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2015 Institut Pasteur Korea Annual Report

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2015 Institut Pasteur Korea Annual Report

2015 Institut Pasteur Korea

ANNUAL REPORT CONTENTS

Institut Pasteur Korea

Translational Research Performance in 2015

Teaching & Training

Achievements

Mission & Goals

Mission

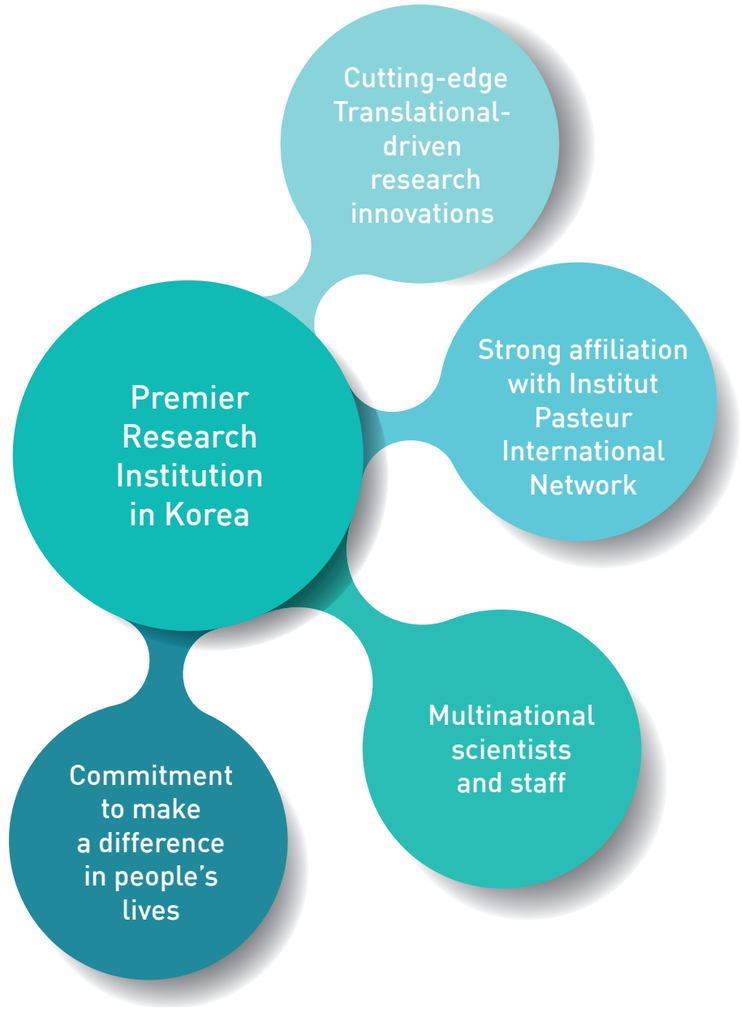
Institut Pasteur Korea (IPK) is an international research institute that focuses on infectious diseases to generate transformative discoveries that will enhance human, animal and environmental health. IPK utilizes proprietary platforms to accelerate translation of these discoveries into clinical applications, identify novel molecular targets and discover small molecules to diagnose, treat, and address serious unmet global public health needs.

Goals

With the excellence of an international team of scientists and staff, cutting-edge research innovations, and our affiliation with the Institut Pasteur in Paris and its global network of 33 institutes, IPK is committed to make a difference in people's lives, upholding Louis Pasteur's tradition, and be one of the leading research institutions in Korea. Together, we are Pasteurians making strides to improve health through research.

Core Values

We emphasize the importance of interpersonal understanding, communication and cooperation. IPK promotes building positive human relationships inside and outside the working place, the ability to effectively communicate and share our passion for science with colleagues and the public, as well as teamwork to achieve a common objective with a sense of responsibility for the group.



Strategy & Major Objectives in 2015

Our research operations are currently focused on six well defined programs, namely, I. Tuberculosis, II. Hepatitis, III. Respiratory Viruses (Influenza), IV. Antibacterial Resistance, V. Leishmania, and VI. Cancer Biology. IPK provides superb opportunities and support for outstanding young scientists to establish their reputation, places special attention to promote educational and training programs to Korean students and scientists, and encourages domestic and international collaborations.

Success Story of IPK

First-in-Class Tuberculosis Drug Discovery

Q203 is a molecule, discovered by IPK, which has a novel mechanism of action and is highly effective against both multi-drug-resistant and extensively drug-resistant mycobacterium tuberculosis. Q203 has successfully advanced through preclinical testing.

Hepatitis C Drug Discovery

The well-developed Hepatitis C virus (HCV) program at Institut Pasteur Korea has delivered a highly active lead series that has a novel mechanism of action with therapeutic efficacy against HCV.

Establishment of a Biotech Company

Qurient is a spin-off biotechnology company of Institut Pasteur Korea dedicated to developing novel therapeutics from late discovery to human proof of concept.

We are Pasteurians

From Louis Pasteur to Institut Pasteur Korea,
we fight disease for you and your loved ones.

History

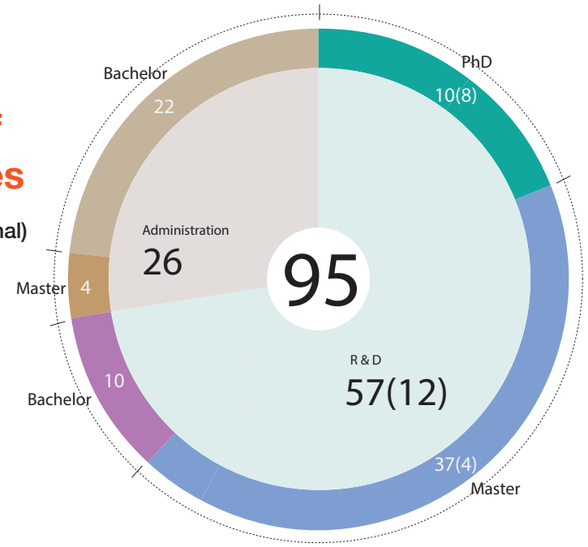
- **2003.12** Agreement on establishment of Institut Pasteur Korea between Institut Pasteur and Korea Institute of Science and Technology (KIST)
- **2004.04** Inauguration of the Institut Pasteur Korea at KIST campus in Seoul, supported by the Ministry of Science, ICT and Future Planning (MSIP)
- **2005.07** Agreement between Gyeonggi Province and Institut Pasteur Korea on the relocation of Institut Pasteur Korea
- **2007.09** First screening agreement with DNDi: Technical Agreement for HTS assay for Leishmania
- **2008.05** The 1st Bio Safety Level 3 certified by Korean Government (Certification issued by KCDC)
- **2008.07** Spin off of Qurient
- **2009.05** Relocation to and inauguration ceremony at Pangyo Techno Valley in Gyeonggi Province (supported by Gyeonggi Province)
- **2010** Awarded for the Partnership of the Year by DNDi
- **2011** Awarded for the Partnership of the Year by DNDi
- **2013. 08** Publication on the new compound for the treatment of tuberculosis in Nature Medicine
- **2014.12** 10th Anniversary Ceremony
- **2015.07** Q203, a first-in-class tuberculosis drug candidate in Korea, was approved for FDA clinical trial phase I
- **2015.08** Master research agreement with DNDi for research collaboration on Leishmania and T. Cruzi
- **2015.12** Q203 was designated for FDA orphan drug

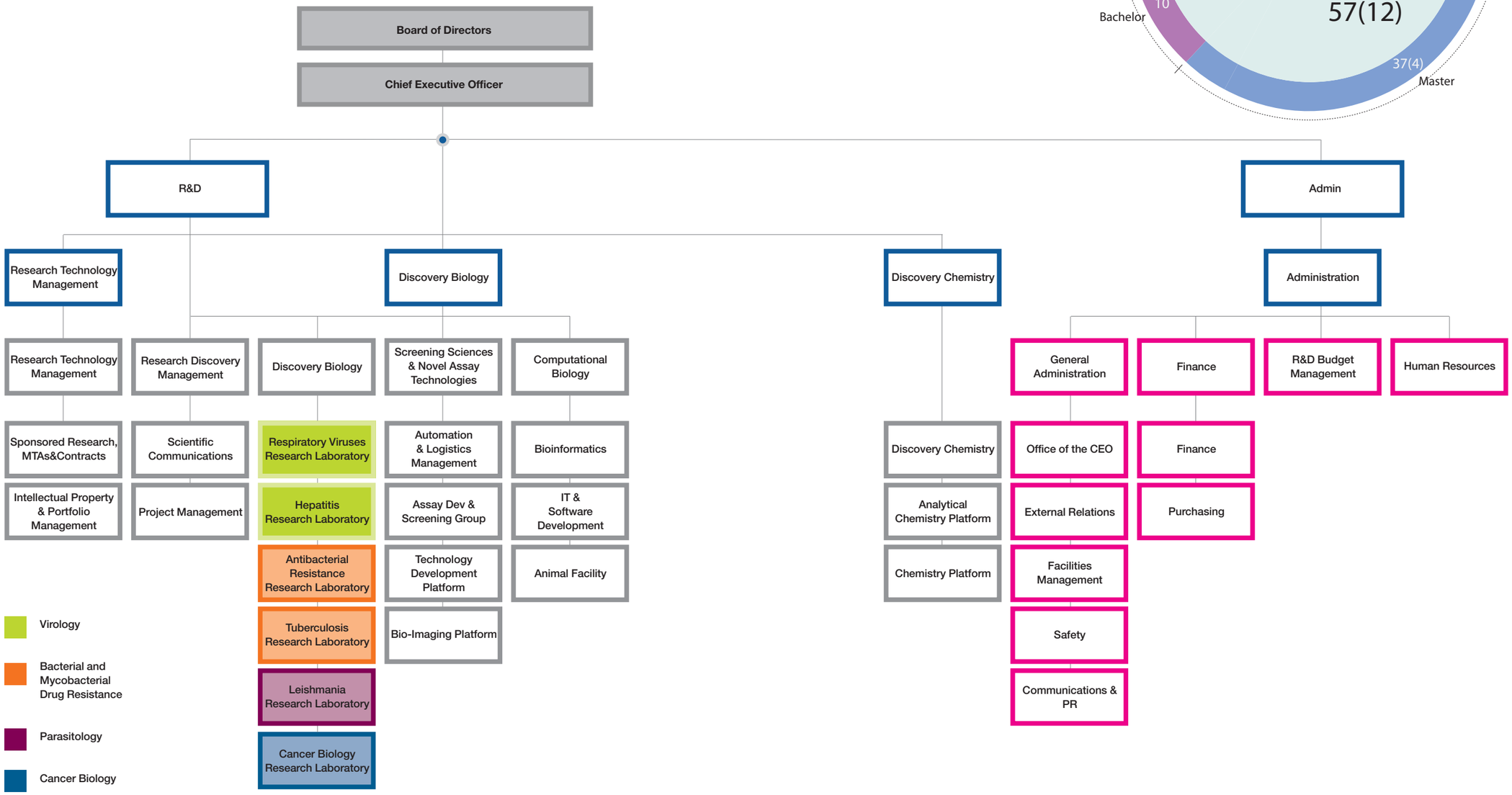
Organization

Organization and Human Resource Profile

Current Profile of Human Resources

※(International)





Structure

Discovery Biology

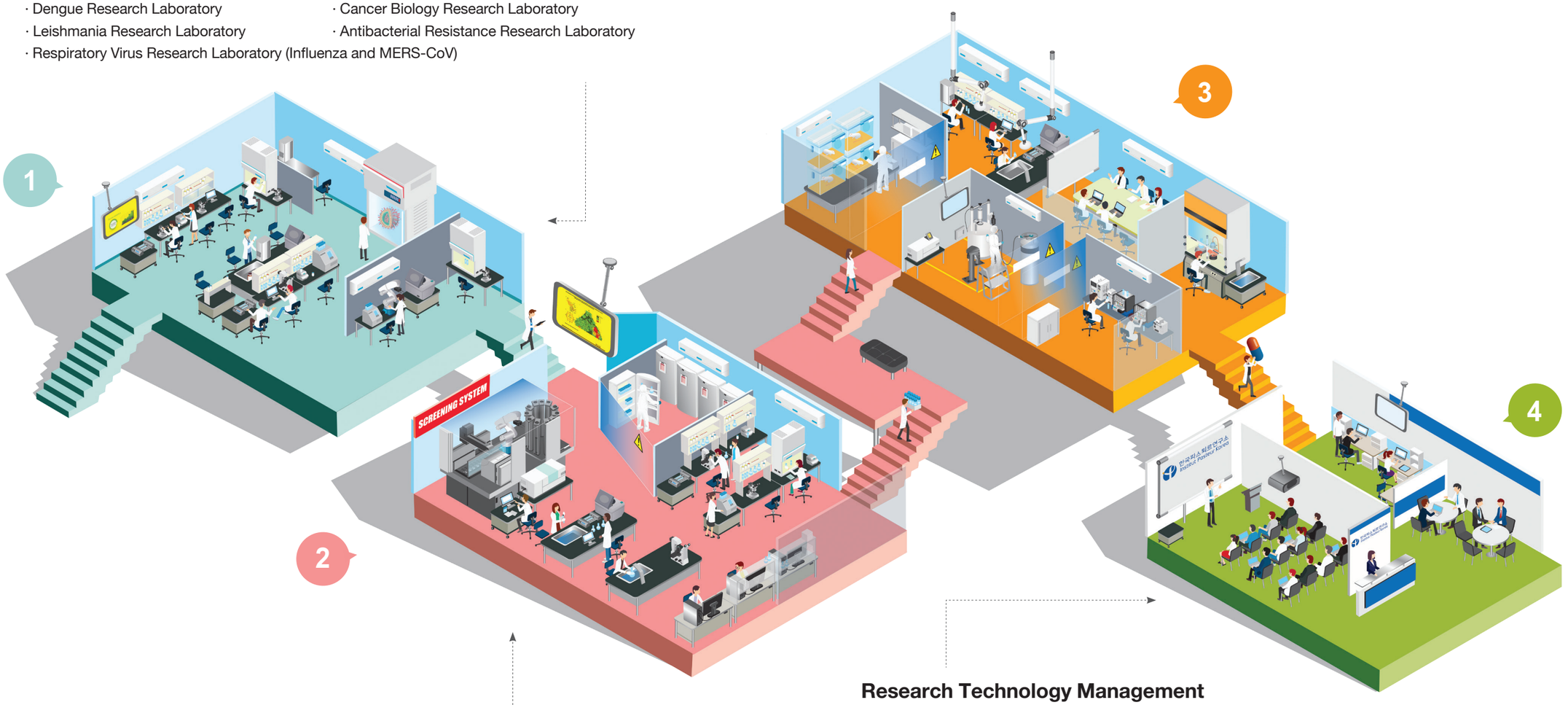
Institut Pasteur Korea has been fighting infectious and neglected diseases.

- Tuberculosis Research Laboratory
- Dengue Research Laboratory
- Leishmania Research Laboratory
- Respiratory Virus Research Laboratory (Influenza and MERS-CoV)
- Hepatitis Research Laboratory (HBV, HCV and Ebola)
- Cancer Biology Research Laboratory
- Antibacterial Resistance Research Laboratory

Discovery Chemistry

Discovery chemistry group supports all IPK translational research programs. The group also plays a key role in optimizing hits identified during screening activities. Their expertise cover the following areas:

- Structure activity relation studies
- Lead optimization
- Drug-like properties



Assay Development & Screening Platforms

Institut Pasteur Korea has been building the best High Content Screening platform in both BSL-2 and BSL-3 laboratories to enable discovery biology to understand diseases, and develop novel therapies.

- Technology Development Platform
- Assay Development & Screening
- Computational Biology
- Automation & Logistics Management

Research Technology Management

Institut Pasteur Korea works closely with industry and academia to increase collaboration and partnerships. With these connections, our technologies will be developed into future medicinal therapies.

- Invention disclosure
- Knowledge and practice
- Intellectual property
- Consulting
- R&D collaboration
- Patent
- Material transfer agreement
- Licensing

Discovery Biology

Tuberculosis Research Laboratory

Principal Investigator: Vincent Delorme, PhD.

Research focus:
(1) Mycobacterium tuberculosis / host immune system interaction: latent tuberculosis
(2) Novel therapies for the treatment of MDR and XDR TB

Laboratory members: Doyoon Kwon, MSc. (Senior Researcher), Minjeong Woo, MSc. (Junior Researcher)

Core support members: Moonhwan Kim, PhD. (CHP), Sunhee Kang, MSc. (CHP), David Shum, MSc. (ADS), Jinyeong Heo, MSc. (ADS)

CHP: Chemistry Platform; ADS: Assay Development & Screening Group

A. Research Progress in 2015

A.1 Novel therapies for the treatment of MDR and XDR Tuberculosis

A.1.1 Development of TTCA and Uracil chemical series

Two lead compounds have been identified from previous screening activities at IPK. This year we continued their biological and pharmacokinetic profiling. Both TTCA lead compounds showed efficacy at 20 mg/kg daily oral dosing in the murine model of chronic tuberculosis. After four weeks treatment, the best compound showed an efficacy similar to isoniazid. The lead compound from the Uracil chemical series was tested against 26 drug-resistant clinical isolates and demonstrated 100% inhibition. Sequencing of spontaneous resistant mutants obtained on cholesterol medium revealed the involvement of adenylyl cyclase and AMP cyclization as a potential pathway by which the pathogen resists the drug. Currently, we are focusing more on the adenylyl cyclase pathway to better understand its role in drug resistance/latency within macrophages.

A.1.2 Natural extract screening

During this period, we have screened 11,088 extracts from actinomycetes. The natural extract library was obtained from the Center for Nutraceutical and Pharmaceutical Material (CNPM), Korea. Despite the moderate signal to noise ratio, we were able to select extracts with inhibitory effect on Mycobacterium tuberculosis replicating within macrophages. CNPM scientists performed the 16S rRNA sequencing of these strains and concluded that all positive extracts belong to the Streptomyces genus. CNPM is scaling up extracts production from five strains for confirmatory studies.

A.2 Mycobacterium tuberculosis/host immune system interaction: latent TB

A.2.1 Development of latency model using SS18b strain

In order to address host/pathogen interaction we focused on developing new assays to mimic the latency of Mycobacterium tuberculosis in macrophages. We generated a modified SS18b strain constitutively expressing a green fluorescent protein (GFP) amenable for imaging within the cells. Macrophages derived from THP-1 cell line were infected and incubated in the presence of reference compounds (isoniazid and rifampicin) to investigate their potency to eradicate intracellular, non-replicating Mycobacterium tuberculosis-GFP **(Figure 1)**.

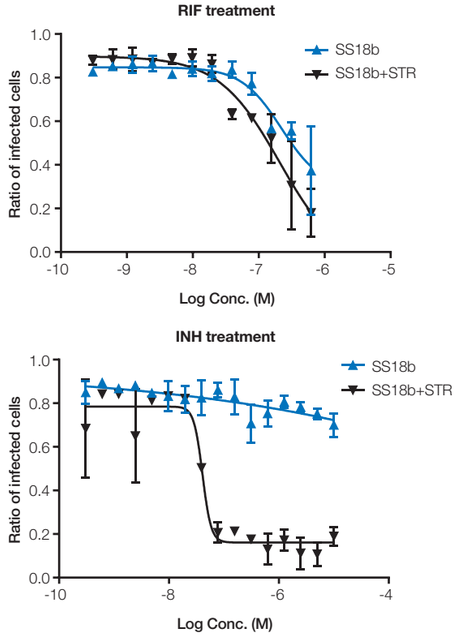
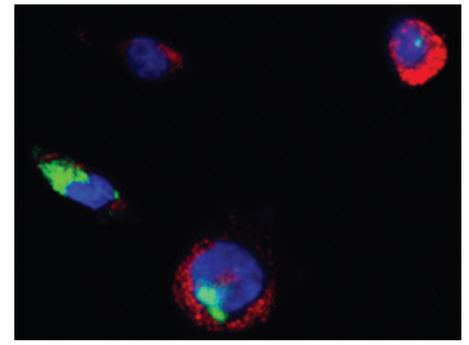


Figure 1. Adaptation of the SS18b-GFP strain to the infected macrophage assay. The ratio of infected cells is plotted as a function of the compound concentration. SS18b-GFP strain grown with Streptomycin (STR) is used as a control. RIF: rifampicin; INH: isoniazid.

