Institut Pasteur Korea

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R&D STRATEGIC PLAN

INSTITUT PASTEUR KOREA

Asia-Pacific Regional Hub of Infectious Disease Research

Contributing to Global Public Health

Institut Pasteur Korea

2022-2026 R&D Strategic Plan

Institut Pasteur Korea (IPK) is an international research institute with a primary mission to develop tools to control infectious diseases, including drug development. The institute was established in April 2004 through collaboration between the Institut Pasteur Paris (IPP) and the Korea Institute of Science and Technology (KIST). The Ministry of Science and ICT (MSIT), and the Gyeonggi Provincial government have provided continuous support for IPK, and during the last several years, IPK made full efforts to diversify funding sources.

Celebrating the 18th anniversary in 2022, IPK leadership and teams are proposing a new strategic plan to guide our operations in the immediate future and throughout 2022-2026. The 2022-2026 strategic plan proposes a rejuvenation of IPK's scientific mission, including the development of new infrastructure and technology and new scientific thematic. Amidst the international response to the COVID-19 pandemic, this strategic plan complements the new Korea Virus Research Institute (KVRI) of the Institute for Basic Science (IBS), a unique instrument for Korean scientific cooperation and outreach, building the capacity to provide an open platform for international partners. The time has come to prepare for and implement the next phase of strategies for IPK.

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INSTITUT PASTEUR KOREA

TODAY

IPK's Role and Impact

COVID-19 as a case study of our relevance

Since its conception 18 years ago, the IPK has reached a pivotal moment to reset the ways to collaborate with both Korean and international partners. It is important to reflect on the lessons learned from the events during the last two years of COVID-19, the pandemic that constitutes the public health emergency of international concern.

The Korean government initiative to establish IPK in 2004 created the basis for the preparedness that allowed cutting-edge translational research capacity to be deployed for accelerated therapeutics discovery in response to a newly emerged infectious disease, COVID-19 in 2020. IPK's research experience with SARS-CoV-1, and MERS-CoV enabled a prompt drug repositioning screening approach to SARS-CoV-2. In this context, IPK has excelled as readily "fit for purpose," mobilizing and focusing its resources and research capacity within days to weeks to quickly identify therapeutic options to help fight current and future pandemics.

- The COVID-19 crisis is one of the series of public health events caused by infectious pathogens that speaks to the future need for drug discovery resources to be dedicated to fighting emerging infectious diseases. Furthermore, an epiphany during this crisis is the realization that not only vaccines but also therapeutics are integral to a robust public health response.
- Within just a few months of the first COVID-19 cases in Korea in January 2020, IPK adopted drug repositioning strategy and discovered four promising drug candidates that are currently undergoing several domestic and international clinical trials. Significantly, collaboration through the Pasteur Network and partnership with the French Ministry of Foreign Affairs and the Korean Ministry of Science and ICT played significant roles in initiating international and domestic clinical trials by demonstrating the leadership to ensure coordination between industry, government, and clinical/public health and academic partners. IPK has not only proved as a pre-clinical R&D vehicle, but also demonstrated its value as a strategic partner by working closely with public-health sectors.
- Of the government (National Research Council of Science & Technology [NST], IBS, Daegu-Gyeongbuk Medical Innovation Foundation [DGMIF], etc.) and private industry laboratories working on infectious diseases and therapeutics in Korea, none has been as well placed as IPK to successfully pivot resources to address the immediate needs precipitated by the COVID-19 pandemic. This response is testimony to the founding stakeholders' vision of IPK being singularly fit-for-purpose as an R&D institution that directly benefits public health.
- IPK's performance in response to the COVID-19 crisis clearly highlights the value of 18 years of investment by MSIT into research capacity-building for drug discovery in the field of infectious diseases.

> IPK has demonstrated that it represents Korea's preparedness for future infectious disease outbreaks, precisely as a result of the MSIT's prior investment. Accordingly, the premise of IPK's new 2022-2026 Strategic Plan must consolidate a "preparedness strategy," with R&D capacity ready to mobilize against emerging infectious disease threats while maintaining active research on continuing threats, such as anti-microbial-resistant pathogens.

Current Status Quo

- Founded in 2004 under the auspices of the MSIT and Gyeonggi Provincial government, IPK is an international research institute aimed at therapeutics discovery for treating infectious diseases to benefit public health.
- IPK is a private, non-profit institute governed by a board of directors (BoD) and an executive/management leadership of CEO, CSO, and Administrative-Director.
- IPK's annual budget is around $17M, and the yearly umbrella budget of approximately $5M funded by the MSIT will terminate at the end of 2022. The remaining $10-12M of the annual budget is raised from variable sources, including fee-for-service(FFS) activities, technology transfer, and indepen dent project-driven grant incomes. With its current annual budget, IPK maintains only about 100 personnel (~75% research-staff of which each 44% and 49% are PhD and Master's qualified and 18% are international) cf. physical capacity of ~250 personnel.
- IPK has built a top-level research capacity connecting biocontainment infrastructure, equipment, and know-how for infectious diseases studies. The discovery biology teams spe cializing in different pathogens covering viruses, bacteria, and parasites are dedicated to developing cell-based phenotypic assays, which are then implemented in a technology division equipped with high-throughput/high-content screening and medicinal chemistry expertise to facilitate drug discovery to combat infection. IPK has a strong convergence of expertise in advanced technologies for infectious disease drug screening using cell-based phenotypic assay. IPK's globally renowned expertise has no equivalence on the Korean peninsula and is comparable internationally with only a few sites in the world.
- IPK distributes its resources according to public health in terests and research needs. IPK's discovery biology programmes include tuberculosis, antibiotic resistant bacteria (including nosocomial), viral hepatitis, and emerging zoonotic viruses such as Zika, Ebola, influenza, SFTSV, and human coronaviruses(including SARS, MERS, and SARS-CoV-2).
- IPK has proven technology-transfer ability, bringing new drug discovery into clinical trials. For example, IPK discovered the anti-tuberculosis compound (Q203; Telacebec*), which has completed Phase IIa clinical trials. First-in-class telacebec has been described as "...the first all-new pan-tuberculosis regimen of the 21st century; making the distinction between drug-susceptible and drug-resistant TB obsolete." (Jager et al., 2020; NEJM 382;13).
- Most recently, IPK has excelled as a COVID-19 frontline research laboratory at the forefront of identifying FDA-approved drugs as candidates for the treatment of COVID-19. (Jeon S, et al.2020; Antimicrob Agents Chemother 64:e00819-20, Ko M, et al. 2021; J Med Virol. 93(3);1403-1408). Four lead clinical candidate are sponsored in ongoing international clinical trials.

* Licensed out to and currently under development by Qurient Therapeutics Co., Ltd. (www.qurient.com)

Challenges Ahead

Three key areas to be bolstered by a new strategic plan aligning R&D efforts in the post-COVID-19 era

New strategies will provide insights to accelerate the translational drug discovery pipelines. Furthermore, basic research and therapeutics discovery will be prioritized for infectious disease preparedness and research readiness.

LEADING INFECTIOUS DISEASE TECHNOLOGY INNOVATION

AI-driven technologies combining image-based morphology, transcriptomics, proteomics, metabolomics, cytometry and cheminformatics will allow data analysis multiplexing to enable next-generation high-content screening (HCS) for antimicrobial drug discovery. Image-based high-content screening (HCS) will again be the catalyst for change, specifically, in connection with i) deep learning/AI technology and ii) the multiplexed and multi-omics data and analysis that define the next generation of drug discovery tools. With image data at its core, IPK is well-positioned to lead the next generation of HCS technology development the benefits of which will primarily impact Korean researchers by boosting their arsenal of tools for therapeutics discovery in infectious diseases.

WORLD-CLASS PATHOGEN BIOCONTAINMENT INFRASTRUCTURE

IPK's BSL-3 and ABSL-3 biocontainment infrastructure and expertise ensure its ability to handle a broad-spectrum of new and emerging infectious disease pathogens. IPK is heavily invested in establishing specialized (BSL-3/ABSL-3) bio-containment infrastructure to enable manipulation of equipment, reagents, and high-risk BSL-3 pathogens. With research knowledge and expertise in drug discovery targeting infectious diseases, IPK can manage a variety of high-risk pathogens, including viruses, bacteria, parasites, and fungi. IPK's BSL-3 expertise is at the disposition of Korea's biomedical research community, both as a service and as a facility resource.

AGILE INFECTIOUS PATHOGEN RESEARCH CAPACITY

IPK has proven research resources that can be rapidly reconfigured to face new challenges. In the decades leading up to COVID-19, pandemic risk swelled and ebbed with SARS, MERS, H1N1, and other viral diseases, including Zika, chikungunya, and Ebola. In addition to these, there have been several other serious global infectious disease risks, for example, antibiotic-resistant bacteria (both nosocomial and community-acquired), including multidrug resistant tuberculosis, MRSA, foodborne and intestinal pathogenic bacteria, and other emergent multidrug-resistant nosocomial pathogens like the yeast Candida auris, which has manifested in major urban healthcare networks worldwide, including Seoul. IPK's research resources have proven sufficiently agile to rapidly pivot and redeploy to handle previously unknown new infectious disease challenges. Expanded broad-spectrum BSL-3 biocontainment infrastructure that will be completed by the end of 2022 will further ensure the efficient management of new pathogens, thereby providing a unique contribution to the preparedness of Korea's research capacity to fight new infectious diseasessuch as COVID-19.

