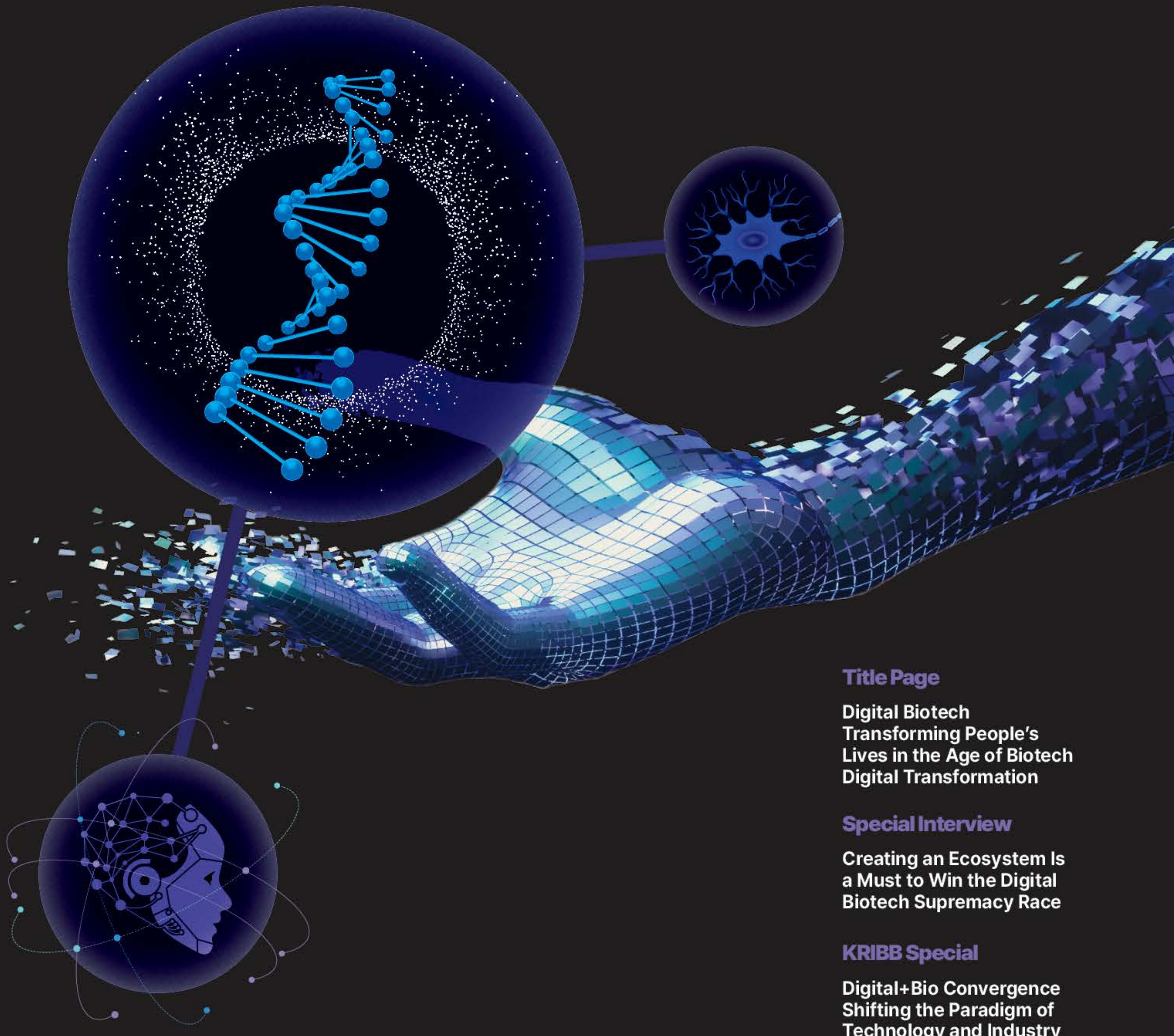
KRIBB *focus*

15th ISSUE | 2023

Preparing for the future of digital biotech



Title Page

Digital Biotech Transforming People's Lives in the Age of Biotech Digital Transformation

Special Interview

Creating an Ecosystem Is a Must to Win the Digital Biotech Supremacy Race

KRIBB Special

Digital+Bio Convergence Shifting the Paradigm of Technology and Industry

KRIBB *focus*

Korea Research Institute of Bioscience and Biotechnology(KRIBB) is research institute that specializes in bioscience and biotechnology. It is the hub of national bioindustry research based on global standard research on the origin of life and the establishment and dissemination of public infrastructures.

