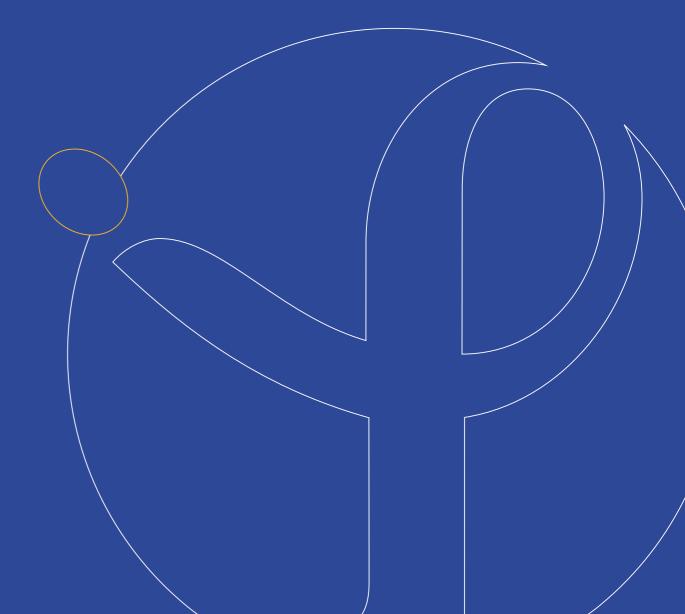
Institut Pasteur Korea 2020 Annual Report





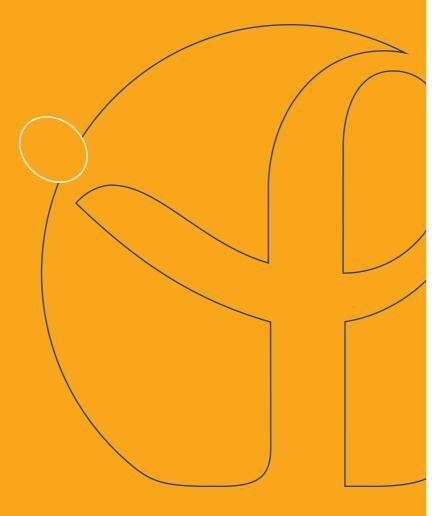
Institut Pasteur Korea 2020 Annual Report



Institut Pasteur Korea 2020 Annual Report

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For Research, For Health, For Our Future



Youngmee JEE, MD, PhD
CEO of Institut Pasteur Korea

The COVID-19 crisis has renewed our awareness of the significance of infectious disease preparedness research. It has created many challenges, but it has also provided chances for the Institut Pasteur Korea(IPK) to establish itself as a global center of excellence. The Institute successfully discovered COVID-19 therapeutics candidates by drug repositioning. The platforms developed through these efforts will facilitate research and development on future emerging infectious diseases.

In 2021, mid-and long-term research priorities for the IPK will be developed and implemented. We will enhance collaboration with leading research groups and industry partners forging successful practical application of research outcomes by commercialization.

With a strategic scientific vision centered on reinforcing relations among our partners across the Institut Pasteur International Network in the Asia-regional hub, the IPK will work closely with new partners such as the *Global Virus Network* (GVN) and the *Global Research Collaboration for Infectious Disease Research Preparedness* (GloPID-R). IPK will also continue to work with established partners such as the *Drugs for Neglected Diseases initiative* (DND*i*) and the *Global Antibiotic R&D Partnership* (GARDP) aiming to enrich educational and training programs, consolidating scientific engagement from domestic to international levels.

With the goal to establish IPK as a world leading institute in infectious disease research and therapeutics development, we will continue to expand our research portfolio in cutting-edge areas, including: viral immunology, antimicrobial resistance, and bioinformatics. To achieve this, we will focus our efforts on projects aimed at cross-fertilization of domestic and international scientific resources, skills and expertise; for example, in multi-discipline research programs such as Al-based therapeutics research with the *Pasteur International Joint Research Unit*.

The IPK can capitalize on both the availability of cooperative resources deriving from the international network, and Korea's excellent research infrastructure. Focused on scientific excellence, taking a leading role as the Asia-Pacific regional hub of infectious disease research and becoming a global partner to major international public health bodies, the Institut Pasteur Korea will deliver value for public health globally.

Fighting Infectious Disease



Mission and **Strategy**



Institut Pasteur Korea is a nonprofit research institute established through international collaboration between Korea and France, focusing on infectious diseases.

Institut Pasteur Korea (IPK) is an international research institute striving to address global health issues with a combination of cutting edge approaches in order to understand disease mechanisms and develop new treatments. By promoting multi-disciplinary projects, IPK is at the forefront of drug discovery and contributes to Korea's future.

RESEARCH

IPK is a growth engine for Korea's biomedical research industry, working successfully with biotech to develop multi-disciplinary R&D technology and translate fundamental discovery-based research to enhance public health. IPK combines front-line biology, IT, and chemistry with innovative cell-based drug discovery platforms that identify novel molecular targets for potential new therapies to treat diseases. With world-class drug discovery capabilities and a talented team drawn from all over the world, IPK scientists aim to uncover various physiological and pathological processes to devise new strategies for diagnosing, preventing and treating disease. IPK currently focuses on global infectious diseases that represent today's health challenges such as zoonotic virus infections, viral immunity, tuberculosis, antibiotic resistance, viral hepatitis, cancer, dengue, and neglected diseases, as well as preparing for emerging diseases that may impact future health needs.

EDUCATION

Education and teaching are an important part of Louis Pasteur's legacy and the establishment of IPK. The institute contributes to Korea's knowledge economy, fanning the spirit of discovery and innovation by nurturing the development of the next generation of scientists and health professionals. IPK is committed to sharing scientific expertise and technologies with early-career researchers and scientists. IPK provides a variety of educational and training opportunities throughout the year, such as internships for undergraduate and graduate students, international practical courses for select scientists with support from the Institut Pasteur International Network, and Master and Doctoral programs.

PUBLIC HEALTH

IPK is contributing to national and global public health efforts to fight infectious diseases and is at the forefront of responding to the current COVID-19 pandemic. IPK pioneered drug repositioning research and identified COVID-19 therapeutic drug candidates, for which clinical trials are ongoing in collaboration with Korean pharmaceutical companies. This work leveraged significant earlier IPK results from the 2015 Korean MERS outbreak.

INTERNATIONAL

Present on 5 continents, through 33 institutes, the Institut Pasteur International Network (IPIN) plays a major role in research, education and public health via numerous cooperation and training programs and provides a front-line response against emerging, re-emerging and endemic infectious diseases. As a hub institution, IPK plays a key role in the IPIN leading drug discovery research and serves as a bridge between Korea and global biopharma science.

Science knows no country, because knowledge belongs to humanity, and is the torch which illuminates the world.

- Louis Pasteur



2020 Summary

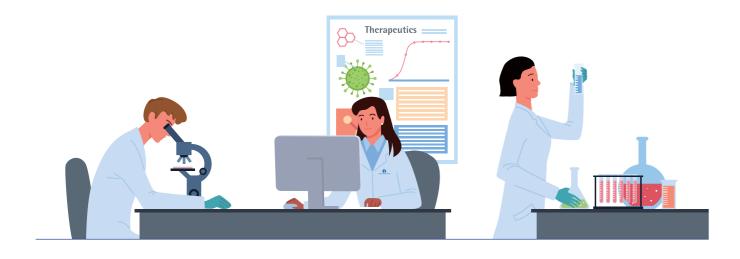
Institutional Highlights
COVID-19 Special Report





Institutional Highlights

COVID-19 evoked many challenges, but also opened the way for Institut Pasteur Korea to forge the creation of a Global Centre of Excellence.



These accomplishments placed IPK at the forefront of therapeutics research against COVID-19.

Contributing to Public health

COVID-19 Drug Repositioning Research

In 2020 IPK launched "Drug Repositioning" research in efforts to identify drug candidates among those already licensed or currently in clinical development, hoping to fast-track COVID-19 therapeutics. We discovered excellent SARS-CoV-2 antiviral activity in four drugs: nafamostat, camostat, ciclesonide and niclosamide. Through IPK's international network, clinical trials were initiated in Senegal, Australia, Mexico, etc. Making significant strides in identifying candidate drugs for COVID-19 treatment, these results were published in: Antimicrobial Agents and Chemotherapy (May 4), and the Journal of Medical Virology (Aug 7). These accomplishments placed IPK at the forefront of therapeutics research against COVID-19.



Joining Global Efforts Tackling Neglected Diseases

IPK, together with Fundación MEDINA and the Drugs for Neglected Diseases *initiative* (DND*i*), was awarded a research grant from "La Caixa" Health Research 2020 program that supports the identification of novel natural products potentially effective for treatments of leishmaniasis and Chagas disease for three years. The joint project targets to explore MEDINA's vast microbial natural product libraries' chemical diversity using the whole-cell phenotypic screening platform of IPK.

Moments to Capture

President Moon Supporting IPK's Research

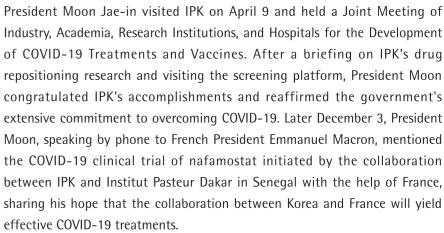




Photo Source: CHEONGWADAE(Blue House) Homepage

PARIS PEACE FORUM A Global platform for Governance projects

Presented at the 2020 Paris Peace Forum

IPK's global effort in establishing an international scientific framework facilitating COVID-19 therapeutics discovery was presented at the 2020 Paris Peace Forum (November 11-13) as one of a few selected flagship projects. Therein, IPK-CEO Dr. Wangshick Ryu delivered a live pitch titled 'Pasteurian Spirit to Fight COVID-19' highlighting the collaboration among Institut Pasteur in Korea, Senegal, and France within the trusted Institut Pasteur International Network in establishing international clinical trials.



Key Milestones 2020 Summary

Key Milestones

Feb. 11



Dr. Hangran Seo, Head of Cancer Biology Research Lab, and Mr. David Shum, Head of Screening Discovery Platform, was awarded the 2019 Gyeonggi Province Science and Technology Merit.

[COVID-19] IPK initiated the screening of licensed drugs and drug candidates, including the US FDA-approved ones, searching for their antiviral efficacy against COVID-19 using SARS-CoV previously received through scientific collaboration with HKU-Pasteur Research Pole.

[COVID-19] SARS-CoV-2* was received from the Korea Disease Control and Prevention Agency. * NCCP No. 43326

Feb. 17

[COVID-19] Based on the collaboration with IPK. Institut Pasteur Dakar received approval for the Phase III clinical trial of nafamostat in Senegal.

Jul. 27

Aug. 13

[COVID-19] Camostat was approved for the Phase II clinical trials in Mexico which will be conducted by Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán(INCMNSZ) in collaboration with IPK and its partners.

Aug. 19

[COVID-19] IPK began joint research for international Investigator-initiated clinical trials of camostat with Daewoong Pharm and KIRAMS.

[COVID-19] Based on the collaboration with IPK, INCMNSZ received approval for the Phase II clinical trial of nafamostat in Mexico.

Oct. 8

IPK, Fundacion MEDINA, and DNDi initiated global collaboration through "La Caixa" Health Research project with an aim to discover new natural products against leishmaniasis and Chagas disease.

Sep. 29



[COVID-19] Bruno Figueroa, the Ambassador of Mexico to Korea, discussed strategies for promoting Korea-Mexico collaborations to fight against COVID-19 at IPK.

Oct. 22

[COVID-19] Dr. Amadou Sall, Director of Institut Pasteur Dakar, visited IPK and discussed the latest status and strategies to facilitate ongoing clinical trials of nafamostat in Senegal.

[COVID-19] Choi Ki-young, the Minister of Science and ICT, discussed various strategies to facilitate the research in the COVID-19 Drug Repositioning Research Roundtable Meeting held at IPK.



[COVID-19] IPK joined forces with Chong Kun Dang Pharma and the Korea Institute of Radiological & Medical Sciences (KIRAMS) to promote the development of nafamostat as a COVID-19 drug.



[COVID-19] IPK presented a crossborder scientific collaboration framework facilitating the clinical development of COVID-19 therapeutics at the 2020 Paris Peace Forum. Image Source: 2020 Paris Peace Forum Online Platform

Mar. 20

Dedicated researchers and staffs are doing the best to guide

Institut Pasteur Korea to a new level of service for global health

[COVID-19] IPK reported on bioRxiv the result of the drug screening in Vero cell experiments where about 20 drug candidates were identified with strong antiviral activity against SARS-CoV-2.

May. 12

human lung cells.

[COVID-19] IPK reported on

bioRxiv that nafamostat and

camostat exhibited highly potent

antiviral efficacy against SARS-

CoV-2 in its screening based on

research labs and acknowledged its leading role in COVID-19 drug discovery at the Joint

[COVID-19] President Moon Jae-in visited IPK's Meeting with Industry, Academia, Research Institutions, and Hospitals for the Development of COVID-19 Treatments and Vaccines. Photo Source: CHEONGWADAE(Blue House) Homepage



[COVID-19] Philippe Lefort, the Ambassador of France to Korea, discussed at IPK how to further optimize the Franco-Korean collaboration to help stop COVID-19.



[COVID-19] Phase III clinical trial of nafamostat in Australia, as a part of ASCOT, began, which was enabled and conducted by the international collaboration of IPK, the University of Melbourne, and so forth.

Dec. 14



Dr. Seungtaek Kim, Head of Zoonotic Virus Lab., was awarded a commendation from the Minister of Science and ICT for his contribution to development in the bio field through advancing COVID-19 drug repositioning.