To implement our new strategic plans and meet expectations in the field of infectious disease research, IPK clearly needs to secure highly qualified scientists and experts and connect with international research partners and funders.

INSTITUT PASTEUR KOREA
2022 – 2026

Institut Pasteur Korea pursues scientific excellence and performs the role as the Asia-Pacific regional hub for the Pasteur Network by strengthening its engagement with public health initiatives.

Vision and Path

To contribute to global pandemic preparedness, Institut Pasteur Korea (IPK) sees a post-COVID world where our priorities must focus on preparedness research on emerging infectious diseases and anti-microbial resistance (AMR) with "One-Health" approach. Accordingly, IPK scientific leadership has identified five strategic areas for key actions. The five strategic areas articulate codependency and interplay between: scientific-technology R&D, infrastructure, shared resources, education/ teaching and international networking.

We propose to progress our new strategic vision by reinforcing our research, collaboration and partnership role both domestically, and internationally in the Asia-Pacific region. To achieve this our strategy is founded on goals developing our strengths: innovative technology for drug-discovery in infectious pathogens, sharing access to biological and infrastructure resources with our domestic and international infectious disease communities, and accelerating technology transfer for faster delivery of research discovery and innovation. This way IPK aims to establish itself as a motor to the Asia-Pacific biohealth research hub.

Our scientific strategic goals outlined in the following pages include developing immunological studies and expertise among our faculty. In particular, immunological research studies seeking to validate antibody therapeutics, and therein discover immunomodulatory molecules able to boost desirable immune responses (e.g. novel adjuvants), and/or minimize undesirable immune effects (e.g. unwanted inflammatory responses).

Further, in our new strategic plan we have prioritized methodologies and technologies aimed at improving the speed and precision of hit-to-lead prediction in the pre-clinical drug screening pipeline. For example, using advanced immunomonitoring single-cell flow-cytometry, and emerging multi-omics technologies and workflows.

Along these lines we consolidate and build upon our Pasteur International Joint-Research Unit embedded to our screening platform elaborating research-initiatives for deep-learning driven data analysis, and optimizing phenotypic high-content high-throughput drug screening.

These research efforts are aimed to have transversal comple-mentarities with our established BSL-3 image-based screening facilities, and to bolster the traditional small-molecule drug development pipeline.

Similarly, we will focus efforts on ADMET- based rationalization of compound formulation for enhanced hit-lead identification to improve the early drug development workflow using biophysical, biochemical and medicinal-chemistry insight to provide added value.

Naturally these research aims demand improved infrastructure for pre-clinical research implementing new R&D technologies into biocontainment laboratories equipped adequately to handle high-risk pathogens. For this reason, we will reinforce our animal team expertise and enhance preclinical infrastructure with new technologies for in vivo small-animal imaging. With the support of the Ministry of Science & ICT, Research Resource Center IPK will be equipped with additional BSL-3, ABSL-3, and Bioresource Center to help infectious diseases research for IPK and external researchers, including the Pasteur international Network.

Operational and implementation challenges characterize the burgeoning need for access to limited BSL 3 biocontainment laboratory infrastructure, and bioresources. Accordingly, IPK aims at expanding BSL-3 lab space equipped with the latest research tools open-access sharing with our domestic, and Asia-hub partners.

We invite you to share and join in our strategic vision, which we believe will further IPK's contribution to global infectious disease research, hoping to advance Pasteur's mission assuring excellent basic and translational-science to benefit public health by knowledge-sharing, innovation and savvy technology-transfer.

Five-Year Roadmap

Vision

Institut Pasteur Korea pursues scientific excellence and performs the role as the Asia-Pacific regional hub for the Pasteur Network by strengthening its engagement with public health initiatives.

Mission

- **Reseach** — Reinforce the connection between basic/translational infectious disease research and commercialization.
- **Public Health & International Collaboration** — Strengthen partnerships with the Pasteur Network, especially in the Asia-Pacific region, and expand collaboration with domestic/international research institutes, health organizations, industry and academia.
- **Education** — Activate scientific exchange through training courses utilizing the Pasteur Network, and advance the education, including the Master's and Doctoral programs of the University of Science and Technology-IPK Campus, in collaboration with domestic/international universities and related institutes.

R&D Strategic Plan

01	02	03	04	05
Expand research areas to broaden responsiveness to emerging diseases	**Empower AI-based research** to establish IPK as a world-class center for excellence in infectious disease high-throughput screening (HTS) serving Korea and the Pasteur Network	**Reinforce preclinical research** to accelerate the translation of scree-ning results to public health	**Establish a Research Resource Center** as a ONE-STOP research support system for responding to infectious disease threats	**Activate internation-al networks** and lead the Asia-Pacific region as a research hub

Core Values

Communication | **C**ollaboration | **C**ompetency

Professionalism | **P**articipation | **P**artnership

3Cs & 3Ps

R&D STRATEGIC PLAN

Pillar 1

Expand research areas to broaden responsiveness to emerging diseases

Key Projects

01. Introducing immunological perspectives and antibody therapeutics
02. HTS approaches in early drug formulation and ADMET for drug development
03. Supporting real time surveillance with global genomic database of emerging infectious diseases

Pillar 2

Empower AI-based research to establish IPK as a world-class center for excellence in infectious diseases HTS serving Korea and the Pasteur Network

Key Projects

01. Pasteur international research unit: Artificial intelligence for image-based drug discovery & development (Ai3D)
02. Chembioinformatics-driven drug discovery and development to combat pathogens causing infectious diseases
03. Multi-omics and orthogonal big data analysis: Combining phenomics, cheminformatics, genomics, and transcriptional data analysis

Pillar 3

Reinforce preclinical research to accelerate the translation of screening results to public health

Key Projects

01. Enhancement of preclinical infrastructure and networking for infectious disease research
02. *In-vivo* imaging and quantification of pathogens and host inflammatory responses
03. Establishment of a cutting-edge in-vivo 3D ultra-high content imaging system
04. Single-cell analysis of host responses to infection using preclinical models

Pillar 4

Establish a Research Resource Center as a ONE-STOP research support system for responding / to infectious disease threats

Key Projects

01. Establishment of infectious disease bioresource cluster for emerging and dangerous infectious disease preparedness
02. Expansion of ABSL-3 and BSL-3 facilities
03. Providing open access to the core facilities specializing in infectious disease research
04. Education and training of experts specialized in infectious disease research

Pillar 5

Activate international networks and lead the Asia-Pacific region as a research hub

Key Projects

01. Fostering a global network and cooperative system for research in infectious diseases
02. Using a One Health approach to tackle antimicrobial resistance (AMR)
03. Building international collaboration around emerging viral diseases

Pillar 1

Expand research areas
to broaden responsiveness to emerging diseases

IPK has made tremendous efforts to adopt and utilize state-of-the-art technologies for effective drug screening and further development, primarily focusing on infectious diseases that range from neglected diseases to pandemic viral diseases and cancer. As a result, IPK has been positioned as a central hub for drug discovery in South Korea and beyond. Strategies for intervening in pathogen–host cell interactions have been successful because high-throughput (HT) and cell phenotype–based screening can generate efficient and reliable hits and candidates, which have at times led to license-outs and progression to clinical trials.

However, some niches must be filled to better prepare IPK for emerging or reemerging infectious disease challenges as an institute rooted in translational research. During the last two decades, advances in immunology have allowed for novel approaches to controlling various diseases, including pathogenic infections, and antibody-based drugs have become a major target-specific therapeutic platform. Furthermore, early formulation and ADMET (absorption, distribution, metabolism, elimination, toxicity) characterization of lead/candidate compounds may contribute to successful drug development. Finally, global surveillance and diagnostic infrastructure must be established for proactive preparedness to emerging infectious diseases.

Therefore, IPK seeks to maximize its capability to adequately respond to emerging diseases by expanding its research areas including immunology, antibody therapeutics, early drug formulation and ADMET studies for the development of preventive and therapeutic measures and construct diagnostic infrastructure to proactively reduce the impact of the global health threats

Goal

The goal of this expansion is to equip IPK's platforms to develop effective therapeutic and preventive countermeasures, leading to success in the fight against emerging and re-emerging infectious diseases. IPK aims to enhance its research capacity by appending several key study fields:

01. Immunology and antibody therapeutics
02. HT drug formulation and ADMET studies
03. Supporting real time surveillance based on genomic database of infectious diseases

Key Project 1

Introducing immunological perspectives and antibody therapeutics

To quickly develop both prophylactic and therapeutic methods to successfully control emerging infectious diseases, IPK now seeks to include immunological aspects in addition to its drug development methods that directly target pathogens or pathogen–host cell interactions. The institute has recently added the Viral Immunology Laboratory (VIL) to conduct immunological studies of viral infections and prophylactic vaccine development. By understanding how pathogens cause immune system malfunction, critical immune-mediated symptoms can be targeted in drug development.

Moreover, advances in genetic engineering, along with the hybridoma technique for producing large amounts of monoclonal antibodies (mAb), have enabled the successful translation of antibody-mediated drugs to clinical use. By taking advantage of antibody-based drugs and leaning into its infectious disease expertise, adding to its expertise in small molecule drug screening, IPK will launch an antibody therapeutics research program to improve its preparedness for infectious diseases with methods other than chemical-based drug discovery.

Aim & Priorities

The aim of immunological research at IPK is to understand the immunological mechanisms of pathogenesis and immunity triggered by pathogenic infections and establish preventive and therapeutic strategies.