MISSION, FUNCTION, VISION & GOALS

KRIBB conducts research on the fundamental principles of biological phenomena that contributes to the safe and healthy life of people and the advancement of the national bioeconomy.

MISSION

To carry out R&D activities and related projects in the field of bioscience and biotechnology in joint effort with other research institutes, academia, and industries at home and abroad

FUNCTION

Develop and disseminate sophisticated core technology in bioengineering and bioeconomy
- Innovative bio-convergence
- Creation of future growth engine
- Resolutions for the national bio-agenda

Support public infrastructures bioengineering R&D both at home and abroad
- Supporting for public infrastructure
- Think tank for national policy
- Institute that foster professionals
- Support for small to medium businesses towards commercialization

VISION

A Global Leader for Healthy Life and Bioeconomy

GOALS

Global Research Institute Leading the New Waves of K-BIO

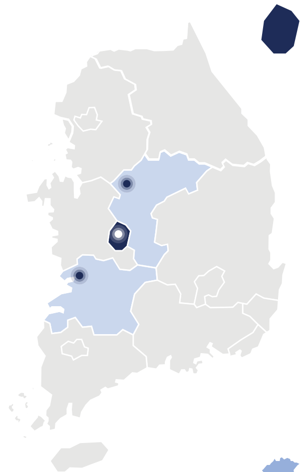
- **W** World-class R&D
- **A** Accelerating Open Innovation
- **V** Vitalizind Bio-industry
- **E** Enhancing sustainability

HISTORY OF KRIBB

SINCE 1985 THE PATH OF KRIBB

- **1985. 2.** Established the Genetic Engineering Center (Seoul and Hong Kong)
- **1990. 7.** Relocated to a new building in Daedeok Innopolis in Daejeon
- **1995. 3.** Renamed as "Biotechnology Research Center"
- **1999. 5.** Became an independent legal entity under the Korea Research Council of Fundamental Science & Technology(KRCF)
- **2001. 1.** Renamed as "Korea Research Institute of Bioscience and Biotechnology(KRIBB)"
- **2005. 9.** Established the Ochang Branch (Ochang, Chungbuk)
- **2006. 11.** Established the Jeonbuk Branch (Jeong-eup, Jeonbuk)

ORGANIZATION



DAEJEON HQ BIO CONVERGENCE & SOURCE TECHNOLOGY

Bio Convergence Research / Basic Source Technologies for National Agenda / Bio Infrastructure Hub / Center for Domestic·Global Cooperation

- Aging Convergence Research Center
- Critical Diseases Diagnostics Convergence Research Center

- Korea Bioinformation Center
- Digital Biotech Innovation Center

SYNTHETIC BIOLOGY AND BIOENGINEERING RESEARCH INSTITUTE
- Synthetic Biology Research Center
- Genome Editing Research Center
- Cell Factory Research Center

DIVISION OF BIOMEDICAL RESEARCH
- Personalized Genomic Medicine Research Center
- Microbiome Convergence Research Center
- Rare Disease Research Center
- Biotherapeutics Translational Research Center
- Immunotherapy Research Center
- Disease Target Structure Research Center
- Metabolic Regulation Research Center

DIVISION OF RESEARCH ON NATIONAL CHALLENGES
- Infectious Disease Research Center
- Environmental Diseases Research Center
- Biodefense Research Center
- Stem Cell Convergence Research Center
- Bionanotechnology Research Center
- Plant Systems Engineering Research

DIVISION OF BIOTECHNOLOGY INNOVATION
- Technology Transfer Center
- SME Support Center
- BioProcess Engineering Center
- Bio-Evaluation Center
- Core Research Facility & Analysis Center