A.2.2 Development of the foamy macrophage model

Mycobacterium tuberculosis can be found within granulomas, organized clusters of cells hosting macrophages heavily loaded with lipids, called foamy macrophages. These foamy cells are thought to be reservoirs for latent bacteria. We are currently investigating an in vitro model of foamy macrophages to test this hypothesis. THP-1 cells were first differentiated with PMA for 3 days, then infected with Mycobacterium tuberculosis at low multiplicity of infection (MOI) and finally treated with very low density lipoproteins (VLDL). Bacterial replication within THP-1 cells was monitored kinetically using fluorescence microscopy. Results from these studies revealed a decrease in growth rate in foamy cells versus non-foamy cells (**Figure 2**). Validation using primary cells is underway to confirm these findings.



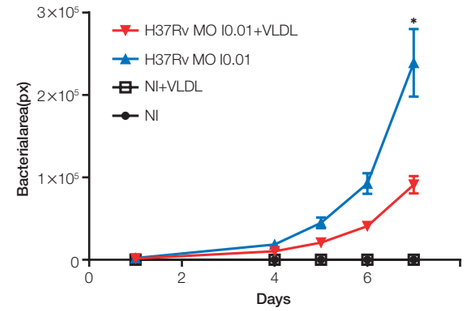


Figure 2. THP-1 macrophages were infected with Mycobacterium tuberculosis-GFP (MOI 0.01) and incubated with VLDL. Left: at day 7, cells were fixed, stained and observed by fluorescence microscopy. Lipids appear in red (lipid-Tox), nuclei in blue (DAPI) and bacteria in green (GFP). Scale bar: 25μM. Right: kinetic of bacterial growth in foamy macrophages. At day 7, the number of bacteria was statistically lower in the foamy cells as compared to control (P value < 0.005).

B. Achievements

B.1 Patents

1. PCT/EP2015/063982 (filed): Anti-infective compounds (TB TTCA). Jaeseung Kim, Sunhee Kang, Min Jun Seo, Mooyoung Seo, Jeongjea Seo, Sumi Lee, Juhee Kang, Dongsik Park, Ryang Yeo Kim, Kevin Pethe, Jichan Jang, Jonathan Cechetto, Heekyoung Jeon, Ki Deok Kim. 2015

B.2 Publications

We have accumulated a series of experimental

data since March 2015 and we are preparing manuscripts to publish in 2016.

B.3 Presentations

1. Vincent Delorme, Infected macrophage as a platform for drug-discovery in tuberculosis, Institut Pasteur International Network Symposium, Paris, ***France***, 15-Oct-2015 (***oral presentation***)
2. Vincent Delorme, Cellular models to study tuberculosis latency and persistence, Institut Pasteur International Network Symposium, Paris, France, 14-Oct-2015 (*poster presentation*)
3. Vincent Delorme, Identification of anti-tuberculous compounds by high-content screening using a model of infected macrophages, Hallym University, ***Korea***, 09-Sep-2015 (***oral presentation***)
4. Vincent Delorme, Q203 discovery and mechanism of action. Targeting respiration for TB drug discovery - The future of QcrB, National Institutes of Health (NIH), Bethesda, MD, ***USA*** ,13-May-2015 (***oral presentation***)
5. Vincent Delorme, Identification of anti-tuberculous compounds by high-content screening using a model of infected macrophages, Chungnam University, ***Korea***, 12-Mar-2015 (***oral presentation***)

B.4 Ongoing & new collaborations

1. Screening of natural extracts libraries, Pr. Joo-Won Suh, Director, Center for Nutraceutical and Pharmaceutical Materials, ***Myongji University, Korea***
2. Compound-target interaction study using NMR in entire bacteria cells, Dr. Nadia Izadi-Pruneyre, Structural and Chemical Biology Department, ***Institut Pasteur, Paris, France***
3. Drug potency against MDR/XDR and non-tuberculous mycobacteria (NTM) clinical isolates, Dr. Sungweon Ryoo, Chief of Molecular Mycobacteriology Unit, Korean Institute of Tuberculosis, ***Chungbuk, Korea***
4. Optimization of Zmp1 inhibitors as new antitubercular leads, Dr. Sandra Gemma, Department of Biotechnology, Chemistry and Pharmacy, ***University of Siena, Italy***
5. Investigation of lipolytic enzymes from Mtb as biomarkers to discriminate active and latent TB, Pr Sunghan Kim, Department of infectious diseases, ***Asan Medical Center, Seoul, Korea*** and Dr Stephane Canaan, EIPL (UMR7282), ***CNRS, Marseille, France***

Hepatitis Research Laboratory

Principal Investigator: Marc P. Windisch, PhD.

Research focus:

(1) Identification and characterization of novel therapies for hepatitis C virus (HCV)

(2) Identification and characterization of novel therapies for hepatitis B virus (HBV)

(3) Identification and characterization of novel therapies for Ebola virus (EBOV)

Laboratory members: Hee Young Kim, PhD (Senior Researcher), Sangchul Lee, PhD (Senior Researcher), Myung Eun Lee (PhD student), Jae Won Yang, M.Sc. (Researcher), Yoojin Cho, M.Sc. (Researcher), Eun Ji Jo, M.Sc. (Junior Researcher), Sanghyun Park, M.Sc. (Junior Researcher), Saehong Min, M.Sc. (Junior Researcher)

Core support members: David Shum, M.Sc. (ADS), Tae-Hee Kim, PhD (ADS), Soonju Park, M.Sc. (ADS), Constantin Radu, M.Sc. (SMA), Honggun Lee, M.Sc. (SMA), Kideok Kim, M.Sc. (SMA), Moonhwan Kim, PhD (CHP), Suyeon Jo, M.Sc. (CHP), Jaeheon Lee M.Sc. (CHP), Sunhee Kang, M.Sc. (CHP), Young Mi Kim, M.Sc. (CHP), Inhee Choi, PhD (CHM), Yoonae Ko, M.Sc. (CHM), Regis Grailhe, PhD (TDP), Seonhee Kim, M.Sc. (TDP).

ADS: Assay Development & Screening Group; **SMA:** Sample Management & Automation; **CHP:** Chemistry Platform; **CHM:** Cheminformatics; **TDP:** Technology Development Platform

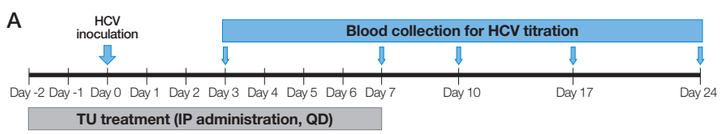
A. Research Progress in 2015

A.1 Novel therapies for HCV and HBV

A.1.1 Identification and characterization of novel HCV inhibitors

A.1.1. 1 Lead optimization and characterization of IPK00260330 as a new hepatitis C virus lead compound

In 2015, the HRL team along with internal collaboration, significantly improved the drug like properties of the TU chemical series by synthesizing and evaluating more than 300 derivatives. Among these derivatives, two advanced lead compounds have been selected for in depth DMPK evaluation, in vivo toxicity and in vivo efficacy studies. One optimized lead compound (IPK00260330) has been nominated as a Lead compound, as determined by its drug-like profile. IPK00260330 also demonstrated potent inhibitory effect on patient derived HCV isolates in a humanized mouse model. 50 mg/kg, oral once a day treatment with IPK00260330 did not show any adverse effects in mice (**Figure 1A & B**).



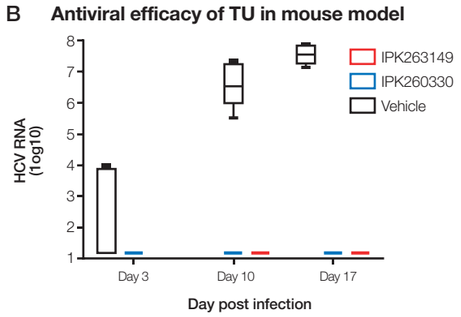


Figure 1. (A) HCV in vivo efficacy study in humanized mice (study design). Mice were treated with 50mg/kg of TU derivatives (IPK263149 in red and IPK260330 in blue) or vehicle control (in black) 2 days prior infection, followed by inoculation with patient derived HCV. Blood samples were taken as depicted. (B) Quantification of HCV RNA level in blood samples. In black vehicle control and IPK263149 and IPK260330 in red and blue, respectively. The average of at least 4 mice per group is shown.

A.1.1.2 Hits identification from natural and small compound libraries for HCV

Furthermore, by screening of natural compound libraries, we identified Micrococcin P1 (antibacterial, antiprotozoal and antimalarial agent), an inhibitor of HCV genotypes 1 and 2 (**Table 1**). Micrococcin P1 interferes with an HCV E1/E2 mediated entry as shown by using HCV pseudo-particle. However, Micrococcin P1 does not interfere with HCV RNA replication. It has been found that Micrococcin P1 is highly synergistic with FDA-approved HCV drugs in cell cultures.

IDPP was also identified by screening small molecule libraries and shown to inhibit transduction of HCV pseudo-particle without affecting viral RNA replication. IDPP potently (IC50=46±26 pM) inhibits exclusively HCV genotype 2 viruses (**Figure 2**) and prevents cell-to-cell spread which is the major route of transmission in the liver. Furthermore, IDDP treatment of HCV producing cells led to intra-cellular retention of ApoE.

Table 1. EC_{50} and CC_{50} of Micrococcin P1

Virus	HCV genotype	Micrococcin P1 treatment		SI[c]
		EC_{50} (μM)[a,b]	CC_{50} (μM)[a,b]	
TN-Luc	1a	0.54 ± 0.01	15.17 ± 3.53	28.1
Jc1-Luc	2a	0.52 ± 0.08	11.5 ± 0.01	22.1

[a] Values represent the average ± SD of two independent experiments.
[b] The CC50 and EC50 values of each compound were calculated based on the cell viability and antiviral activity data.
[c] Selectivity index (SI) = CC50/EC50.

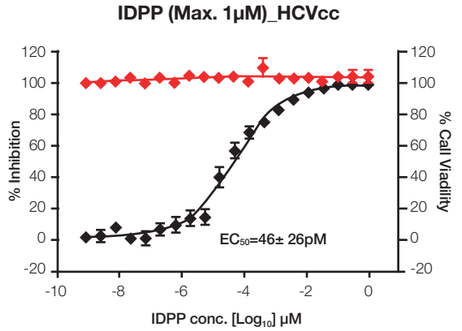
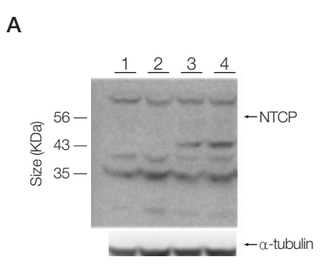


Figure 2. Antiviral effect of IDPP in the HCV genotype 2 infectious cell culture system. Dose dependent antiviral effect is show by black diamonds. Cell viability is measured by the detection of cell nuclei and is shown in red.

A.2 Identification and characterization of novel HBV inhibitors

A.2.1 Characterization of the infectious hepatitis B virus cell culture system

In order to identify a suitable HBV target cell line, we evaluated the expression of sodium-taurocholate co-transporting polypeptide (NTCP), a crucial HBV receptor, in various hepatoma cell lines and determined the expression by Western-blot analysis (**Figure 3A**). After selection of suitable target cells we inoculated these with cell culture derived HBV and determined HBV infection rates. At day 6 post HBV infection in 384-well plates infection rates were evaluated by immunofluorescence analysis of the hepatitis B core (HBc) protein (**Figure 3B**). Furthermore, we are currently evaluating the option of developing a genome wide RNAi screen by testing transfection efficiencies of reference siRNAs (e.g. NTCP).



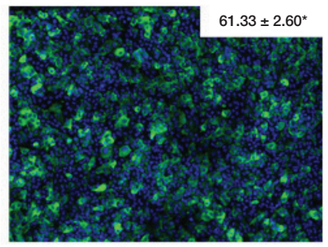
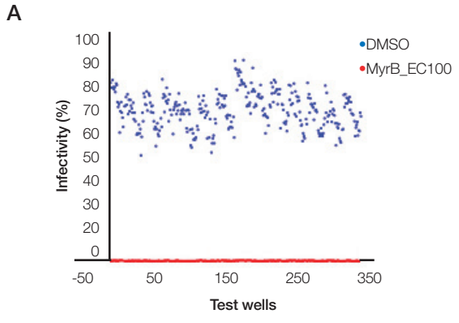


Figure 3. Characterization of HBV susceptible cell line assay. (A) Western-blot analysis of HepG2 cells. Lane 1, HepG2; Lane 2; mock DNA transfection, Lane 3; hNTCP-HepG2 from Heidelberg University and Lane 4; hNTCP-HepG2 from Yonsei University.(B) HBc-specific immunofluorescence (green) analysis at 6 days post infection. Nuclei are stained with Hoechst (blue).

A.2.2 Identification and characterization of novel HBV inhibitors

Using the infectious HBV cell culture system IPK developed a phenotypic HTS assay and screened 1,822 FDA-approved drugs and biologically active molecules. Assay robustness was demonstrated by well-to-well, plate-to-plate and batch-to-batch variation evaluation with positive (MyrB HBV entry inhibitor) and negative controls (DMSO) (**Figure 4A**). Compounds inhibiting HBc antigen expression were considered as inhibitors whereas compounds increasing HBc expression were preliminarily classified as activator (potentially inhibitors of cellular viral restriction factors) (**Figure 4B**). Hit confirmation is being performed and assays for mechanism-of-action studies such as detection of HBV covalently closed circular DNA (cccDNA), have been established for detailed characterization of inhibitors.



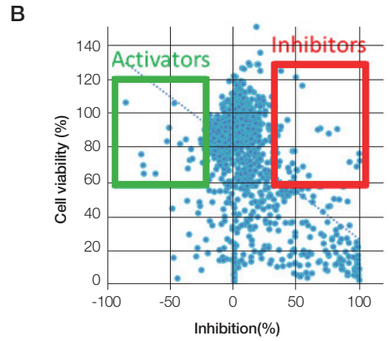
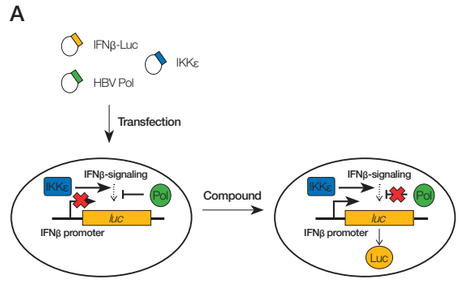


Figure 4. Pilot screening results. (A) Demonstration of assay robustness in pilot screening. In fourteen 384-well plates, 24 wells in each plate HBV infection was evaluated either with DMSO treated (blue dots; infected) or with of MyrB (entry inhibitor) treated cells (red dots; infected and inhibited). Infection rate of each well is depicted as individual point. (B) Hit selection. 17 compounds were selected with >50% HBV inhibition (reduced HBc expression) and >50% cell viability (DAPI stain of cell nuclei). Additionally, 12 compounds were selected increasing >30% HBV infection rates (increased HBc expression) and >50% cell viability.

In order to identify compounds restoring innate immunity (interferon beta signaling) in HBV replicating hepatoma cells, IPK performed a pilot screen of approx. 5,500 compounds using an interferon beta (IFNβ) reporter-based system. The assay is based on the overexpression of the viral polymerase (Pol) and IKK? an IFNβ-signaling inducer (**Figure 5A**). Under this condition Pol completely abolishes signaling; however compounds interfering with Pol-DDX3 interaction were identified restoring signaling. Hits were triaged in order to select for HBV-specific immuno-modulator (**Figure 5B**) and evaluation of them in stable HBV replicating- and in infected cells is ongoing.



B

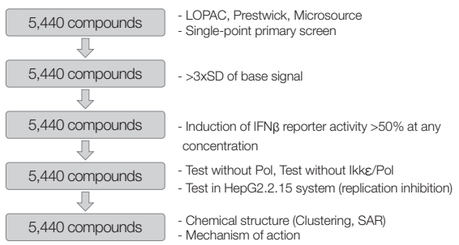
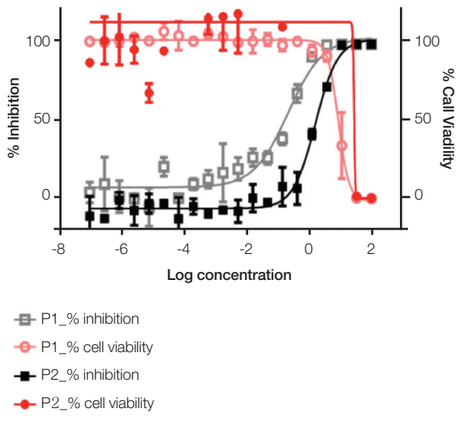


Figure 5. Identification of compounds restoring innate immunity in HBV-infected cells (A) Assay principle to identify compounds restoring IFNβ-signaling in HBV Pol expressing cells. (B) Screening and hit triage. After screening of FDA-approved drugs, hits were confirmed by dose-response analysis and non HBV-specific IFNβ-signaling activator rejected. Confirmed HBV Pol-specific hits are being further analyzed.

A.3 Identification and characterization of novel Ebola virus inhibitors (Institut Pasteur Ebola Task Force)

The EBOV trVLP system was successfully adapted to 384-well plates using HEK293T cells and tamoxifen was selected as reference compound showing inhibition of viral entry (**Figure 6A**). Furthermore, YFP was cloned into the EBOV coding region to have an alternative read-out option beside luciferase (**Figure 6B**).

A



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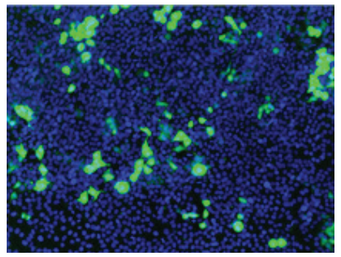


Figure 6. (A) Tamoxifen, a known EBOV entry inhibitor, was used as control. Luciferase-based assay, transduction of p1 target cells (grey) followed by supernatant transfer to p2 target cells (black). Cell viability is shown in red. (B) Visualization of EBOV replication by YFP expression (green) and cell nuclei are show in blue (Hoechst).

B. Achievements

B.1 Patents

1. PCT/EP2015/058421 (filed): COMPOUNDS FOR TREATING VIRAL INFECTIONS. Marc P. Windisch, Hee-Young Kim, Jaewon Yang, Jongyeon Hwang, Suyeon Jo, Jeongjin Kwon, Dongsik Park, Jihyun Choi, Jaeheon Lee, 2015

B.2 Publications

1. Dong-Kyun Ryu, Yeji Ahn, Wang-Shick Ryu and Marc P. Windisch. (2015) Development of a novel hepatitis B virus encapsidation detection assay by viral nucleocapsid-captured quantitative real-time RT-PCR. Biotechniques. 2015 Nov 1;59(5):287-93. doi: 10.2144/000114354. eCollection 2015.
2. Lee S, Yoon KD, Lee M, Cho Y, Choi G, Jang H, Kim BS, Jung DH, Oh JG, Kim GW, Oh JW, Jeong YJ, Kwon HJ, Bae SK, Min DH, Windisch MP, Heo TH, Lee C (2015) Identification of a resveratrol tetramer as a potent hepatitis C virus helicase inhibitor. Br J Pharmacol (accepted)
3. Grünvogel O, Esser-Nobis K, Reustle A, Schult P, Müller B, Metz P, Trippler M, Windisch MP, Frese M, Binder M, Fackler O, Bartenschlager R, Ruggieri A, Lohmann V. (2015) DDX60L Is an Interferon-Stimulated Gene Product Restricting Hepatitis C Virus Replication in Cell Culture. J Virol. 89(20):10548-68
4. Ko CK, Lee SY, Windisch MP, Ryu WS. (2015) DDX3 DEAD-Box RNA Helicase is a Host Factor that Restricts Hepatitis B Virus Replication at the Transcriptional Level. J Virol. 88: 13689-98
5. Chunkyu Ko, Park WJ, Park SH, Kim ST, Marc P Windisch, Ryu WS. (2015) The FDA approved drug irbesartan inhibits HBV-infection in HepG2 cells stably expressing sodium taurocholate co-transporting polypeptide, Antivir Ther.