By studying animal and human viral infections, IPK seeks to understand the role of immunity in mediating path-ogenesis and immune responses in the context of respiratory viral infections, including influenza and SARS-CoV-2. The results of this research will form the foundation for exploring the relevant immunomodulatory molecules with IPK's outstanding screening resources. Studies to improve vaccine platforms for pathogens, in collaboration with academic/industrial partners, will refine vaccine platforms and thoroughly profile vaccine-mediated immunogenicity. Regarding the development of antibody therapeutics, IPK will explore approaches including humanized mouse immunization or single B-cell isolation from immunized/infected humans for the initial screening of target-specific mAbs.

- Define the immunological mechanisms of pathogenesis and immunity after pathogenic infections and vaccinations.
- Screen immunomodulatory (stimulatory/suppressive) substances.
- Sorting single B cells specific to desirable antigens and cloning variable regions of antibodies.
- Establishing a humanized mouse immunization model to produce human mAbs.

Expected Outcomes

1. Defined immunological targets of intervention to alleviate infection-mediated pathogenesis and symptoms.
2. An experimental platform to test immunomodulatory effects.
3. Capacity to initially screen antigen-specific human mAb.
4. Rapid development of antibody therapeutics during the emergence of new infectious diseases.

Key Project 2

High-throughput screening (HTS) approaches in early drug formulation and ADMET for drug development

One of the most important features in drug discovery is oral bioavailability, for which the key parameters are the capacity of the active pharmaceutical ingredient (API) to cross the intestinal barrier, access the portal system (the liver), and finally reach the general circulation intact. Although API should also be soluble in aqueous biological fluids to reach the target tissue, approximately up to 75% of compounds currently in development are poorly water-soluble, requiring substantial investments for formulation studies usually in the late stages of the development process.

This solubility factor is crucial because it also affects *in vitro* and *in vivo* efficacy, as well as drug metabolism and pharmocokinetics. It is estimated that up to 40% of drug candidates have failed due to drug–drug interactions or toxicity. Thus, both regulators and drug developers consider that chemical absorption, distribution, metabolism, excretion, and toxicity (ADMET) studies are required to evaluate the viability of a drug candidate.

The formulation and ADMET studies are critical as it is difficult to synthetically improve solubility and ADMET weaknesses when they are intrinsic to the main scaffold. Leveraging the versatility of IPK's HTS platform could allow formulation screening to be performed in the early stages of drug discovery and development (hit-to-lead) to better understand the properties and requirements of the scaffolds of interest, or to potentiate therapeutic efficacy by improving ADMET properties for both water-insoluble and -soluble APIs.

Aim & Priorities

IPK has been actively developing small-molecule drugs for potential therapeutic cures. An HT early formulation and ADMET related HTS platform must be versatile and robust to evaluate drug candidates. Some development is necessary to ensure compatibility with pre-existing pipelines:

- Generation of a library of bio-compatible excipients (e.g., co-solutes, polymers, surfactants, and lipids).
- Building of a customizable lipid nanoparticle (LNP)-formulation platform, with assessment of drug-loading efficiency.
- Establishing a phenotype-based HTS platform for cell-based metabolic and plasma drug stability.
- Automation of enzyme-based in-vitro ADMET studies using HTS platforms (CYP450 enzymes, UGT, and MDR1 [P-gp]) for inhibition or induction assays.
- Outsourcing and establishing business-to-business (B2B) contracts with contract research organizations for, e.g., *in-vitro* permeability and toxicity studies (with hERG, Ames, Comet assays, etc.).

Expected Outcomes

Knowledge of solubility and ADMET properties allows medicinal chemists to understand the efficacy and safety of a compound as a potential drug candidate in the early drug discovery stage.

1. A versatile, and easy-to-use multi-dimensional HT formulation platform.
2. Improved hit-to-lead optimization and preclinical studies using a rational formulation strategy.
3. A better understanding of the scaffolds of interest and their developability as drug-like candidates in the early stages of drug discovery.
4. Streamlined ADMET data handling.
5. ADMET big data results for small-molecule drugs that can be used for future AI-based drug discovery.

Key Project 3

Supporting real time surveillance with global genomic database of emerging infectious diseases

Emerging and re-emerging infectious diseases are unpredictable and create a gap between planning and responsive action. To overcome this gap, there is a need to come up with proactive systems that would ensure preparedness and response in anticipation of pandemic potential in infectious diseases. Proactive and comprehensive preparedness must be in place to reduce the impact of the public health threats.

After experiencing the rapid spread of high risk infectious diseases some information-based surveillance programs have been introduced in public or private institutional level, but still in short of the full expectation of the outbreak of infectious diseases. It is more and more important to gather and analyze the information of infectious disease occurrence world-widely in real time.

Identifying an infectious disease outbreak is crucial for both the initiation of health intervention measures and timely informing of the global health agencies. It needs to apply the information-based rapid detection methods in real time, and share the data with public database systems. IPK is set to coordinate and support the gathering genomic database of global infectious diseases utilizing the Pasteur Network.

Aim & Priorities

IPK has been actively participating in preparedness and responsive plan for the prevention and effective control of emerging and re-emerging infectious diseases world-widely. Our priorities for this goal include:

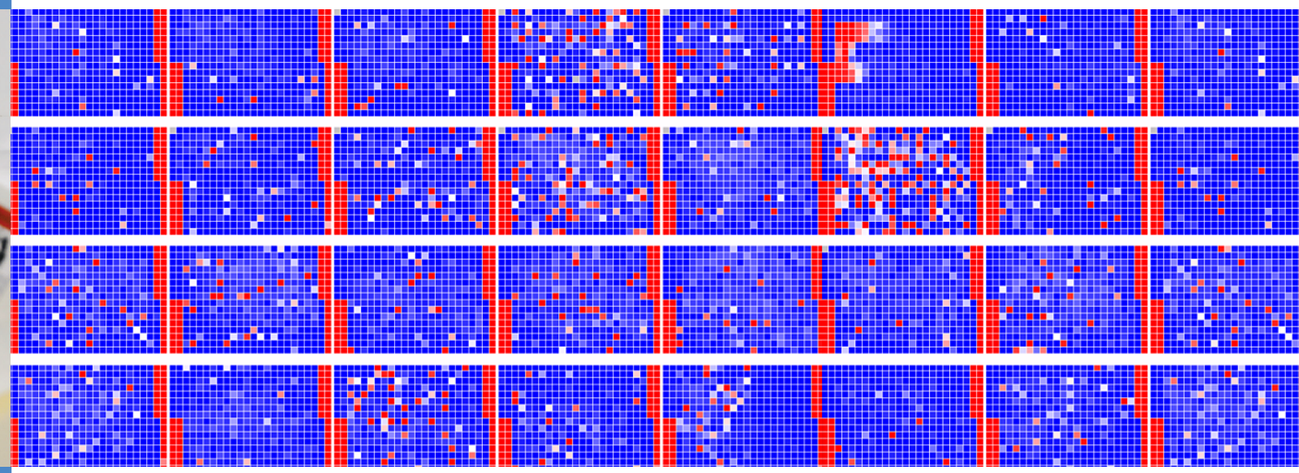
- Coordinated networks of infectious diseases: Organize adequate and efficient systems of coordination among network of infectious diseases both public and private needed in emerging infectious disease detection, preparedness, and response at national and international levels.
- Gathering information from global institutions and satellite labs to enhance disease surveillance: Improve case detection and surveillance of emerging and re-emerging infectious diseases with establishment and utilization of global infectious disease database to prevent and minimize its spread.
- Development and application of rapid diagnostic platform: Identification of high risk infectious diseases is crucial for the effective control of the possible outbreak with real time detection method established with the information of the database.

Expected Outcomes

Establishment and utilization of the global database linked to national bio-information system allows to prepare the real time surveillance system and the effective rapid diagnostic methods in advance of the outbreak.

1. Establishment and utilization system of the global surveillance network with the global database.
2. Development and application of rapid diagnostic methods based on the global database.

Pillar 2



Empower AI-based research
to establish IPK as a world-class center for excellence in infectious disease HTS serving Korea and the Pasteur Network

IPK was founded to establish the emergent new technology at that time: image-based HCS. Now advanced HCS technology development will again be the catalyst for change, specifically in combination with i) deep learning and AI technology and ii) multiplexed data analysis, which will define the next generation of drug discovery tools. With image data at its core, IPK is well positioned to be at the forefront of the next generation of HCS technology development, the benefits of which will primarily impact Korean researchers by enhancing their armory of tools for the discovery of infectious disease chemotherapeutics.

In addition to the emerging need to re-establish a strong image informatics team, IPK must also face a deluge of data. High-content, HT, and automated image-based screening and medicinal chemistry facilities are notably associated with certain data science and bioinformatics needs. IPK is therefore making a focused effort to establish new expertise in single-cell analyses (flow cytometry, immunological analyses), transcriptomics, bacterial metagenomics, image-based single-cell analysis (phenomics), bioresource biobanking, and cheminformatics (in silico structure–activity relationship [SAR] and structure–property relationship [SPR] modeling).

Toward IPK's mission to establish cutting-edge, next-generation drug screening and maintain competitiveness in today's data-driven world, the institute is compelled to build a robust, sustainable team for bioinformatics and data science. Innovative computational methods will allow compound screening data to be re-purposed and combined with knowledge of chemical/structural biology, bioactivity, transcriptomics, and interactome data. These approaches will promote the unparalleled sensitivity of phenotypic screening to complement in silico–based compound modeling in the prediction of new lead compounds and drug targets.