Image Source: Korea Science & Technology Fair Homepage Capture

Fighting Infectious Disease Institut Pasteur Korea 2020 Annual Report



COVID-19 Special Report

Drug Repositioning Targets COVID-19
Therapeutics

At the time of writing and unprecedented in the 21st century, the COVID-19 pandemic has witnessed over 152 million people infected with SARS-CoV-2, and more than 3.2 million deaths.

Committed to discovering fast-track COVID-19 therapeutics, IPK pioneered a drug repositioning strategy using our Biosafety Level 3 facilities to evaluate the efficacy of thousands of approved and proposed drugs including approximately 1,500 US-FDA-approved compounds. IPK's state-of-the-art high-throughput/high-content 'Phenomic' screening platform enabled accelerated identification of drug candidates that had potent antiviral activities against SARS-CoV-2 in cell-based infection assay experiments*. Based on these studies the lead-drug candidates identified: nafamostat, camostat, ciclesonide, and niclosamide, were selected for further development and/or clinical trials.

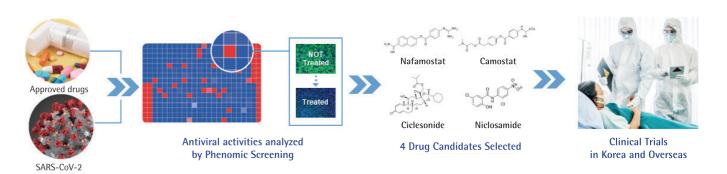
For clinical trials, the Institut Pasteur International Network consisting of 33 members located in 25 countries worldwide benefitted IPK's efforts to initiate international clinical trials for COVID-19 therapeutics. In particular, combined with the support of the Korean and French authorities IPK successfully established a bridge between Korean pharmaceutical companies and international clinical partners convergent on the goal to fast-track COVID-19 therapeutics. Thanks to these efforts, the identified drug candidates are currently undergoing Phase II and III clinical trials in Korea and overseas.

1) Jeon S, et al. Identification of antiviral drug

candidates against SARS-CoV-2 from FDAapproved drugs. (2020) *Antimicrob Agents Chemother 64:e00819-20 (Selected as Editor's Pick)*

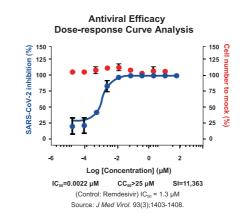
 Ko M, et al. Comparative analysis of antiviral efficacy of FDA-approved drugs against SARS-CoV-2 in human lung cells. (2021) J Med Virol. 93(3);1403-1408. (Accepted: 1 Aug 2020)

IPK COVID-19 Drug Repositioning



STOP-PRESS (April 2021): IPK's latest studies reveal selected anti-SARS-CoV-2 drug candidates are equally effective against the SARS-CoV-2 variants identified from the UK and South Africa compared to the original SARS-CoV-2 isolates*. This promising result provides hope that COVID-19 therapeutics may provide important clinical therapy recourse to emerging variants.

IPK's COVID-19 Drug Candidates



Ingredient Nafamostat mesylate Brand Name Varies, including Nafabelltan Inj. of Chong Kun Dang Pharmaceutical Corp. Original Indication Anti-coagulant and treatment for acute pancreatitis Usage Intravenous (IV) Injection Antiviral Efficacy Over 100 folds superior to remdesivir in Calu-3 cell experiments Mode of Action Inhibit TMPRSS2 in human cells (Reference: Hoffmann et al. (2020), Cell 181, 271-280)

Potent antiviral efficacy and a dual effect as anti-coagulant

Antiviral Efficacy Dose-response Curve Analysis $\begin{pmatrix} 8 \\ 8 \\ 150 \\ 125 \\ 125 \\ 125 \\ 100 \\$

Camostat

Characteristic

Nafamostat

Ingredient	Camostat mesylate	
Brand Name	Varies, including Foistar Tab. of Daewoong Pharmaceutical Co., Ltd.	
Original Indication	Treatment for chronic pancreatitis and postoperative reflux esophagitis	
Usage	Oral (Tablet)	
Antiviral Efficacy	Stronger than remdesivir in Calu-3 cell experiments	
Mode of Action	Inhibit TMPRSS2 in human cells (Reference: Hoffmann et al. (2020), Cell 181, 271–280)	
Characteristic	Strong antiviral effect and advantage of oral use	

^{*} Korea Disease Control and Prevention Agency, National Culture Collection for Pathogens, NCCP43326, NCCP43381, NCCP43382

2020 Summary 2020 Major Achievements

Antiviral Efficacy Dose-response Curve Analysis 140 120 100 80 60 40 20 0 100 Concentration [log µM] IC...=4.33 CC...>50 SI=11.56

(Control: Remdesivir) IC₅₀ = 11.41µM

Source: Antimicrob Agents Chemother. 2020 64(7):e00819-20

Antiviral Efficacy

Ciclesonide Ingredient Ciclesonide **Brand Name** Alvesco Original Indication Treatment for asthma Inhaler Usage **Antiviral Efficacy** As effective as remdesivir in Vero cell experiments Target NSP15 of SARS-CoV-2 **Mode of Action** (Reference: Matsuyama et al. (2020) J Virol. 95(1):e01648-20) Characteristic Dual effect of antiviral and inflammation treatment

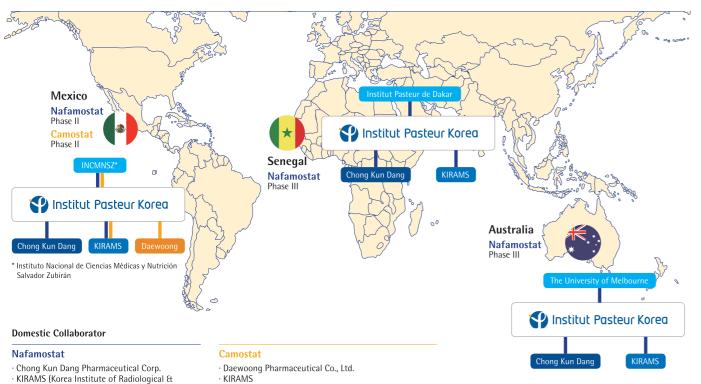
Medical Sciences)

Niclosamide

Ingredient	Niclosamide	
Brand Name	Varies	
Original Indication	Anthelmintic drug	
Usage	Oral (Tablet)	
Antiviral Efficacy	Superior to remdesivir in Vero cell experiments	
Mode of Action	Activate autophagy in human cells (Reference: Gassen, N.C., Niemeyer, D., Muth, D. et al. (2019) Nat Commun 10, 5770)	
Characteristic	Formulation changed to increase absorption into body	

International Clinical Trials Conducted by IPK

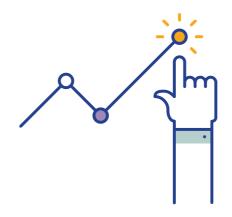
(As of 1Q 2021)





2020 Major Achievements

2020 In Numbers



Sharing Knowledge



peer-reviewed scientific publications



80% publications with international partners



Technology Transfer

90% published in openaccess journals

filed patents

issued patents

Clinical Trials



4 drug candidates



4 countries

Funding Received



10 newly funded projects



20 continually funded projects



5,493 mio. KRW



75% internationally issued patents



3 out-licensing agreements

Research Collaboration



5
memorandum of understanding agreements



19 joint research agreements



18 material transfer agreements



sponsored researches

2020 Institut **Pasteur** Korea

IPK's **Drug Discovery Approach**

Translational Research

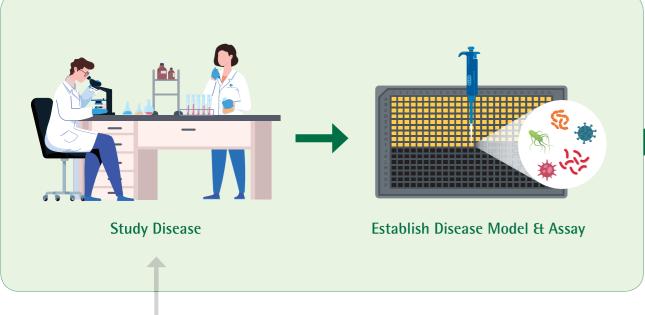
Translational Research Division evaluates the drug efficacy of thousands of compounds through the cell- and image-based screening operated in the BSL-2 and BSL-3 laboratories and identifies novel candidates. The identified candidates are further developed to have more drug-like properties by SAR, toxicity, and lead optimization studies and their invivo efficacy is evaluated in animal experiments.

. Screening Discovery Platform

. Animal Facility and Lab Support

. Technology Development Platform

. Medicinal Chemistry



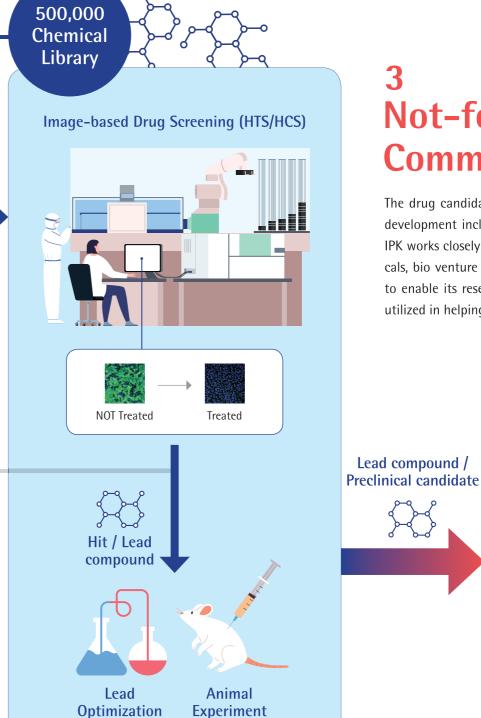
Target Identification

Discovery

Biology

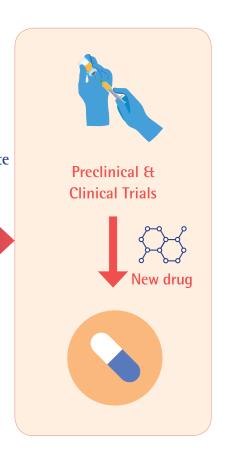
Discovery Biology Division studies diseases and pathogens, from which researchers establish disease models and assays for drug screening. Additionally, target identification and studies for the mechanism of action (MoA) are conducted for the candidates identified from screening. . Zoonotic Virus Lab

- . Viral Immunology Lab
- . Applied Molecular Virology Lab
- . Tuberculosis Research Lab
- . Antibacterial Resistance Lab
- . Leishmania Research Lab
- . Cancer Biology Research Lab



Not-for-profit **Commercialization**

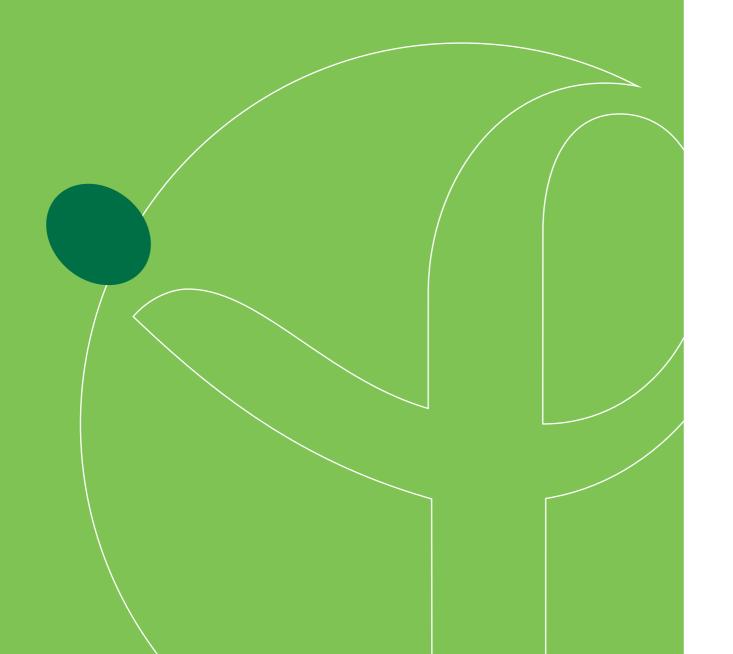
The drug candidates are transferred for subsequent development including preclinical and clinical trials. IPK works closely in collaboration with pharmaceuticals, bio venture companies, academia and hospitals to enable its research technology and output to be utilized in helping the patients in need.



Fighting Infectious Disease 16 Institut Pasteur Korea 2020 Annual Report

2020 Research Highlights

- **Oiscovery Biology**
- Translational Research
- Bio Start-up Incubation





For diseases like COVID-19, we ideally need orally available drugs capable to prevent progression to severe disease or death.



Four weeks after obtaining the SARS-CoV-2, we identified 24 drug candidates for treament of COVID-19.



Our paper on COVID-19 drug repositioning* was cited 280 times as of May 12, 2021.

* Jeon et al. (2020) Identification of antiviral drug candidates against SARS- CoV-2 from FDA -approved drugs. Antimicrob Agents Chemother.
64:e00819- 20 (Selected as Editor's Pick)



We have supported more than 70 domestic and international organizations in their efforts of COVID-19 drug development.

Zoonotic Virus Laboratory

Prepared and ready to respond to emerging viruses!



We study viruses, especially emerging viruses such as SARS-CoV-2 and Zika virus. We believe being prepared is the best way to address outbreaks and this was demonstrated in our recent response to the COVID-19 pandemic. Although we are focusing on the coronaviruses now, our research scope covers other viruses as well including mosquito-borne flaviviruses (e.g. dengue and Zika viruses) and tick-borne bunyaviruses (e.g. SFTS virus). Our ultimate goal is to understand the biology of these viruses and to develop therapeutic interventions (e.g. small molecule inhibitors and therapeutic antibodies).