B.3 Presentations

1. Marc Windisch, Characterization of a novel inhibitor acting on early and late steps of the hepatitis C virus life cycle, Annual Symposium on Hepatitis Viruses 2015, Gang-won, ***Korea***, 21-Jan-2015 (***Invited talk***)
2. Myungeun Lee, Characterization of a novel small molecule inhibitor interfering with early steps of the hepatitis C virus life cycle, Annual Symposium on Hepatitis Viruses 2015, Gang-won, ***Korea***, 21-Jan-2015 (***Invited talk***)
3. Sangchul Lee, Development of a phenotype hepatitis B virus infection assay in 384-well plate format, Annual Symposium on Hepatitis Viruses 2015, Gang-won, ***Korea***, 21-Jan-2015 (***poster Presentation***)
4. Marc Windisch, Characterization of novel inhibitors acting on early and late steps of the hepatitis C virus life cycle, seminar course for Biomedical Science Department, Graduate School of Ajou University, Gyeonggi-do, ***Korea***, 1-April-2015 (***Invited talk***)
5. Marc Windisch, Viral Hepatitis, KCS symposium: Infectious Disease Research in Biochemistry and Structural Biology, Gyeonggi-do, ***Korea***, 16-April-2015 (***Invited talk***)
6. Sangchul Lee, Development of a phenotypic hepatitis B virus infection assay to evaluate inhibitors with novel mechanism of action, The spring symposium for the Korean Association of Immunologists, Gyeonggi-do, ***Korea***, 17-Apr-2015 (***Poster presentation***)
7. Myungeun Lee, Characterization of a Novel Small Molecule Inhibitor Targeting Hepatitis C Virus Glycoprotein E1, the Spring Symposium for Korean Association of Immunologists, Suwon, ***Korea***, 17-April-2015 (***Poster presentation award***)
8. Marc Windisch, Characterization of novel inhibitors acting on early and late steps of the hepatitis C virus life cycle, Hepatitis mini-symposium, Catholic Univ. of ***Korea***, 14-May-2015 (***invited talk***)
9. Marc Windisch, Discovery, identification and characterization of novel hepatitis C virus inhibitors, International seminar on pharmaceutics 2015, ***Indonesia***, 4-August-2015 (***Invited talk***)
10. Sangchul Lee, Development of a phenotypic hepatitis B virus infection assay in 384-well plates and screening of small molecule compound libraries, The 27th international conference of the Korean Society for molecular and cellular biology, Seoul, ***Korea***, 22-Sep-2015 (***Poster presentation***)
11. Hee-Young Kim, Characterization of a small molecule inhibitor interfering with hepatitis C virus entry by targeting viral glycoprotein E1, The 27th international conference of the Korean Society for molecular and cellular biology, Seoul, ***Korea***, 22-Sep-2015 (***Poster presentation***)
12. Sangchul Lee, Development of a phenotypic hepatitis B virus infection assay in 384-well plates and screening of small molecule compound libraries, 2015 International meeting on molecular biology of hepatitis B virus, Bad Nauheim, ***Germany***, 7-Oct-2015 (***Poster presentation***)
13. Eunji Jo, Benzothiazepinecarboxamides: novel hepatitis C virus inhibitors interfering with viral entry and secretion of infectious virions, 22nd International Symposium on Hepatitis C Virus and Related Viruses, Strasbourg, ***France***, October 9-13, 2015 (***Poster presentation***)
14. Marc Windisch, Characterization of a novel small molecule inhibitor targeting hepatitis C virus glycoprotein E1, 22nd International Symposium on Hepatitis C Virus and Related Viruses, Strasbourg, ***France***,

October 9-13, 2015 (***Poster presentation***)

15. Saehong Min, Characterization of a small molecule inhibitor interfering with hepatitis C virus entry by targeting viral glycoprotein E1 and associated lipids, 22nd International Symposium on Hepatitis C Virus and Related Viruses, Strasbourg, ***France***, October 9-13, 2015 (***poster Presentation***)
16. Marc Windisch, Towards the identification and characterization of novel Ebola virus interventions by screening of small molecule compound libraries, International Scientific Symposium Institut Pasteur International Network, Paris, ***France***, October 14, 2015 (***Invited talk***)
17. Myungeun Lee, Characterization of a novel small molecule inhibitor targeting hepatitis C virus glycoprotein E1, International Scientific Symposium Institut Pasteur International Network, Paris, ***France***, October 15, 2015 (***Poster presentation***)
18. Marc Windisch, Characterization of an novel HCV inhibitor targeting E1/E2 glycoproteins, Institut Pasteur Virology Department retreat, Paris, ***France***, November 17, 2015 (***Invited talk***)

B.4 Ongoing & new collaborations

1. Development of a screening assay using Ebola virus trVLP system (new/external/Dr. Hoenen, ***NIH, Rocky Mountain Laboratories, USA***)
2. Evaluation of micro RNAs interfering with HCV (new/external/Prof. Yoon, ***Catholic University, Seoul, Korea***)
3. Evaluation of nanoparticles in HBV and HCV cell culture systems (new/Prof. Kattesh, ***University of Missouri, USA***)
4. Evaluation of HBV inhibitors (new/Prof. Kim, Ajou University, Suwon, Korea)
5. Determination of ApoE level in TU treated hepatoma cells (new/Prof. Seungtaek Kim, ***Yonsei Severance Hospital, Seoul, Korea***)
6. Evaluation of protease/polymerase/helicase inhibition of resveratrol tetramer (new/external/Prof. Choongho Lee, ***Dongkuk University, Seoul, Korea***)
7. HCV inhibitors MoA study (new/external/Prof. Ralf Bartenschlager, ***University of Heidelberg, Heidelberg, Germany***)
8. Evaluation of novel anti-HCV agent targeting cyclophilin A. (old/external/Prof. Sung Soo Kim, Department of Biochemistry and Molecular Biology, School of Medicine, ***Kyung Hee University, Seoul, Korea***)
9. Evaluation of kinase inhibitors interfering with HCV entry. (old/external/Prof. Soon Bong Hwang, Ilsong Institute of Life Science, ***Hallym University, Anyang, Korea***)
10. Novel cell culture adapted chimeric HCV to characterize the viral life cycle. (old/external/Prof. Jens Bukh, Department of Infectious Diseases and Clinical Research Centre, ***University of Copenhagen, Denmar***k)
11. Analysis of HCV and ethanol induced dysregulation of MHC class I-dependent antigen presentation in liver cells. (old/external/Prof. Natalia Osna, Dept Internal Medicine, ***University of Nebraska Medical Center, USA***)
12. Analysis of siRNA targeting conserved RNA regions of HCV. (old/external/Dr. Mahmoud M. Elhefnawi, American University in Cairo Informatics and systems Department, ***The National Research Centre, Egypt***)
13. Development of a phenotypic HTS using HCV reporter cells. (old/external/Prof. Charles M. Rice ***Rockefeller University, New York, USA***)
14. Identification of HBV assembly inhibitors (old/external/***Sanofi***)
15. Identification of immune modulators restoring innate immunity in HBV replicating cells. (old/external/***Sanofi***)
16. HBV infection of NTCP expressing hepatoma cells. (old/external/Prof. Stephan Urban; Department of Molecular Virology, ***Heidelberg University, Germany***)
17. Development of epsilon HBV Pol and IRF3 nuclear translocation assay. (old/external/Prof. Wang Shick Ryu, Department of Biochemistry, ***Yonsei University, Seoul, Korea***)

Respiratory Viruses Research Laboratory

Principal Investigator: Ji-Young Min, PhD.

Research focus:

(1) Development of Pan-Influenza inhibitors

(2) Elucidation of mechanism of action and characterization of new therapeutic targets for Influenza infection

(3) Investigation of the interaction influenza virus/host immune modulators

(4) Mechanisms inhibiting MERS entry, replication and spreading

Laboratory members: Ji Hoon Park, PhD. (Senior Researcher), Soyoung Chang, MSc. (Researcher), Jihye Lee, MSc. (Junior Researcher), Dong Jo Shin, MSc. (Junior Researcher), Jinhee Kim, MSc. (Junior Researcher)

Core support members: Moon Hwan Kim, PhD. (CHP), Sunju Kong, MSc. (CHP), David Shum, MSc. (ADS), Constantin Radu, MSc. (SMA)

CHP: Chemistry Platform; **ADS:** Assay Dev & Screening Group; **SMA:** Sample Management & Automation

A. Research Progress in 2015

A.1 Selection of Pan-influenza inhibitors for the development of universal influenza treatment

a. Confirmed the anti-influenza activity of primary hits (103 total, 6 clusters and 2 singletons) showed dose response. Newly purchased and purity checked compounds were used.
b. Completed selection of scaffold based on their activity profiles and novelty as anti-influenza agents
c. Conducted additional cell-based target free HTS with natural extracts library established by working groups in the Center of Diseases Biology & Chemical Genomics.

A.2 Target identification of potential lead influenza therapeutic compounds

a. Established biological assay systems to distinguish host or viral factors, which may interact with identified compounds.

b. Several in vitro techniques have been used for the investigation of protein-chemical and protein-protein interactions, including GST pull-downs, thermal stability testing using protein expressed in vitro, and RNA interference technology.

A.3 Immunomodulators as influenza treatment

a. Established immunomodulator screening platform utilizing Luc-reporter system and human lung epithelial (A549) cells stably expressing GFP tagged NF-kB.
b. Completed validation of platform using known cytokines in regulation of innate immune responses.

A.4 Identification of potential drug targets using siRNA technology

a. Conduct well-based screening with human druggable Dharmacon ON-TARGETplus2® SMART pool2® siRNA library set (2732 siRNAs) in human lung epithelial cells infected with influenza viruses.
b. Identified seven novel human genes down-regulating replication of influenza virus and validated these genes in the biochemical assays (**Figure 1&2**).

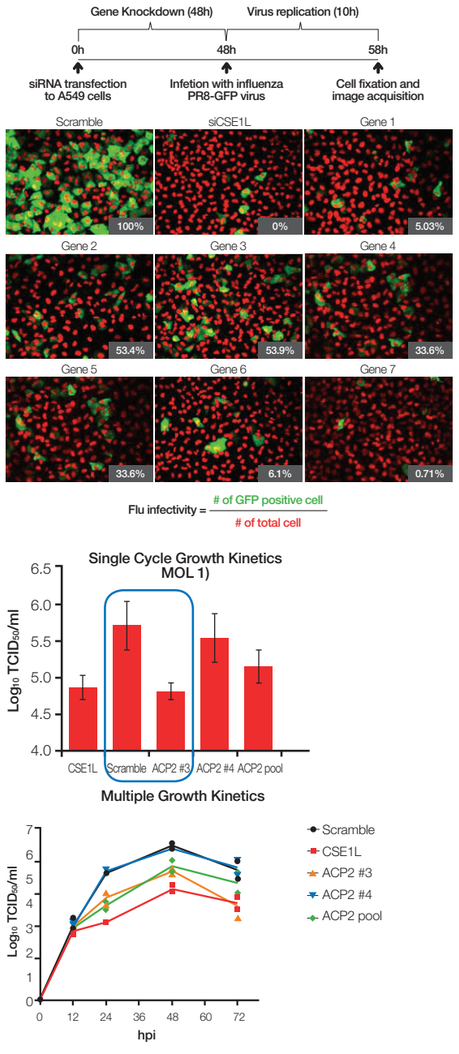


Figure 1. Identification seven human genes down-regulating replication of influenza viruses.

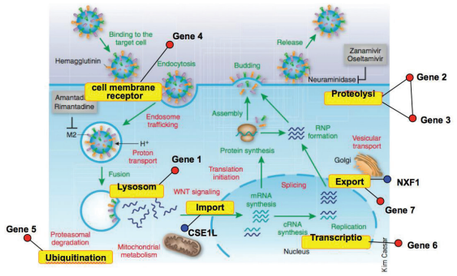


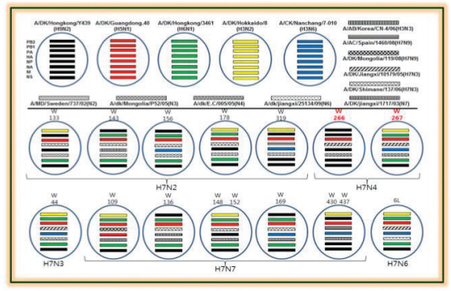
Figure 2. Identification seven human genes down-regulating replication of influenza viruses.

A.5 Pathogenesis of H7 avian influenza viruses in Korea

a. Screened >200 aquatic bird fecal samples and isolated H7 avian influenza viruses by phylogenetic analysis.
b. Determined EID50 and MLD50 of Korean H7 isolates
c. Selected H7 Korean isolates representing high and low pathogenic models for further studies.

Virus	Subtype	EID_{50}/ml	MLD_{50}/30ul
A/EM/Korea/W178/07	H7N2	8.75	7.0<
A/AB/Korea/W44/05	H7N3	9.25	7.0<
A/EM/Korea/W266/07	H7N4	9.4	6.0
A/MD/Korea/6L/07	H7N6	7.1	6.0<
A/EM/Korea/W152/06	H7N7	8.25	6.0<
A/Anhui/1/13 (RG)	H7N9	7.5	6.0

Table 2. Virulence of H7 avian influenza viruses isolated in Korea



B. Achievements

B.1 Patents

1. US Provisional US62/168903 (filed): Anti-Influenza compounds PPA. Ji-Young Min, Deu John Cruz, and So Young Chang, May 31 2015
2. US Provisional US62/218547 (filed): Compounds for Treatment of Influenza A virus. Ji-Young Min, September 14, 2015

B.2 Publications

1. Yoon A, Yi KS, Chang SY, Kim SH, Song M, Choi JA, Bourgeois M, Hossain MJ, Chen LM, Donis RO, Kim H, Lee Y, Hwang DB, Chung J, and Min JY. (2015) An Anti-influenza virus antibody inhibits viral infection by reducing nucleus entry of viral nucleoprotein. PLoS One. EMID:eaf6a16993c61ed8
2. Park JH, Park EB, Lee JY, and Min JY. (2015) Identification of novel membrane-associated prostaglandin E synthase-1 (mPGES-1) inhibitors with anti-influenza activities in vitro. Biochemical and Biophysical Research Communications. DOI: 10.1016/j.bbrc.2015.11.129

B.3 Presentations

1. Ji-Young Min, Opportunity for drug discovery in Korea to complement vaccine development. MERS-CoV Vaccine workshop, ***Saudi Arabia***, Nov 14-15, 2015. (**Invited talk**)
2. Ji-Young Min, Opportunity for drug discovery in Korea to complement vaccine development. Global MERS-CoV Symposium, K-CDC/K-NIH, ***Korea***, Sep 10, 2015. (**Invited talk**)
3. Ji-Young Min, Opportunity for drug discovery in Korea to complement vaccine development. Global MERS-CoV Symposium, International Vaccine Institute, Seoul, ***Korea***, Sep 10, 2015. (**Invited talk**)
4. Ji-Young Min, Novel broad-spectrum antiviral against influenza blocks dsRNA binding to NS1A protein and restores antiviral responses. The 4th International Society for Influenza and other Respiratory Virus Diseases ? Antiviral Group, Austin ***TX, USA***, June 2-June 5, 2015. (invited talk)
5. Ji Hoon Park, Anti-influenza activities of membrane associated prostaglandin E synthase-1(mPGES-1) inhibitors. The Korea Society of Virology, ***Yangyang, Korea***, Aug 29, 2015. (**Invited talk**)
6. So Young Chang, A natural product from Euborphia humifusa exerts broad-spectrum antiviral activity against influenza A and B viruses by blocking nuclear export of viral ribonucleoprotein. The 4th International Society for Influenza and other Respiratory Virus Diseases ? Antiviral Group, ***Austin TX, USA***, June 2-5, 2015. (**Poster**)
7. Jihye Lee, Role of H3N8 equine influenza A virus NS1A in viral growth and host immune responses. 2015 Korea Society of Biochemistry and Molecular Biology International Conference, Seoul, Republic of ***Korea***, May 12-14, 2015. (**Poster**)
8. Ji Hoon Park, Anti-influenza activities of membrane associated prostaglandin E synthase-1(mPGES-1) inhibitors. International meeting of MSK, ***Changwon, Korea***, Apr 15-18, 2015. (**Invited talk**)
9. Deu John Cruz, A new class of small molecule inhibitors block entry of adamantine-resistant influenza A virus. The 4th International Society for Influenza and other Respiratory Virus Diseases - Antiviral Group, ***Austin TX, USA***, June 2-5, 2015. (**Poster**)

B.4 Ongoing & new collaborations

1. Pathogenesis of emerging avian influenza viruses in Korea. Young-Ki Choi, DVM, Ph.D., ***Chungbuk National Univ. Korea.***
2. Surveillance of human influenza viruses in Korea. Kisoon Kim, Ph.D., NIH, ***Korea.***
3. Transmission of MERS-CoV. Sung-Han Kim, M.D. Asan Medical Center, ***Korea.***

Antibacterial Resistance Research Laboratory

Principal Investigator: Soojin Jang, PhD.

Research focus:

(1) Investigation of bacterial physiology and antibiotic resistance

(2) Discovery of new antibacterial molecules active against drug resistant bacteria

(3) Target identification of new antibacterial molecules

Laboratory members: Yunmi Lee, MSc. (Researcher), Hyungjun Kim, MSc. (Junior Researcher)

Core support members: David Shum, MSc. (ADS), Nam Youl Kim, MSc. (ADS), Jinyeong Heo, MSc. (ADS), Constantin Radu, MSc. (ALM), Ki Deok Kim, MSc. (ALM), Honggun Lee, MSc. (ALM)

ADS: Assay Dev & Screening group; **ALM:** Automation & Logistics Management

A. Research Progress in 2015

We previously identified oxythiamine from a small-molecule screening against Pseudomonas aeruginosa and demonstrated that it inhibits the bacterial growth by interfering thiamine-dependent enzymes such as acetolactate synthase and pyruvate dehydrogenase. We further demonstrated that oxythiamine is intracellularly pyrophosphorylated through bacterial thiamine biosynthetic pathway and it is essential for the activity. With these results, one manuscript is in preparation targeting early next year publication and some parts of the results have been presented at two conferences as posters and an oral presentation. Moreover, our extensive experience on small molecule screening and physiological study of P. aeruginosa have attracted other research teams with invited talks and new collaborators (refer to Major Accomplishment section). New projects to combat against two other notorious superbugs, S. pneumoniae and S. aureus, have been significantly progressed in this year. We have developed a new screening assay against S. pneumoniae. The developed assay is now ready to screen antipneumococcals for various S. pneumoniae strains including multidrug resistant ones. Our effort to track down the development of antibiotic resistance in S. aureus identified a hypothetical protein (protein-13280) by analyzing bacterial transcriptomic changes in the presence of antibiotics. We demonstrated that the induction of protein-13280 is an early bacterial response to antibiotic treatment, which may be associated with resistance development. We are also investigating community-based antibiotic resistance as a pilot project with the goal to identify new mechanism(s) of bacterial resistance.

A.1 Development of the assay system and discovery of novel antibacterial molecules against superbugs

A.1.1 Identification of oxythiamine activation mechanism

We previously hypothesized that phosphorylation of oxythiamine is necessary for its activity. This hypothesis was supported by in vivo detection of phosphorylated oxythiamine collaborating with Prof. Uwe Sauer in ETH Zurich in Switzerland. Furthermore, the whole genome sequencing of an oxythiamine resistant mutant suggested that thiamine monophosphate kinase (ThiL) is likely involved in phosphorylation of oxythiamine (**Figure 1**).

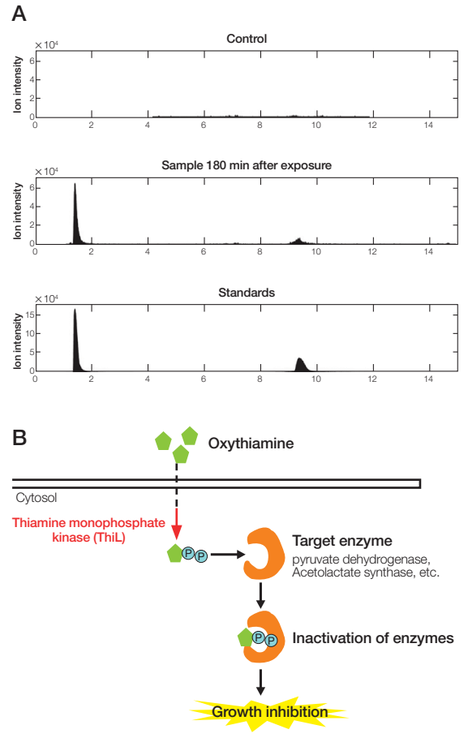


Figure 1. Detection of intracellular phosphorylation of oxythiamine and a postulated model. Phosphorylated oxythiamine was detected in P. aeruginosa PAO1 (A). P. aeruginosa PAO1 incubated with oxythiamine was harvested and mono- and pyro-phosphorylated oxythiamine was measured. The experiments were repeated at least three times. Synthesized oxythiamine mono- and pyro-phosphates were used as controls. A process of oxythiamine activation is postulated based on an oxythiamine resistant mutant study (B).

