentially expressed proteins of mononuclear blood cells (MBCs) in bone marrow between some subtypes of leukemia and controls were detected including: 48 protein spots in the M_6 (25 protein spots were up-regulated, 11 protein spots were down-regulated and 12 protein spots were only appeared obviously in one gel including 7 proteins in the patients and 5 proteins in the control), 100 protein spots in the M_2 (20 spots only obviously appeared in patients, 13 absent spots, 37 up-regulated and 30 down-regulated spots) , 73 protein spots in the M_5 (16 spots only appeared in patients, 16 absent spots, 23 up-regulated and 18 down-regulated spots).

Using MALDI-TOF MS peptide mass fingerprint method with the MASCOT search program (www.matrixscience.com), proteins was identified. 44 proteins were identified including 22 named proteins and 22 hypothetical proteins. They were divided in to four protein groups: the immune group (22.73%), cell cycle group (36.36%), apoptosis group (18.18%) and other proteins (22.73%). Some of the remarkably different expressed proteins were: MHC class II Cw chain (down-regulated), Cdk 6 (up-regulated), BAX protein (up-regulated), PP2A (up-regulated), PMRT4 (up-regulated). Particularly, cdk 6 and BAX were up-regulated in leukemia patients; they were valuable proteins for the investigation about the biomarkers. Using SSCP-PCR, the mutation/alteration in exon 2-3 of BAX gene was detected in one AML patient.

HOANG Thi My Nhung, Ph.D.

"Identification of new Aurora kinase inhibitors from compounds extracted from Vietnamese herbs"

A challenge in cancer therapy is the specific targeting of cancer cells with no damage on quiescent cells. The chromosomal passenger proteins complex plays a central role in cell division. The functions of the four passenger proteins of the complex: INCENP, Survivin, Borealin and Aurora B are tightly connected. This complex insures accurate mitosis; therefore its members may be very relevant targets towards mitosis abortion. In this line, these proteins are proposed as druggable candidates in cancer therapy. Among this complex, Aurora B is the only enzymatic member Aurora B is expressed exclusively in mitosis and controls chromosome alignment and microtubule tension as well as cytokinesis. It may thus be proposed as a druggable target for cancer therapy. In fact mitotic kinases represent a tremendous hope towards targeting of cancer cells. The aim of this project is to extract natural substances from plants used by Vietnamese pharmacopoeia. Among them, we expect to find Aurora kinase inhibitors that may be proposed as new anti-mitotic drugs. First we will screen in vitro for kinase inhibition and then positive extracts will be tested ex-vivo on cell culture. The more interesting compounds will be evaluated on nude mice bearing tumors.

BUI Thi Viet Ha, Ph.D.

"Using microbial preparation for controlling root-pathogenic microfungi (*Phytophthora* spp) in citrus trees"

Worldwide, post-harvested losses of fruits and vegetables including citrus have been estimated about 25%, much of which is due to fungal and bacterial infections. In the last decades, pesticides have been commonly used to control phytopathogenic fungi and bacteria. These pesticides cause many problems on environment and human health. That is why there is a global trend of using microbial agents as an alternative method to control fungal and bacterial pathogens in plants. These microbial agents show some advantages such as: rapidly colonize fruit surfaces, wounds and soils, compete against the pathogens for nutrients and survive in a wide range of temperature conditions.

Our present work aims to investigate the effects of a microbial preparation that is antagonistic toward pathogenic fungi.

From soil, sea water samples, 105 bacterial strains, 165 actinomycete strains and 32 fungal strains were isolated. Among them, 2 strains (XS2 and T1) have the strongest activities against phytopathogenic fungi in mycorhiza such as *Phytophthora* spp and *Fusarium* spp. These two active strains were chosen for further experiments.

Based on the 16S rDNA sequence analysis, the strains XS2 belongs to *Streptomyces hygroscopicus* and it is named as *Streptomyces hygroscopicus* XS2. Based on the sequence of the D1/D2 region of 26S rDNA, strain T1 belongs to *Trichoderma atroviridae* and it is named as *Trichoderma atroviridae* T1.

Streptomyces hygroscopicus XS2 and *Trichoderma atroviridae* T1 were used to produce a microbial preparation and it was found in our experiments that the obtained microbial preparation could control well *Phytophthora* spp and *Fusarium oxysporum* growth on the citrus tree. The compound XS2 isolated from *Streptomyces hygroscopicus* XS2 has a structure belonging to enterocin group.

David HELFMAN, Ph.D.