Global Challenges

Precipitated by the pandemic, our major research challenge in 2020 has been the discovery of drugs capable to intervene as therapeutics for COVID-19 treatment. Although several COVID-19 vaccines were successfully developed very quickly, we do not have effective treatment options for COVID-19 except for monoclonal antibodies and some steroid drugs. For diseases like COVID-19, we need orally available drugs which can be used for patients with mild COVID-19 in order to prevent progression to severe diseases and deaths.

Flavivirus (e.g. dengue and Zika viruses) and bunyavirus (e.g. SFTS virus) infections also need development of therapeutics since these viral infections are already a substantial burden in public health and likely to be epidemic in the near future. Currently, no therapeutic intervention is available for these diseases.

Fighting Infectious Disease

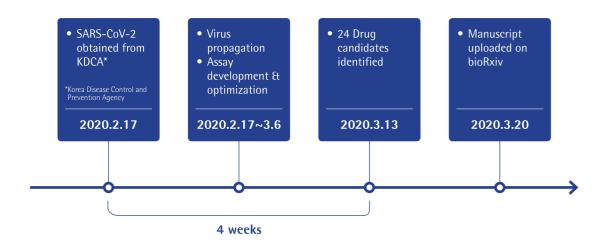
2020 Research Highlights
Zoonotic Virus Laboratory

2020 R&D PROGRESS

From MERS to SARS we've learned a lot...

Our main progress in year 2020 was the drug repositioning study in response to the COVID-19 pandemic. We were very successful in this effort in part because we were well prepared by working on MERS drug development (small molecule inhibitors and monoclonal antibodies) even before the COVID-19 pandemic. Although working with BSL-3 pathogens such

as MERS-CoV was not easy, our efforts paid back. MERS and COVID-19 are similar to each other in that both diseases are caused by the same group of coronaviruses. The knowledge and experiences that we had gained in this MERS research program had prepared us well for the unprecedented COVID-19 global challenge.



SARS-CoV-2 is just one episode in a long saga. Once it is overcome, we will still continue to prioritize studies on zoonotic viruses because the threat of future pandemics remains.



R&D HIGHLIGHTS

Beyond discovery the objective is to assure delivery to those in need

We were faster in drug repositioning study than any other research group in the world in our scale of drug screening. Some drug candidates (i.e. nafamostat, camostat, niclosamide, ciclesonide) that we identified are being further developed in multiple clinical trials in collaboration with pharmaceutical companies. Our

successful drug discovery efforts have drawn a huge global attention to our research program, which led to numerous research collaborations to support COVID-19 drug discovery of other research institutions and pharmaceutical companies.

Our ultimate goal is to understand biology of these viruses and to develop therapeutic interventions (e.g. small molecule inhibitors and therapeutic antibodies).



Photo Source: CHEONGWADAE (Blue House) Homepage

66

We feel great responsibility during the current COVID-19 pandemic and have had a privilege to serve the people, our country, and the global community with our own research. We will continue to devote ourselves to understand underlying biological principles of emerging viral pathogens to come up with better therapeutic options.

99

Dr. Seungtaek Kim, Head of Zoonotic Virus Lab



Immune system is a central part of the natural defense we have against viral infection. Critically we need to understand how to support and bolster immunological defense against disease.



According to WHO, 13.9% (7.7 million) of global total death was due to infectious diseases in 2019.



11 times higher

Approximately, 11 times higher COVID-19 in-

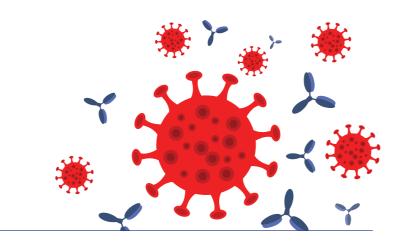


10

10 months, Record-breaking speed of COVID-19 vaccine development and approval for use

Viral Immunology Laboratory

Harnessing immunity to protect people from infectious diseases!



The Viral Immunology Laboratory (VIL) aims to understand immunological principles underlying response to viral infections and vaccinations in effort to develop interventions for immune-associated diseases including infectious diseases and cancer. Specifically, VIL studies molecular and cellular mechanisms of immuno-pathogenesis during viral infections such as influenza virus and SARS-CoV-2 (COVID-19 virus). We are particularly interested in how the innate immune system bolsters antibody and T cell responses, and seek to establish the basis for preventive and therapeutic strategies to modulate the strength and longevity of immune protection.

Global Challenges

The COVID-19 pandemic has catalyzed the rapid development and emergency use of preventive vaccines based on classical and novel vaccine platforms. However, questions like 'how do these vaccines work?' and 'what is the best vaccination strategy to gain protection from variants?' remain. Likewise, understanding the impact of emerging viral infections on disease progression and immunity is critical to develop effective therapies. VIL aims to answer these important questions by performing immunological studies including the analysis of innate and adaptive immunity in the context of animal models for basic research, and clinical studies for translational research.

2020 R&D PROGRESS

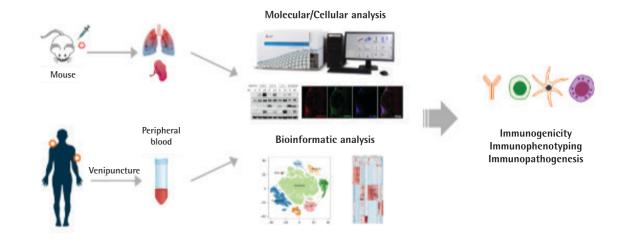
New IPK research program launched to tackle infectious diseases from an immunological perspective

In the spring of 2020, the VIL was newly created at IPK with the mission to establish basic and translational research programs focused on understanding immune response to viruses.

A novel immunological function of local damage upon vaccination, in addition to the immune-stimulatory effect of microbe-derived patterns, has been investigated in the lab. Our study highlights the role of molecular pathways triggering inflammation and immune response to the administration of vaccine adjuvant. We are currently examining the role of this pathway in viral infection-generated immune response and pathogenesis.

Serendipity brought the founding of our team at IPK to

be concurrent with the emergence of the SARS-CoV-2 pandemic and the imperative to adapt our research strategy to help in the fight against COVID-19. In active collaboration with IPK's Zoonotic Virus Laboratory, we have tested antiviral drug candidates in cell lines and animal models. Moreover, in collaboration with the Korea Cancer Center Hospital and Asan Medical Center, we began translational studies analyzing immunogenicity and immunological longevity of COVID-19 vaccine response in humans. For these studies we are using advanced multiplexed flow-cytometry technologies allowing transcriptomics and immune-profiling of animal models and human samples from clinical studies.



R&D HIGHLIGHTS

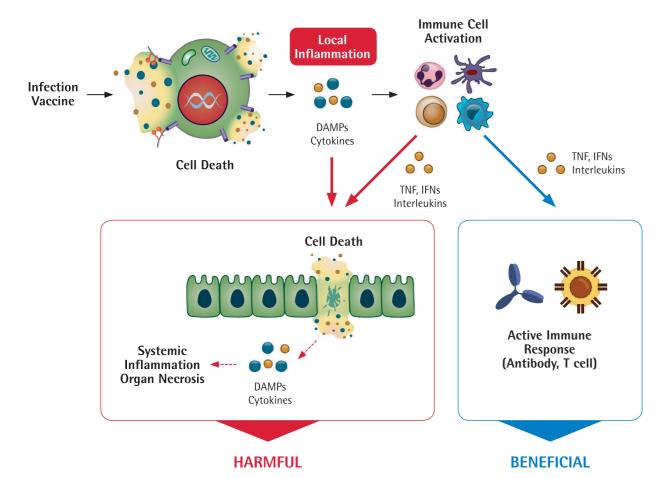
Selected publications include discovery of the role of damage-response in triggering inflammation, characterization of adjuvant-induced honed immune response, and identification of virucidal peptide activity:

- We interrupt your regular programming to bring you necroinflammation. 2019 Cell Death and Differentiation
- Squalene emulsion-based vaccine adjuvants stimulate
 CD8 T cell, but not antibody responses, through a
 RIPK3-dependent pathway. 2020 Elife

A collaborative study on screening and developing antiviral peptides to Zika and Dengue viruses was accepted for publication in 2021.

• The amphibian peptide Yodha is virucidal for Zika and dengue viruses. 2021 *Scientific Reports*

Also, VIL secured research grant awards for: 'New investigator support' and 'Source technology development in response to newly emerging viruses' from the National Research Foundation of Korea, and 'Screening antiviral and anti-inflammatory agents from natural substances' from the National Institute of Biological Resources.





What can immunology provide us? Tremendous advances in science and technology have brought immunological research to flourish. In the past, people used to think immunology equaled and was merely limited to the vaccine. However, now immunological concepts are all around us; not just in the vaccine, but also in diagnosis, immune-modulatory drugs, antibody-therapy, cell-therapy, microbiome and so on. As an immunologist, my goal is to utilize my expertise in immunology to fight against infectious diseases and contribute to wellbeing and global health equity.



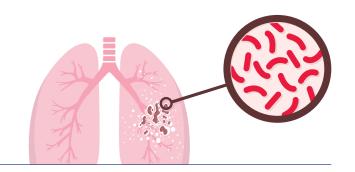
Dr. Eui Ho Kim, Head of Viral Immunology Lab



World Health
Organization seeks
to put an end to the
global TB pandemic
by 2030. However,
the emergence of
drug-resistant
strains casts a
shadow of doubt on
this ambitious target.

Tuberculosis Research Laboratory

Developing tools to help the discovery of new drugs against tuberculosis



With an estimated 1.4 million deaths per year worldwide, tuberculosis (TB) remains a major challenge for public health. While largely affecting developing countries, this disease also plagues three economic superpowers: India, China and Russia. Despite considerable improvements due to the efforts of the World Health Organization seeking to put an end to this pandemic by 2030, the emergence of drug-resistant strains cast a shadow on this ambitious target. Introduction of new drugs is still largely needed, together with methodologies to reduce the duration of the therapy. In this context, the Tuberculosis Research Laboratory (TRL) is committed to providing the field with means to facilitate the discovery and evaluation of new drugs against TB.



Long and laborious antibiotic treatment (1 to 2 years) needed for drug-resistant TB.



62% without treatment

62% of drug-resistant TB patients do not receive treatment.



30% treatment rate

Low treatment success rate (30%) for the extensively drug-resistant (XDR) infections

Global Challenges

TB is caused by *Mycobacterium tuberculosis* (*Mtb*) species. Working with these bacteria is made tedious by their slow growth rate (2 to 3 weeks to get colonies on a plate, cf. 1 day for *Escherichia coli*) and requires highly specialized containment facilities (BSL-3). These constraints, together with the low market profitability of TB drugs, discourage pharmaceutical companies from pursuing TB drug discovery programs. As part of the solution addressing this shortfall, TRL develops assays and methods for identification of new molecules active against *Mtb*, and the corresponding target mechanisms that could be exploited therapeutically.

2020 Research Highlights

Tuberculosis Research Laboratory

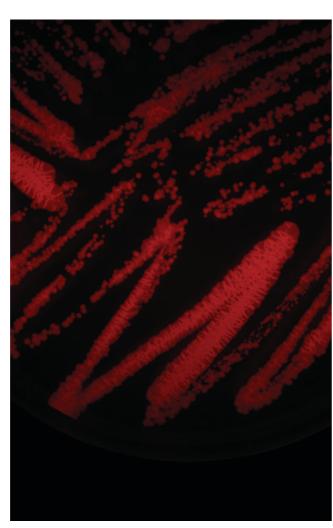
2020 R&D PROGRESS

Fighting TB on three fronts

Drug discovery: in 2020, we focused on the multifunctional protein FolB, which has been shown to be essential for bacterial growth by deletion and mutagenesis studies. Following purification of the native enzyme, we developed a miniaturized assay allowing monitoring of the aldolase activity by fluorescence, in a micro-well plate format (96, 384-well plates). The assay was used to screen about 9,000 compounds, allowing the selection of a handful of hits that were re-synthesized for confirmatory studies, together with a couple of derivatives.

Pre-clinical models: we assessed the *Kramnik* mouse model in order to test the capacity of compounds to diffuse in and sterilize necrotic lesions, for which blood circulation is absent. To support this project, we used a unique in vivo animal imaging method developed in collaboration with IPK's Technology Development Platform (Dr. Regis Grailhe).

New first-in-class anti-TB drugs will come from innovation in new pre-clinical models and advances in cellular immunology. Cellular immunology: we continued the investigation of the Max Planck Institute (MPI) cells, which are murine embryonic liver cells self-replicating in the presence of granulocyte macrophage stimulating factor (GM-CSF), in collaboration with Plymouth University in UK (Prof. Gyorgy Fejer). We successfully prepared new cell lineages from C3HeB/FeJ (Kramnik), IFN- α/β receptor K0 (Ifnar1tm1Agt), as well as hCD68GFP mice. These cells will help better understand and counteract how Mtb evade our immunity.



Mycobacteria expressing Crimson far-red reporter, as seen by fluorescence imaging

R&D HIGHLIGHTS

Against TB, share and conquer

We published the results of our findings describing the antitubercular potential of thienothiazolocarboxamide (TTCA) series together with the chemistry team of IPK, highlighting a new scaffold with activity in vivo against a murine model of TB (*Bioorg Med Chem.* 2020 Dec 1;28(23):115797).

A book chapter highlighting the importance of phenotypic screening for the field of TB drug discovery was published (Phenotypic Drug Discovery. B. Isherwood and A. Augustin, Royal Society of Chemistry: 198-216).

We also gave 2 oral presentations (virtual meeting) about TB to students and researchers in India.

Lastly, we developed a web-based application for the management of multi-well plate layouts, called PlateEditor, and made it freely available online to everyone (https://plateeditor.sourceforge.io/). This tool has been designed to fasten the process of data analysis for experiments performed in multi-well plates, which we use frequently in our laboratory.