A.1.2 Assay development for S. pneumoniae

A new assay for S. pneumoniae has been developed to identify new anti-pneumococcal agents. The developed assay based on bacterial viability test using resazurin was applicable for three different S. pneumoniae strains including a reference strain and multidrug resistant strains.

A.1.3 Investigation of S. aureus responses to antibiotics

In order to investigate the process of antibiotic resistance development, antibiotic-mediated transcriptional changes of S. aureus were monitored by RNA sequencing. We found that a hypothetical protein, protein-13280 is significantly induced upon various antibiotic treatments and its induction is time-dependent and dose-dependent (**Figure 2**).

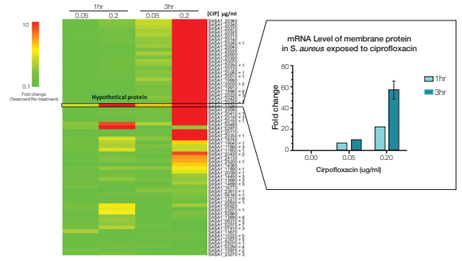


Figure 1. Transcriptomic analysis of antibiotic effect on S. aureus. S. aureus were treated with two different concentrations of ciprofloxacin (0.05 and 0.2 ug/ml) and they were harvested after 1 and 3 hour incubation. Changes of bacterial gene expression were measured by RNA sequencing.

A.1 Investigation of community-based antibiotic resistance

Our pilot experiment to analyze community associated antibiotic resistance was conducted with collected samples from various places in our institute that represents a small community. We have isolated a total of 52 morphologically different bacteria and found that 33% of them are resistant to at least one antibiotic with 30 % of multidrug resistance among them.

B. Achievements

B.1 Patents (N/A)
B.2 Publications

1. Jang S (2015) Efflux pumps of Staphylococcus aureus and their clinical implication. J. Micro. TJOM-D-15-00159R1. (accepted)
2. Hong YF, Lee HY, Jung BJ, Jang S, Chung DK, Kim H (2015) Lipoteichoic acid isolated from Lactobacillus plantarum down-regulates UV-induced MMP-1 expression and up-regulates type I procollagen through

the inhibition of reactive oxygen species generation. Mol Immunol. 67(2 Pt B):248-55

3. Kim H, Kim HR, Kim NR, Jeong BJ, Lee JS, Jang S, Chung DK. (2015) Oral administration of Lactobacillus plantarum lysates attenuates the development of atopic dermatitis lesions in mouse models. J Microbiol. 53(1):47-52.

B.3 Presentations

1. Soojin Jang, Discovery of new antibacterial molecules to combat bacterial infections, 2015 international Meeting of the Microbiological Society of Korea, ***Changwon, Korea***, 15-04-2015 (***Oral***)
2. Hyungjun Kim, Yunmi Lee, and Soojin Jang, The application of alamar blue assay for large-scale compound screening system against Klebsiella pneumoniae assay in 384-well plate, 2015 international Meeting of the Microbiological Society of Korea, ***Changwon, Korea***, 15-04-2015 (***Poster***)
3. Yunmi Lee, Hyungjun Kim, and Soojin Jang, Determination of antibacterial activity of natural products against Pseudomonas aeruginosa, 2015 international Meeting of the Microbiological Society of ***Korea, Changwon, Korea***, 15-04-2015 (***Poster***)
4. Soojin Jang, Discovery of new antibacterial molecules to combat bacterial infections, CHA University College of Pharmacy, ***Sungnam, Korea***, 03-06-2015 (***Oral***)
5. Soojin Jang, Discovery of new antibacterial molecules to combat bacterial infections, Sungkyunkwan University College of Medicine, ***Suwon, Korea***, 09-06-2015 (***Oral***)
6. Soojin Jang, Validation of thiamine metabolism as an antipseudomonal drug target using oxythiamine, Scientific Symposium of the Institut Pasteur International Network, Paris, ***France***, 10-15-2015 (***Poster***)

B.4 Ongoing & new collaborations

1. Compound screening against Pseudomonas aeruginosa, Dr. Chul Min Park, Korea Research Institute of Chemical Technology, ***Korea***
2. Metabolic analysis regarding oxythiamine project, Dr. Uwe Sauer, Institute of Molecular Systems Biology, ***Switzerland***
3. The effect of efflux pumps on oxythiamine activity, Prof. Herbert Schweitzer, Colorado State University, ***USA***
4. Genetic study of Staphylococcus aureus, Prof. Alexander Horswill, University of Iowa Carver College of Medicine, ***USA***
5. Mutant generation of Staphylococcus aureus, Prof. Tarek Msadek, Institut Pasteur, Paris, ***France***
6. Morphological screening of Pseudomonas aeruginosa, Dr. Sven van Teeffelen, Institut Pasteur, Paris, ***France***
7. International consortium MetaSUB, Prof. Christopher Mason, Weill Cornell Medical College, ***USA***

Leishmania Research Laboratory

Principal Investigator: Joo Hwan No, PhD.

Research focus:

(1) Discovery of novel antileishmanial inhibitors and drug targets through phenotypic approach

(2) Identification of inhibitors targeting trypanothione synthetase of Leishmania

Laboratory members: Gyong Seon Yang, MSc. (Senior Researcher), Gahee Choi, MSc. (Researcher)

Core support members: David Shum, MSc. (ADS), Sooyoung Byun, MSc. (ADS), Nakyung Lee, MSc. (ADS), Moonhwan Kim, PhD. (CHP), Sun-ju Kong, MSc. (CHP), Inhee Choi, PhD. (CHM)

ADS: Assay Dev & Screening group; **CHP:** Chemistry Platform; **CHM:** Cheminformatics

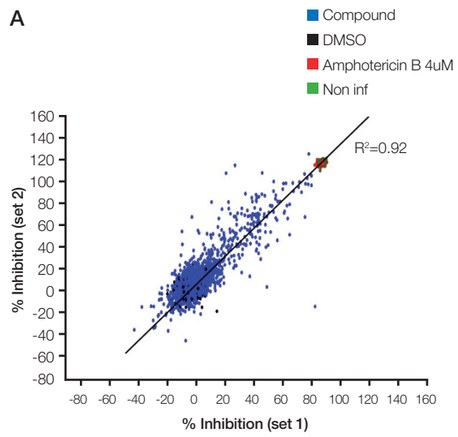
A. Research Progress in 2015

A.1 Discovery of novel anti-leishmanial compounds and drug targets through phenotypic approach

We have achieved the list of items as proposed during the early phase of the project.

1. Adapt Leishmania infected Macrophage (THP-1) model to HTS format: The assay has been adapted to 384 well plate format and confirmed with reference compounds (amphotericine B; EC50 ~ 300nM and miltefosine ~ 3μM) as well as Z' factor > 0.8
2. Pilot screening of 1,742 bioactive and FDA approved compounds: The duplicate run resulted in R2=0.92 to validate the reproducibility of the assay (**Figure 1A**). We have identified 20 new antileishmanial compounds with known mode of actions or targets. Among them, mammalian Target of Rapamycin (mTOR) inhibitors were found possess potent antileishmanial activity with EC50 values ranging from < 96nM to 4.2uM which is comparable to the activity of reference compounds (~300nM to ~3μM) as shown in **Figure 1B-F**.

A



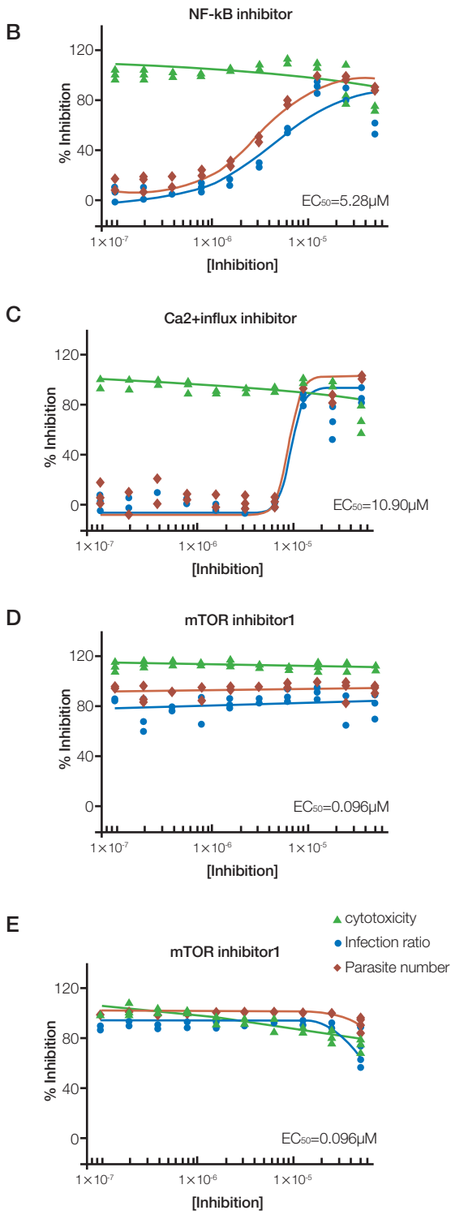


Figure 1. Validation of phenotypic Leishmania assay using pilot library and confirmation of hits with dose-responsive curves. (A) Screening of 1,742 compounds using Leishmania infected THP-1 cell based assay in duplicate with R2 values; compounds (blue), DMSO for negative controls (black), amphotericin B (red) or none infected (green) for positive controls Conformational 10 point 2 fold dilution DRC forof NF-kB (B), Ca2+ influx (C), mTOR (D,E) inhibitors; host cell viability (green), inhibition in infection ratio (blue) and parasite number (red).

3. Screening of 50,000 compounds (diversity set): We have screened 50,000 compounds and overall Z' was 0.81, validating the quality of the screening Figure 2A). 154 positives (>50% activity and <50% host cell toxicity) were identified and structural analysis identified 17 clusters and 46 singletons. 29 compounds were repurchased and dose-response activity test have confirmed that the activities of compounds ranges from EC50 of ~1μM to >10μM (**Figure 2B**).

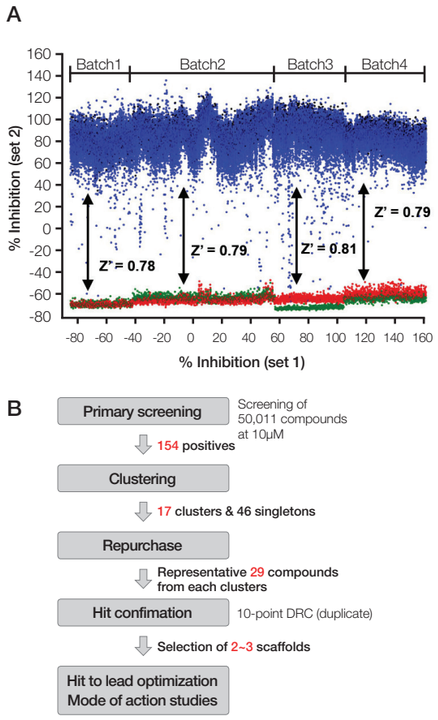
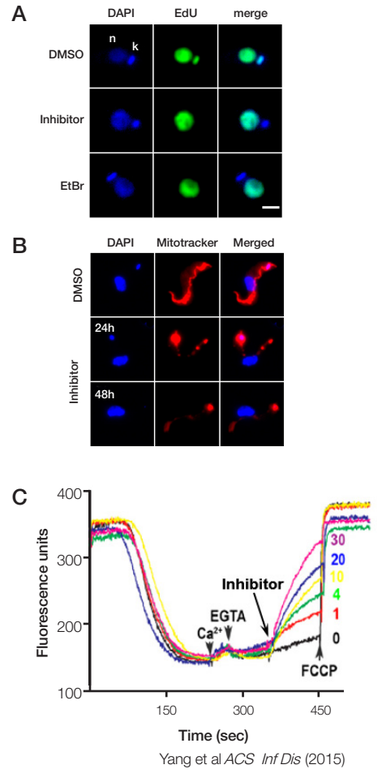


Figure 2. Selection of antileishmanial compounds by screening diversity set library. (A) Screening of 50,000 compounds at 10μM concentration; compounds (blue), positive (red) and negative controls (black and green) with acceptable Z factors (B) Selection procedures of the compounds for further investigations.

4. Establishment of kinetoplast replication assay: In order to select hits with kinetoplast replication specific activity from 50,000 compounds, we have developed click-chemistry based replication assay to specifically label newly synthesized or replicating DNA. Pentamidine, DB75 and a set of diamidines were found active in the assay which was used as a reference compounds to validate the assay. A set of identified diamidines were also found active against related kinetoplastids parasite (**Figure 3 A-C**), thus, proof of concept (PoC) in vivo efficacy test was conducted with Trypanosoma brucei (T. brucei, model organism for Leishmania) mouse model resulting in 100 % parasite clearance at 3mg/kg intraperitoneal injection (Yang et al., ACS Infect Dis, 2015).



Yang et al *ACS Inf Dis* (2015)

Figure 3. Development of kinetoplast replication and mitochondrial membrane potential assays and validation with tool compounds. (A) Visualization of newly synthesized DNA through labeling incorporated EdU with click-chemistry and effect with diamidine inhibitor; nucleus (n) and kinetoplast DNA (k). (B) Visualization of mitochondrial membrane potential and effect of identified inhibitor at 625nM after 24 and 48 hours and (C) biochemical quantification of the depolarization effect with various inhibitor concentrations (1, 4, 10, 20 and 30uM)

5. Validation of Farnesyl Pyrophsophate Synthase as a target for Kinetplastid parasite: We have attempted to reposition human osteoporosis drug, bisphosphonates, for the treatment of Kinetoplastid parasite infection. We used T. brucei as a model parasite. A series of biochemical, biophysical and molecular parsitological technique was used to validate the target with PoC experiement in vivo as shown in (**Figure 4**).

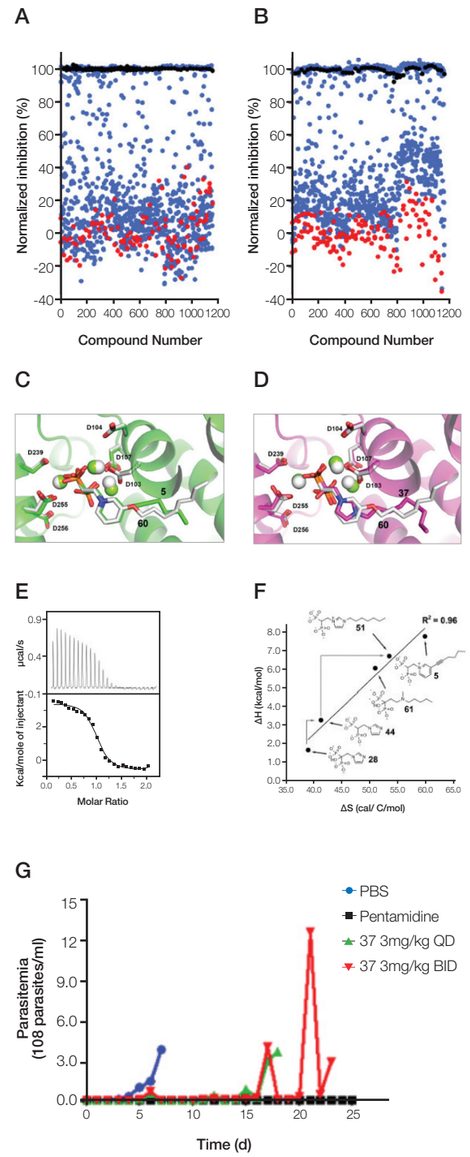


Figure 4. Inhibition of Trypanosoma brucei Cell Growth by Lipophilic Bisphosphonates: An In Vitro and In Vivo Investigation (A) T. brucei FPPS, Z' = 0.63. Red = DMSO negative control; black=positive control (15 μM zoledronate); blue = compound. 925 compounds were screened in each assay. (B) T. brucei, Z' = 0.59. Red = DMSO negative control; black=positive control (100 nM pentamidine); blue = compound. (C) Superimposition of crystallographic structures of 5 (green, PDB ID code 5AEL) and 60 (white, PDB ID code 3EFQ) bound to TbFPPS; (D) Superimposition of crystallographic structures of 37 (green, PDB ID code 5AFX) and 60 (white, PDB ID code 3EFQ) bound to TbFPPS. (E) Isothermal titration calorimetry (ITC) results for bisphosphonates binding to FPPS (F) Replacement of the 1-OH group in zoledronate by a 1-H and addition of a C7 sidechain (51) results in an increased entropic contribution to the overall binding energy. (G) parasitemia at 3 mg/kg administrated by intraperitoneal injection once (QD) and twice (BID) per day. Blue line/circles, PBS control; black line/squares, 5 mg/kg pentamidine; green line/triangles, 3 mg/kg 37 (QD); red line/triangles, 3 mg/kg of 37 (BID).

A.2 Target-based drug discovery of compounds interfering with trypanothione biosynthesis in trypanosomatids (Institut Pasteur International Network)

Trypanothione is a virulence factor for Leishmania, and the enzyme responsible for the biosynthesis is Trypanothione synthetase (TryS) which is known to be essential for the parasite survival. Through this project, we aim to identify inhibitors against TryS and use those as starting points for target based drug discovery. Currently we have expressed and purified TryS in a large quantity and developed an assay to conduct HTS against the protein.

B. Achievements

B.1 Patents (N/A)

B.2 Publications

1. Yang G, Zhu W, Kim K, Byun SY, Choi G, Wang K, Cha JS, Cho HS, Oldfield E, No JH (2015) Inhibition of Trypanosoma brucei Cell Growth by Lipophilic Bisphosphonates: An In Vitro and In Vivo Investigation Antimicrob Agents Chemother (accepted)
2. Yang G, Zhu W, Wang Y, Huang G, Byun SY, Choi G, Li K, Huang Z, Docampo R, Oldfield E, No JH (2015) In vitro and In vivo Activity of Multi-Target Inhibitors Against Trypanosoma brucei. ACS Infect Dis 1: 388-398
3. Jin JH, Park EB, Kim KJ, Kim M, Lee S, Lee KT, Yang G, Byun S, Lee N, Goo J, No JH, Choo DJ, Lee JY (2015) In vitro Evaluation of s-Triazine Derivatives for African Trypanosomiasis. Bull. Korean Chem. Soc (accepted)
1. Li K , Wang Y, Yang G, Byun S, Rao G, Shoen C, Yang H, Gulati A, Crick DC, Cynamon M, Huang G, Docampo R, No JH, Oldfield E (2015) Oxa, Thia, Heterocycle, and Carborane Analogues of SQ109: Bacterial and Protozoal Cell Growth Inhibitors. ACS Infect Dis1(5):215?221ACS

B.3 Presentations

1. Joo Hwan No, Discovery of antileishmanial compounds utilizing high content intracellular Leishmania assay, Seoul/Republic of ***Korea***, 24-October-2015 (***Oral***)
3. Joo Hwan No, Leishmaniasis: Fighting against New Emerging NTD with Bad Old Arsenal. Where do we stand?, Seoul/Republic of ***Korea***, 25-October-2015 (***Oral***)
4. Joo Hwan No, Identification of starting points for antileishmanial discovery using high content cell-based assay, Seoul/Republic of ***Korea***, 26-October-2015 (***Oral***)
5. Joo Hwan No, Gyongseon Yang, Soo Young Byun, Gahee Choi Lipophilic Analogs of Zoledronate Inhibit T. brucei by Targeting Farnesyl Diphosphate Synthase and Exhibit in vivo Efficacy, Paris/***France***, 15-Oct-2015 (***Poster***)
6. Gahee Choi, Gyongseon Yang, Wei Zhu, Yang Wang, Guozhong Huang, Soo young Byun, Kai Li, Zhuoli Huang, Roberto Docampo, Eric Oldfield, and Joo Hwan No, Biological evaluation of multitargeting diamidine inhibitors against kinetoplastida parasites, Seoul/Republic of ***Korea***, 23-October-2015 (***Poster***)
7. Gyongseon Yang, Inhibition of Trypanosoma brucei cell growth by lipophilic bisphosphonate: An in vitro and in vivo investigation, Seoul/Republic of ***Korea***, 22-Oct-2015 (***Oral***)
8. Gyongseon Yang, In vitro and In vivo Activity of Multi-Target Inhibitors Against Trypanosoma brucei, Paris/***France***, 15-Oct-2015 (***Poster***)

B.4 Ongoing & new collaborations

1. Host-Leishmania interaction, Dr. Gerald Spaeth, Institut Pasteur Paris, Paris, ***France***
2. Trypanothione synthetase inhibitor discovery, Dr. Marcelo Comini, Institut Pasteur de Montevideo, Montevideo, ***Uruguay***
3. Diamidine MoA study, Prof. Eric Oldfield, University of Illinois at Urbana-Champaign, IL, ***USA***
4. Intracellular parasite assay development, Dr. Jean-Robert Ioset, Drugs for Neglected Diseases initiative, Geneva, ***Switzerland***
5. X-ray crystallography of inhibitor-protein complex, Prof. Hyun-Soo Cho, Yonsei Univeristy, Seoul, Republic of ***Korea***

Cancer Biology Research Laboratory

Principal Investigator: Haengran Seo, PhD.