"Oncogenic Signaling"

Cancer is a major health problem throughout the world. Understanding the molecular mechanisms underlying cancer is important for the development of strategies aimed at preventing, diagnosing and treating different types of cancer. Alterations in cell architecture (morphology) are an important criterion used by pathologists to identify and define cancerous tissues. It is well established that the three-dimensional architecture of cells and tissues is important for normal cellular and physiological function. The actin cytoskeleton plays a critical role in the spatial organization of cells and tissues. Over thirty years ago cell biologists observed that transformed cells exhibit loss of stable actin filaments, called stress fibers. Subsequent studies have demonstrated that alterations in the organization of the actin-based cytoskeleton are an established characteristic of cells transformed by oncogenes, viruses and chemical carcinogens. Changes in the organization of the cytoskeleton and its associated adhesive structures (e.g., focal adhesions) are associated with abnormal processes linked to cancer including regulation of cell proliferation, programmed cell death (apoptosis), anchorage independent cell growth, cell adhesion, migration, and metastasis. We are investigating the mechanisms by which spatial organization of cells and the actin cytoskeleton are de-regulated by oncogenic signaling pathways, and how disruption of cellular architecture contributes to the properties of transformed cells. This information is being used to identify potential targets for the treatment of cancer.

CHOI Giltsu, Ph.D.

"Collaborative regulation of seed germination by PIL5 and other transcription factors"

PIL5, also known as PIF1, is a phytochrome-interacting basic helix-loop-helix transcription factor that inhibits seed germination in Arabidopsis. It binds to G-box elements (CACGTG) present in various promoters and regulates the expression of genes associated with those promoters. A genome wide analysis of its binding sites coupled with a gene expression analysis indicated that PIL5 binds to 748 sites and regulates the expression of 166 genes either positively (105 genes) or negatively (61 genes) in imbibed seeds. The 166 genes include various hormone signaling genes including *RGA*, *ABI3*, *ABI5*, *JAZ1*, *ARF18*, and *CRF1* to 3, as well as various cell wall modifying enzyme genes including the expansin and xyloglucan endotransglycosylase genes. In addition to these direct target genes, PIL5 indirectly regulates various hormone metabolic genes. These analyses suggested that the phytochrome-PIL5 signaling module regulates seed germination by coordinating hormone signaling and cell wall properties in imbibed seeds. We further investigated why PIL5 binds to only a subset of G-box elements out of 29,251 G-boxes in the genome. Our analysis indicates that many PIL5-bound G-boxes are coupled with other elements. These coupling elements can also partially explain non G-box PIL5-binding sites. Taken together, our data suggest that that PIL5 binds to its target in the presence of coupling transcription factors.

LIM Dae-Sik, Ph.D.

"Aurora A and B kinases regulate mitotic progression by phosphorylating the tumor suppressor RASSF1A"

The Aurora A and B kinases play important roles in the regulation of mitosis in eukaryotic cells, with their aberrant expression resulting in aneuploidy and tumorigenesis. The tumor suppressor RASSF1A regulates mitotic progression by inhibiting anaphase-promoting complex (APC)–Cdc20 activity, but the regulation of this action and the possible role of RASSF1A in cytokinesis have remained unknown.

We newly found that Aurora A and B sequentially associate with RASSF1A and catalyze its phosphorylation on serine-203 *in vivo* during mitosis. Depletion of Aurora A or expression of the nonphosphorylatable S203A mutant of RASSF1A led to a marked delay in mitotic progression as a result of the failure of RASSF1A to dissociate from Cdc20 and the consequent delayed destruction of mitotic cyclins. Expression of the phosphomimic S203D mutant of RASSF1A normalized the delay in mitotic progression in Aurora A–depleted cells. Moreover, phosphorylation of RASSF1A by Aurora B during late mitosis is required for the interaction of RASSF1A with Syntaxin16, a member of the t-SNARE family, and for the proper recruitment of Syntaxin16 to the spindle midzone and the midbody for successful completion of cytokinesis. These findings implicate Aurora-mediated phosphorylation of RASSF1A in regulation of both the timing of mitotic progression and cytokinesis.

KIM Mi Young, Ph.D.

"Tumor self-seeding by circulating cancer cells"

Cancer progression is commonly segregated into processes of primary tumor growth and secondary metastasis. In this conventional model, the high cell density and rapid growth rate of primary tumors are attributed to an ability of cancer cells to sustain unlimited proliferation and to favorably influence their microenvironment. In contrast, metastasis is thought to depend on cancer cell dissemination and adaptation to distant organs. Shedding of tumor cells into the circulation may occur in large numbers and from early stages of tumor formation. Yet overt metastasis is achieved only by a minority of these dispersed cells due to tight vascular wall barriers and unfavorable conditions for survival of disseminated cells in distant organs. However, these impediments may be less stringent as regards the ability of circulating tumor cells (CTCs) to re-infiltrate their tumors of origin. The neovasculature of tumors is typically leaky, a feature that would facilitate not only the passage of tumor cells into the circulation but also their entry from the circulation back into the tumor. CTCs would likely need no further adaptation to thrive in the microenvironment of their source tumor. In the present study, we demonstrate that CTCs can also colonize their tumors of origin, in a process that we call "tumor self-seeding". In addition, this study provides experimental evidence for the features, the mediators, and the potential consequences of tumor self-seeding.