Overview of the PlateEditor web application

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The path to a TB-free world by 2030 is hindered by rushing torrents made of social and economic issues. Our team can help by bridging academic research to pharmaceutical companies, thus making the crossing easier and safer.

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Dr. Vincent Delorme, Head of Tuberculosis Research Lab



The only way to mitigate the threat of antibiotic resistance is by understanding bacterial physiology and the underlying fundamental mechanisms.



With the availability of antibiotics (c.1940's) average life-expectancy increased by 30 years during the 20th century.



100 trillion USD

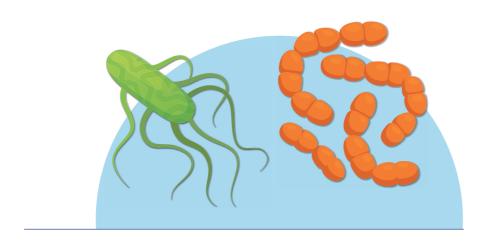
The O'Neill report estimates that by 2050, annual mortality caused by antibiotic resistance will be over 10 million and cost globally over \$100 trillion USD.



According to the Pew Trust latest figures of 43 candidate antibiotic molecules in development, 19 have potential to be active against Gram negative "ESKAPE" bacteria. However, only 1 in 4 represents a new mechanism of action, and none of these is active against *Gram negative* bacteria, or so-called "critical threat pathogens" identified by WHO.

Antibacterial Resistance Laboratory

Fighting against antibiotic-resistance through understanding bacterial physiology



Antibiotic resistance is a global public health threat estimated to risk a mortality rate of over 10 million people a year by 2050. The Antibacterial Resistance Laboratory (ARL) team aims to contribute to the solution of this emerging infectious disease problem by discovery of new antibacterial agents and targets. Our experimental approach is distinguished by our focusing priority on understanding bacterial physiology and fundamental mechanisms of antibiotic resistance.

Global Challenges

Antibiotic resistant bacteria are rapidly spreading all around the world, and only immediate action is likely to prevent the worst-case scenario: a *post-antibiotic era*. In order to effectively combat antibacterial resistance, a more comprehensive knowledge on bacterial physiology and antibiotic resistance is required, opening the way to new anti-bacterial therapeutics.

2020 R&D PROGRESS

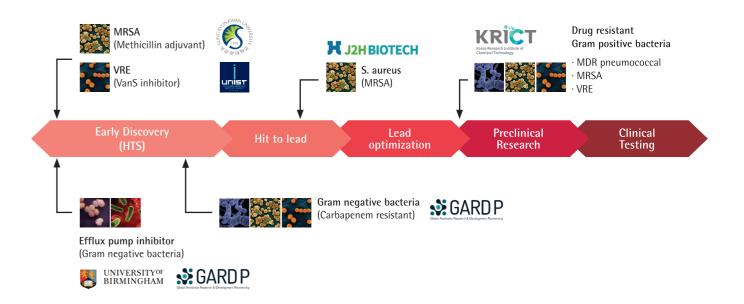
Global collaboration to fight antibiotic resistance.

Discovery of new antibacterial molecules:

ARL discovered new antibacterial molecules against Streptococcus pneumoniae, Staphylococcus aureus, Pseudomonas aeruginosa, Klebsiella pneumoniae, and Acinetobacter baumannii collaborating with various domestic and international partners. Our new antistaphylococcal molecules that are also active

against methicillin-resistant *S. aureus* (MRSA) have been licensed-out.

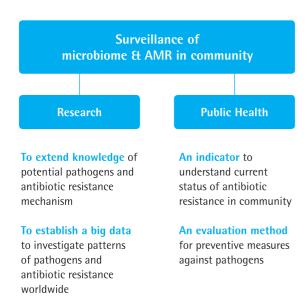
Working with GARDP and University of Birmingham (UK) we began a research program focused on multidrug resistance, aiming to identify efflux pump inhibitors for Gram negative bacteria.



Surveillance of community based antibiotic resistance:

The Metagenomics and Metadesign of Subways and Urban Biomes (MetaSUB) is an international consortium whose goal is to understand the urban microbiome. Currently, 62 teams from 32 countries participate in the consortium. As a consortium member, ARL investigated community-based microbiome and antibiotic resistance in samples from Seoul Subway stations revealing

abundant resistant genes: TEM beta-lactamase gene and APH aminoglycoside resistant gene. Inasmuch as beta-lactams including penicillin and cephalosporin are TEM substrates and among the most widely prescribed antibiotics in Korea, our results suggest detection of antibiotic resistance in microbiome sampled from masstransit is a powerful surveillance method for detecting community-based antibiotic resistance.



R&D HIGHLIGHTS

Strategic partnering to deliver solutions

Despite the unprecedented challenge presented by COVID-19 in 2020, we made significant research progress resulting in three significant publications, two patent applications, and a successful technology transfer of new antibacterial molecules to J2HBlotech, a Korean pharmaceutical company.



Antibiotic resistance becomes a great threat to all mankind. No one can be safe from the threat until we develop effective therapeutic agents against antibiotic resistant bacterial infections. Antibacterial Resistance Laboratory (ARL) has focused on discovery of new antibacterial molecules based on understanding bacterial physiology and resistance mechanisms working with domestic and international partners. I believe that all our efforts will facilitate new antibiotic development that can save millions of people around the world.

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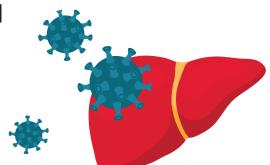
Dr. Soojin Jang, Head of Antibacterial Resistance Lab



We are dedicated to translational research developing therapeutics for viral diseases. Our strategy is to quickly translate basic science into therapeutic options.

Applied Molecular Virology Laboratory

The Quest for the Achilles Heel of Viruses



The Applied Molecular Virology Laboratory (AMV) is dedicated to conducting translational research developing therapeutics for viral disease. The main research focus is viral hepatitis; however, Zika- and Ebola viruses are being investigated, too. Our work aims to identify the Achilles heel of viruses, meaning we study virus-host/human interactions to identify viral weaknesses. Therefore, we do cell-based drug- and genome-wide RNAi experiments and apply chemical genomics and OMICS strategies to quickly translate high-quality basic science into therapeutic options.



Approx. 250 million people are chronically infected with HBV worldwide.



Among them, approx. 20 million people are chronically co-infected with hepatitis D virus (HDV).



million dead

Approx. 1 million patients die annually due to HBV- and HDV-related liver diseases.

Global Challenges

Hepatitis B virus (HBV) infection is a leading cause of life-threatening liver diseases, including hepatocellular carcinoma (HCC). Chronically infected patients are treated with drugs that control the virus's multiplication, but do not cure. For decades, the lack of a cell culture system to study the entire HBV life cycle has hampered research and new drug development. About 5 years ago, significant progress was made with the discovery of the viral entry receptor. Since then, it became possible to infect cells with HBV in research laboratories. However, very limited viral progeny are secreted for unknown reasons, and cell-to-cell spread, the major route of virus transmission in the liver, could not be studied. To overcome this bottleneck, we developed a new HBV platform supporting the entire HBV life cycle (*J Hepatol.* 2019 Aug;71(2):289-300) and started screening for antivirals and cellular factors crucial to the virus, with the ultimate goal to identify curative treatment options.

2020 Research Highlights
Applied Molecular Virology Laboratory

2020 R&D PROGRESS

Bringing light into the dark

To shed light on how human pathogenic viruses are using their hosts, us humans, we have conducted drugand RNAi screening campaigns to evaluate the effect of host-targeting inhibitors and selected host genes on the HBV life cycle, respectively. Therefore, a target-free high content screening (HCS) assay was developed using infectious HBV particles to investigate the entire viral life cycle (Fig. 1). As a result, we identified novel factors crucial to HBV, which are being further characterized. Among them was a new inhibitor, preventing HBV from

entering liver cells and spreading from one infected cell to another, that was further developed by conducting structure-activity relationship studies. Furthermore, we are also using our novel HBV platform to investigate hygiene measures. Thus, we developed a virus end-point dilution assay to determine the number of infectious HBV particles in the presence of virucidal measures like chemicals, heat, UV light, etc. Thereby we can determine which measures are appropriate to inactivate HBV to provide a safe environment for users.

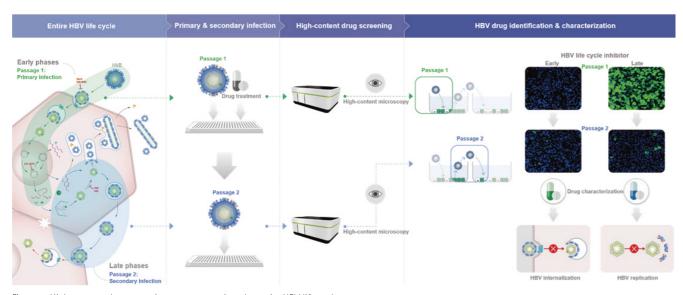


Figure 1: High-content drug screening assay to monitor the entire HBV life cycle.

R&D HIGHLIGHTS

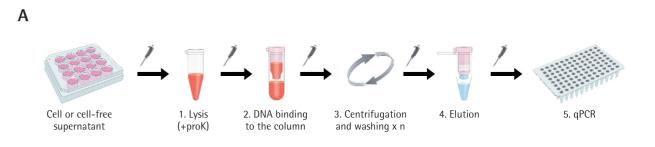
Viruses know no borders

The year 2020 was the year when life nearly came to a standstill due to COVID-19. However, we accelerated and engaged in even more international collaborations. We teamed up with laboratories in Morocco, Pakistan,

Vietnam, New Caledonia, Czech Republic, Norway, Estonia, and Finland, working on HIV, HCV, HBV, ZIKV, and SARS-CoV-2. As a result, eleven scientific manuscripts were published that generated knowledge benefiting

humankind in the future. Furthermore, we developed a technique that enables quantifying DNA viruses in a fast and inexpensive way. A total of 96 samples can be tested simultaneously without the need for expensive reagents or robots (Fig. 2) (*Viruses.* 2020 Aug 24;12(9):928).

Moreover, we devised a strategy for a novel target-based high throughput screening (HTS) assay to identify a new class of HBV inhibitors targeting viral RNA encapsidation (Fig. 3) (*Antiviral Res.* 2020 Mar;175:104709). In 2021, our team will continue the development of novel platforms supporting the investigation of liver-tropic viruses. In addition, we will conduct in vivo proof-of-concept experiments to determine whether our new inhibitors could add value to existing therapies.



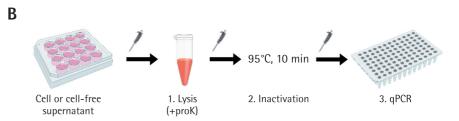


Figure 2: A Simple and cost-effective DNA preparation method suitable for high-throughput PCR quantification of HBV genomes. (A) A standard procedure to prepare viral DNA. (B) A new, improved approach to prepare viral DNA.

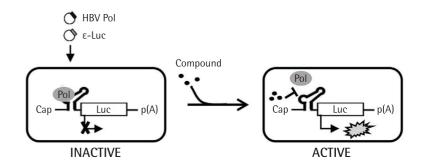


Figure 3: Identification of novel HBV pregenomic RNA encapsidation inhibitors.

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We are working on solutions that benefit patients directly and indirectly by developing first-in-class drug candidates and state-of-the-art platforms to study all aspects of viral diseases, respectively.

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Prof. Marc P. Windisch, Head of Applied Molecular Virology Lab



Affordable therapeutics and diagnostics for leishmaniasis and other neglected parasitic diseases is a major preoccupation of Institut Pasteur worldwide and constitutes a major global health need.



Among neglected tropical diseases, leishmaniasis causes the highest mortality rate (25,000 / yr), and among parasitic diseases is surpassed only by malaria.



1.6

With 1.6 million new cases each year leishmaniasis is distributed across all continents (Europe, America, Africa and Asia) except Australia.

Interestingly, there are recent reports on autochthonous leishmaniasis cases (canine and human) in South Korea, whereas previous cases were imported.

Leishmania Research Laboratory



Leishmaniasis is caused by the protozoan parasite *Leishmania* species and is one of the ten most lethal neglected tropical diseases (NTDs) infecting over 12 million people worldwide who are associated with a high risk of either mortality or stigmatization due to deformity. The disease is distributed globally across tropical regions and its global health impact exposes over 350 million people to infection in some of the most vulnerable regions of the world. Current treatment options are limited mainly by adverse effects, and there is no vaccine. The Leishmania Research Laboratory (LRL) aims to discover next-generation therapeutics for leishmaniasis and develop rapid diagnostics. In addition, we study the biology of the host-cell/pathogen infection, notably the underlying mechanisms by which *Leishmania* hijacks macrophages for its survival and propagation.

Global Challenges

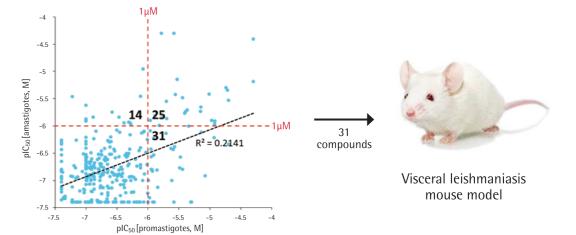
Current leishmaniasis treatment options such as antimonials, amphotericin B and miltefosine have drawbacks related to severe adverse effects, route of administration and parasitic drug resistance. Further, there is no clinically (Phase IIb) validated drug target to pursue the discovery of inhibitors in a target-specific manner. New drugs are needed to help overcome these challenges. The LRL uses high-throughput high-content (phenotypic) screening to identify candidate drugs as therapies against *Leishmaniasis*. Further, towards affordable technology for improved early and rapid detection of visceral and cutaneous leishmaniasis we are working in collaboration with industry (BioSquare Inc.) to develop more sensitive diagnostics.