Research focus:

(1) Establishment of 3D tumor microenvironment for liver cancer therapy

(2) Development of therapies to regulate drug resistance mediated by radiation-induced endothelial to mesenchymal transition

Laboratory members: Yeonhwa Song, MSc. (Junior Researcher)

Core support members: David Shum, MSc., (ADS), Soonju Park, MSc. (ADS), Jinyoung Heo, MSc. (ADS), Constantin Radu, MSc. (SMA)

ADS: Assay Dev & Screening Group; **SMA:** Sample Management & Automation

A. Research Progress in 2015

During 2015, our research effort focused on two major programs: 1) Establishment of 3D tumor microenvironment for liver cancer therapy, and 2) Development of a biological system that monitors radiation-induced endothelial transition to mesenchymal cells, which are known to mediate resistance to chemotherapy treatment.

A.1 Establishment of 3D tumor microenvironment (TME) for liver cancer therapy

Hepatocellular carcinomas (HCC) is resistant to conventional chemotherapeutic agents and remains an unmet medical need. The 3D cell culture system is highlighted as a new method to screen for new cancer therapies. The multicellular tumor spheroid cultures are closely similar to pathophysiological gradients of in vivo tumors and subsequently an ideal screening model for new drugs. The multicellular tumor spheroids (MCTS) cultures (**Figure 1**) composed of Huh7 (HCC cells), WI38 (fibroblasts), LX2 (hepatic stellate cells) and HUVEC (endothelial cells) to replicate HCC tumor microenvironments. After several iterative attempts, the right cell ratio to grow spheroid tumors was established. The right cell combination was used to develop tumor spheroids-based high-throughput assay in a 96-well format to identify new drugs to treat HCC (**Figure 2**).

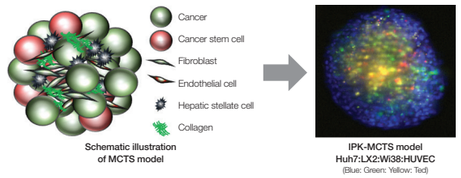


Figure 1. MCTS models: Miniature systems to mirror human tumors in vitro: HUVEC (as red), WI38 (as yellow) and LX2 (as green) were stained by VybrantTM cell-labeling solution before making the spheroid. Ultra-low attachment 96-well round bottomed plates were used for forming of MCTS. This image was obtained by Operetta HCS system.

We also used the MCTS model to investigate the effect of sorafenib on the growth of spheroids composed of Huh7 alone or MCTS. Results from this study indicate that reciprocal crosstalk between HCC and stromal cells can enhance drug resistance to sorafenib in MCTS models when compared to liver cancer cell (Huh7) culture alone, suggesting that tumor microenvironment play a key role in liver cancer drug resistance. Similar results were obtained when HCC patient tissue-derived tumor spheroids were used. Results from these studies showed that patient tissue-derived spheroids were more resistant to sorafenib (IC50 = 12.8 uM) when compared to HCC (Huh7) cell line-derived tumor spheroids (IC50 = 3.8 uM). Based on these findings, we established and validated highly reproducible MCTS?based HTS system to identify new drugs to treat HCC and other types of cancer. Once we identify compounds of interest, we can further apply whole genome-wide siRNA screening platform to identify the molecular target(s) that could be involved in cancer drug resistance.

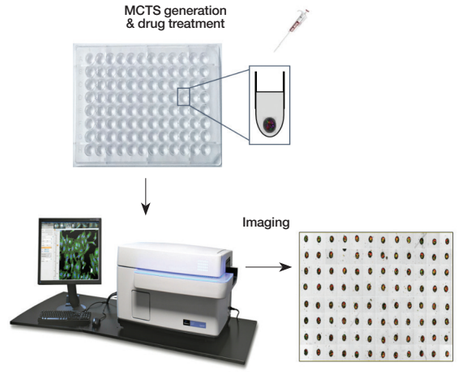


Figure 2. Schematic illustration of MCTS-based drug screening platform MCTSs for HCC drug discovery

A.2 Development of therapies to regulate drug resistance mediated by radiation-induced endothelial to mesenchymal transition

The structure of the vascular endothelium is composed of endothelial cells (EC), smooth muscle cells and a basement membrane. The endothelial cells form a continuous and uniform monolayer in normal tissues and express various receptors involved in angiogenesis such as VEGFRs, Tie-2, EGFR, PDGFR, and chemokine receptors. Activation of receptors in endothelial cells trigger several signaling cascades to regulate survival, proliferation, and invasion. Endothelial cells emerged as an additional source of fibroblasts during endothelial-to-mesenchymal transition (EndMT). EndMT is a phenotypic conversion of endothelial cells to fibroblast-like cells, which is involved in cardiac development and tissue fibrosis. In a tumor microenvironment endothelial cells generate carcinoma-associated fibroblasts supporting cancer progression. In this context, we aimed to investigate the radiation-induced transition of endothelial cells to fibroblasts-like and drug resistance in a non-small cell lung cancer to understand lung cancer fibrosis after radiotherapy and its effect on chemotherapy. Results from our studies led to the development of cell-based assay using human-derived endothelial cells (HUVEC) and stress fiber formation as an endpoint to measure the radiation-induced fibrosis (**Figure 3**) for high throughput screening.

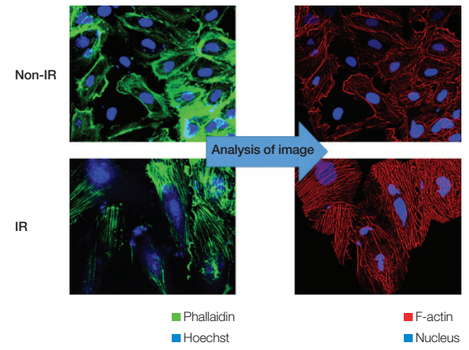


Figure 3. Development of phenomic screening platform to identify inhibitor of IR- induced fibrosis in endothelial cell

Radiation-induced fibrosis is characterized by an enlargement of cell size and increasing of actin stress fiber without serious toxicity (panel IR) in endothelial cells. Screening a chemical library of 622 compounds identified 6 hits as demonstrated in (**Figure 4**). Two compounds, CHIR-98014 and Oxaliplatin significantly reduced radiation-induced fibrosis in HUVEC.

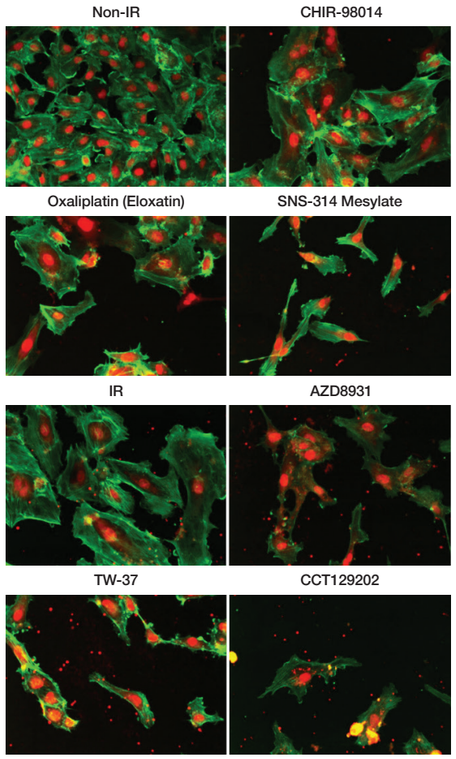


Figure 4. Images of 6 inhibitory compounds on radiation-induced fibrosis in HUVEC. Nuclei count, nuclei area, cell area and degree of actin stress fiber were measured by staining Hoechst (as red) and Phalloidin (as green).

B. Achievements

B.1 Patents (N/A)

B.2 Publications

1. Seo HR (2015), Stromal cells in tumor microenvironment: promising target for hepatocellular carcinoma therapy, Curr Cancer Ther Rev. Vol. 11, No. 2, 2015 issue. (Accepted)

B.3 Presentations

1. Yeonwha Song, Sulfasalazine inhibits cellular growth through impairment the ROS pathway in CD133+ Hepatocellular Carcinoma Cells, Korean Society for Molecular and Cellular Biology, Seoul, ***Korea***, 22-Oct-2014 (***Poster***)
2. Haengran Seo, Establishment of 3D tumor micro-environment for liver cancer therapy, Seminar, Catholic University of Korea, Seoul, ***Korea***, 19-March-2015 (***Invited talk***)
3. Haengran Seo, Establishment of novel assay system for liver cancer therapy, The 2nd collaborative symposium on drug discovery, Seoul, ***Korea***, 06-April-2015 (***Invited talk***)
4. Yeonwha Song, Establishment of Multicelluar Tumor Spheroids-Based Phenomic screening Platform for Hepatocellular Carcinoma Therapy, Korean Society for Molecular and Cellular Biology, Seoul, ***Korea***, 22-Sep-2015 (***Poster***)
5. Haengran Seo, Crosstalk between HCC and Hepatic stellate cells Contributes to the Chemoresistance of HCC in Multicellular Tumor Spheroids, Korean Society for Molecular and Cellular Biology, Seoul, ***Korea***, 22-Sep-2015 (***Poster***)
6. Haengran Seo, Assay Development for Hepatocellular Carcinoma (HCC) Drug Discovery using High Content Screening Technology, Seminar, KIRAMS, Seoul, ***Korea***, 12-Oct-2015 (***invited talk***)
7. Haengran Seo, Establishment of Multicelluar Tumor Spheroids-Based Phenomic screening Platform for Hepatocellular Carcinoma Therapy, International scientific symposium Institut Pasteur International network, Paris, ***France***, 15-Oct-2015 (***Poster***)

B.4 Ongoing & new collaborations

1. Establishment of 3D-tumor microenvironment (TME) for liver cancer therapy, Dr. Kang Mo Kim, ASAN Medical Center, Seoul, ***Korea***
2. Development of radiotherapy through regulating radiation-induced endothelial to mesenchymal transition, Dr. Yoon-Jin Lee, KIRAMS, Seoul, ***Korea***
3. Drug discovery for overcoming radiotherapy-resistance in lung cancer, Dr. Seong-Yun Jeong, and MD/Ph.D., Eun Kyung Chio, ASAN Medical Center, Seoul, ***Korea***
4. Assay development for personalized cancer therapy, Dr. Chungsu Kim, ASAN Medical Center, Seoul, ***Korea***

Core Support Structures

Technology Development Platform

Principal Investigator: Regis Grailhe, PhD.

Laboratory members: Jiho Kim, PhD (Senior Researcher), Seonhee Kim, M.Sc. (Researcher), Hyeju Eun, M.Sc. (Researcher)

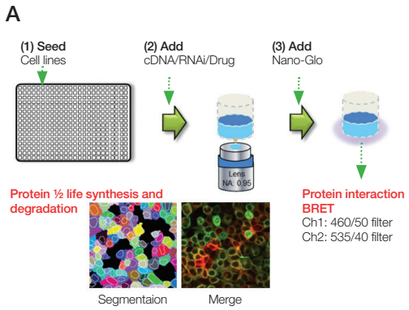
A. Capabilities

In 2015, we focused on two axes of research: (1) we developed a novel method to quantify protein-protein interaction (PPI) using RET technique in living cells. This approach which enabled measurement of protein-protein inter-distance as well as protein-protein affinities was used to characterize the protein network occurring between NFKB and TNF host cell pathway and rabies virus proteins (M & P) in collaboration with the group of Herve Bourhy from the Institut Pasteur; (2) In order to track, in live animals, pathogenicity caused by infectious agents, we developed transgenic mice reporting inflammation using novel near-infrared probes. As a proof of concept, we built transgenic mice expressing near-infrared fluorescent proteins, E2-Crimson under the control of the Glial fibrillary acidic protein (GFAP). We selected astrocytes (GFAP) promoter for their known strong induction to infection, ischemic injury, immune stimuli and inflammation. We showed that this method is reliable and can be used to track inflammation in live animals but as well in post-mortem using high resolution microscopy. Based on this successful result, we are applying this technology to track inflammation response occurring during infection.

A.1 Development of a method to quantify protein-protein interaction in living cells

Many important biological processes are controlled by protein complexes comprised of protein-protein interactions (PPIs). PPI sites represent potential targets for compounds to be developed against for modulation of specific disease processes. Furthermore, successful examples of small-molecule modulators of PPIs have been growing in recent years. Unfortunately PPI techniques are of invasive nature, lack of physiological conditions, and are not adapted to higher-throughput formats. Because of the need for proper PPI screening techniques, we developed a novel approach to quantify PPI occurring in living human cells. Our technique which combines Bioluminescent Resonance Energy Transfer (BRET) and High Content Screening (HCS) shows high sensitivity and specificity, two prerequisite for High Throughput Screening (**Figure 1A**). More importantly, we show that our method allows quantification of protein proximities and PPI relative affinities (**Figure 1B**).

A



B

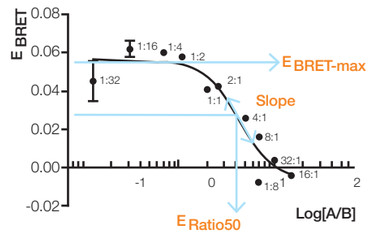


Figure 1. RET-HCS based protein-protein interaction platform. A Upon transient transfection of A and B protein of interest respectively tagged with NanoLuc and yellow fluorescent proteins, we quantify the expression level as well as the protein subcellular expression and the protein-protein interaction level. Three steps are necessary: (1) Cell seeding, (2) HCS and (3) BRET. B Upon expression of variable given A/B proteins, we were able to visualize the AB interaction (EBRET) which follow a single exponential curve. Such representation can be used to measure EBRETmax and ERatio50 respectively related to protein-protein distances and affinities.

The goal of our research program is to validate the applicability of our technology to protein-protein interactions inhibitor drug screening. In addition we aim to apply our technology to study of the innate immune signaling and monitor host?pathogen interactions using Rabies, Measles and MERS virus models. Understanding, when and how an interaction between host and microbe leads to disease opens the perspective to develop prevention strategies.

A.2 Development of small animal optical imaging technology to track inflammation

Small animal as well as ex-vivo tissular model has been an important test bed for basic and translational biomedical study followed by clinical propagation. It has enabled the study of complex disease pathophysiology in great detail at a cellular and molecular level. While all of major clinical imaging has been modified and adapted for small animal model, optical imaging technologies are still the only ones readily providing cellular and subcellular resolution. Unlike conventional methods that require euthanizing groups of animals at multiple time points, imaging techniques allow longitudinal studies in the same cohort of mice.

As of today, the most convenient and adapted solution to physiological response specific to subpopulation cells, as compared to injected molecular probes, is the use of optical imaging technology based on transgenic expressing bioluminescence or fluorescent proteins. Although few examples in the literature propose the use of infrared protein, we show that such a technique as compared to bioluminescence present numerous advantages such as the lack of substrate injection, and the dual imaging capability in vivo and post mortem. This year, we developed transgenic mice reporting inflammation using fluorescence protein near-infrared probes under the control of the Glial fibrillary acidic protein (GFAP) promoter. We selected astrocytes (GFAP) for their known strong induction to infection, ischemic injury, and inflammatory or immune stimuli. The first transgenic model was found to show a detectable reporter signal emitting specifically from the brain tissue in living animals using various small animal imaging equipment (IVIS Spectrum CT, Lumina K and FMT2500) (**Figure 2A**), as well as post mortem with subcellular resolution using microscopy technique (**Figure 2B**). Such animal models are planned to be used to perform longitudinal studies to track inflammation induced upon systemic bacterial lipopolysaccharide (LPS) challenge, as well as rabies virus infection.

A

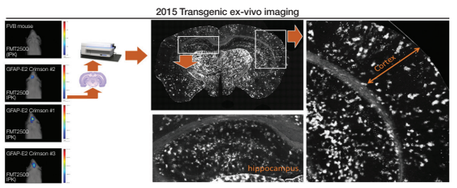


Figure 2. Generation and characterization of the GFAP-E2-Crimson. A. We developed transgenic mouse reporting inflammation using fluorescence protein near-infrared probes under the control of the Glial fibrillary acidic protein (GFAP) promoter. Using this small animal optical imaging technology allows longitudinal studies in the living mouse. The Infra-Red signal can be found localized in the brain of three transgenic mice. B. Images acquired using HCS microscope shows the brain localization using microscopy of the Infra-Red protein expressing astrocytes distributes in coronal brain sections.

B. Achievements

B.1 Patents (N/A)

B.2 Publications

1. Nam S, Chang HR, Jung HR, Gim Y, Kim NY, Grailhe R, Seo HR, Park HS, Balch C, Lee J, Park I, Jung SY, Jeong KC, Powis G, Liang H, Lee ES, Ro J, Kim YH. (2015); A pathway-based approach for identifying biomarkers of tumor progression to trastuzumab-resistant breast cancer. Cancer Lett.28:880-90.

B.3 Presentations

1. Seeing the invisible by bioluminescence energy transfer. Pohang University of Science and Technology (POSTECH), 26-10-2015, ***Korea (Invited speaker)***
2. Elucidating protein interaction network, Yearly retreat of the Infectious et Epidemiology department of Institut Pasteur, 20-10-2015, Paris, ***France (Invited speaker)***
3. Live cell screening platform to study the dynamic organization of protein-protein interaction networks, International Conference Korean Society for Molecular and Cellular Biology, 22-09-2015, ***Korea, (Poster)***
4. FLIM software for automation of lifetime based FRET analysis. KSBMB, 13-05-2015 ***Korea, (Poster)***
5. Nanoluciferase as an efficient bioluminescent resonance energy transfer donor for protein-protein interaction studies. KSBMB, 13-05-2015, ***Korea, (Poster)***

B.4 Ongoing & new collaborations

1. Role of neuronal, microglial and glial cells during rabies virus infection in the modulation of innate immune response. Interaction with three research group from the ***Institut Pasteur***; Fabrice Chretien, Herve Bourhy, and Jean Yves Coppe. ***France***.
2. Quantitative analysis of protein-protein interaction of with host target proteins, Herve Bourhy, Unit Lyssavirus dynamics and host adaptation (DyLAH), ***Institut Pasteur France.***
3. Development of FarRed fluorescent transgenic reporting using non-invasive imaging approach inflammation, Taekwan Lee, Daegu-Gyeongbuk Medical Innovation Foundation (DGMIF), ***Korea***.
4. Optimization of high-throughput phenomic analysis based siRNA microarray. Young IL Yeom, Ph.D, Korea Research Institute of Bioscience & Biotechnology (KRIBB), ***Korea***.
5. Quantitative analysis of measles virus (MV) protein-protein interaction of with host target proteins, Anastasia V. Komarova, Unit Viral Genomics and Vaccination (Group head Fr?d?ric Tangy), ***Institut Pasteur, France.***
6. Study of hepatitis type C virus (HCV) E1 protein dimerization properties and effect of TU small molecule, Marc Windisch, Hepatitis Research Laboratory, ***Institut Pasteur Korea.***
7. Quantitative analysis of MERS protein-protein interaction of with host JAK/STAT pathway, Ji-Young Min, Respiratory Viruses Research Laboratory, ***Institut Pasteur Korea.***
8. Development of Heterodimeric Topoisomerase I of Leishmania donovani PPI assay for PPI inhibitor screening. Joohwan No, Leishmania Research Laboratory, ***Institut Pasteur Korea.***

Computational Biology

Principal Investigator: Sangchul Lee, PhD.

Laboratory members: Inhee Choi, PhD (Senior Researcher), Yoonae Ko, MSc. (Researcher)

A. Capabilities

We focused our activities at improving software for in-house microscopy to improve lifetime imaging and accuracy of cell detection and segmentation. The generic functionality for the old imaging software IM3 was significantly extended by adding the analysis of the time-lapse data, which allows for the detection of aggregates for better data output. Tools for more accurate processing of images were implemented, such as additional algorithms for detection and quantification of nuclei and cells, removal of biased illumination, and exclusion of the fields from analysis. Both IMG and CHM groups were involved in the deployment of the integrated information system for analysis of biological, chemical and image processing data initiated in collaboration with Assay Development and Screening and Sample Management and Automation groups. IMG and CHM groups analyzed various cheminformatics tools to select a system appropriate for chemical structural determination, and methods and databases to analyze images, screening data from chemical and RNAi libraries.