These emerging technologies will leverage the complex biological relevance of phenotypic screening to accelerate high-efficacy therapeutic discovery for to fight infectious diseases.

Goal

The goal is to establish in-house excellence in image informatics and chem-/bioinformatics.

01. Pasteur international research unit
02. Chembioinformatics-driven drug discovery and development
03. Multi-omics and orthogonal big data analysis

Key Project 1

Pasteur international research unit: Artificial intelligence for image-based drug discovery & development (Ai3D)

HT imaging–based phenotypic screening of chemical compound libraries has proven effective in identifying molecules that are active against pathogens responsible for infectious diseases. One result of its inherent biological relevance is the resurgence of phenotypic screening (compared with *in-vitro* target-based approaches) with enhanced predictivity in the discovery of first-in-class small-molecule drugs with improved therapeutic outcomes.

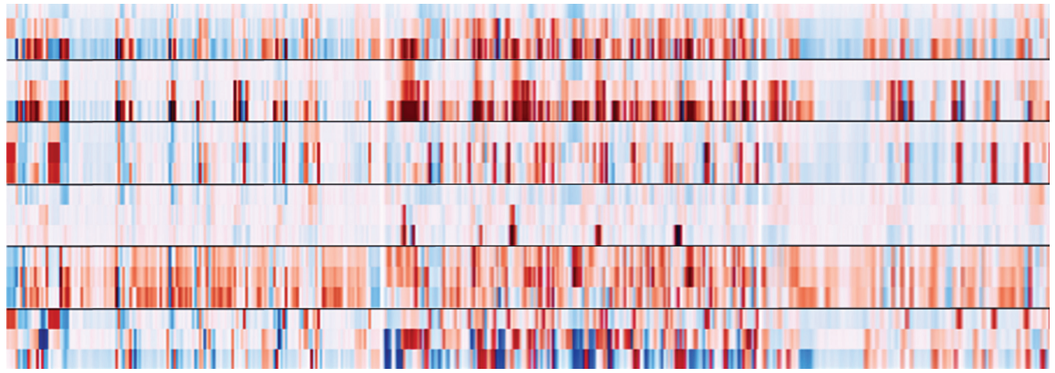
Internationally, IPK has been among the leaders in HT cell-based phenotypic imaging for chemical compound screening. However, key limitations of conventional phenotypic screening are its lack of insight into molecular mechanisms of action (MoAs), low sensitivity, and inability to distinguish activities in complex mixtures. We propose to address these limitations by developing strategies based on cutting-edge imaging methods complemented by new deep learning approaches, such as artificial neural networks. Major advances in HT automated microscopy have been accompanied by similar advances in computational methods for analyzing large-scale, image-based data.

There has been a recent renaissance in AI approaches based on machine learning and deep learning, which uses artificial neural networks to predict relevant information from complex unstructured data. Accordingly, these approaches have begun to appear throughout the drug screening pipeline, from single-cell analyses, to tissue histopathology, all the way to cheminformatics, transcriptomics, and gene target identification.

The Pasteur International Unit, focused on using AI for image-based drug discovery and development (PIU-AI3D), will establish innovative methods using AI, machine learning,and deep learning technologies applied to imaging for drug discovery. These methods will be powered by manifold databases, which notably include our HT chemical screening assay platform for phenotypic analysis of infected and non-infected cell-based paradigms. Automation to produce massive data outputs characterized by low system noise and high biological relevance will help us establish an unprecedented AI-amenable database resource for infectious disease drug discovery.

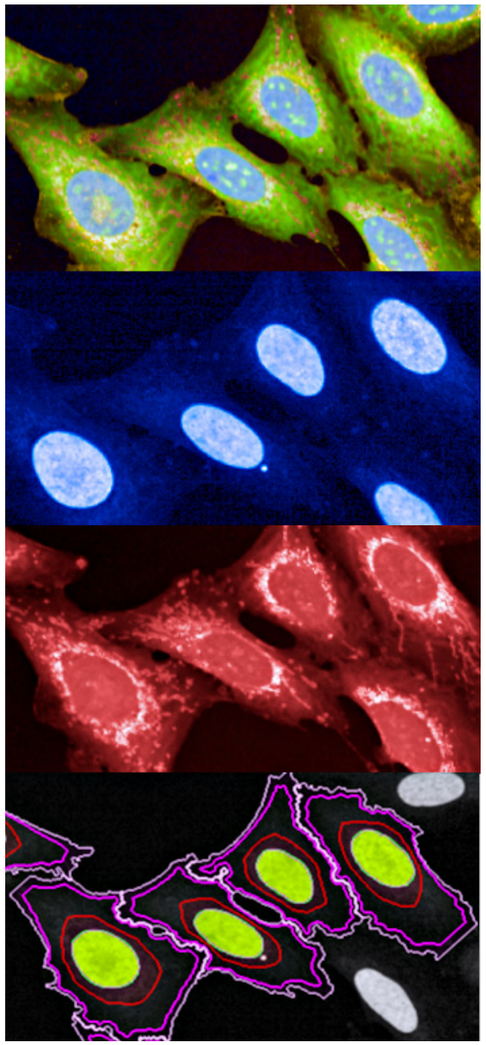
Aim & Priorities

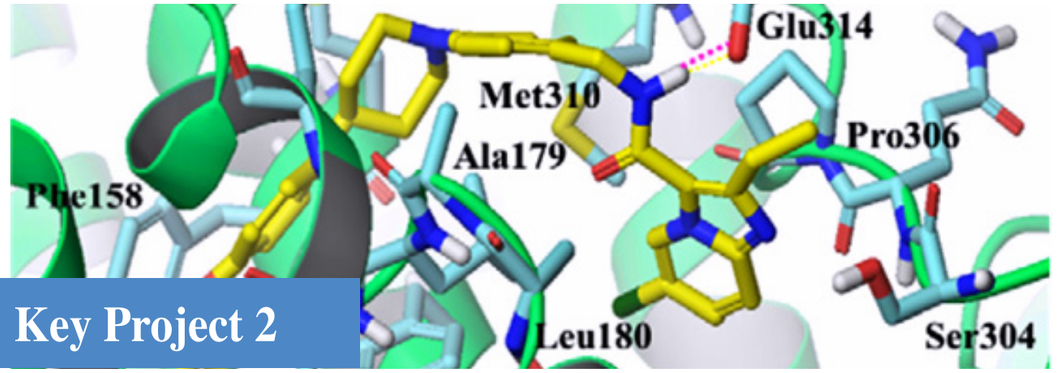
- Identification of drug targets with deep learning analysis of image-based phenotypic screens of isolated bacteria.
- High-sensitivity screening using “Cell Painting”: morphological cell profiling/fingerprinting in higher eukaryotic cell models (cell lines, primary fibroblasts, engineered immortal and stem cell lines).
- AI-/phenomics-driven target identification and drug discovery in viral infection models of host cell–pathogen interactions (using bright-field transmission and/or fluorescence imaging).
- Data sustainability, quality control, biological relevance, rigor, and reproducibility following Factor Analysis of Information Risk (FAIR) data principles and policies.
- Orthogonal, multiplexed multi-omics analysis using phenomics, transcriptomics, proteomics, and metabolomics to map functions to phenotypes.
- AI-driven phenotypic screening for bioactivity in diverse natural extract collections (marine, freshwater, and terrestrial sources).



Expected Outcomes

1. Systematic and robust research pipeline (service) for i) drug target identification using deep learning analysis of image-based phenotypic screens in selected clinically relevant bacterial, and ii) routine super-high-sensitivity screening with morphological cell profiling.
2. End-to-end AI-/phenomics-driven black-box screening pipeline for antiviral drug discovery in selected clinically relevant viral infection models of host cell– pathogen interactions.
3. Routine and sustainable image data generation, and storage based on transparent and standardized quality control, rigor, and reproducibility.
4. Implementation of orthogonal, multiplexed multi-omics analysis using phenomics, transcriptomics, proteomics, and metabolomics capable of mapping functions/MoAs to phenotypes.
5. AI-driven phenotypic screening service for screening bioactivity in diverse natural extract collections.





Key Project 2

Chembioinformatics-driven drug discovery and development to combat pathogens causing infectious diseases

The COVID-19 crisis has underscored the urgent need to develop and assess potential new therapies against viral and bacterial diseases and build a strong pipeline of anti-infective drugs. IPK has been at the forefront of drug discovery, mainly focusing on infectious diseases, by promoting multidisciplinary projects. Strategic determination of plausible drug targets of causal pathogens at the beginning of development will help us save time and improve effectiveness.

Genomic analysis of the causal pathogens will provide a more thorough understanding of the mechanisms of infection, leading to focused targets for drug discovery, vaccine development, and antibody therapeutics and highlighting genes for diagnostic strategies.

With more than 10 years of experience in the field of small-molecule synthesis and drug design considering both SAR and SPR, IPK will further synthesize novel compounds through data- and AI-driven drug design.