DIVISION OF RESEARCH STRATEGY
- Biotech Policy Research Center
- Korea Biosafety Clearing House
- National Research Safety Headquarters

OCHANG BRANCH INSTITUTE BIOMEDICAL SCIENCE

Natural Pharmaceuticals Research & Industrialization / Infrastructure Hub for Biological Resources / Linked Development with Local Bio Cluster Cooperation

- Natural Product Research Center
- Chemical Biology Research Center
- Nucleic Acid Therapeutics Research Center

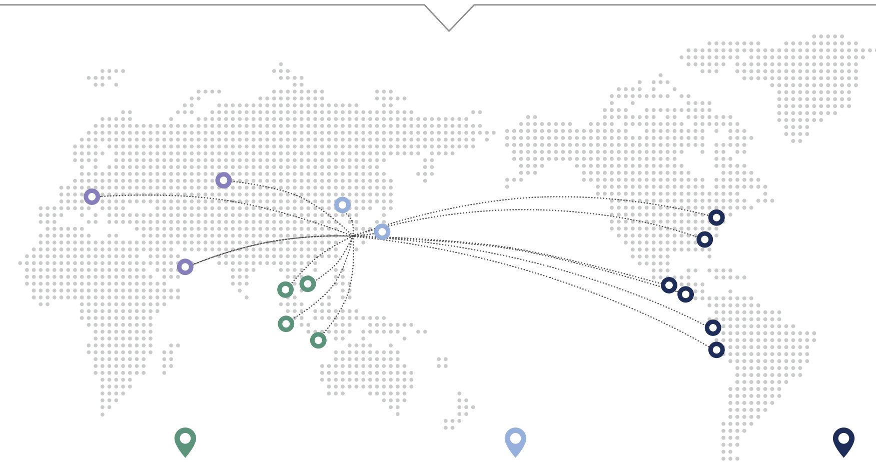
DIVISION OF NATIONAL BIO-INFRASTRUCTURE
- Laboratory Animal Resource & Research Center
- National Primate Research Center
- Futuristic Animal Resource & Research Center
- Bio-Resource Central Bank
- International Biological Material Research Center
- Korea Preclinical Evaluation Center
- Bio-Infrastructure Policy Support Center

JEONBUK BRANCH INSTITUTE BIO MATERIALS

Functional Bio Material Research & Commercialization / Infrastructure Hub for Microorganisms & Cell Line / Linked Development with Local Bio Agriculture Convergence Research

- Functional Biomaterial Research Center
- Microbial Biotechnology Research Center
- Biological Resource Center
- Primate Resources Center

INTERNATIONAL NETWORK



OECD
Working Party on Bio Nano and Converging Tech(BNCT)

KAZAKHSTAN
NCB

IRAN
Univ. of Tehran

THAILAND
NANOTEC

MALAYSIA
InterAcademy Panel in Biology(IAP)

INDONESIA / BPPT
Korea-Indonesia Biological Material Research Center

VIETNAM / IEBR
Korea-Vietnam Biological Material Research Center

CHINA / ISWC, YAAS
Korea-China Biological Material Research Center

JAPAN / RIKEN
Chemical Biology Joint Research Center

USA / NIH, University of Pennsylvania
Research Fellowship

USA
Korean-American Scientist and Engineers Association(KSEA)

COSTA RICA / INBIO
Korea-Costa Rica Biodiversity Material Research Center

NICARAGUA / UNAN-LEON

PERU / UNALM

ECUADOR / INABIO

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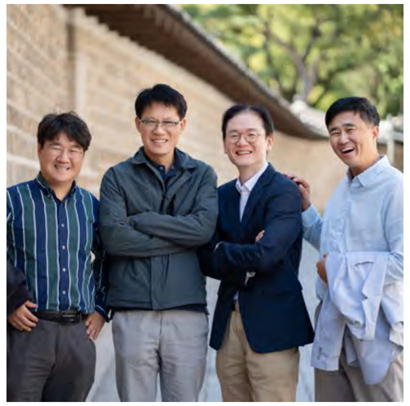