A sponsored research project for development of the specialized software tool for the Samsung Medical Center was also initiated during 2015. The tool allows performing visualization and statistical analysis of the screening results of patient derived samples against a drug panel. The analysis takes into account genomic alterations to carry out more detailed analysis of the drugs efficiency.

A.1 Image Processing Platform

The algorithm for automated clustering of cellular morphology was proposed. In collaboration with Technology Development Platform, a method for visualization of the cells belonging to the same phenotypic clusters was investigated for standardization of cluster cells orientation and computation of averaged image. The software for analysis of the single cell data was extended by adding tools for flexible selection and analysis of cellular subpopulations. A specialized module for the FRET analysis was also implemented which allowed performing computations for every cell.

A.2 Cheminformatics

In collaboration with chemistry, our role was to cluster chemical structures from primary screening based on substructures defined by both the cheminformatics analysis program and the chemistry platform. The screening collections were analyzed based on similarities in compounds and substructures in comparison with reported biologically active compounds such as antivirals. We also conducted annotation of the FDA-bioactive compound libraries. Annotation was based on information provided by chemical vendors and public database. Structural and physicochemical properties representing 2D and 3D features of compound libraries have been updated and combined with biological activities to facilitate current and future SAR studies.

B. Achievements

B.1 Patents (N/A)

B.2 Publication

1. Nguyen TT, Tsoy YR (2015). A kernel PLS based classification method with missing data handling. Statistical papers, pp 1-15.
2. Song M, Jeonga E, Leeb TK, Tsoy Y, Kwon YJ, Yoona SJ (2015) Analysis of image-based phenotypic parameters for high throughput gene perturbation assays. Computational Biology and Chemistry, 58:192-198

B.3 Presentations

1. Yury Tsoy, Through synergy of cheminformatics, bioinformatics, image processing, and data analysis to interdisciplinary research and knowledge discovery in the context-rich environment, International Network for Data Analysis Scientific Meeting, France, 17-March-2015 (short talk)
2. Inhee Choi, Strategic HTS Compound Procurement at Institut Pasteur Korea, International Scientific Symposium - Institut Pasteur International Network, ***France***, 15-October-2015 (***invited speaker***)

B.4 Ongoing & new collaborations

1. Software development with Dr. Nam Do Hyun, Professor, Institute for Refractory Cancer Research, ***Samsung Medical Center, Korea.***

Discovery Chemistry

Laboratory members: Suyeon Jo, M.Sc. (Senior Researcher), Sunhee Kang, M.Sc. (Senior Researcher), Sunju Kong, M.Sc. (Senior Researcher), Jaeheon Lee, M.Sc. (Junior Researcher), Youngmi Kim, M.Sc. (Senior Researcher)

A. Capabilities

The chemistry group supports all programs at IPK by providing expertise in hit to lead optimization by synthesizing focused chemical compounds libraries to address SAR (Structure Activity Relationship) studies as well as optimizing drug-like activities of lead compounds. While in-vitro efficacy is screened in-house, ADME, pharmacokinetic and non-GLP toxicity studies are conducted through CROs. This year, the chemistry group was supporting the translational research activities heralded by the tuberculosis, hepatitis C, respiratory viruses and leishmania groups.

B. Achievements

* Lead optimization and nomination of one optimized lead compound from the hepatitis C virus program
* Finalizing the lead optimization for the tuberculosis program
* SAR studies for influenza pan-inhibitors program
* SAR studies for anti-leishmania program
* Quality control and structural confirmation of synthesized and imported chemical compounds
* Filed two patents to cover lead compounds for tuberculosis and hepatitis C program

Assay Development & Screening

Group Head: David Shum, M.Sc.

Laboratory members: Tae-Hee Kim, PhD (Senior Researcher), Hi Chul Kim, M.Sc. (Senior Researcher), Soonju Park, M.Sc. (Researcher), Namyoul Kim, M.Sc. (Researcher), Jinyeop Kim, M.Sc. (Researcher), Nakyung Lee, M.Sc. (Researcher), Jinyeong Heo, M.Sc. (Researcher), Sooyoung Byun, M.Sc. (Researcher)

A. Capabilities

Our role at IPK is to provide expertise in assay development and optimization as well as chemical and RNAi screening. The ADS group works in close collaboration with each investigator through all stages of: 1) assay development, 2) assay validation, 3) assay automation, 4) high-content or high-throughput screening, and 5) data analysis. Our research activities enable discovery of small molecules for drug development, biomarkers, and elucidation of biological targets for disease mechanisms. We use fully-automated robotic platforms located in BSL-2 and BSL-3 laboratories for pathogen and biological research. We validate and format assays to 96/384 well format to perform screening activities. We are also capable of screening assays covering a wide range of detection readouts including fluorescence, bioluminescence, absorbance, and imaging (confocal and epi-fluorescent). Our chemical library collection is comprised of ~400,000 molecules covering diverse sources including synthetic, natural products, extracts, and FDA approved drugs. We also use genomic platforms (siRNA and shRNA technology) to identify new targets and signaling pathways as well as uncover mechanism of actions.

B. Achievements

* Optimized and validated all screening assays for IPK discovery biology programs such bacterial (streptococcus pneumoniae, mycobacterium tuberculosis), parasitic (visceral leishmaniasis), and viral research (hepatitis B, EBOLA, MERS-CoV)
* Ran all screenings to support the Drugs for Neglected Disease initiative (DNDi-IPK) with focus on Trypanosomal pathogens with the goal to identify small molecules for therapies against visceral leishmaniasis and chagas disease
* Assay development and screening using siRNA technology on an infectious lyssavirus system for essential host determinants; a collaboration with Dr. Herv? Bourhy at Institut Pasteur Paris
* Development of an arrayed electroporation prototype was developed and successfully screened against a focused siRNA library in primary CD4+ T cells. This was a collaboration between ADS at IPK and Dr. Thierry Rose laboratory at Institut Pasteur Paris.

Successfully ran external screening collaboration programs and training courses for young and well established scientists in Korea

Automation & Logistics Management

Group Head: Constantin Radu, M.Sc.

Laboratory members: Honggun Lee, M.Sc. (Senior Researcher), Kideok Kim, M.Sc. (Researcher), Adrien Mesnard, M.Sc. (Researcher), Bumsuk Jean, B.S. (Senior Assistant), Heeyoung Na, M.Sc. (Senior Assistant), Jungjin Lee, M.Sc. (Senior Assistant), Eunhye Kim, B.S. (Senior Assistant)

A. Capabilities

The core facility's mission is to provide dependable services for all research activities for internal and external projects that help with the current activities for infectious and neglected diseases as well as oncology. We provide cutting edge technologies and platforms to principal investigators to help with their translational research programs. Our services include performing sample transfers for exploratory biology, assay development and screening campaigns, supplying de-ionized water, media preparation, reagents sanitization and compound preparation as well as an uninterrupted service to automated robotic platforms for the screening activities. In line with the Korean regulation, we collect diverse set of chemical and RNAi libraries to expand IPK's chemical libraries and manage the import of compounds from domestic and international collaborators to IPK. In order to cut cost and manage consumables efficiently, we implemented IPK warehouse as a service to all scientists at IPK to ensure sustained consumables and reagents supply. With increasing demand from internal and external projects, we are also looking at updating the current automation platforms and replacing aging infrastructure within the BSL-2 and BSL-3 environment laboratories.

B. Achievements

* Expanded IPK's compounds and RNAi libraries (Enamine, NCI Natural Extracts, Selected FDA Approved Set & Human Genome wide RNAi libraries.)
* Supported internal and external screening projects
* Managed sample libraries storage in environmentally controlled conditions
* Supported screening activities for DNDi Drug Discovery (Sanofi, Anacor, and TB alliance) and NTD Booster Drug Discovery (TAKEDA, Eisai, AstraZeneca and Shionogi).
* Established a system for recovering consumables used by the SMA group while supporting assay development and screening activities
* Updated technology tools for liquid handling to obtain optimal transfer performance
* Implemented training sessions on using IPK's different technologies for super and backup users from all laboratories
* Established an organized and transparent platform for instrument scheduling and maintenance for IPK common equipment
* Established a warehouse management system, controlling all consumables used by IPK researchers and thus reducing costs.

Animal Facility

Group Head: Regis Grailhe, PhD.

Laboratory members: Sully Lee, DVM (Junior Researcher), Sinyoung Park, M.Sc. (Junior Researcher), Seungbin Lim, B.Sc., (Researcher)

A. Capabilities

Animal facility group oversees all in-vivo experimental studies pertaining to research programs at IPK. Our expertise spans from establishing disease models to pharmacokinetic and toxicological studies in rodents under a biosafety level 2 and 3 conditions. Our experience in disease models includes tuberculosis mouse model, ovariectomy-induced osteoporosis model, osteoarthritis model, stroke model and cerebral palsy model. We successfully dosed animals via different routes such as oral gavage, intravenous, subcutaneous, intra-dermal, intramuscular, intraperitoneal, intra-nasal, intra-tracheal, intra-articular and intrahepatic. Our in-house expertise also covers small animal surgery, organ harvest, paraffin and cryo-section preparations and tissue immunostaining for confocal microscope imaging. For pharmacokinetic studies we are able to execute urine and feces sample collection as well as blood collection from retro-orbital plexus, tail vein, abdominal vein, jugular vein, saphenous vein and cardiac puncture. This year, we conducted a series of efficacy and pharmacokinetic studies to support the tuberculosis program and we are establishing in-house models for the hepatitis B and liver cancer programs. We have also renewed the IPK-IACUC committee and updated ongoing animal study protocols.

Significant Events in 2015

Symposia and Education Programs
MOU and Other Activities

January
28 MOU with Yonsei University

February
6 MOU with Armed Forces Capital Hospital

9 Visit of Economy, Science & Technology Committee of 9th Gyeonggi Province Assembly

24-25 Scientific Review

25 Visit of the Minister of Science and Technology of Ethiopia

March
24 MOU with Innovating Center for Bio-Imaging Guided Drug Discovery and Development of Seoul (iCBigD3)

April
3 Joint Workshop with Chun Lab

6 Collaborative Symposium on Drug Discovery with Asan Medical Center (AMC)

6 MOU with Asan Medical Center (AMC) and Center for Bio-imaging of New Drug Development (C-BiND)

22 Visit of Ireland Ambassador

May
11-15 High Content Assay for Target Discovery using RNAi Technology Training Program

13 MOU with Catholic University

15-17 2015 Gyeonggi Ansan Science Festival

28-29 Global Symposium on the Climate Change & Emergence of Infectious Diseases

June
3 Visit of Philippine Delegation

9 MOU with Korea Research Institute of Chemica Technology (KRICT)

9 Collaborative Symposium with Korea Research Institute of Chemical Technology (KRICT)

23 Science Council Meeting

29 2015 Summer Internship Orientation

30 2015 Fire Fighter Training

August
21 Completion Ceremony of 2015 Summer Internship Program

September
3 2015 Open House

4 Visit of Anthony Chaumuzeau (Director of Institut François Corée)

16-18 Visit of Dr. Rose-Marie Van Lerberghe, Chairman of the Board of Institut Pasteur

22 IPK-Independent session at the 27th International conference of the Korea Society of Molecular and Cellular Biology (KSMCB)

October
7 The 7th Scientific Advisory Committee

13 Visit of French Delegation

20 IPK-CICI Gala Dinner

November
2 IPK Press Conference on MERS & Ebola

Promote Science in Korea

One of the main objectives of IPK during 2015 was to promote knowledge transfer to young and established Korean scientists in academia and industry. To this end, IPK has launched four programs; a yearly educational and training program for middle and high school students around the Gyeonggi province, the 2015 drug discovery collaboration, the open house program and a high content assays for target discovery using RNAi technology program. While the middle and high school students program focused on educating the young generation about science and technology, the 2015 drug discovery collaboration, the open house program and high content screening program were directed towards life sciences professionals in academia and industry. The 2015 drug discovery collaboration was a free-of-charge offer to academic laboratories in Korea to run a pilot screening activity to promote drug discovery in academic laboratories. The open house program was an invitation to researchers from industry and academia in Korea to execute a screening campaign using IPK-chemical libraries or IPK RNAi technology. Finally, the high content assays for target discovery using RNAi technology program is a two week-long hands-on laboratory course, consisting of theoretical and practical sessions lectured by IPK, Korean and international scientists. These training courses not only provided the chance to learn the best practices of cutting-edge technologies at IPK but also an opportunity to interact between local and international participants. Due to the success of this course, Institut Pasteur Korea has decided to offer the next course in May 2016.

Scientific Symposiums - International

Global Symposium on the Climate Change and Emergence of Infectious Diseases

Institut Pasteur Korea held a global symposium on the climate change and emergence of infectious diseases on 28-29 May, 2015. IPK was honored at this event by the presence of speakers from Korea and abroad. The symposium was well attended and IPK made it an open symposium to all scientists to a wider group. The impact of global warming on the spread of infectious diseases was captured into two themes; emerging infectious diseases and intermediate hosts and therapeutics. The following speakers were invited to this meeting: Dr. Gerald Parker (Former Deputy Assistant Secretary of Defense, Department of Defense, USA, Vice President, Public Health Preparedness & Response, Texas A&M Health Science Center, USA), Dr. Quynh Mai Le (Vice Director, National Institute of Hygiene and Epidemiology, Hanoi, Vietnam), Dr.Toby Merlin, MD (Director, Division of Preparedness and Emerging Infections, National Centers for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention, USA), Dr. Jin Gwack, (Director, Climate Change Response TF, Korea Centers for Disease Control and Prevention, Korea), Dr. Haryoung Poo (Korea Research Institute Bioscience and Biotechnology, Korea), Dr. Kisoon Kim (Korea National Institute of Health, Korea), Dr. Laurent Renia (Executive Director, Singapore Immunology Network, A*STAR, Singapore), Dr. Dolores Fernandez-Garcia Senior (Institut Pasteur of Dakar, Senegal), Dr. Thomas Hoenen (National Institute of Allergy and Infectious Disease, National Instiutes of Health, USA), Dr. Woo-joo Kim (Korea University Guro-Hospital, Korea), Dr. Hyun Park (Wonkwang University, Korea), Dr. Linfa Wang (Director & Professor, Duke-NUS Graduate Medical School, Singapore), Dr. Osamu Kobayashi (Kyorin University, Japan), Dr. Chris Mok (HKU-Pasteur Research Pole, The University of Hong Kong, Hong Kong). This was a successful event where scientists, industry researchers, government officials, and policy makers exchanged ideas and discussed outlines for future preparedness.

Scientific Symposiums - Domestic

IPK- Asan Medical Center (AMC)

ASAN Medical Center

Institut Pasteur Korea held the 2nd collaborative symposium on drug discovery with Asan Medical Center on April 6, 2015, followed by MOU signing ceremony. The symposium was highlighted by presentations and discussions focusing on the latest advances in the field of cancer, bio imaging and infectious diseases. Speakers from AMC introduced their bio-imaging techniques, while speakers from IPK discussed strategies for new therapies to tackle influenza, and hepatitis B and C. This event led to new collaboration between IPK-Tuberculosis research group and Dr. Sunghan Kim at Asan Medical Center, Korea.

IPK- Korea Research Institute of Chemical Technology (KRICT)

KRICT Korea Research Institute of Chemical Technology

In June 2015, Institut Pasteur Korea had a collaborative symposium with KRICT to go over their respective research programs and capabilities of each institution. Also, the event was an opportunity for scientist to exchange ideas and discuss collaborations. Speakers from KRICT introduced Korea Chemical Bank, Virus Research and Testing Center, and Drug Discovery Platform, while speakers from IPK talked about the discovery biology program, specifically focusing on the tuberculosis program and automation solutions for high content screening. This meeting was followed by initiating two collaborations in the field of dengue fever and antibacterial resistance.

IPK- Korean Society for Molecular and Cellular Biology (KSMCB)

한국분자·세포생물학회 Korean Society for Molecular and Cellular Biology

Based on the Memorandum of Understanding agreement executed in 2013, Institut Pasteur Korea is bound to present at the satellite symposium session at the annual conference of KSMCB. The theme of IPK satellite session this year was ‘Targets to Clinical Success: The Science of Translating Basic Research into Better Health’. For this session, Institut Pasteur Korea invited three speakers to highlight drug-resistant tuberculosis and latent tuberculosis which is recognized as a major health threat to immuno-compromised and HIV-patients. IPK-invited speakers were Dr. Mohamed Hachicha, Ph.D. (Discovery Biology, Institut Pasteur Korea, Korea), Dr. Said A. Goueli, (Promega Corporation/ University of Wisconsin School of Medicine and Public Health, Madison, WI, USA), Dr. Sang-Nae Cho (Yonsei University College of Medicine, Korea) and a KSMCB guest-speaker Loraine Kay D. Cabral, M.Sc. (St. Luke’s Medical Center, Philippines). More than 100 people attended the IPK session, including students and researchers from academia, government and industry.

HCA RNAi Training Program

The course entitled “High Content Assays for Target Discovery using RNAi Technology” was held from May 11th to 15th, 2015 in Pangyo, Republic of Korea.
This newly created course provided a learning platform for those interested or working in the fields of chemical biology and functional genomics to interact and learn the best practices in setting up cell based assays using automated microscopy for RNA interference (RNAi) technologies and leading to the discovery of novel gene targets. This course is open to newcomers to RNAi as well to seasoned research scientist familiar with the technology which are highly interested in unbiased approaches towards developing cell based assays, automated microscopy, performing small focused up to genome scale screens, and analyzing large RNAi screening data sets with relevance in target discovery and cellular pathways.
Due to the success of this 2015 HCA course and its over subscription from local interest, Institut Pasteur Korea has decided to offer the course twice a year with the hope and expectations to help train the next generation scientists on cutting edge technologies in Korea and beyond. As a result, we provided the 2015 HCS training program in November 2015, focusing on the Asia-Pacific region.

Regis Grailhe

Organizer of the program/
Group Head of Technology
Development Platform, IPK

What was the planning intention for 2015 HCA training course?

The main mission of this course is to reinforce interaction with the Institut Pasteur Network. However, we are as well open to the international and domestic scientific community. Our objective is to provide researchers to access to our core technology platforms built over the past decade through these short courses enabling scientific interactions, learning opportunities, and with the ultimate goal of initiating and fostering new research collaborations. In the process, we are reinforcing the value of our institute in South Korea and within the network as an educational center on the use of cutting edge technologies to perform both target and small molecule discovery.

Please tell me what you have felt during the HCA program.

The course gave me a lot of pleasure to prepare and to give to young scientists looking to integrate cutting edge technology in their research. It was a rich experience for us to teach international trainees originating from seven different countries. I was very impressed to see that the students were very motivated and eager to learn through their active participation. In particular, the last day of the course during a case study analysis, I knew the course was a success when I witnessed the students’ true enthusiasm and interest, as they were openly debating.

Thierry Rose

Head of Networks and Signaling group, Center for Innovation & Technological Research, Institut Pasteur

There are various training programs in the IP-Network. We wonder why you decided to attend IPK's HCA training program in May 2015.

We are starting a siRNA screening campaign using HCA to identify the proteins functionally involved in IL7 signaling transduction regulating differentiation, activation, survival and proliferation of human primary T lymphocytes. The training program proposed by IP-K was the perfect introduction to build up the strategy and define the best technology fit for our project with the IP-K screening team.

Please tell me what you have felt or learned during the HCA training.

The HCA training was intense and enlightening. The workshop was covering the theoretical description and practical training of RNAi and drug screening, high content image acquisition and analysis with field experts. I really appreciated the open discussion on the strategy of screening campaign, the expectation of results, the risks and pitfalls.

This course is useful for engineers and scientists but also for PI and heads of lab as well because of the discussion about strategy and expectations. A wide screening requires a large budget and work force. I really encourage PI to attend this course before they write down a screening project in order to save time and disillusions and focus on winning paths and decisive choices: relevant cells and reads out are critical.

What do you expect from the future HCA program? Please give us the feedback of HCA program.

The HCA should stay an introduction to screening at the technical and project definition level. The program and the duration were well balanced, the format should be kept. I really encouraged the organizer to give a copy of the slides to the attendants as a PDF document. This is very important to extend the efficiency of the workshop when attendees go back to their laboratories. They sent it to all attendees and I am deeply grateful to them for that, knowing all the work put in this document.