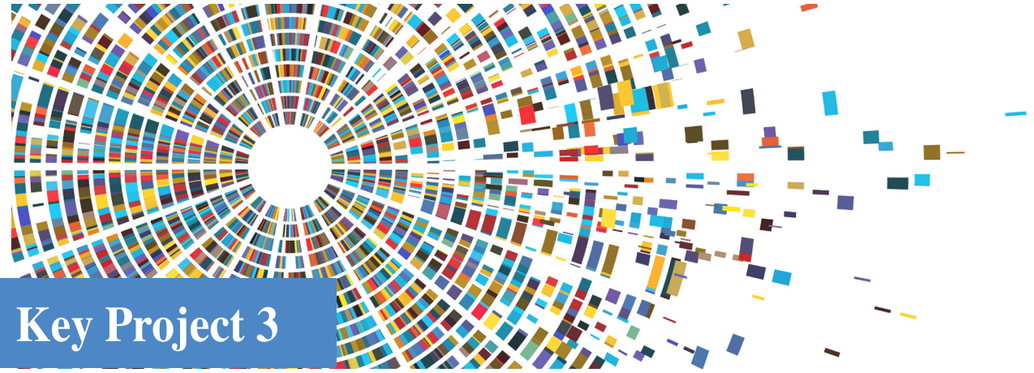
In addition to future target- or MoA-based drug design and the current ligand-based drug design with phenotypic screening, we will make a quantum leap in the effectiveness of drug development to cure infectious diseases.

Aim & Priorities

- Establish a state-of-the-art next-generation sequencing infrastructure for infectious diseases, including RNAseq, ATAC-seq, whole-genome sequencing for SNP analysis, and single-cell sequencing in BSL-2 and BSL-3 environments.
- Molecular modeling and virtual screening for structure-based drug design: protein structures of emerging pathogen targets will be virtually built using either de novo (Alphafold) or homology modeling techniques.
- HT screening and repurposing of synthesized compounds for potential drug candidates.
- Scaffold-, fragment-, and ADMET-based cheminformatics analysis of physicochemical properties and design of drug candidates.
- Establish an integrated drug discovery database with protection technology (blockchain).

Expected Outcomes

1. Sequencing and bioinformatics analyses of in vitro and clinically derived cells and pathogens generated via compound treatment to predict targets and MoAs of drug candidates.
2. Compounds of interests simulated together with virtually generated 3D structures and confirmed experimentally for structure-based drug design.
3. Synthesized therapeutic compounds identified as hits or lead candidates from HT screening and data-driven repurposing as potential drug candidates.
4. Hit compounds designed and synthesized for lead optimization from ligand- and structure-based drug development stages through combinatorial cheminformatics analysis.
5. A drug discovery database with integrated genomics/proteomics data, chemical structures, and experimental results, with data authenticity ensured by blockchain technology.



Key Project 3

Multiomics and orthogonal big-data analysis; Combining phenomics, cheminformatics, genomics and transcriptional data analysis

Finding new drugs depends on discovering novel chemistries that modulate biological processes based on their interaction with tangible molecular targets, ideally understood in terms of known MoAs. Establishing the MoA of a new drug candidate is a bottleneck and risk point in the drug discovery pipeline and a common reason for failure. Consequently, much R&D effort focuses on establishing MoAs, often using genomics- and/or proteomics-based technologies.

For example, next-generation HT sequencing yielding drug-induced transcriptomic profiles can reveal those profiles that are unique to any given MoA. Drug–target interactions can be extrapolated from a variety of data sources to deliver rich insights into drug MoAs, including both on-target and off-target effects, and identify novel indications for failed drugs.

To expand its screening competence by implementing multi-omics analyses, IPK will establish the links between the chemical database, in-house screening results (both single-point and dynamic reaction cell data), and corresponding images, and pursue any multi-omics data approach. Multi-omics integrates diverse-omics data to find a coherently matching genotype/phenotype relationship or functional associations. Performed in conjunction with high-performance/-sensitivity cytological profiling, this type of analysis promises to become a high-value asset in the discovery workflow for hit-to-lead characterization, SAR studies, and high-sensitivity screening of bioactivities in natural extracts.

Aim & Priorities

- Establish compound-/disease-profiling multi-omics matrices that are transparent and accessible to IPK researchers by deploying effective multi-omics database management software (commercial or open-source).
- Generate AI-based infectious disease models using the above approach (multi-omics matrices).
- Establish a FAIR-based open-innovation and open-data deployment of multi-omics analyses and data visualization using open-source or commercial software tools to benefit all IPK researchers.

Expected Outcomes

1. Compound-/disease-profiling multi-omics matrices that are transparent and accessible to IPK researchers, deployed with effective multi-omics data management software (commercial or open-source).
2. AI-based model generated from the multi-omics matrices focused on clinically relevant infectious diseases.
3. FAIR-based open-innovation and open-data deployment of multi-omics analyses and data visualization to benefit all IPK researchers.

Pillar 3

Reinforce preclinical research to accelerate translation of screening results to public health

A pandemic presents many challenges. For example, some scientists are tasked with determining how the infectious disease came to be, while others work to predict case counts.

IPK maintains a state of readiness to respond to emerging infectious diseases while simultaneously studying various diseases, pathogens, and compounds through cell- and image-based screening operated in BSL-2 and BSL-3 laboratories and identifying novel drug candidates. The identified candidates are further developed via evaluation of in-vivo efficacy in animal experiments.

Animal models play a critical role in infectious disease research, and selecting an appropriate model for each disease is key. Both immunocompetent and immunodeficient mice are important to such infectious disease studies. Inbred, immunocompetent mice are often chosen for infectious disease studies, and different inbred strains can show varying susceptibility to a particular virus, parasite, or bacteria.

We intend to maximize the efficiency of drug efficacy verification by securing animal models customized for various infectious diseases and building innovative in-vivo technology platforms that apply the in vitro image-based drug screening system to animal models.

Goal

To control various life-threatening infectious diseases, we must focus on gaining an in-depth understanding of the target pathogen's biology and disease pathogenesis, using appropriate systems to test the safety and efficacy of new treatments through strengthened networks for preclinical research.

To this end, we aim to establish an *in vitro–in vivo* translation(IVIVT) system by grafting a cutting-edge, *in vivo,* ultra-high content 3D imaging system to the development of several preclinical models for various future infectious diseases that can be quickly applied to the development of therapeutics, vaccines, and diagnostics with the following four key projects:

01. Enhancement of preclinical infrastructure and networking for infectious disease research
02. *In-vivo* imaging and quantification of pathogens and host inflammatory responses
03. Establishment of a cutting-edge, in vivo, ultra-high content 3D imaging system
04. Single-cell analysis of host responses to infection using preclinical models

Key Project 1

Enhancement of preclinical infrastructure and networking for infectious disease research

Since its establishment, IPK has maintained unsurpassed operations of ABSL-2 and ABSL-3 laboratories, where animal models of pathogenic infection are conducted with the support of biosafety staff, veterinarians, animal care technicians, and professional facility management teams. Because Korea continues to lack a systematic translational research organization to secure a new drug pipeline for infectious diseases, IPK's development of innovative drugs for infectious disease treatment candidates is indispensable.

Although the demand from external institutions for the use of our special facilities for animal experimentation continues, it is difficult to meet this demand due to active internal use. However, the excellence of IPK's animal testing facility and its operating system has already been proven, and the facility contributes substantially to the study of animal models of infectious diseases.

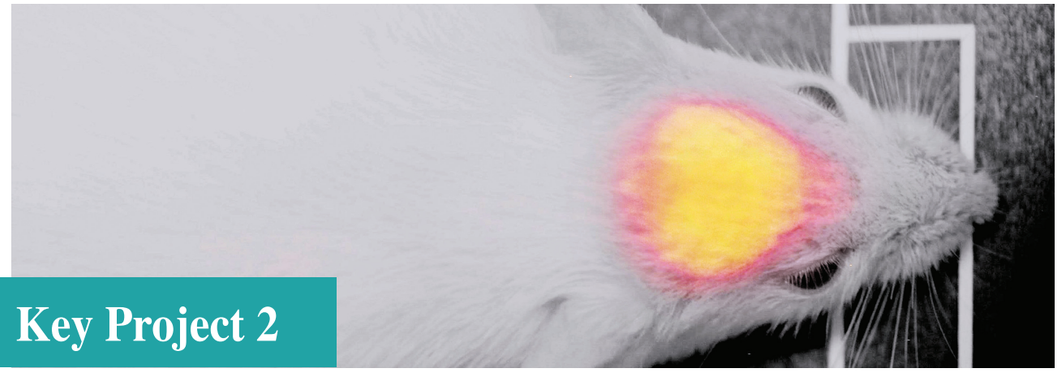
Aim & Priorities

Because IPK's infectious disease animal testing platform occupies an important position in the domestic drug development ecosystem, we aim to expand our specialized animal facilities, upgrade our animal models and techniques, and strengthen existing domestic andoverseas networks for preclinical research.

- Expand the rodent-based therapeutic efficacy evaluation platform to prepare for new infectious diseases.
  - Measurement of serological, histological, and immunological changes by infection time and analysis of viral kinetics for each organ.
  - Pharmacokinetic analysis of therapeutic agents for infectious diseases.
  - Specialized animal facilities: development of bio-behavioral evaluation technology for infectious disease treatment using bio-imaging equipment.
- Establishment of a preclinical R&D support council to respond to infectious diseases.
  - Comprised of infectious diseases and preclinical research experts (and organizations) for rapid research responses to outbreaks
  - Technical and human resources exchanges to unite and complement infectious disease research between organizations.
- Reinforcement of guidelines and approval processes for animal use in preclinical research
  - Establishment of an electronic documents approval and management system for the activities of the Institutional Animal Care and Use Committee.
  - Refinement and enhancement of guidelines for protocol preparation, compliance with regulations, and inspection of animal use in preclinical research.