2020 R&D PROGRESS

Drug repurposing for visceral leishmaniasis (VL)

Previously, LRL has developed high-throughput high-content screening for intracellular amastigotes. The assay mimics the physiological infection where the host macrophage is infected with amastigotes isolated from infected hamsters. Using the system, 9,695 bioactive compounds (including U.S. FDA approved drugs) have

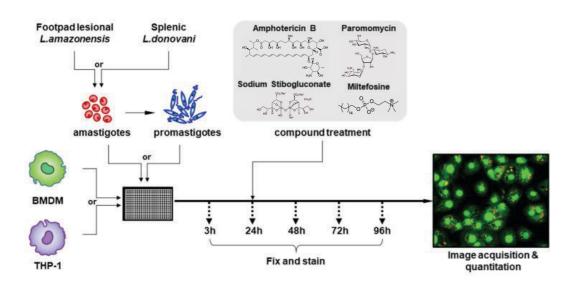
been screened yielding 70 compounds with high potency in terms of half maximal concentration. Among them, 31 compounds with favorable pharmacokinetic properties were selected for in vivo efficacy assessment using a leishmaniasis mouse model.



Infectivity and Drug Susceptibility Profiling of Different Leishmania-Host Cell Combinations

Designing and applying a physiologically relevant in vitro assay is key to identifying inhibitors for phenotypic screening. Based on the importance of intracellular Leishmania assay development, we characterized the infectivity, morphology, and drug susceptibility of different Leishmania and host cell infection combinations. Primary bone marrow-derived macrophages (BMDM) and differentiated human acute monocytic leukemia (THP-1) cells were infected with amastigote or promastigote

forms of *L. amazonensis* and *L. donovani*. Regardless of host cell types, amastigotes were generally well phagocytosed and showed high infectivity, whereas promastigotes, especially those of *L. donovani*, had predominantly remained in the extracellular space. In the drug susceptibility test, miltefosine and sodium stibogluconate showed varying ranges of activity with 14 and >10-fold differences in susceptibility, depending on the host-parasite pairs, indicating the importance of assay conditions for evaluating antileishmanial activity.



R&D HIGHLIGHTS

Multidisciplinary approaches to tackle Leishmania: from treatments to diagnostics

In year 2020, we have published results related to characterization of intracellular Leishmania in vitro model in which different hosts (THP-1 and BMDM) and parasite species (*L. amazonensis* and *L. donovani*) were used to create infections. The results are of interest since the selection of in vitro model is the first critical step of leishmaniasis drug discovery (Baek et al. (2020) *Pathogens* 9:393). Also, mTOR and Pl3K kinase inhibitors that are active against in vitro and in vivo model of *L. donovani* and *Trypanosoma brucei* was identified and published (Phan et al. (2020) *Molecules* 25:1980).

We secured funding from the Research Investment for

Global Health Technology Fund supporting a project (PI: BioSquare Inc.) on the development of rapid diagnostic test against cutaneous and visceral leishmaniasis. Also, in collaboration with Fundación MEDINA and Drugs for Neglected Diseases *initiative*, a funding from La Caixa foundation was secured supporting a project on identifying antileishmanial and antitrypanosomal lead compounds from natural product sources. Also, in terms of basic biology, a project to elucidate the mechanism by which *Leishmania* parasite hijacks the host macrophage has been funded by Korean National Research Foundation.

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Leishmaniasis remains a neglected disease because therapeutics development in the private sector is not engaged. As a not-for-profit research organization, IPK has partnered with NGO's like DND*i* (Drugs for Neglected Diseases *initiative*) in efforts to find new therapeutics for leishmaniasis.

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Dr. Joo Hwan No, Head of Leishmania Research Lab



We aim to think outside of the box by developing physiologically relevant assay systems allowing to enhance early drug discovery.

Cancer Biology Research Laboratory

The development of new drugs for liver cancer and liver fibrosis

Hepatocellular carcinoma (HCC) is one of the most frequently occurring types of cancer made especially severe by its high mortality rate. The highest incidence of liver cancer occurs in Eastern Asia and sub-Saharan Africa, and South Korea has the highest rate among countries worldwide. Since 2013, the Cancer Biology Research Lab (CBL) was established with the aim to develop drugs to treat HCC. We aim to think outside of the box by developing physiologically relevant assay systems recapitulating the tumor microenvironment and enhancing the early drug discovery pipeline converging to HCC therapeutics.

18% 5-year survival rate

As the second-most-common cause of cancer associated with death worldwide, HCC has a five-year survival rate of 18%. Furthermore, its incidence in the United States has rapidly increased by 3-4%, making hepatocellular cancer the fastest-rising cause of cancer-related death.



90% from liver cirrhosis

HCC is the most common primary malignancy of the liver. The majority of cases (80-90%) arise from underlying liver cirrhosis.



Following liver transplantation, recurrence rates are approximately 40%, with a median time to recurrence of 12.3 months.

Global Challenges

In general, the histopathology of liver cancer involves fibrosis, cirrhosis, and liver-related metabolic pathophysiology. Accordingly, drug-induced properties of interest include: anti-fibrotic, anti-inflammatory, and metabolic-regulation. Effective assay for such properties is challenging because of the complex environment of diseased liver tissue. Our team has therefore developed a unique three-dimensional (3D) multi-cellular tumor spheroid (MCTS) assay to achieve multiplexed screening aiming to optimize early identification of interesting drugs likely to be active in diseased liver. Our innovative technology has opened the way to address the challenge of screening small molecules, recombinant proteins, natural products, and traditional herbal medicines in search for new HCC therapeutics.

2020 Research Highlights

Cancer Biology Research Laboratory

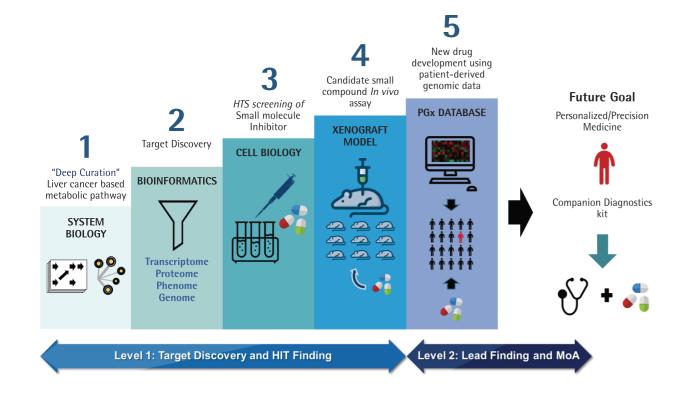
2020 R&D PROGRESS

Enhancing the early drug discovery pipeline

Identification of novel therapeutic targets and hits from multicellular tumor spheroids for HCC therapy

Metabolic alterations in liver cancer cells are numerous, including: aerobic glycolysis, amino acid metabolism, and reduced oxidative phosphorylation; the increased

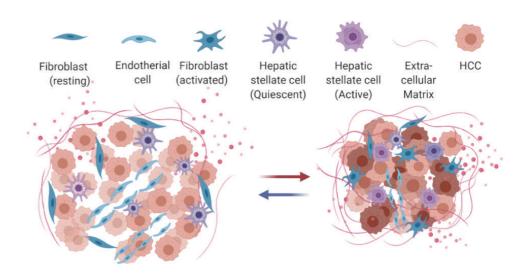
generation of biosynthetic intermediates supports cancer growth and proliferation. Hence, we elucidated the functional roles of metabolic regulators (GRP78, SORD, ASS1) from the 3D-HCC microenvironment and then identified novel drugs against metabolic regulators.



Development of innovative strategy for liver cancer therapy through reprogramming of liver fibrosis

A chronic, local inflammatory milieu can cause tissue fibrosis that results in Epithelial to Mesenchymal Transition (EMT) and Endothelial to Mesenchymal Transition (EndMT), increasing abundance of fibroblasts, and further acceleration of fibrosis. Using our 3D-tissue phenotypic

screening strategy we identified compounds attenuating MCTS compactness, and inhibiting Extracellular Matrix (ECM) proteins. Moreover, when the cell proliferation and angiogenesis inhibitor Sorafenib was added along with anti-fibrotic compounds, apoptosis was increased, suggesting that anti-fibrosis drugs may improve tissue penetration enhancing the action of anti-cancer drugs.



R&D HIGHLIGHTS

Fighting cancer!

Multidisciplinary research to overcome limits in drug discovery for HCC therapy

In 2020, we published the results that our MCTS model provides a new paradigm for high-throughput drug screening and we proposed that it will optimize identifying drugs and targets for HCC treatment. (*Cancers* 12(5):1193, *Sci Rep.* 10 (1):5318 and *Mol Cells.* 44(1):50-62). Based on these research activities, our researchers

won an excellent poster award from the Korean Society for Biochemistry and Molecular Biology (KSBMB), and our results were selected as an excellent research achievement by the National Research Foundation of Korea (NRF). The CBL also secured three patents and four grants from NRF for further investigation. Finally, we achieved successful know-how transfers to several Korean pharmaceutical venture companies.

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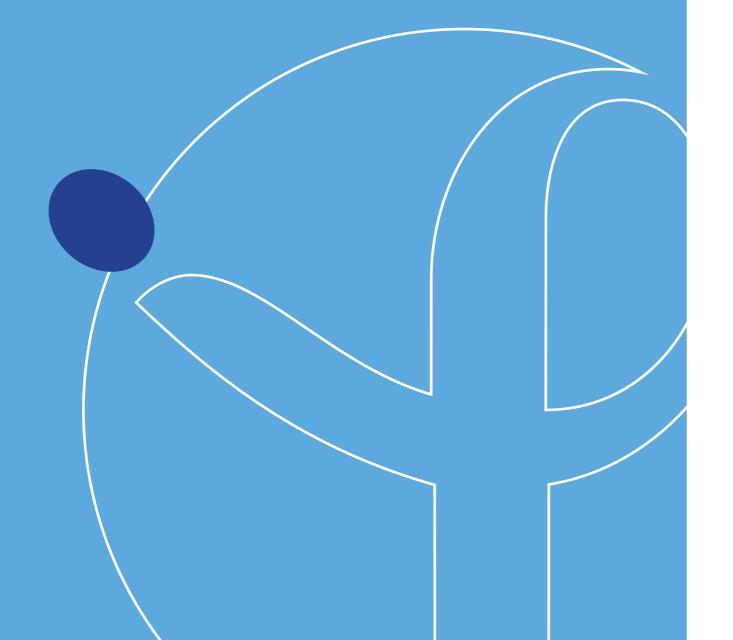
Working at the hospital for joint research, I felt a great deal of pain to witness the patients suffering. I would like to commit my talents and knowledge to research, hoping to alleviate patients' pain. I wish my children will feel proud of my sincere efforts.

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Dr. Haengran Seo, Head of Cancer Biology Research Lab

2020 Research Highlights

- O Discovery Biology
- **⊘** Translational Research
- Bio Start-up Incubation





Automated robotics, advanced imaging microscopes, and disease models allow screening of massive chemogenomic libraries for clues to develop new therapies.



Five automated HTS/HCS screening platforms @ IPK in BSL-2+ & BSL-3+ & BSL3 labs dedicated to infectious disease research



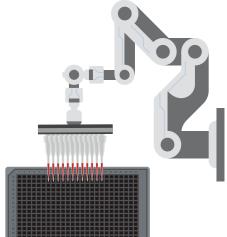
Millions of data points gathered from disease models covering bacteria, viruses, and parasites



Over 50 terabytes of disease-specific information

Screening Discovery Platform

Accelerating the pace of drug discovery for global health



New treatments are urgently needed to meet global health and future pandemic threats. Drug discovery programs encompassing high-throughput / high-content screening (HTS/HCS) are a hallmark feature of the research and development landscape. At IPK, we combine automated robotics, advanced imaging microscopes, and infectious disease models to probe the chemical and genomic landscape for "hits" that reverse disease-specific phenotypes. These large data sets are then interrogated with computational engines and informatic databases to identify the most promising candidates for drug development. An emerging trend recognizes that data will power Al-driven approaches to allow for better understanding of diseases, the mechanism of action, and translational purposes. Through a combination of multidisciplinary approaches and new technologies, the drug discovery process times and failure rates will be greatly reduced leading to overall improvements in pipelines for emerging global health needs.

Global Challenges

Traditional drug discovery is a time consuming and expensive process, lasting 10–15 years and costing approximately \$1.8 billion. For the thousands of compounds that enter the R&D pipeline, ultimately less than 10% will achieve approval to clinical use. The emergence of the 2020 pandemic has highlighted the need for robust technology platforms to be rapid, scalable, and provide high success rates. The Screening Discovery Platform (SDP) provides the comprehensive tools and network to meet these challenges.

Fighting Infectious Disease

2020 Research Highlights
Screening Discovery Platform

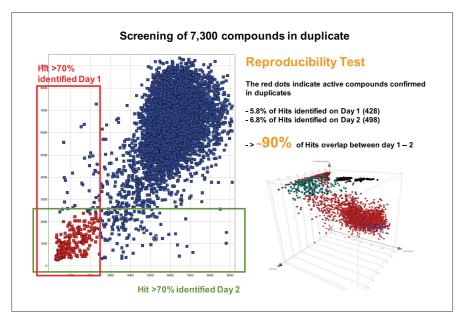
2020 R&D PROGRESS

High-throughput Research Services for Success!

SDP is the core technology platform linking basic biological research to the early drug discovery pipeline with over 20 projects completed in 2020. We have provided support to IPK biology groups by scaling their cell-based assays into HTS/HCS pipelines capable of screening large chemical libraries and whole genome

perturbations. Several promising hits were identified in key areas of infectious diseases and hit-to-lead studies are now underway. Additionally, SDP is the key collaborator in screening programs across Korea and international companies.