Do you have further plans of collaboration with IPK in the future?

I really plan to keep our collaboration ongoing. Our partnership is built on complementary strengths and expertise. The first screen has established the proof of concept. We are using these preliminary results to apply to grant call to raise money for our project. We are aiming to a wider screen in order to extend the technological performance to a scientific achievement of medical interest. Interleukin-7 is tuning the survey and the response of the immune system to infections and cancer through the control of T-cell number and their level of activation. Many proteins involved in the intricate network transducing signals from the interleukin-7 receptor to the expression of gene sets controlling survival, proliferation and activation have to be discovered for a better understanding of the mechanism of the signalling transduction and for the identification of molecular causes of the autoimmune diseases, leukaemia and immunodeficiency induced by the alteration of interleukin receptor activity in T-cells.

Hae Ryung Chang

Post-doctoral researcher, National Cancer Center

What is the background behind your participation in the HCA training program offered by Institut Pasteur Korea in November?

Our lab focuses on cancer drug and biomarker discovery for precision medicine. siRNA screening is an essential tool for biomarker discovery, and we had collaborated with Institut Pasteur Korea in the past for few screening experiments. Because it was my first experience conducting such research, we heavily depended on our IPK collaborator to design the entire experiment, and as always, both parties always aim for the best results, but because of my lack of experience and technical knowledge, we had a few hiccups. Research always requires collaboration, but as we all know, it can be limited if one's knowledge is limited. At my institute, we do not have a screening facility, and most work is done manually, which could be daunting at the initial screening phase. So automated screening system is a process that we find very necessary, and I felt the need to educate myself, seeing that it will most likely be done as a collaborative function for the time being. When I heard that a new training program specifically for RNAi high content screening technology was being offered, I couldn't think of a better opportunity to learn about HCA.

Share with us your thoughts and opinions during and after the program. What was the best part of the program? Do you have any comments regarding aspects of the program in need of improvement?

The program was extremely helpful in several ways. I found that the content touched a variety of topics that are needed to have an overall understanding of RNAi high-content screening experiments. I liked how it was not only focused on the experimental part, but we had hands-on opportunity from sample preparation all the way to data processing. The lectures/seminars were also very helpful, because we were able to hear the pros and cons of such an assay system, the issues and hurdles, which all come very handy for trouble-shooting and data analysis. It was also an opportunity to hear the different perspectives, because the field I work in (cancer research) is very specific in the desired results. The facility tours were impressive and engaging, and it is always good to see how samples are handled throughout the whole process.

For being the 1st training course offered, I was surprised at how detailed and meticulous the program was structured. With that in mind, we had some bumps on the hands-on lab work, which is always the case. One issue that we faced was when manually plating cells in 384 well plates, there is a certain technique that is required, or else cells don't actually touch the bottom. We were confused as to why there were no cells on the plate, but later realized we had to spin the plates down. Also, some portions of the lab took longer than expected and felt a little rushed. I don't think anyone anticipated these issues, and can certainly be improved next time.

What would you expect to see in future HCA programs?

It would be nice to have a prepared course material or a booklet to go back to later. It was a packed training course with loads of information, and having a reference to go back to would be very nice to have for the future.

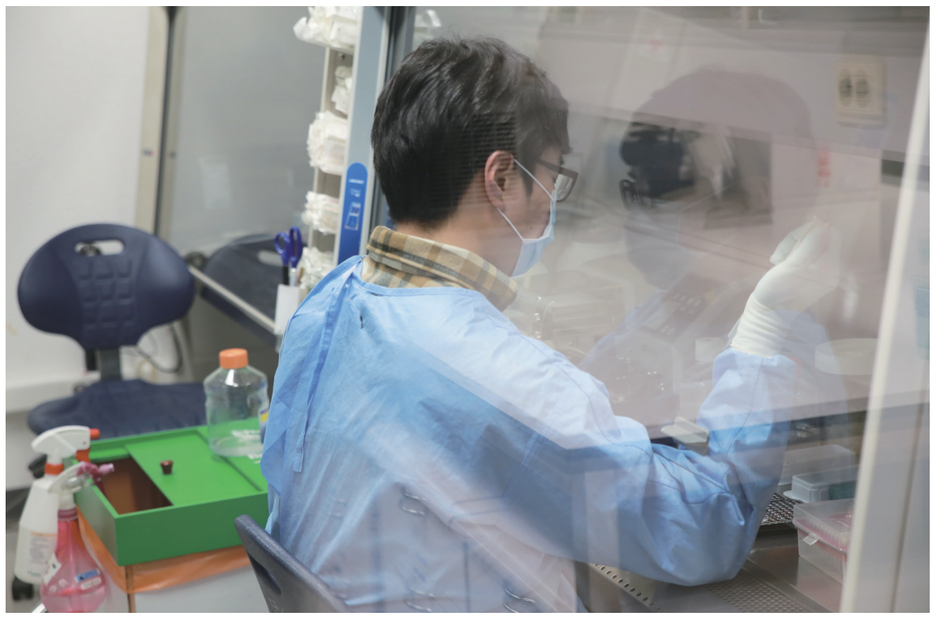
Share any comments or opinions about the Institut Pasteur Korea.

The HCA training course was a great opportunity to learn many aspects of RNAi screening, and thank you IPK for organizing this course. It was also a great experience meeting scientists from other countries and share the differences we experience as scientists, but also what we have in common. Thank you for being a wonderful host for the whole week, and for your generosity to share your expertise with all of us.

HCS RNAi Training Program

The course entitled “High Content Assays for Target Discovery using RNAi Technology” and was held from November 16th to 20th, 2015 in Pangyo, Republic of Korea.

The course was made possible by the generous financial support from the Insitut Pasteur Paris, the Institut Pasteur International Network, and in-kind contribution from GE Korea Healthcare Life Sciences. The international faculty was composed of experts from France, Republic of Korea, Russia, United Kingdom, and USA. The curriculum included theoretical lectures covering topics from cell based assay development, liquid handling, assay automation, HCS, RNAi technologies, image mining to data analysis. The course also allowed trainees to get lab experience on setting up experiments for HCS. Among the 33 applicants, 20 trainees were selected to participate in this first international course; they were either graduate students, post-doctoral research fellows or principal investigators, from 14 different affiliations in 7 countries including China, Hong Kong, France, Republic of Korea, Tunisia, USA, and Vietnam. The trainees had comprehensive interactions with faculty, with some of them formalizing potential collaborative research projects.



Regis Grailhe

Organizer of the program/
Group Head of Technology Development Platform,
IPK

You opened a new learning platform, HCS training course in November. What is the difference between HCA and HCS courses?

Both courses are very similar regarding their contents. They both address High Content Assay (HCA) and High Content Screening (HCS) as well as RNAi technologies. Though the HCS course given in November is open to applicants located in Asia-Pacific region, the HCA course given in May has no geographical limitations. One additional difference is the funding source, for which the HCA course in May comes mostly from the Institut Pasteur Network, and the HCS course originates from local sources.

What was the planning intention for the 2015 HCS training course?

Since its discovery in 1998, RNA interference (RNAi) was adapted to become a powerful tool for biological research and target discovery. Although in the past five years, High Content Analysis adoption has today significantly increased the adoption of all technologies required to perform High Content Screening, target discovery using RNAi Technology remains limited. We believe such technology requires a strong education commitment from the institution.
Our mission therefore is to provide knowledge and experience to young researchers to become familiar to core technology platforms using HCS. Such training provides important learning opportunities for the new generation of scientists who aim to develop an expertise in the field. Importantly, this course is a first and important step to be followed up with continuous support after the course.

Please tell me what you have felt during the HCS program.

The students gave good feedback about the course and showed strong motivation and determination to apply their fresh knowledge to their research. We worked very hard to make this course happen, and it is always provides satisfaction to see that the knowledge was transferred and assimilated.

What is the score that you give to the HCS training course? (Total 100 points)

90 points! There is always room for improvement. The course will always evolve based on feedback collected from students. We are looking to expend the image and data mining bioinformatics part of the course for the next years to come. We plan as well to teach low content technique for those that do not have HCS equipment.

Jose Enrico H.Lazaro

Assistant Professor, National Institute of Molecular Biology and Biotechnology, UP Diliman

What is the background behind your participation in the HCS training program offered by Institut Pasteur Korea in November?

I was invited to attend discussions with Dr. Djaballah when he came to the Philippines a few months ago. I was selected because I do research in antimalaria natural products. When the DOST made the selection for this month's trip they selected me again. In my application to IPK, I also stated that RNAi was a possible way for me to validate putative drug targets. My research involves identifying targets using comparative genomics.

Share with us your thoughts and opinions during and after the program.
What was the best part of the program? Do you have any comments regarding aspects of the program in need of improvement?

The best part were the hands-on and the data analysis. The theoretical classes showed strengths and weaknesses in a frank manner. I would suggest 1) that the exercise software be the downloadable kind; 2) that during the hands on session, the lecturer goes slowly or stays focused on a few parts of the software, since it is difficult to listen and click and mistakes happen when clicking at the same time.

Although not part of the program, the socials allowed me to gather information about the corporate culture of IPK and of Korea. I was also able to obtain insights about administrative efficiency, quality control, and biosafety. I was impressed by how IPK protects its libraries. I have made my recommendations to the DOST, to the effect that we have much to learn in the area of procurement in particular. I have emphasized that if IPK and the Philippines were to work together, organization practices and even corporate cultures should be compatible, aside from the fact that the PI's should talk and agree.

What would you expect to see in future HCA programs?

I would have liked to process our RNAi screening plates ourselves. Dr. Regis gave the data analysis all finished up, giving us an idea what the output should be. THEN, we could have done the analysis all over again to see if we could get the same outputs. That was an excellent session by the way, 20/20!

Share any comments or opinions about the Institut Pasteur Korea.

IPK lacks a bookstore! I asked Dr. Regis if I could buy a biography of Dr. Pasteur, and perhaps a jacket. I have always been a great admirer of Dr. Pasteur, and it was wonderful to see how his vision and mission are incarnated in earnest by the people of the IPK. Having spent some time in Lille, I also noticed the same dedication, the same smoothness of organization.

Sohee Lee

Researcher, Samsung Genomic Institute

What is the background behind your participation in the HCS training program that was offered by the Institut Pasteur Korea in November?

In the Samsung Genome Institute (SGI), several teams playing different roles are operated as one organized body. We proceeded with primary screening based on a database collected from patient samples and cancer cell lines, then conducted secondary screening by modularizing genes by cancer and function. Our team's current project is secondary screening of genes using a Human shRNA Library and liquid handling. We participated because it would be helpful to establish a concept and use the program for the HTS data analysis that we are dealing with, and because we can actually carry out experiments besides holding seminars.

Share with us your thoughts and opinions during and after the program.
What was the best part of the program? Do you have any comments regarding aspects of the program in need of improvement?

In contrast to general education programs that are hard to conduct as both seminar and practice, it was great that both the seminar and practice were well composed. In particular, an intelligible explanation made me have more interest in the fundamental concepts of a data network. I was able to understand faster because of an explanation via appropriate examples of quantification procedures by detection through a cell imaging process and because I was able to observe installation equipment and the test procedures right after HCS theory explanation. The composition of the program itself and the seminar was great, and asking team managers for advice about personal projects was also great. I loved that they printed out and shared feedback and related articles and answered questions about things that I couldn't understand outside of the seminar hours with the utmost sincerity.

What do you expect to see in future HCA programs?

Actually, there are not many expectations about the future because we obtained more information and knowledge than we thought, but unexpected recesses on the third and fourth days were a bit of an inconvenience. Also, insufficient publicity to domestic research facilities and universities that these programs are hosted by the IPK is another inconvenience.

Share any comments or opinions about Institut Pasteur Korea.

I didn't notice the CEO, even when he was close to me. I was impressed that the company is free to exchange ideas about research with everyone. I hope that these programs are instituted in many research facilities other than the IPK, so that lively discussions about research occur continuously.
Thank you for the good program. I hope you will get good results in your research.

Weekly Seminar Series

Institut Pasteur Korea holds weekly research seminars every Wednesday to provide a forum for interaction between scientists and to promote an exchange of the latest advances in the field of infectious disease and oncology. All IPK scientists are encouraged to present their research activities or present seminal scientific findings. Wednesday seminars are also open for attendance to Korean scientists from academia and industry when these scientists are invited as speakers to IPK to present their research activities. The following invited scientists presented their research activities at IPK: Dr. Jean-Marc Cavallion (Institut Pasteur Paris, France), Dr. Sang-Sun Youn (Yonsei University College of Medicine, Korea); Dr. Xavier Saelens (University Gent, Belgium), Dr. Samy Olivier Gobaa (Swiss Federal Institut of Technology Lausanne, Switzerland), Dr. Samuel Rulli (Global Product Manager, Qiagen), Dr. Sunghan Kim (Asan Medical Center, Korea) Dr. Ji-Chang Yoo (Catholic University Medical School, Korea), Dr. Junho Chung (Seoul National University, Korea), Dr. Alexandre Florimond (INSERM, France) , Dr. Kang-yell Choi (Yonsei University, Korea), Dr. Jin Zhong (Institut Pasteur of Shanghai ? Chinese Academy of Sciences, China), Dr. Herv? Bourhy (Institut Pasteur Paris, France) Djalal Meziane-Cherif (Institut Pasteur, Paris, France), Eun-Jeong Yoon (Institut Pasteur Paris, France), Dr. Hanki Lee (Myongji University, Korea), Dr. Chul Min Park (Korea Research Institute of Chemical Technology, Korea), Dr. Ivan Biros (GE Healthcare), Dr. Thierry Rose (Institut Pasteur Paris, France), Dr. Pillhan Kim (Korea Advanced Institute of Science and Technology, Korea), Dr. Dong-Kun Yang (Animal and Plant Quarantine Agency, Korea), Dr. Sunghoon Kwon (Seoul National University, Korea), Dr. Said A. Goueli (Promega Corp. & University of Wisconsin School of Medicine, USA), Dr. Yun H. Choe (LUCAS & MERCANTI, LLP), Dr. Yi Ni (Heidelberg University Hospital, Germany), Dr. Dimitri Lavillette (Institut Pasteur Shanghai & Chinese Academy of Sciences, China).

Internship

Research units of Institut Pasteur Korea study various topics of integrated sciences such as biology, bio imaging technology, and chemistry. Our Internship Program provides specialized hands-on experiences and advanced training opportunities to undergraduate and graduate students in related fields with the goal of helping them successfully pursue professional occupations in research environments. We offer two types of internship programs: the Summer/Winter Regular Internship Program for domestic undergraduate students, and the Irregular Internship Program for domestic and international graduate students.

The Summer/Winter Regular Internship Program is an eight-week program held during summer/winter breaks. The program is designed to expose students to the role and responsibilities of researchers and provide work experience in a relevant field at research facilities. During the internship period, students have a chance to learn basic knowledge of working in a laboratory, assist with an ongoing research project, as well as function as a team member. Since the program was established in 2009, 111 undergraduate students from various universities in Korea have been trained.

The Irregular Internship Program offers a long-term work experience as a team member at a research unit. The program is available to both domestic and international graduate students who are seeking special training in a multi-national and advanced research institute and are willing to contribute to our infectious diseases-focused research and drug discovery efforts.

Christina Ramirez

Rutgers, The State University of New Jersey
short-term intern

What do you think about IPK's internship program?

I thoroughly enjoyed my experience with IPK's internship program. Overall, I learned a great deal and met some amazing people.

Please tell me what you have felt or learned during the internship program.

As a visiting student, I was extremely grateful I was able to reside in IPK's guesthouse for the duration of the internship. I felt the transition from the US to South Korea could have been coordinated more smoothly with the HR department. I was unsure about the logistics until about a week prior to my arrival. In addition, I was advised of obtaining a domestic account and utility responsibilities after my arrival. It would have been best to learn about these things prior to my arrival to be able to coordinate more efficiently. As an intern in the Hepatitis Research Laboratory, I learned a great deal during my internship about the Hepatitis C Virus and viral pathogenesis.

What was the most valuable experience at IPK?

My most valuable experience at IPK was interacting with so many intelligent and genuine people. Not only within my laboratory but also many members in neighboring laboratories.

What do you expect from the future internship program?

The internship can be improved with an orientation strictly for interns. This may have happened for domestic students. As a visiting student, I did not receive all the necessary information at one time but rather in bits and pieces throughout the internship. It would also be improved with an increase in compensation commensurate with an intern's experience and year of study. In addition, it would be great if interns could exhibit their work at an internship symposium (poster and oral presentations). I was fortunate to present my work at the conclusion of the internship but others weren't.

Young Pyo Ryu

Dongguk University
summer intern

What was the background behind your application to the Institut Pasteur Korea Internship Program?

During the summer semester in my university, I came across a notice that said the Institut Pasteur Korea was hiring interns. I became curious about what the institute does and how math is applied in its activities, so I applied for the internship program.

Share the impressions you had of the program you completed with us.

Through the internship program, I gained my first experience in a work environment using English, and I felt that the 8 weeks was very short. The subject, machine learning, was something I never experienced before, and as I studied it, I came to the conclusion that it is applied in many areas and there is still more space for computers to evolve, and I started to develop the drive to study about it more. The institute also featured great welfare programs where I participated in weekly soccer games. The team members were nice to me, allowing me to adapt to the environment easily, and our team chief Yury always answered my questions kindly despite the busy schedule of the facility, which gave me an overall positive impression.

After the internship program end and I returned to my school semester, I wanted to learn more from Yury, but unfortunately, my school schedule did not allow me to do so. But I do feel strongly that if I am given the chance, I would love to continue studying in the program.

Share with us what you would like to see from the internship program in the future.

The chief of the team was so busy during the internship program that I was not able to make proper questions, and as I only read articles most of the time, I feel like I was not able to really learn how things were utilized in practice. I think it would be better to fully learn about one theme and one program. Also, on the last day of the program, a final presentation took place where the intern presented what he or she learned during the program, but I was a little disappointed as I felt like I was reading an article rather than studying. It was a time when 8 weeks simply felt too short. I wish I was able to learn more or had more time to spend with the program.

Sohee Kwon

Hanyang University
ERICA campus
summer intern

What was the background behind your application to the Institut Pasteur Korea Internship Program?

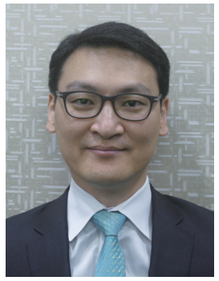
I have a keen interest in new medication development and I wanted to have practical experience in the medical-bio field. At the time, my school was conducting a collaboration program with IPK, so I applied for the intern program. My professor also recommended the program, saying that the experience would be a great opportunity to learn about the work environment and processes of an active research facility. Also, some of my friends who had undergone an internship program commented that they were able to gain knowledge that they could not learn at school, so I did not hesitate in applying. Also, as contagious diseases such as Ebola and MERSC have become social issues in many countries, I became further interested because the research facility specializes in contagious diseases. Furthermore, the fact that I would be able to work with global researchers also contributed to my decision to apply for the internship program.

Share the impressions you had of the program you completed with us.

The 2-month internship program offered me a lot more than I had expected. I was able to learn how initial substances are discovered for new medication development, actually operate the latest equipment such as the BSL-2 laboratory, and experience life in a research facility. The thing I liked the most during the Institut Pasteur Korea Internship Program was that the intern and supervisor were matched 1:1. In particular, my supervisor, Honggun Lee, did his best to teach me just a little more despite his busy work schedule. Furthermore, the chief and team members were willingly helping me by teaching me and giving me opportunities to operate the latest equipment, which constantly made me become more motivated. As all official meetings and work were implemented in English, and documents as well as emails were all written in English, I was able to foster my business English skills as well. In particular, working with the team chief, who is a foreigner, allowed me to have flexible and multiple-perspective thinking, and it also offered me an opportunity to share cultures with each other. The work life with global researchers fostered a global mind which I believe will definitely help me work with foreigners when I start a career in the future. Despite the short 2-month program, the seminars held every Wednesday allowed me to understand what research was being performed by other teams, and I was able to learn about the latest trends and technologies in the bio industry. Also, the Happy Hour held after the seminars provided a time to develop friendship with various people. On the last day of the internship program, the final presentation session was a particularly fond moment as it allowed me to reflect on what I had learned and practiced during the program.

Share with us what you would like to see from the internship program in the future.