Expected Outcomes

1. Rapid characterization of Disease X and facilitation of interventions development with cutting-edge preclinical platforms
2. Creation of an infectious disease preclinical research ecosystem to support investigations in academia and industry
3. Effective and reliable animal research with ethical and scientific justifications to ensure responsible and humane treatment of animals



Key Project 2

In-vivo imaging and quantification of pathogens and host inflammatory responses

When pathogens infect humans, they propagate in certain organs, and the immune system is activated to defend the body. Clinical symptoms mainly emerge from the organism's pathogenesis and the resulting immunopathology. An experimental model system must be established to monitor these dual perspectives of infections because such a model can guide intervention development. This is exemplified by the drugs available to COVID-19 patients, which are divided into those that inhibit the replication of the virus and those that suppress an excess immune response.

IPK aims to use its strengths in bio-imaging and infectious disease research to develop an in vivo imaging system to simultaneously quantify pathogenic infections and host inflammatory responses via bioluminescence or fluorescence imaging. With these techniques, researchers can monitor both the spread of pathogens to different host organs and the kinetics of the immune response.

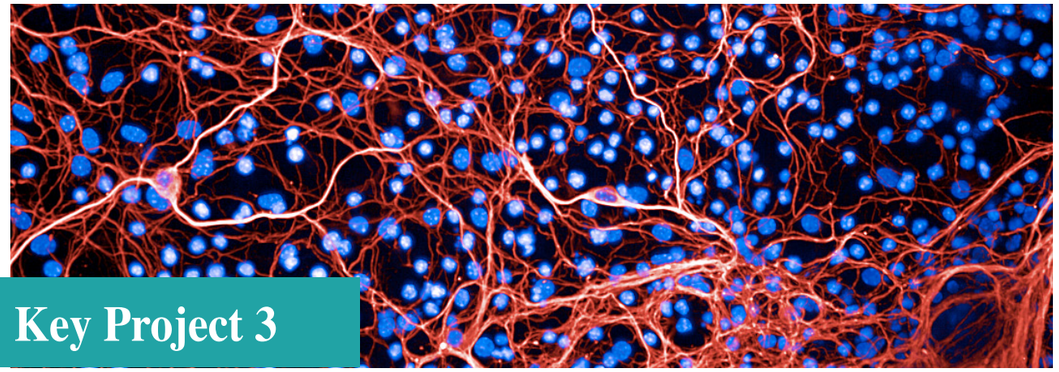
Expected Outcomes

1. Virus, bacteria, and parasite in vivo infection system that can monitor and characterize both pathology and immunopathology.
2. Experimental platform to evaluate drug efficacies and design treatment schemes for clinical applications.

Aim & Priorities

IPK aims to develop noninvasive in-vivo imaging model systems to efficiently monitor infection and host immune response. The technique involves tagging the pathogen of interest and developing a mouse with an immune reporter system. The reporting system will be implemented in various mouse organs to monitor the responses by different types of pathogens.

- Develop selective bioluminescent and fluorescent molecular labeling of pathogen and host rodent model.
- Implement real-time tracking of infectious events and physiological responses.
- Establish high-accuracy preclinical evaluation of drug effects.



Key Project 3

Establishment of cutting-edge in-vivo 3D ultra-high content imaging system

Traditionally, modalities such as immunohistochemistry and fluorescence microscopy have been used to localize cells in pathologic conditions. However, these methods provide limited information because the data are mostly 2D images and may omit cells.

To avoid these limitations, recent advances in total-organ imaging with tissue clearing methods have improved our understanding of the organization of intact tissues. However, the current staining methods are too laborious and inefficient for thick 3D samples.

Here, IPK aims to develop a novel strategy for visualizing immune reactions, cell–cell communication, and host–pathogen interactions within the pathologic tissue by establishing a cutting-edge in vivo ultra-high content 3D imaging system.

Ultra-high content 3D tissue imaging could be a versatile tool for discovering therapeutic agents for infectious diseases when used in combination with other experimental techniques.

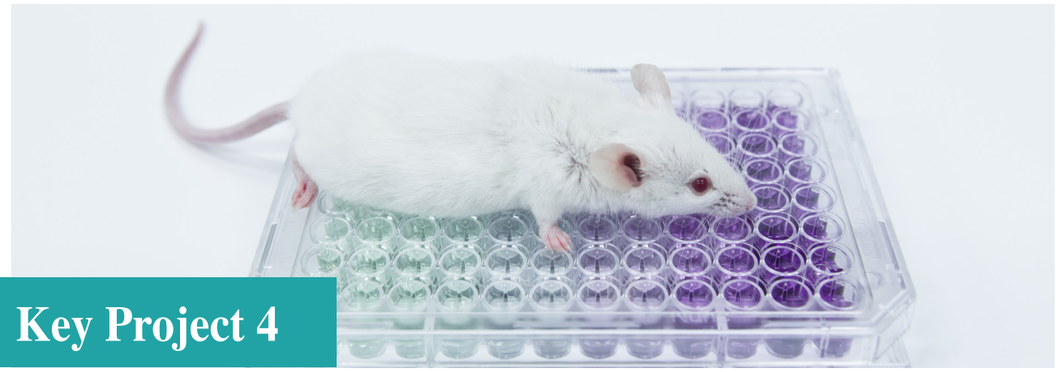
Aim & Priorities

We aim to apply innovative technologies to study detailed molecular and structural information in 3-dimensional tissues. With super-fast immunostaining technology, we can observe the complete 3D features of network architectures and molecular signatures that have never been seen before. A high-end 3D imaging platform for analyzing the 3D molecular signatures of deep tissues and organoids can be used for diagnostic purposes and to evaluate drug efficacy.

- Develop deep tissue immunolabeling procedures using active immunostaining followed by 3D scanning microscopy.
- Implement ultra-high content 3D tissue imaging for infectious diseases

Expected Outcomes

1. Rapid analysis of molecular signatures of disease pathogenesis in vivo with a versatile and reliable staining platform.
2. Fast and accurate 3D quantitative analysis and phenotyping of pathologic tissues for diagnostic purposes and evaluation of drug efficacy.



Key Project 4

Single-cell analysis of host responses to infection using preclinical models

Single-cell technologies have dramatically improved in the past decade. Research in genomics, transcriptomics, and proteomics at the single-cell level has unveiled diversity in cell subsets and individual cell heterogeneity in organisms, identifying new cellular features that have been overlooked by conventional bulk population studies.

Immunology, cancer biology, and developmental biology have benefited the most from these advances. In recent years, single-cell studies have been further extrapolated to investigate infectious diseases, revealing molecular details of host–pathogen interactions and immune responses, including rare molecules and sub-cell types that have crucial functions in such interactions.

In this key project, the most advanced single-cell technologies will be implemented as a cutting-edge tool for preclinical studies at IPK to investigate host responses during infection and facilitate not only basic research, such as infection pathophysiology, but also the discovery of vaccines, therapeutic agents, and diagnostic biomarkers.

Aim & Priorities

This project aims to integrate single-cell technology into IPK's preclinical research and use it to expand our comprehension of host responses to infectious agents and treatments and facilitate the translation of fundamental scientific discoveries to the clinical setting.

- Implementation of infrastructure for single-cell techniques at IPK in collaboration with leading domestic academic and industrial partners.
- Application of single-cell analysis to investigate host responses in different organs and cell types, such as immune cells, during infection.
- Expansion of single-cell analysis to pharmacodynamics in preclinical models to explore heterogeneous host responses to pathogens and drugs.

Expected Outcomes

1. Advancement of preclinical research, enabling comprehension of host behaviors and immune responses during infections as well as immune evasion mechanisms of different pathogens at the single-cell level.
2. Facilitation of translational research for the development of therapeutic and diagnostic targets and drug candidates against infectious agents.

Pillar 4

Establish a Research Resource Center as a ONE-STOP research support system for responding to infectious disease threats

When a new infectious disease emerges and causes a significant epidemic, the emergency response relies on research efforts toward understanding the newly discovered pathogen to develop diagnostics, vaccines, and therapeutics. The bioresources and core research infrastructure necessary to lead infectious disease research will play a crucial role in serving these goals.

IPK, as a member of the Pasteur Network for research on global infectious diseases, has begun to establish the Research Resource Center (RRC) to support infectious disease research. IPK RRC will be a core component in the research infrastructure for infectious diseases and will operate with the ONE-STOP support system to address the challenges of research responses to emerging epidemics and pandemics.

Goal

IPK RRC systemically operates a user-friendly Open Lab to provide bioresources, facilities, equipment, and education according to consumer needs. The Open Lab supports full-cycle R&D to overcome infectious disease outbreaks. IPK RRC has 4 main goals:

01. Establish a Bioresource Center (BRC) to collect high-risk or newly emerging infectious bioresources
02. Expand BSL-3 and ABSL-3 facilities
03. Construct the ONE-STOP Open Lab environment
04. Educate and train the experts specialized in infectious disease research

Key Project 1

Establishment of infectious disease bioresource cluster for emerging and dangerous infectious disease preparedness

Bioresources are essential experimental research materials for life sciences and bio industry. The infectious disease BRC, once established, will become a core component of the infectious disease research infrastructure. Rooted in 3 principles—Trust, Sustainability, and Initiative—IPK BRC is committed to receiving depositions/donations of bioresources from the medical/scientific research areas, confirming the authenticity of the bioresources, and preserving and distributing them appropriately. IPK BRC's mission is to provide the high-quality, standardized bioresources needed to create novel therapeutics, vaccines, and diagnostic tools.