- During the course of the COVID-19 pandemic, the SDP facilitated rapid assessment of anti-viral properties of FDA-approved drugs, bio-actives, and clinical investigational compounds. Numerous hits were identified and a few are in clinical trials for repurposing against SARS-CoV-2.
- Screening programs with IPK biology teams including: viral research (hepatitis B, hepatitis E, dengue), hepatocarcinoma (novel targets, fibrosis), bacterial (TB, gram negative strains), and parasites (Leishmania, Chagas, malaria).
- International partners in early drug discovery for infectious diseases included: GARDP (antimicrobial resistance), DNDi (neglected tropical diseases), and the Institut Pasteur International Network (SARS-CoV-2 protease, anti-venom therapies, dengue prognosis, and Bordetella inhibitors).
- Partnered with KaiPharm for a transcriptomic profiling database and global service program.
- Collaborations and screening programs in Korea for academic, biotech, and government.

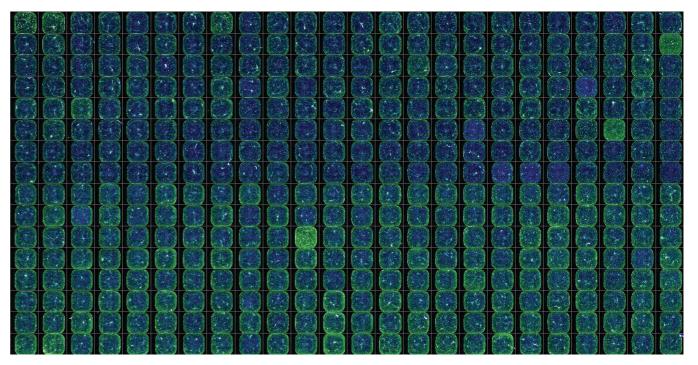


HTS Data Analysis & Visualization

R&D HIGHLIGHTS

Phenotypic screening for drug discovery

- Publication of a proof-of-concept study using functional genomics to predict treatments in certain cancer types.
 Identification of potential targets to understand the efficacy of DNA-methyltransferase inhibitors. (*Proc* Natl Acad Sci USA 118(13):e2016289118)
- Publication of a collaborative screening environment for neglected tropical diseases. Virtual studies were performed at DNDi and several world-leading pharmaceuticals submitted compounds to IPK for testing, yielding a lead candidate against visceral leishmaniasis. (RSC Med Chem 12:384-393)
- Publication of virtual screening results and proof-ofconcept study for Bcl-2 proteins. This protein family is an attractive target for development of anti-cancer inhibitors. (*Biochem Biophys Res Commun* 527(3):709-715).
- Review publication of next-generation approaches in drug discovery trends for the future. Highlights datadriven omics and phenotypic screening for infectious disease research. (*Trends Parasitol* 35(7):559-570).



Phenotypic Screening Mosaic in 384-well plate

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SDP is accelerating the pace of drug development through HTS/HCS screening, target deconvolution, omics, and data. We are committed to providing solutions to meet current global challenges as well as preparing for the future.

Mr. David Shum, Head of Screening Discovery Platform



IPK drug screening is founded upon use of advanced imaging technologies allowing the study of diseases in situ in animal, tissue and cell models.

Technology Development Platform

Probes and optical imaging techniques measuring chronic and infectious disease

The maintenance of IPK's phenotypic screening facility requires a steady and consistent improvement of advanced cutting-edge high-content screening technologies. In this context the Technology Development Platform (TDP) serves to provision non-invasive imaging technologies in cell, tissue and small-animal models for quantitative phenotypic measurement enabling screening. Taking advantage of our multi-disciplinary team composed of molecular biologists, immunologists, and imaging specialists, our work includes, but is not limited to development of optical molecular probes, and imaging technologies for studying disease in situ across macro- to microscopic spatial and temporal scales.

Once infected, becomes more susceptible

Although the central nervous system is extremely resistant to infection due to a combination of protective layers, once the infection has initiated, it is generally more susceptible to infection than most extens tiesues.



The occurrence rate of viral encephalitis is about 1 in 200,000 per year affecting mainly children, the elderly, and those with suppressed immune systems.



Post-mortem pathology reveals Alzheimer or other dementia in over 30% of seniors.

Global Challenges

Optical imaging technologies help understand disease pathologies at multiple spatial and temporal scales, bridging the gap between molecules, cells, tissues, and animal models. The main research challenges addressed by TDP are:

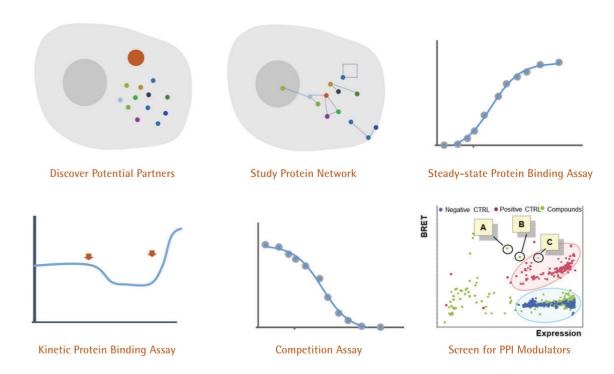
- Measuring protein-protein networks using bioluminescence & fluorescence in living cells.
- Therapeutics discovery for neuropathic viruses and neurodegenerative
- Measuring inflammation in vivo to quantify inflammation in chronic and infectious disease models.

2020 R&D PROGRESS

We have developed a portfolio of tailor-made assay services that allow for precise, robust, fast, and costefficient analysis of almost any type of protein-protein interaction, or protein binding to various targets. Moreover, we can analyze protein stability, and protein aggregation using state-of-the-art, label-free, in situ Bioluminescence Resonance Energy Transfer method (BRET) imaging. Using BRET, we can follow protein-protein interaction networks directly inside living cells during pathological events.

We are developing improved biological relevance cellular models by adapting stem cells and induced pluripotent stem cell (iPSC) for HCS to study neuropathic viruses.

Using a near-infrared (NIR) reporter protein expressed in astrocytes, we demonstrate that it is possible to non-invasively quantify brain inflammation in living animals. Furthermore, with a newly designed in-vivo imaging hardware, brain inflammation quantification can be now measured with high sensitivity allowing to perform longitudinal studies, measuring the effect of chronic and infectious diseases on brain inflammation.



Services for protein network study in living cells

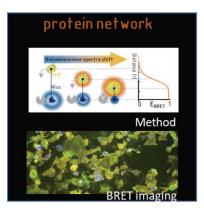
R&D HIGHLIGHTS

Application of optical imaging approaches to study diseases

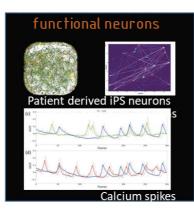
Combining the use of optical-based technologies and photonic probes, TDP renders methods enabling non-invasive quantification of the biological pathways involved in infectious and chronic diseases. Our technology has enabled direct investigation of key molecular events occurring during Parkinson's disease,

Alzheimer's disease, Amyotrophic lateral sclerosis disease, and Dystonia. Likewise, key interactions between viruses and host cells were studied for Measles (PMID: 33515806 *Mol Cell Proteomics* 2021 Jan 27;20:100049) and Rabies (*mSphere* 2019 May 22;4(3):e00047-19) viruses.

Nano-scale



Micro-meso-scale



Micro-scale



Multi-scale optical imaging methods in living biological models

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We are committed to technology innovation that we believe is an important driving force behind the democratization of medicine into the future.

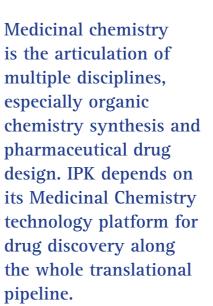
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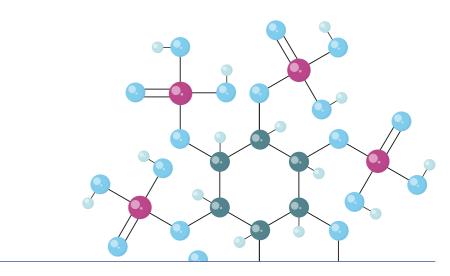
Dr Regis Grailhe, Head of Technology Development Platform



Medicinal Chemistry

Data Inspired Medicinal Chemistry!





The Medicinal Chemistry (MC) team seeks to efficiently optimize candidate drugs iteratively using chemical design and synthesis based upon: phenotypic/target-based screening, SAR (structure-activity-relationship) and ADMET (absorption, distribution, metabolism, elimination, toxicity) analysis. Our work aims ultimately to improve candidate compounds by enhancing drug potency and "drug-like" properties.

The MC platform provides a "one-stop solution" from drug design up to preclinical stage development.



1,800 FDA-approved drug collection, more to be discovered

It is estimated that the drug-like small molecule chemical space is vast comprising of about 10⁶⁰ chemical entities, of which 6 × 10⁶ molecules are druggable. The fact that the current FDA-approved drug collection comprises only 1,800 compounds suggests that there are many more compounds remaining to be discovered. Hence, we are limited practically by the speed and cost of screening such a vast chemical space.

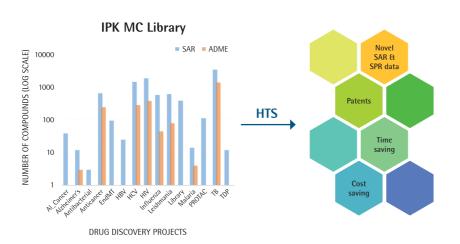
Global Challenges

Developing compounds to better perform as therapeutics requires chemical design and synthesis be driven iteratively by SAR/SPR (structure-property-relationship) analysis. However, in the case of infectious disease there is not much data available compared to cancer or metabolic diseases. Over the years IPK MC team has synthesized more than 9,400 proprietary compounds under the auspices of just a dozen or so different infectious disease targets. Accordingly, about 2,300 compounds are annotated with experimentally confirmed ADMET data, comprising a unique "big data" SAR/SPR resource for infectious disease studies.

2020 Research Highlights

Medicinal Chemistry

Figure 1. IPK proprietary MC compound library: distribution of compounds across different thematic project areas. Datadriven drug-discovery strategies of MC team will save cost and time.



2020 R&D PROGRESS

High tech chemistry driving innovative drug discovery

Discovery of new anti-microbial and anti-chagas agents

The IPK proprietary MC compound collection was screened against *S. aureus* WT (wild type) and MDR (multi-drug resistant) strains with the aim to identify compounds with antibacterial properties. Interesting scaffolds were found, which previously were identified as anti-leishmanial compounds. Additionally, the IPK proprietary MC compound collection was screened against *T. cruzi*, and *L. donovani* amastigotes to develop novel anti-chagas and/or anti-leishmanial drugs. Interestingly, scaffolds of interest were previously identified as HIV hits. Additionally, the MC team has secured Korea Health Industry Development Institute (KHIDI) grant for novel TB drug discovery driven by chembioinformatics.

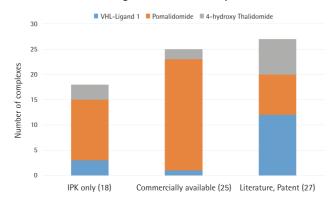
New platform technology – PROTAC

PROTAC (PROtyeolysis TArgeting Chimera) exploits target protein binder, E3-ligase binder and linker complexes to target protein degradation and has therapeutic potential to target otherwise "undruggable" proteins. The MC team

Figure 2. Introduction of E3-ligase and linker complexes for PROTAC platform technology. Distribution of number of complexes based on types of three different E3-ligases and linker lengths. Notably, 'IPK only' complexes are uniquely designed by the MC team.

has uniquely designed and synthesized to create the database of E3-ligase and linker complexes which can be flexibly applied when designing PROTAC compounds (Figure 2). The three main E3 ligases are VHL-1, pomalidomide and 4-hydroxy thalidomide. Various linkers are distributed up to 20 carbons in lengths. Most of them have drug-like molecular weight distribution. IPK-MC PROTAC derivatives were designed, synthesized and assayed for AIMP2-DX2 targeting aiming to establish a first-in-class lung cancer drug. SAR study of linker attachment positions was explored, and found that Position 2 in AIMP2-DX2 Hit compound 1 is optimal for biological activities. Appropriate PROTAC combinations for the AIMP2-DX2 inhibitor, linker and E3-ligase were found with inhibition percentage of 50% from luciferase assay.



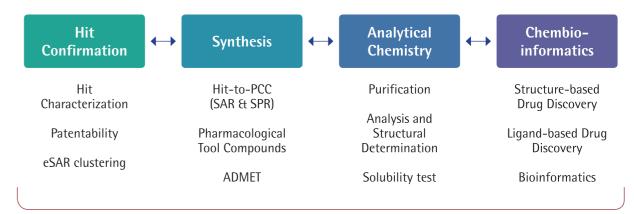


2020 R&D HIGHLIGHTS

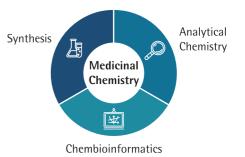
Medicinal Chemistry Service, Collaboration and Development

In 2019/2020 the MC team has been recognized by internal and external partners for excellence in fee-for service (FFS) and collaborative drug discovery projects. Provisioning FFS including: synthesis for two high-profile domestic Korean Al drug discovery companies and molecular modeling for a Korean bio start-up company. We also provided analytical chemistry services for start-ups as well as pharmaceutical companies.

The MC team published eight peer-reviewed manuscripts in reputable journals describing syntheses of two chemical series, molecular modeling, and chembioinformatics analysis. Notably, reporting lead optimization of anti-TB lead candidate: the thienothiazolocarboxamide (TTCA) series. This work formed basis for five patents and two-year grant support for TB drug discovery.