I hope the internship program of the Institut Pasteur Korea will be a representative program that students in the fields of life science and chemicals can look up to. One thing I would like to see addressed is to indicate which department is looking for interns to allow participants to apply for departments of their liking or have picks (first pick, second pick, etc.) to allow students to have a better experience and understanding related to their major studies. Also, I think that 2 months was too short to gain practical knowledge and experience. In addition to a short-term program, designing a long-term program (about 6 months) for students on leave would be efficient for the institute which is hiring interns and an opportunity to gain in-depth knowledge for the intern.



Dongil Kim

Manager, Intern Program at Hanyang University ERICA Campus Teaching Affairs Office

What is your opinion about the Institut Pasteur Korea's internship program?

Hello, I am Director Kim Dong-il of the field education support center of Hanyang University ERICA Campus. The ERICA Campus introduced an official field education system in 2004, and since then, more students and participating companies have joined the program. At the moment, the program has nearly 300 organizations, and more than 1,000 students apply for internships.

The relationship with IPK started during the 2014 summer semester. A total of seven students (two in 2014 Summer, one in 2014 Winter, and four in 2015 Summer) from the ERICA Campus underwent the internship program, and I believe they were able to gain beneficial experiences in various aspects such as an indirect experience of corporate/social culture, promoted motivation for their career, strengthened resume building and more. A student survey also showed that the students who participated in the IPK internship program are generally satisfied with the program. In particular, students are highly satisfied with the environment, relation to their major, safety management and overall program operation.

I believe that outstanding organizations, like the Institut Pasteur Korea, participating in the fostering of future talent with practical capabilities is critical. If a few aspects can be improved, I am certain that the program will become one of the finest programs in fostering high-quality talent.

Share with us what you would like to see from the internship program in the future.

I found the following two suggestions as I reviewed the suggestions made by students and considerations of the current field education system and policies of Korea.

1) Details in Hiring Notification: There was enough information about which field of study, how many students can enroll and application requirements, but there was not enough information regarding what kind of work the students would be undertaking during the program. The work descriptions were too brief and summarized, resulting in students becoming curious as to what kind of work was being done. If future notifications would describe details of the work and work per team/department, students would better understand the program and apply with more passion.

2) Financial Aid Increase: Students spend money for transportation and meals, and the aid offered by the IPK appears to be on the short side. The amount offered is surely defined considering the educational perspectives of the program, but I believe that a slight increase will be able to provide greater satisfaction and educational effect. Currently the Ministry of Education is said to be preparing a policy to prevent the so-called "passion payment," which is a social issue regarding the exploitation of labor and field education. Announcing a defined guideline for the financial aid will become mandated to benefit both the company and students. As the Ministry of Education's policy is headed in that direction, if the Institut Pasteur Korea can reflect these future policies in its program, it will not only build a better talent fostering program but also be a social contribution program as well.

I would like to ask for your continuous efforts and passion in field education and talent fostering.

Marie Brosset

short-term intern

What do you think about IPK's internship program?

I think it's a huge opportunity for students like me to work I in a big structure as IPK, with professionals who are able to teach, and supervise our work.

Please tell me what you have felt or learned during the internship program.

During the internship I improved my experience in molecular biology, and I liked it. My supervisor was very patient and explained to me very well when I did not understand. She has been an excellent supervisor for me.

What was the most valuable experience at IPK?

What I preferred during my internship was the good relation between IPK's members and the committee each Wednesday.

What do you expect from the future internship program?

I expect a little more independence in the lab work, and an internship lasting more than 2 months.

Institut Pasteur Korea - University of Science and Technology (UST) Program

Helping young researchers and advancing the R&D culture of Korea by sharing our unique expertise and research facilities are important responsibilities of Institut Pasteur Korea. In 2014, Institut Pasteur Korea has joined a member campus of The University of Science and Technology (UST), which is a government supported graduate school specializing in fostering prospective researchers in the fields of science and technology. Institut Pasteur Korea was the first non-profit research organization to be selected as a member of 33 UST Campuses.

The Institut Pasteur Korea - UST Program aims to provide opportunities for students to participate in ongoing disease research and drug discovery projects in an international R&D environment. The program is scheduled to begin the second semester of 2016 and will offer a PhD course for two students.

Jae-in Park

Associate, UST Global Collaboration Team

Tell us what you expect from the UST-IPK campus and the significance of the campus.
IPK is the only global research facility among the 32 campuses contributing to UST. In particular, there should be no objection to saying that IP is the world's top research facility in epidemic research. With the global research network of IPK, we hope to foster leading talent not only in the epidemic field but also in the bio research field.

What is the background behind the training partnership with the Institut Pasteur of France and what do you expect from the partnership?
The world is more closely connected than it has ever has been before. Advancements in transportation and communication technologies have created an open field of competition within Korea as well as the world. In order to strengthen its research and education competitiveness, UST has established a partnership with IP with the belief that UST is in need of a partnership with a leading global research facility. With the education experiences of IP and IPK, we hope that UST students will be able to mature as leading global scientists.

What kind of international programs does UST perform? What is your speciality and what role do you undertake in the partnership with Institut Pasteur Korea?
Currently, UST is implementing various partnerships with numerous overseas institutions. About 30 to 40 students participate in training programs in universities overseas annually, and there are many international exchange programs such as Korea-Japan joint seminars. Also, to manage approximately 30% of foreign students in the institute, we implement talent attraction through agreements among institutes and in fairs. I am in charge of international collaboration, which performs overseas VIP welcoming and oversees the overall relationships with overseas institutes.

IPK is aware that UST is leading the "Korean Wave" of Korean science. Can you tell us how you feel about it and share your goals?
UST is still a young institute (11 years), and the international collaboration team is very small with only one chief and two staff members. Between 2011 and February 2015, I had to do international collaboration work by myself. As I worked alone, there were times when the work overwhelmed, but at the same time, I was able to experience the entire work process. The times when I feel most proud of what I do is when I see students trained in our school return to their countries and make contributions to their countries' scientific development. If I may share one moment that I feel most proud of from the 4 years and 4 months of my career at UST, it would be the interview with the Minister of Science and Technology of Ethiopia. Despite that country's poverty, I was impressed by the strong will and vision of the leaders of the country who never reflected its poverty. My current goal is to help students to be able to fully make use of their potential fostered from the training and education offered by UST and its affiliated institutes.

Collaborations & Memorandum of Understandings

In order to promote domestic and international collaborations, we encouraged all scientists to present their scientific findings at domestic and international conferences, including the Annual Institut Pasteur Symposium meeting in Paris. The latter event was funded mainly by Institut Pasteur Paris and the French embassy in Korea. We believe these types of international interactions will lead to short and long term collaborations between IPK scientists and Institut Pasteur Paris. We also signed new MOUs with Korean institutions to promote research collaboration within Korea, such as KRICT, Asan Medical Center, Armed Force Capital Hospital, Yonsei University College of Medicine, the Innovative Center for Bio-Imaging Guided Drug Discovery and Development of Seoul National University Bundang Hospital (iCBigD^3), and the Catholic University of Korea.

Korea Research Institute of Chemical Technology (KRICT)

KRICT
Korea Research Institute of Chemical Technology

IPK and KRICT entered into a new partnership in June 2015 by signing an MOU to develop novel therapeutics to combat infectious diseases. The two organizations aimed to strengthen joint research activities, including discovery of small molecule inhibitors of infectious agents, investigation of the modes of action of small molecule inhibitors, and development of biological assay systems. To achieve these goals, both institutes will initiate collaborative research projects, hold joint scientific conferences, and exchange researchers. They will also combine their research technologies, such as chemical libraries, ADMET assays, and high-throughput/high-content screening to accelerate drug discovery research. Two joint programs are underway and are investigating new therapies for antibacterial resistance and dengue fever.

Yonsei University College of Medicine

YONSEI UNIVERSITY
COLLEGE OF MEDICINE

IPK has initiated a partnership with Yonsei University College of Medicine by signing a Memorandum of Understanding in January 2015 that covers scientific collaborations in drug discovery research. To strengthen and expand cooperation, IPK and the Yonsei University College of Medicine have agreed to collaborate in 1) discovery of therapeutics against human diseases, 2) evaluation of efficacy and safety of novel drug candidates, 3) drug development for improving public health, 4) drug resistance studies and 5) development of imaging technologies for high content screening (HCS). Additionally, both organizations will carry forward the training of scientists in the field of bioscience and technology, the operation of a joint PhD program as well as technology sharing. Both organizations will promote human networking through researcher exchange programs, such as visiting scientists and adjunct research professorships, and to expand research activities to other scientists within the Institut Pasteur network.

Korean Armed Forces Capital Hospital

IPK and the Korean Armed Forces Capital Hospital have signed an MOU in February 2015 covering various scientific collaborations in fighting against infectious diseases, with a strategic focus on drug discovery and development of effective diagnostic methods for bacterial and viral infections. IPK and the Korean Armed Forces Capital Hospital will initiate collaborative research projects, provide support with research facilities and laboratory techniques, and exchange of scientists and scientific information. Currently, one scientist of the Korean Armed Forces Capital Hospital is training on drug discovery techniques and the high throughput/content screening technologies at IPK

Asan Medical Center (AMC) & Center for Bio-imaging of New Drug Development (C-BiND)

ASAN
Medical Center

An MOU was signed for various scientific collaborations with an aim to develop new therapeutics for infectious diseases and cancer, and also to leverage bio-imaging technologies in drug discovery research. The parties are partnering to advance the drug discovery capabilities of Korea in a global market. Under the term of the agreement, they will combine together the clinical research expertise of Asan Medical Center and the visual-based high throughput/content screening platform of IPK in order to accelerate drug discovery research. The current collaboration with Asan Medical Center is demonstrated by three ongoing joint-programs covering research activities on infectious diseases and cancer.

Innovative Center for Bio-Imaging Guided Drug Discovery and Development of Seoul National University Bundang Hospital (iCBigD^3)

SNUH 분당서울대학교병원

Institut Pasteur Korea and the Innovative Center for Bio-Imaging Guided Drug Discovery and Development of Seoul National University Bundang Hospital (iCBigD^3) signed an MOU covering various scientific collaborations with the objective to combine proprietary assets and know-how in bioimaging and drug discovery. Both organizations plan to collaborate in expert training, researcher exchange and education programs as well as efficacy and safety studies of novel drug candidates.

Catholic University of Korea

가톨릭대학교
THE CATHOLIC UNIVERSITY OF KOREA

IPK and Catholic University of Korea have signed a Memorandum of Understanding, agreeing to create new co-educational programs for their students and to develop new therapeutics to fight human diseases. The collaboration with Catholic University of Korea will be very unique to IPK as it provides IPK with a great opportunity to search natural products for potential drugs.

Education Outreach

Life Science Program

The Institut Pasteur Korea Life Science Program is a yearly program launched in 2009 as a part of the Gyeonggi Mentor Project of the Gyeonggi Provincial Government, which financially supports the program. In pursuit of encouraging local middle school students interested in science, this program offers monthly classes that include field trips and multidisciplinary activities with international researchers. The classes consist of a lecture followed by a simple experiment. They are coordinated with actual research for new drug discovery so that the students will gain knowledge of various diseases and new drug discovery, as well as learn basic science and research technology by the end of the program. Another unique feature of this program is the mentor-mentee activities in which a small group of students engages with a mentor, usually a young and enthusiastic PhD, to work on a scientific project, such as creating a scientific magazine. Throughout the mentor-mentee activities, students not only explore new scientific ideas, but also learn how to work as a team.
In 2015, 279 students in the Gyeonggi province have participated in the program, which began in 2009.

Hyun Myung Kim

Senior Researcher of Gyeonggi Province Mentor Program

What is the intention of the Gyeonggi-do Mentor Program?
The Gyeonggi Science Mentor Program is mentor-mentee matching program that has been promoting the scientific motivation and capacity of youngsters since 2004, and the program's final objective is to present a blueprint for future careers to natural science and engineering students.
It offers various programs for social contributions by science engineers and to lessen scientific inequality among the isolated through creativity/personality education for youth and region-specific science infrastructure.

What do you think of the Gyeonggi Mentor Program offered by Institut Pasteur Korea?
IPK has been offering high-quality education content and various mentor programs with special programs unique to the institute through the Gyeonggi Science Mentor Program. I am aware that the satisfaction levels of clients, a direct beneficiary, are very high, and in particular, the publication that contains details of the program offered throughout the year is impressive. I believe it is proof that IPK is passionate about the program, and the institute is making a large amount of practical effort in the program.

Dong Hoon Lee

Team Leader of Gyeonggi Province Mentor Program

Share your opinion or things you expect from Institut Pasteur Korea with us.
I would like to ask for your continuous dedication to the initiative and creative programs as IPK has always been doing. I hope that the mentor program and IPK will be able to contribute to finding the next Pasteur in Korea.

Special Invitation Program

Widely sharing the benefits of our unique capabilities and resources to foster prospective scientists and researchers is one of the important social roles of Institut Pasteur Korea. We operate a one-day program twice a year to young students from families with special needs. The program includes interesting lectures and an exciting trip to a major National Science Museum. From 2010 to December 2015, approximately 418 students and children participated in the program.

We also offer a half-day program for science teachers designed to help them develop innovative educational approaches. We discuss the latest research in the field of infectious disease and new drug discovery.

Touring the advanced research facilities and laboratories, exploring the mission and scientific achievement of Dr. Louis Pasteur, and having discussions with researchers and scientists can inspire teachers to develop new teaching methods that can enhance student performance. This program is currently being operated in collaboration with Gyeongin National University of Education, from which 60 teachers have participated since 2014.

Pasteur Junior Program

The Pasteur Junior Researcher Program, established in 2014, is a community program sponsored by congressman Jong-hun Rhee for local middle school students interested in life science, diseases and medicine. The program allows students to briefly experience the exciting field of new drug discovery research.

The program operates twice a year, in spring and fall, on Saturdays, and both students and parents are welcome to attend. Throughout the program, students can learn about different phases of new drug discovery research, as well as participate in a series of simple experiments. Parents participate in a separate program that includes a state-of-the-art research facilities tour.

The program covers basic knowledge of biology, chemistry and technology, as well as applied sciences and research. New drug discovery research is also presented. Bio-safety training and a presentation by the CEO and international scientists of the institute are also a part of the program.

In 2015, 65 students from eight local middle schools, including Hatap Middle School, Seohyun Middle School, Imae Middle School, Naejeong Middle School and Neulpuren Middle School, Pangyo Middle School, Sampyung Middle School, Saetbyul Middle School and their parents participated in the program.

Eun young Park

A parent of Pasteur Junior Researcher Program participant

What was the background of you and your child's participation in the Pasteur Junior Researcher Program?

When I visited Congressman Yi Jong-hun's office in 2014, Secretary Park Gyeong-hyeon provided me with interesting information about this program. I was told that the highly recognized Institut Pasteur Korea was providing a hands-on scientific experience to students who applied for the program. I thought it was a different program from the others, so I applied with high hopes and curiosity.

What was your impression of the program offered by Institut Pasteur Korea?

In two different aspects, the Pasteur Junior Researcher Program has proven to be an outstanding program.

The first aspect is that the program offered a chance for junior high school students to visit the secret, advanced research facility and undertook the role of being the leading figure in offering practical education in research.

The second aspect is that students are able to have a chance to learn from leading researchers in their field at the most advanced research facility in Korea rather than learning biology or chemistry in a school environment. I am certain that the various experiences offered through the program will assist in deciding future careers and foster more passion in the field of their interest.

I am also certain that it will be a fruitful time to learn about the attitude of a scientist, their knowledge and problem-solving methods.

Can you share your impressions or thoughts about the Pasteur Junior Researcher Program?

From the perspective of a parent, the content of the program has no drawbacks as the program is implemented by highly trained professionals and the main subject of the program is students. My son, who is a high school freshman, appears to have developed a great fondness for the program as time went by. Hearing him say that he wants to study life science in college, I am sure the experience here in the program has contributed to it. I also enrolled in an in-depth program of 2 hours over two sessions with students, and the sessions focused on the Ebola virus and MERSC. The sessions gave me the strong impression that the research conducted here has a close relationship with our daily lives. The rigid safety procedures also made a strong impression. From the program contents to the details of each program, the passion of each staff member was reflected, and I found myself thankful for the passion in developing this program.

I am aware that you are the chairwoman of the Pasteur Junior Researcher Program mothers' gathering, the "Spectrum." Please share the background of how it was established and also its activities and future plans.

"Spectrum" is a local community sharing group in which all students and parents can participate. The name of the group means that everyone with different characters can come together and form a beautiful ray of light with different colors. It was established as a talent donation program by parents as a way to thank the Institut Pasteur Korea, which has been practicing the sharing of knowledge with local students. Since last May, the mothers of Spectrum have been visiting a local center for the disabled, Hanmaeum Welfare Center, once a month to help in the kitchen. The free meals offered by the center made the site a popular location. Also, we have opened an internet caf? site to record and spread the activities performed by the group. At the moment, we are planning a voluntary activity in which students can participate. At the September 2015 regular meeting, we decided to register the Spectrum Students Group as a voluntary group of the Seongnam Community Service Center. I am sure that the students who participated in the Pasteur Junior Researcher Program will be able to help the local community with the teachings learned through the program.

Is there something you would like to see in the Pasteur Junior Researcher Program in the future? Also, please share us your ideas or opinions about Insitut Pasteur Korea.

I first want to thank the staff members of IPK who have invested a great amount of passion and effort in developing the Pasteur Junior Researcher Program for our students. I am certain that this will produce valuable outcomes anywhere at any time. As new sessions are held continuously, there must be difficulties that the staff has to withstand, but I would like to ask for your continuous effort to produce opportunities for students to continuously participate in the program with continuing passion and interest. I think that this would also be the hope of many other parents. Any program that offers interesting and beneficial teachings is something we all can hope for. I thank you for your interest in the activities of Spectrum. I would like to ask for your continuous interest in the group, and I pray for the advancement of the Institut Pasteur Korea.

Science Booth

Operating a science booth at festivals is a good way to promote science and make it widely accessible to the general public. Institut Pasteur Korea has operated an experiment-based science booth at festivals where visitors can walk through the process of how we fight diseases and discover new drugs. We provide mini-programs, such as simple presentations related to our research programs, followed by simple, but fun, activities led by our multi-national researchers. These programs are intended to make science interesting and enjoyable for students and families.

Since 2010, nearly 10,000 people have visited our booth. Our science booth was recognized as one of the three most popular booths among 80 organizations that participated in the 2011 Gyeonggi Science Festival.

Ki Chan Kang

Techno Doctor Project
at Gyeonggi Technopark

What is the intention of holding the Gyeonggi Science Festival?

The festival was developed to offer the citizens of Gyeonggi-do an opportunity to learn about and experience the excellence and variety of the science culture of Ansan Science Valley, and to contribute to spreading science technology and fostering creative future talent.

What is your opinion of the operation of the Institut Pasteur Korea's booth during the 2015 Gyeonggi Ansan Science Festival?

IPK operated a very active, dynamic booth during the festival.

What would be a potential goal or additional effect you wish to achieve through the science festival?

We aim to strengthen the science technology education in Gyeonggi-do by promoting the awareness of science technology among citizens and by promoting organizations, companies and universities related to science technology.

Achievements

Achievements in 2015

Scientific achievements in 2015:

- 24 scientific publications
- 65 scientific presentations (39 oral presentations (10 international in 4 countries, France, USA, Indonesia, and Saudi Arabia; and 29 in Korea)
- 26 poster presentations (11 international in 3 countries, France, USA, and Germany; and 15 in Korea)
- 7 scientific meetings organized and hosted by our institute (1 global symposium, 2 global training courses; and 4 domestic symposia)
- Wednesday weekly seminar series (23 invited speakers, 11 foreign speakers (France, Belgium, USA, China) and 12 Koreans)
- 18 issued patents (7 domestic and 11 international).
- 6 filed international patent applications
- Nomination of a lead compound from the HCV program for technology transfer and licensing

Technology for out-licensing

IPK is dedicated to developing and providing innovative technologies through collaborative opportunities including in and out-licensing, co-research, co-development and co-marketing with research institute, pharmaceutical companies and biotech companies domestically and internationally.? The hepatitis C virus (HCV) program identified unique virus entry inhibitors with a mechanism of action different from the currently used therapies. Our technology mediates synergistic effect when combined with current therapies and it is expected to lengthen treatment period in the clinic. IPK is an advanced discussions with Korean biotech/pharmaceutical industry to out-license our HCV program and discuss collaborations to advance new anti-infective compounds with new mechanism of action to treat resistant tuberculosis and hepatitis B virus infection.

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