To achieve this mission, IPK will establish the Human Bioresource center to collect and provide blood materials. IPK will then implement a Customized Pathogen Culture Collection to similarly collect and provide pathogens. Standardized bioresources will be provided to the infectious disease research community. Finally, IPK will provide education and training for the handling of infectious bioresources in BSL-2/-3 facilities to proper consenting and business planning processes to ensure that these samples are used instead of remaining in storage. As the handling (banking) of infectious bioresources has become more professional, there is a specific need for education and training on these procedures. IPK facilitates international cooperation by building capacity in established collaborative platforms, such as PIBnet (Pasteur international Biobanking network), and plans to build a new relationship with an emerging dangerous pathogens biobank, which will play a key role in facing these methodological and ethical challenges.

Aim & Priorities

- Establishment of the Human Bioresource Bank.
  - The bank will collect and provide human specimens containing high-risk viruses/antigens/antibodies/ nucleic acids to the biomedical research and industry communities.
  - To secure human specimens, a global biobank network will be established for sharing bioresources among the research community.
- Establishment of the Customized Pathogen Culture Collection.
  - The Customized Pathogen Culture Collection will collect and distribute pathogens based on the needs of researchers studying new and emerging infections under high-quality BSL-2/-3 facility standards.
- Production of Standardized Bioresources
  - IPK BRC will produce standardized bioresources for quality assurance of biological medicines and diagnostics.
- Education and Training
  - The BRC will develop an appropriate range of education and training opportunities for the diverse needs of researchers who are not familiar with the field but want to conduct infectious bioresources–based research.

Expected Outcomes

1. Provide infectious bioresources to researchers unable to acquire human blood to contribute to the development of basic and medical sciences.
2. Produce quality-controlled materials to ensure consistent production of accurate products, improve the diagnostic accuracy of laboratory medicine, and control the quality of test results.
3. Establishment of partnerships with external institutions (other bioresource centers, hospital-based staff, clinical centers, and companies).
4. Create economic value with materials and maximize import substitution by improving the long-term stability of materials, ensuring material reliability through international standardization, and improving material utilization at home and abroad.
5. Contribution to the utilization network of various infectious bioresources.

Key Project 2

Expansion of ABSL-3 and BSL-3 facilities

IPK was the first organization in Korea to obtain BSL-3 research facility permission and will build and operate a 1,688 m^2 Research Resource Center on its foundation of 15 years of advanced operation and management experience. Through this, we intend to strengthen our emergency response capabilities against infectious disease crises, a common threat to humankind, and play a pivotal role in national and international cooperation between the public and private sectors. We will build additional infrastructure, such as (A) BSL-3 research facilities and resource banks that can handle high-risk pathogens, and open the facilities to ensure easy access for the private sector, thereby supporting direct research activities at the private level. IPK further plans to become a center for strengthening basic and core research on viral infectious diseases together with the KVRI so that industry, academia, and researchers can use it jointly and acquire research capabilities to accelerate the linkage and utilization of basic research results.

Aim & Priorities

Using our strength of private access to virus research infrastructure with limited private investment, IPK will build a research facility capable of handling high-risk pathogens at the national level based on the demand of related companies. We will complete the (A)BSL-3 facility permission process for the Korea Disease Control and Prevention Agency by June 2023. We will use this infrastructure to provide a safe and consumer-oriented research environment.

- BSL-3 facility (Approx. 243 m^2, 4 laboratories)
  : Facilities for testing and researching risk group 3 pathogens, such as COVID-19, MERS, and *Mycobacterium tuberculosis*
- ABSL-3 facility (Approx. 322 m^2, 3 laboratories, 2 breeding rooms, 2 autopsy rooms)
  : Facilities for testing and researching animal infection models, comparable to a general BSL-3 research facility
- : Facilities for rapid acquisition of pathogens, sample production, and storage

Expected Outcomes

1. Core strategic infrastructure that will lead infectious disease research and promote innovation in national research infrastructure, which will be opened to the public for their benefit.
2. Establishment of a domestic infectious disease research hub, strengthening IPK's role of linking the public and private sectors by securing the safety of research labs, reducing costs, and providing quality services through open innovation.
3. Creation of an environment that nurtures experts of viruses and infectious diseases, of whom there are few in Korea.

Key Project 3

Providing open access to the core facilities specializing in infectious disease research

(A)BSL-3 facilities are essential for research involving infectious substances that require a high level of safety management as there may be serious consequences following exposure or leakage. These facilities require professional operation and high maintenance costs, and building and maintaining such facilities at the private level is difficult. After establishing new (A)BSL-3 facilities with support from the government, IPK will facilitate their joint use with the researchers in industry, academia, and research institutes through Open Lab. Our efforts will foster the convergence of outstanding research capabilities to support the development of vaccines and therapeutics needed for infectious disease preparedness and response.

Aim & Priorities

IPK will prepare the regulations and guidelines nesessary for the joint use of the (A)BSL-3 facilities and establish an operating system for effective management.Because compulsory training alone is insufficient to enable research in these facilities, experts in virus research and (A)BSL-3 operations will be invited to support professional research personnel, thus expanding national infectious disease R&D capabilities.

- Establish BSL-3 operation regulations and guidelines
  - Prepare safety management regulations and guidelines for the safe use of (A)BSL-3 facilities.
  - Prepare detailed operation regulations and guidelines for the joint use of (A)BSL-3 facilities in the RRC.
  - Establish a SOP for each facility and type of equipment.
- Implement expert safety training program utilizing BSL-3 facilities
  - Support research personnel through tailored education involving on-site practical training in the (A)BSL-3 facilities.
  - Invite experts in virus research and BSL-3 operation to aid in training professional research personnel and provide high-quality, tailored services to those using the facilities.
  - Carry out regular training of researchers in the facilities and improve the private sector's usage capabilities through continuous management of regulations and guidelines.
- Support and manage the use of research facilities by private-sector researchers
  - Establish an RRC management system for managing facility use requests, equipment/facility reservations, users, equipment, facilities, bioresources, and sales.
  - Establish a biological safety management system consisting of an Institutional Biosafety Officer (IBO) and have the Institutional Biosafety Committee (IBC) ensure biosafety through approval of the users' research plans.
  - Ensure researcher safety and protection by having IPK researchers either conduct externally-requested experiments or support these experiments by monitoring and guiding the entire research process.
  - Install basic research equipment and safety equipment, including biosafety cabinets and autoclaves, which are necessary for the joint use of the facility. Conduct periodic inspections of the facilities and safety equipment to ensure biosafety.

Expected Outcomes

1. Joint use of the facilities by industry, academia, and research institutes by providing an Open Lab for handling high-risk pathogens.
2. Cultivate the virus/infectious disease research expertise currently lacking in Korea.
3. Generate national infectious disease R&D collaboration by providing a space for fundamental research, next-generation technology research, and research based on demand from industry, academia, and research institutes.

Key Project 4

Educate and train the experts specialized in infectious disease research

Human resource is an essential infrastructure axis to cope with the infectious disease pandemic. Most researchers who are not accustomed to high biosafety laboratories cannot apply their skills in using live infectious pathogens.

To support expanded research activities by the companies, research institutes, academies, and hospitals on vaccines and emerging viruses, the training of researchers and industrial workers in the field and environment is highly required.

Expected Outcomes

1. Researchers who can understand infection biology and work in BSL-3 laboratory
2. Reinforcement of national capacity to deal with the infectious diseases

Aim & Priorities

IPK will participate in several training programs for internships in infectious diseases along with other public and private partners. Those training programs will provide basic skills to work in (A)BSL-3 laboratories. In addition to such safety-focused training, IPK will provide research-focused training in the field. By training and working on infectious disease projects, the researchers will equip fundamental competency working in the area.

- Participate in the collaborative internship programs
  - Train interns through KOITA(Korea Industrial Technology Associates), UST(University of Science and Technology), and other established intern programs
- IPK's proprietary research intern program
  - Maximally utilize the BSL-3 and ABSL-3 facilities. The current five rooms will be expanded to 12 rooms at the end of 2022.
  - Experience various infectious diseases research projects of IPK on viral, bacterial, and parasitic pathogens.
  - Focused on pathogen research fundamental in addition to biosafety training

Pillar 5

Activate international networks
and lead the Asia-Pacific region
as a research hub

The current COVID-19 crisis has reminded the world that preparedness for infectious diseases must remain a key focus of research and development. Unfortunately, preparedness has been neglected and underfunded for too long, creating gaps that became overly apparent when COVID-19 first appeared. Through its screening platform and unique infectious disease expertise, IPK has been able to quickly respond to the crisis, creating opportunities for clinical research and attracting collaborators at national and global scales.

With the situation evolving toward a global reckoning of the need to more efficiently fund infectious disease preparedness, IPK remained visible and well-positioned in global collaborations to ensure its early access to newly emerging research initiatives. Among its international partnerships, IPK will play a leading role particularly in the Asia-Pacific region of the Pasteur Network.

The COVID-19 crisis has further reminded the world that AMR is a looming disaster that can only be averted with more effort and collaboration. Multiple actors must participate in addressing each of the One Health components, which is essential to prevent AMR. In this global context, we propose to focus on 3 key projects that could secure IPK's ability to rapidly respond to emerging infectious diseases through a strong presence in the international research scene.

Goal

In this strategic pillar, we propose to focus on strengthening international collaborations specifically for research on AMR and emerging viral diseases by building cooperative systems with local laboratories worldwide, intensively participating in related global consortia and new initiatives, and organizing regular scientific events and workshops. More generally, to include other diseases and research areas, we propose to more actively promote the exchange of scientific staff and students and the opening of joint laboratories by welcoming guest professors to IPK.