Iterative design and synthesis of putative drug molecules



Destination to Innovative Discovery Chemistry Collaboration

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Entering into the Big-Data/AI-driven era, our team is connecting virtual and real chemical spaces for innovative drug development.

Dr. Inhee Choi, Head of Medicinal Chemistry

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Animal Facility & Lab Support

Pre-clinical phase small animal testing for drug development

In vivo disease models are critical to validating the pre-clinical drug development pipeline, and we support our researchers to assure technology transfer to clinical applications.





Lack of ABSL-2, ABSL-3

Due to the lack of ABSL2 or ABSL-3 facilities in Korea there are many restrictions in researching infected animal models exposed to high-risk pathogens and efficacy/toxicity test of new drug candidates using them.



Various types of transgenic mice are imported, generated and used and maintaining them for a long time is a challenge due to problems such as poor mating, microbial contamination and high cost of breeding.



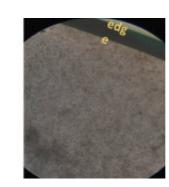
Periodic calibration of equipment and replacement of consumables can prevent laboratory equipment failures and maintain machine performance, thereby obtaining reliable and reproducible experimental data

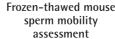
The Animal Facility & Lab Support (ALS) team facilitates studies using in vivo animal models critical to understanding the complex relationships and histopathology at the whole body level during disease and therapeutic intervention. For therapeutics development, this work is essential for preclinical validation of the safety and efficacy of new drug candidates. In addition to this activity, our team designs and fabricates small equipment peripherals and accessories, assures significant equipment maintenance, and provides technical and administrative support to daily research activities of all IPK teams. Animal research can be performed in three types of facilities composed of a Specific Pathogen-free (SPF) laboratory, animal biosafety level 2 (ABSL-2) laboratory, and animal biosafety level 3(ABSL-3) laboratory. In addition to experimental animal research into infectious diseases, we support a broad set of experiments, including new therapies. Furthermore, we provide sperm cryopreservation and in vitro fertilization services, particularly for the storage of transgenic mice. Importantly, we are particularly vigilant to ensure that the highest animal welfare standards adhere rigorously to strict legislative requirements.

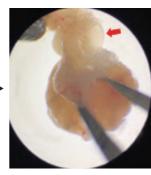
2020 R&D PROGRESS

Expertise supporting scientific services

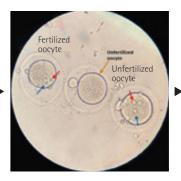
- We support the IACUC protocols accreditation of every research team on 8 different diseases as well as ensure the researcher training to safely conduct animal experiments using pathogens.
- Services provided are husbandry and animal breeding in ABSL and SPF spaces.
- We support the establishment of intranasal infection of tuberculosis bacteria (M.tb H37Rv species) to Kramnik mouse (C3HeB/FeJ) to create a tuberculosis mouse model similar to specific lesions in tuberculosis patients. Moreover, we supported animal experiments to establish an infectious model for acute pneumonia and for preclinical drug efficacy tests of compounds selected against pneumonia using screening platform technology.
- In order to maintain various types of genetically modified mice in IPK, in vitro fertilization using cryopreserved sperm and fertilized egg transplantation methods are being set.







Collection of oocytes (arrow. swollen ampulla)



In vitro fertilzation(IVF)



Two cell stage embryos

2020 R&D HIGHLIGHTS

Quality assurance and accreditation

The animal experiment protocols for each research team that studies eight different types of diseases should be approved in advance of starting the experiment. As a result, 15 new animal experiment protocols were approved in year 2020 by IPK-IACUC [Ref. Table 1].

Study Purpose	IACUC No.	Funding source	Title
	IPK-20001	IPK general fund (NRF)	Establishment of tuberculosis infection model in Kramnik (C3HeB/FeJ) mice.
Tuberculosis	IPK-20003	Middle-Class Research grant (NRF)	Production of Alveolar macrophage-like phagocytes (MPI cells) from mice with various genetic background
	IPK-20015	MSIT-Unmet Medical Needs division	In vivo efficacy of new isoniazid-loaded polymer formulation against Mycobacterium tuberculosis infection in mice
Neuroinflammation	IPK-20004	MSIT20-04	Generation of mouse transgenic primary and embryonic neuronal and glial fluorescent cell lines and study fluorescent transgenic animal models.
MERS-CoV	IPK-20002	Convergent solution for Emerging virus Infection (NO1901-0000) MERS-corona and Zika viruses research (NN1901-0000)	Evaluation of the efficacy of anti-MERS-CoV agants in vivo
	IPK-20005	IPK-general fund (NRF)	Investigagion of macrophage polarization modulator for anti- leishmanial drugs by multi-dimensional screening platform
	IPK-20006	[MSIT2] 2020 LRL	Study of host-Leishmania interaction
Leishmania	IPK-20007	[MSIT2] 2020 LRL	Application of in vivo Cutaneous Leishmaniasis mouse model and drug efficacy testing
	IPK-20013	RIGHT Fund and KOICA CTS program	Establishment of in vivo Leishmania infection model for infected serum collection and diagnostic tool development
COVID-1 and COVID-2	IPK-20008	2020 Drug repositioning for COVID-19 treatment (NN2015-0001), Convergent solution for Emerging Virus Infection (N01901-0000)	Evaluation of the efficacy of anti-SARS-CoV-1/2 agents in vivo
Pneumonia	IPK-20009	2020 Innovate New drug pipeline Development program	Establishment of pneumonia model using the clinical isolates and in vivo efficacy validation of identified antibacterial molecules
SFTSV	IPK-20010	2020 Unsolved treatment development program; Development of therapeutic antibody for treatment of SFTS (KD2003-0001)	Evaluation of the efficacy of anti-SFTSV agents in vivo
T-Cruzi	IPK-20011	[MSIT] 2020 LRL	In vivo evaluation of drug efficacy against Trypanosoma cruzi
Influenza	IPK-20012	2020 Preparedness to Emerging Viruses (MSIT20-0108)	Assessment of immunogenicity of vaccine components in mice
Sperm cryo and IVF	IPK-20014	[MSIT1] 2020 Animal facility preparedness to Emerging viruses	In vitro fertilization and embryo transfer using fresh and cryopreserved inbred mouse sperm

[Table 1] IPK animal experiment protocol approved

7 (

Animal models continue to prove their value in the drug discovery process as they are essential to predict toxicity and efficacy of drug candidates in patients.

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Dr Regis Grailhe, Head of Animal Facility& Lab Support

2020 Research Highlights

- O Discovery Biology
- Translational Research
- **Start-up Incubation**



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Bio Core Facility Start-up Incubator

A core component of the IPK mission is to assure scientific discovery is delivered as applications in the real world to the benefit of Public Health. This requires working closely with industry partners and helping biotech startups build themselves up.





Entrance to the IPK Startup Platform (Located on the 3rd Fl. R&D Building)

Conducting the Bio Core Facility Project supported by the Ministry of Science & ICT, IPK has been incubating bio startups since 2017, helping them reinforce their R&D capabilities, facilitate business operation, and expand the global network. Utilizing the core R&D facility and infrastructure as well as the know-how of establishing spin-off bio ventures such as Qurient Co., Ltd., IPK has been providing customized support based on the needs of each company, their potential and competitiveness.

Based on an assessment of competitiveness and potential synergy with IPK, five startup companies were selected to establish operations for three years in the IPK BioCore Facility Startup Platform. Anticipated benefits for companies include access to IPK R&D-service assets and expertise, plus the Pangyo Techno Valley location, a sought-after biomedical hub. Situated just on the outskirts of the capital city Seoul, IPK's BioCore Facility provides unique opportunities and privileges to selected startups, with manifold access to both academic and industrial collaborators and partners.

Bio Core Facility Project at a Glance

- Purpose: To support growth and advancement of the young start-ups utilizing the core facility, global research network and start-up platform of IPK
- Project Period: June 2017 ~ June 2024 (7 years)
- Funding Agency: Ministry of Science and ICT
- Funding: 1.5 billion KRW per year, 10.5 billion KRW in total for the project
- Supporting Programs
- Provide free use of laboratories and office spaces in the IPK's Startup Platform
- Give access to its research infrastructure (Common facility and equipment needed for basic biology and drug discovery research)
- Mentoring and education for research and operation activities and consultation to advance technology and value up the company
- Support with commercialization strategy and establishment of networks

*Five companies are selected every three years in 2017 and 2020, and the supporting program is no longer than 3 years.

2020 PROGRESS & HIGHLIGHTS

Since 2017, five startups: PiMedBio, Inc.; Cellatoz Therapeutics, Inc; ILIAS Biologics, Inc.; Biosquare, Inc., and Amyloid Solution, Inc., have established themselves at IPK's startup platform for their research and business operations from 2018 to 2020. For three years, IPK provided manifold support through over ninety sessions of education and scientific seminars, twenty mentoring programs, external consultations for business development and globalization strategies, and so forth, which was provided in addition to the spaces and facilities. It was rewarding to witness the significant growth of participating companies.



2020 Research Highlights 2020 Publications

Performance in Number: Growth of the five participating companies (2018-2020)

Promoting commercialization of biotechnology for the benefit of Public Health

350 million KRW 6 patents upfront payment received registered & technology transfers 9 filed 100.8 billion KRW 141 new hires investment secured **GMP** facility established (by Cellatoz Therapeutics)

> Starting 2021, five newly selected companies will replace the previous departed businesses, joining the program for the 2021-2024 2nd phase.











2020 Publications

j.bmc.2020.115797

- 1. Identification of Antiviral Drug Candidates against SARS-CoV-2 from FDA-Approved Drugs.
- Antimicrob Agents Chemother. 2020 Jun 23;64(7):e00819-20. doi: 10.1128/AAC.00819-20
- 2. Identification and Tracking of Antiviral Drug Combinations. Viruses. 2020 Oct 18;12(10):1178. doi: 10.3390/v12101178.
- 3. Squalene emulsion-based vaccine adjuvants stimulate CD8 T cell, but not antibody responses, through a RIPK3-dependent pathway. Elife. 2020 Jun 9;9:e52687. doi: 10.7554/eLife.52687.
- 4. Infectivity and Drug Susceptibility Profiling of Different Leishmania-Host Cell Combinations.
 - Pathogens. 2020 May 20;9(5):393. doi: 10.3390/pathogens9050393.
- 5. Advanced Therapeutics, Vaccinations, and Precision Medicine in the Treatment and Management of Chronic Hepatitis B Viral Infections; Where Are We and Where Are We Going? Viruses. 2020 Sep 7;12(9):998. doi: 10.3390/v12090998.
- 6. In Vitro and in Vivo Activity of mTOR Kinase and PI3K Inhibitors Against Leishmania donovani and Trypanosoma brucei. Molecules. 2020 Apr 23;25(8):1980. doi: 10.3390/molecules25081980.
- 7. Chromenopyrimidinone Controls Stemness and Malignancy by suppressing CD133 Expression in Hepatocellular Carcinoma. Cancers (Basel). 2020 May 8;12(5):1193. doi: 10.3390/cancers12051193.
- 8. Discovery of 4-hydroxy-2-oxo-1,2-dihydroquinolines as potential inhibitors of Streptococcus pneumoniae, including drug-resistant strains. Bioorg Med Chem Lett. 2020 May 1;30(9):127071. doi: 10.1016/ i.bmcl.2020.127071
- 9. Identification and characterization of a novel hepatitis B virus pregenomic RNA encapsidation inhibitor. Antiviral Res. 2020 Mar;175:104709. doi: 10.1016/j.antiviral.2020.104709
- 10. A Simple and Cost-Effective DNA Preparation Method Suitable for High-Throughput PCR Quantification of Hepatitis B Virus Genomes. Viruses. 2020 Aug 24;12(9):928. doi: 10.3390/v12090928.
- 11. Identification of inhibitors of Bcl-2 family protein-protein interaction by combining the BRET screening platform with virtual screening. Biochem Biophys Res Commun. 2020 Jun 30;527(3):709-715. doi: 10.1016/j.bbrc.2020.05.045
- 12. Benzimidazole Derivatives as Novel Zika Virus Inhibitors. ChemMedChem. 2020 Aug 5;15(15):1453-1463. doi: 10.1002/
- 13. An Engineered Microvirin Variant with Identical Structural Domains Potently Inhibits Human Immunodeficiency Virus and Hepatitis C Virus Cellular Entry.
- Viruses. 2020 Feb 11;12(2):199. doi: 10.3390/v12020199.