01. Fostering a global network for infectious diseases research
02. Using a One-Health approach to tackle AMR
03. Building international collaboration around emerging viral diseases

Key Project 1

Fostering a global network and cooperative system for research in infectious diseases

Strong global visibility facilitates the recruitment and retention of talent and access to high-impact, long-term funding of research-based organizations, and, in turn, creates a virtuous circle inside which both the institution and the researchers can thrive. Establishing and maintaining international collaborations and efficient networking are required to initiate and pertain to such a positive environment.

As a board institute of the Pasteur Network, IPK leads research collaboration among the institutes in the Asia-Pacific region. The bi-monthly meetings hosted by IPK provide a space for the regional institutes to share research progress and opportunities. Collaborative research projects on AMR, COVID-19, and others will be initiated through Pasteur or the Global Research Collaboration for Infectious Disease Preparedness (GloPID-R) program.

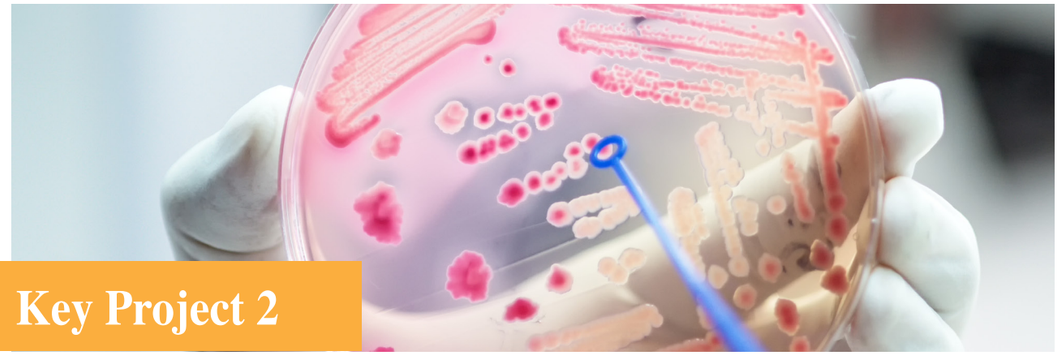
In recent years, IPK has built strong relationships with influential partners and has witnessed a rise in national and international collaborations around COVID-19 research. These achievements mostly rest on the shoulders of IPK's screening platform, and research skills and careful equipment management are required to maintain a highly competitive profile. Balancing this with long-term collaborations that rely on other sets of competencies and themes within the research groups is important to keep a rich network of partners. We will engage resources and put efforts into actively establishing collaborations through scientific exchange and events that can help to promote the institute's achievements and unique expertise.

Aim & Priorities

- Build cooperative system with local laboratories around the world to facilitate international joint researches including establishment of a global pathogen database
- Welcome and send students and researchers to targeted personnel exchange programs to foster collaborations with foreign institutions.
- Secure opportunities to welcome foreign post-doc researchers and high-level research directors using available funding schemes, like the Brain Pool Program.
- Organize workshops, joint seminars, and other scientific events to increase the visibility of IPK at the regional and global levels and create bonds between guest researchers and IPK staff.
- Increase public/private partnerships with global pharmaceutical companies and consortiums able to provide funds or resources for research in specific areas, like AMR and One Health.

Expected Outcomes

1. Facilitate international joint research projects with a unique opportunity to access to the specific information of regional infectious diseases and pathogens.
2. Sign confidential disclosure agreements (CDAs) or memoranda of understanding (MoUs) with private, internationally established companies.
3. Host an international research unit led by a guest principal investigator from a foreign organization or university.
4. Secure the visit of students and researchers from foreign institutions to IPK and vice versa.
5. Organize a workshop, joint seminar, or other scientific event of international reach covering a topic of relevance for IPK and the Asia-Pacific region (including One-Health or AMR).



Key Project 2

Using a One-Health approach to tackle antimicrobial resistance (AMR)

AMR is a survival mechanism of microorganisms against antimicrobial agents. Although AMR is a natural phenomenon, it has been aggravated due to the misuse and overuse of antimicrobials in the clinical and agricultural sectors and has recently grown into a looming tsunami with the potential to become a catastrophic global public health crisis. Because AMR can occur and spread within and between humans, animals, and the environment, One Health is an indispensable approach to controlling it sustainably.

Strong international collaborations are crucial to effectively tackling the current AMR crisis as AMR pathogens respect no borders. Advanced transport technology in modern society has facilitated dramatic increases in population mobility and the trade of agricultural and food products worldwide, expediting the global transmission of AMR. Regional and global collaborative work will save lives at risk of AMR around the world, especially in low- and middle-income countries.

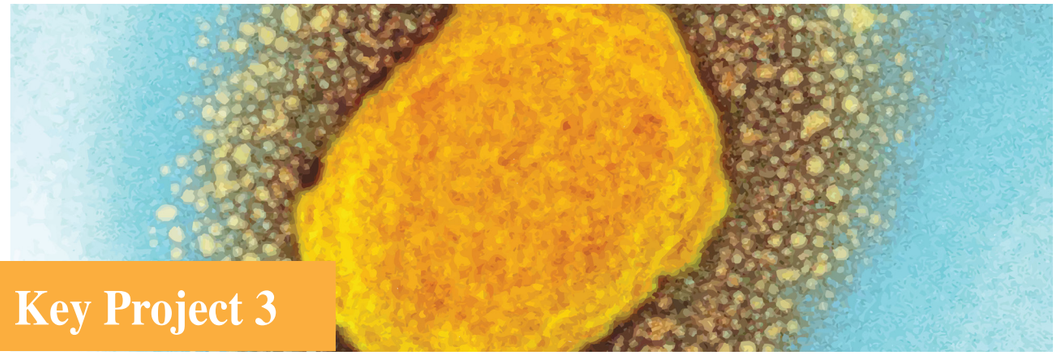
From the founding of IPK, a broad international network has been one of its primary assets. In this key project, we will leverage our existing international network to fight AMR and build even stronger international collaborations with regional and global partners.

Aim & Priorities

- Active cooperation and participation in global AMR and One Health endeavors by closely following up on the actions of major stakeholders, including the World Health Organization (WHO), and GloPID-R.
- Enhance collaborative work with Global Antibiotic Research and Development Partnership (GARDP) with an additional research project to deliver new antimicrobial agents against multidrug-resistant Gram-negative bacteria.
- Build innovative joint research projects on AMR within the Pasteur Network and seek funds from global funding agencies such as Joint Programming Initiative on Antimicrobial Resistance (JPIAMR) and the Wellcome Trust.
- Launch a regional One Health surveillance project among the Pasteur Network Asia Hub by conducting a metagenome analysis of AMR in humans, animals, and the environment
- Initiate an international AMR data-sharing procedure by collecting and sharing the data generated through collaborative research within the Pasteur Network, especially focusing on the Pasteur Network Asia hub.

Expected Outcomes

1. Successful performance of high-impact research that combines IPK's expertise in AMR with new technologies and international experts.
2. Establishment and test-operation of an SOP for an international common database and AMR data repository system.
3. Contribution to global efforts to tackle the current AMR threat by establishing IPK's strong position in AMR and One Health research.



Key Project 3

Building international collaboration around emerging viral diseases

When the WHO declared COVID-19 a pandemic in early 2020, international cooperation became essential in many sectors, and research communities responded rapidly to address scientific difficulties. The WHO played a leading role in this process by facilitating researchers to share early research results and helping countries to plan epidemic control strategies and to gain approval for new drugs/vaccines. Private communities also shared their research expertise beyond borders, succeeding in developing vaccines and therapeutics at unprecedented speeds and providing surveillance data for epidemic prevention.

In pursuit of more efficient and abundant collaboration for future viral pandemic outbreaks, new initiatives are developing around the world. One example is PREZODE (Preventing Zoonotic Disease Emergence), a new international initiative to prevent zoonotic diseases through early detection and resilience by coordinating an extensive portfolio of projects focusing on emerging diseases. Global funders, such as the Wellcome Trust and Bill & Melinda Gates Foundation, have organized a consortium for future pandemic preparedness.

Since 2021, IPK has expanded its international collaboration playing a central role in infectious disease drug screenings as a regional representative of the Pasteur Network. IPK also joined the GVN as a center of excellence and has initiated discussions with Global funders to be a part of new global consortiums on drug development. Through this project, IPK will reinforce its role as a key partner in the global response to emerging viral diseases by further utilizing its robust drug discovery platform.

Aim & Priorities

- Increase the number of Pasteur Network collaboration projects supported by the new Pasteur Foundation. The foundation is organizing a new funding structure for collaboration in the network. IPK, as the board representative of the Asian region, will primarily focus on Asian-regional projects.
- Join the international consortium on drug development organized by international funders, such as the Wellcome Trust, the Bill & Melinda Gates Foundation, and DNDi, potentially contributing through phenomic drug screening in BSL-3 laboratories.
- Expand international collaboration through new global initiatives such as PREZODE. Expand research focus into surveillance and early detection of emerging zoonotic diseases.

Expected Outcomes

1. Participate in new Pasteur Network projects led by the foundation. Engage in at least one project per year.
2. Participate as a partner in at least one global consortium for future pandemic drug development.
3. Project selected by international funders (RIGHT Fund, GloPID-R, etc.), with more than three projects selected in five years.

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