- 14. Discovery of thienothiazolocarboxamide analogues as novel antitubercular agent. Bioorg Med Chem. 2020 Dec 1;28(23):115797. doi: 10.1016/
- 15. Novel structural CYP51 mutation in Trypanosoma cruzi associated with multidrug resistance to CYP51 inhibitors and reduced infectivity. Int J Parasitol Drugs Drug Resist. 2020 Aug;13:107-120. doi: 10.1016/ j.ijpddr.2020.06.001
- 16. Identification of 4-anilino-6-aminoquinazoline derivatives as potential MERS-CoV inhibitors. Bioorg Med Chem Lett. 2020 Oct 15;30(20):127472. doi: 10.1016/ i.bmcl.2020.127472
- 17. Structure-guided discovery approach identifies potential lead compounds targeting Mpro of SARS-CoV-2. Virus disease. 2020 Nov 11:31(4):1-5. doi: 10.1007/s13337-020-00627-6. Online ahead of print.
- 18. Integrative Gene Expression Microarray Meta-analysis Identifies Host Factors and Key Signatures Involved in Hepatitis B Virus Infection. Infect Disord Drug Targets. 2020;20(5):698-707. doi: 10.2174/187152651 9666190807153901.
- 19. The ThiL enzyme is a valid antibacterial target essential for both thiamine biosynthesis and salvage pathways in Pseudomonas aeruginosa. J Biol Chem. 2020 Jul 17;295(29):10081-10091. doi: 10.1074/jbc. RA120.013295
- 20. The Beginning of Ending Hepatitis C Virus: A Summary of the 26th International Symposium on Hepatitis C Virus and Related Viruses. Viruses. 2020 Mar 11:12(3):302. doi: 10.3390/v12030302.
- 21. Inhibitors of Na+/K+ ATPase exhibit antitumor effects on multicellular tumor spheroids of hepatocellular carcinoma. Sci Rep. 2020 Mar 24;10(1):5318. doi: 10.1038/s41598-020-62134-4.
- 22. Application of multi-omics technology for the elucidation of antipneumococcal activity of 3-acyl-2-phenylamino-1,4-dihydroquinolin-4-one (APDQ) derivative against Streptococcus pneumoniae. Sci Rep. 2020 Nov 26;10(1):20685. doi: 10.1038/s41598-020-77694-8.
- 23. Comparative study of different forms of Jellein antimicrobial peptide on Leishmania parasite.
 - Exp Parasitol. 2020 Feb;209:107823. doi: 10.1016/j.exppara.2019.107823



R&D Infrastructure

IPK employs dynamic robotic platforms for high-throughput screening of chemical libraries and RNAi collections. Our fully-automated robotic platforms are located in BSL-2 and BSL-3 laboratories suitable for most pathogens and biological research.



Awards on Biosafety Facility Operation

(2019) Citation award (institution) by the Minister of Trade, Industry and Energy (MOTIE) for contributing biosecurity management

(2019) Citation award (individual) by the Minister of Science and ICT (MSIT) for contributing LMO safety management

Physical Containment Laboratories

Biosafety Level 3 Laboratory (BSL-3)

- Certified with the approval of Korea Center for Disease Control & Prevention (KCDC, currently KDCA) in March, 2009 (Reconfirmed in 2012, 2015 and 2018)
- Designed to handle the risk group 3 pathogens such as M. tuberculosis, SARS-CoV, SARS-CoV-2, MERS-CoV, and SFTSV

Biosafety Level 2 Laboratory (BSL-2)

- Registered in Korea's Ministry of Science & ICT according to the Transboundary Movement, etc. of Living Modified Organisms Act.
- Designed to handle risk group 2 pathogens such as influenza virus, Zika, Dengue, HBV, Leishmania, T. cruzi and S. aureus.

Animal Laboratory

- Composed of specific pathogen-free laboratory(SPF), animal biosafety level
 2 laboratory(ABSL-2) and animal biosafety level
 3 laboratory(ABSL-3) with individual ventilation cage system
- Exquisitely controlled environment for care and maintenance of experimental animals



Researchers in operation of the screening platforms located at the BSL-3 Lab.

Screening Platform

IPK utilizes image- and cell-based high-throughput/high-content screening platform. It quantifies biological events in living cells and allows the cells themselves to identify the most effective drug targets from millions of complex molecular interactions. Disease mechanisms addressed by the identified compounds are likely to be physiologically relevant since compounds are tested and studied in cells.

Chemical Screening

Chemical screening can be used to identify molecules with biological activity from our libraries covering 500,000 compounds including synthetics and natural products. The diverse collection was assembled with the help of the inhouse chemistry and cheminformatics experts, as well as established strategic partners.

RNAi Screening

RNAi technology enables sequence specific knockdown of genes to identify new targets and cell signaling pathways for disease understanding. Our RNAi collections cover both siRNA and shRNA technologies for gene by gene systematic interrogation of our biological models.

Automation Management Solutions

Multimodality instrumentation and automated microscopes are integrated into our robotic platforms for fast reliable data acquisition.

Our detection technologies include fluorescence, bioluminescence, absorbance, and high-content imaging to enable understanding of simple to complex biological interactions.

We are capable of screening assays in a wide range of detection technologies to uncover potential leads for development into biomarkers, probes and drugs.

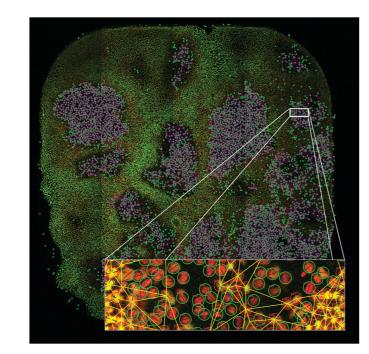


Innovative IPK Screening Platform

Innovative IPK Screening Platforms Accelerating Drug Discovery for All

IPK renders access to our innovative drug screening expertise and technologies in biosafety level-2/-3 laboratories enabling domestic and international partners the opportunity to advance their own drug development programs.

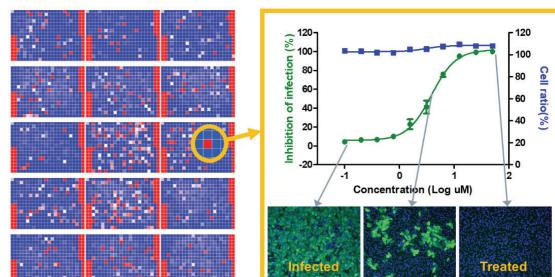
The highly experienced professionals of IPK provide various services through all stages of the screening process including biochemical, cell-based, or custom assay design and adaptation, combinatorial screening, proof-of-concept screening, small to large scale screenings, dose-response studies, as well as chemical analysis and molecular modeling.



High-Content Screening (HCS) refers to the use of automated digital microscopy extracting high-resolution images from biological samples. HCS allows to analyse cellular level changes in tissue organisation and function to reveal effects of disease and/or drugs. IPK HCS screening services use this type of approach to discover new drugs by screening chemical compound libraries for biological effects.



During the fifteen years since our founding, IPK has established itself an international reputation as a go-to-partner for pre-clinical screening in infectious disease. In this context we are sought by many partners from academia, public/private-research institutes, NGO's and industry. This was exemplified in 2020 as IPK expedited fee-for-service support for COVID-19 related screening requests for over 70 organizations that approached us for support and partnership. These activities included the evaluation of antiviral efficacy for candidate compounds and antibodies against SARS-CoV-2 using our already developed cell-based assays. Through these partnerships, IPK has screened over 2,000 third-party molecules and antibodies in 2020. Indeed, our own studies revealed potent candidates now undergoing clinical trials. Importantly, as a member of the Korean government's COVID-19 response R&D supporting group, IPK has been helping Korean domestic companies with in vitro drug efficacy evaluation.



IPK's cell-based screening allows new drug candidates to be identified faster and more reliably.



Research Collaborations & Partners

For a healthier and safer life Let's join forces and work together



MOU Agreement in 2020

- Gachon University
- · Government-wide R&D Fund for Infectious Disease Research
- Korean Society for Molecular and Cellular Biology (KSMCB)
- · Scripps Korean Antibody Institute (SKAI)
- · WuXi AppTec, Inc.

Joint Research Agreement in 2020

- · Atomwise, Inc.
- Chong Kun Dang Pharmaceutical Corp.
- · Daewoong Pharmaceutical Co., Ltd.
- · Drugs for Neglected Diseases initiative (DNDi)
- · GlaxoSmithKline plc. (GSK)
- · Global Antibiotic Research & Development Partnership (GARDP)
- · Institut Pasteur de Dakar
- Institute for Basic Science (IBS)

- Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán (INCMNSZ)
- · J&C Sciences
- · Kainos Medicine, Inc.
- · KaiPharm Co., Ltd.
- Korea Advanced Institute of Science and Technology (KAIST)
- · Korea Disease Control and Prevention Agency (KDCA)
- Korea Research Institute of Bioscience and Biotechnology (KRIBB)
- · Korea Research Institute of Chemical Technology (KRICT)
- Korea Institute of Radiological & Medical Sciences (KIRAMS)
- · Michigan State University
- · MK Consulting
- · National Institute of Molecular Genetics (INGM)
- · NeuroControls GmbH
- · The University of Melbourne

Scientific epilogue

Spencer L. Shorte CSO of Institut Pasteur Korea



During the 2020 pandemic IPK scientists and staff of IPK valiantly doubled their efforts at all levels. From basic to translational research, IPK not only maintained activities, but even increased its output. Much of the increase was reflected in provisioning services, collaboration and support rendered to Korean domestic partners. Driven by the critical public health need both academics and companies alike rallied resources unique to IPK's infrastructure, expertise and know-how. In parallel, international partners were abundantly present both in efforts to fight the pandemic, but also other infectious disease areas

too. Testifying IPK's excellence organizations such as DND*i* and TB-Alliance speak to the professionalism and commitment to high-quality science and service that is a hallmark to IPK's scientific service mission (see below). While 2020 witnessed our fighting SARS-CoV-2 IPK's scientists concomitantly continued fighting other infectious diseases too. This diversity of research know-how is important to maintain and even increase. In the current report we learn of the diversity of IPK scientists' knowledge covering from bacteria, to parasites, and viruses, and dynamized by cutting-edge technology know-how in drug-screening and imaging. In the future, knowledge on the immune system, and inflammation taken together with the study of infection, microbiota, and microbiology will help not only help better fight infectious disease, but also inform upon the etiology and improved therapeutic treatment of other diseases. So, bidding a farewell and thank you to Dr. Wangshick RYU (IPK CEO: 2017-2020) we are excited transitioning to the leadership of our new CEO Dr. Youngmee JEE who will pilot IPK into this future. As IPK scientists continue the search for new therapeutics to mitigate disease, we will assure the benefits are shared with the life science community in Korea, our Asia-regional partners, and beyond eventually through the global Pasteurian international network. To achieve this, IPK will focus strategic priorities on a research program reinforced by ever more cutting-edge technologies targeting anti-microbial resistance, and enhanced infectious outbreak preparedness.

Recognition by collaborators



Dr. Mel Spigelman (MD) President and Chief Executive Officer of TB Alliance

We cannot hope to end TB without dramatically shorter, simpler and better treatments. Institut Pasteur Korea has been (and still is) key in implementing and performing the GARDP screening strategy. The collaboration has been very productive with over 24,000 compounds screened in 2020 and we plan to continue these efforts with Institut Pasteur Korea in 2021 and beyond.



Dr. Jean-Robert loset Senior Discovery Manager of Drugs for Neglected Diseases initiative

Institut Pasteur Korea is an amazing, fully dedicated and extremely competent partner with a long and successful collaboration history with DND*i*. The access to the Institut Pasteur Korea discovery HCS technology platform and associated expertise is definitively one of the critical pillars of the DND*i* drug discovery program targeting Neglected Diseases.



Dr. Anastassia V. Komarova Institut Pasteur (Paris)

The protein-protein interaction platform of the Technology Development Platform of Institut Pasteur Korea was key to validating the molecular mechanisms underlining viral protein regulation of innate immunity and cell death pathways in host cells.



Institut Pasteur International Network



33
Nember Institutes

Member Institutes



25

Countries



Pasteurians



10

Nobel Laureates



The Institut Pasteur International Network brings together 33 institutes, located in 25 countries across the five continents, united by the same missions, the same culture, and the same values. Leveraging vast human and scientific community, the Network is involved in international research projects, public health, teaching and training programs.

For the past century, the Network has served as a sentinel for emerging infectious diseases in several endemic regions of the world, leveraging unique multidisciplinary cooperation in the field of human health by fighting against infectious diseases.

By its diversity and global presence, the Institut Pasteur International Network aims to respond, in an innovative way, to international public health priorities.

Institut Pasteur International Network



Prof. Pierre-Marie Girard

Executive Vice-President for International Affairs, Institut Pasteur (Paris)

"Institut Pasteur Korea has grown over the recent years as an essential partner within the Institut Pasteur International Network. As a key player in the field of Applied Research and Technology Transfer for the benefit of Global Health, IPK's interactions have been shown to be highly beneficial for all. We particularly appreciate its leading role in image-based innovations illustrated by the setup of a Pasteur International Unit with Institut Pasteur on "Artificial intelligence for image-based drug discovery & development (Ai3D)" and the different initiative with African partners for the rapid detection of e.g. malaria infections. Next, we are looking forward to the growing involvement of IPK to place research outputs in a wider clinical research and public health perspective and as such, make other partners gain from their expertise in the business of managing science. Within this context IPK's actions are of national, regional and inter-regional importance for the scientific radiance of our Network."



Dr. Jennifer HeurleyDeputy Vice-President for International Affairs, Institut Pasteur (Paris)

"Korea has remarkably controlled the epidemic by ensuring economic and academic continuity through adaptation measures. In support of this effective health management, Korea was able to take advantage of its scientific and industrial infrastructures, both for the massive production of tests and for research into therapies, to which the Institut Pasteur Korea (IPK) has contributed. Indeed, IPK's expertise in high-content phenotypic screening, using robotics, automation, artificial intelligence and imaging technologies, allowed to contribute effectively to the national effort by testing several thousand molecules from its chemical library in record time. In particular, this highly original approach has enabled it to identify Nafamostat, an anticoagulant used in Korea to treat pancreatitis for over 20 years, as a potential candidate whose in vitro results against COVID-19 have shown promise. The first clinical trial was prepared in collaboration with the Institut Pasteur de Dakar, another member of the Institut Pasteur International Network. The Senegalese authorities, at the highest level of government, were quick to approve the principle of this trial, which was financially supported by the French and Korean governments. The mobilization of the three governments of Korea, France and Senegal around this scientific collaboration aimed at identifying and making available a treatment against COVID-19 as soon as possible and for the benefit of the populations led to the joint invitation of the IPK and the Institut Pasteur de Dakar, to the Paris Peace Forum. This very high-level event bringing together political and civil society leaders with international experts is a recognition for IPK's contribution to science, health and society."



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