KRIBB FORUM

COVER STORY

SPECIAL REPORT

KRIBB PERSONAGE

KRIBB RESEARCH

KRIBB ENTREPRENEUR

KRIBB NEWS

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PUBLISHER	Jang-Seong Kim
EDITOR IN CHIEF	Kyu-Sun Lee
EDITORS	(KRIBB) Kyu-Sun Lee , Hyun Heo , Dong-Hwi Kim , Ji-Yeon Seo (CHAI) Yoo-Li Choi, Na-Ra Ji, Su-Jin Seong
PRODUCTION	CHAI
DESIGN	Seon Lee
IMAGES	KRIBB, Shutterstock.com

DIGITAL BIOTECH

Digital Transformation and **Biotech**

The COVID-19 pandemic brought about considerable changes in various aspects of our lives and society, including healthcare and medicine, as well as the economy. What is especially noteworthy is the fact that it has led to accelerated digital transformation throughout society. Satya Nadella, the youngest person ever to be appointed CEO of Microsoft, said, “We've seen two years' worth of digital transformation in two months.” Digital transformation is also taking place in the biotechnology field. Various attempts are being made to incorporate information and communication technologies such as big data, artificial intelligence, and robots into the bioindustry. A good example would be the development of new drugs using AI. By incorporating digital twin technology, which uses AI to design protein structures and develop biotechnology in a digital space, biological experiments can be performed with greater speed and accuracy for the development of new biomaterials and products. Digital biotech is now regarded as a key resource for R&D, rather than as simple data obtained as a research result.

The Korea Research Institute of Bioscience and Biotechnology (KRIBB) is achieving remarkable results in digital biotech research and development. Researchers use AI to discover new drug candidates and analyze the genome information of viruses and bacteria to develop diagnostic and treatment methods for infectious diseases. Also, to make precision medicine possible, the institute is working to develop gene therapy for rare genetic diseases using gene editing technology and to build a stem cell genome map and database. Since digital biotech is still in its early stages, there are many challenges and opportunities. This is why we must focus our efforts on investing in basic research related to digital biotech and creating an industrial ecosystem. This will allow us to reduce the technological gap and catch up with biotech powerhouses around the world and foster our country's bioindustry as a new driving force for national economic growth. Developed nations worldwide have already joined the heated race to take the lead in global digital biotech. In September last year, the Biden administration issued the Executive Order on Advancing Biotechnology and Biomanufacturing Innovation, which included measures to innovate the economy based on biotechnology. Ahead of this, China announced in May that it would work to hone its bioeconomy capabilities to the level of developed countries by 2035 through its Bioeconomy Plan, and Japan also announced its Bio Strategy in 2019 and 2020. As such, countries around the world are competing to foster the bioeconomy. In December last year, the Korean government announced the Digital Biotech Innovation Strategy with a mission to become an advanced biotech country by 2030 based on the convergence of biotechnology and digital technology. With the goal of reaching 85% of the level of the world's best biotechnologies by 2030, the government has decided to develop new digital biotechnologies and new industries, secure fundamental technologies that are fundamental to various digital biotechnologies, create a data-centered biotech innovation ecosystem, and lay the groundwork for the biotech digital transformation.

Digital biotech is a key technology of the future that will change people's life, and its astounding economic value is impossible to estimate. However, there are some aspects that should not be overlooked. We must consciously ensure that human dignity and balance in nature are respected in the course of researching and applying digital biotechnology, which may involve manipulating genes or the body functions of living things during the research process. Additionally, sensitive data such as personal genetic information or vital signals may be used. Therefore, we must not forget the main premise that digital biotech is “technology for humanity.” Only when digital biotech is rooted in this premise can it be sustainable. As we are pioneering a completely new field, active discussions must take place from multiple viewpoints, covering not only the technological aspect but also legal, institutional, and ethical issues in order to minimize side effects.

Jang-Seong Kim
President of Korea Research Institute of Bioscience and Biotechnology (KRIBB)

15th

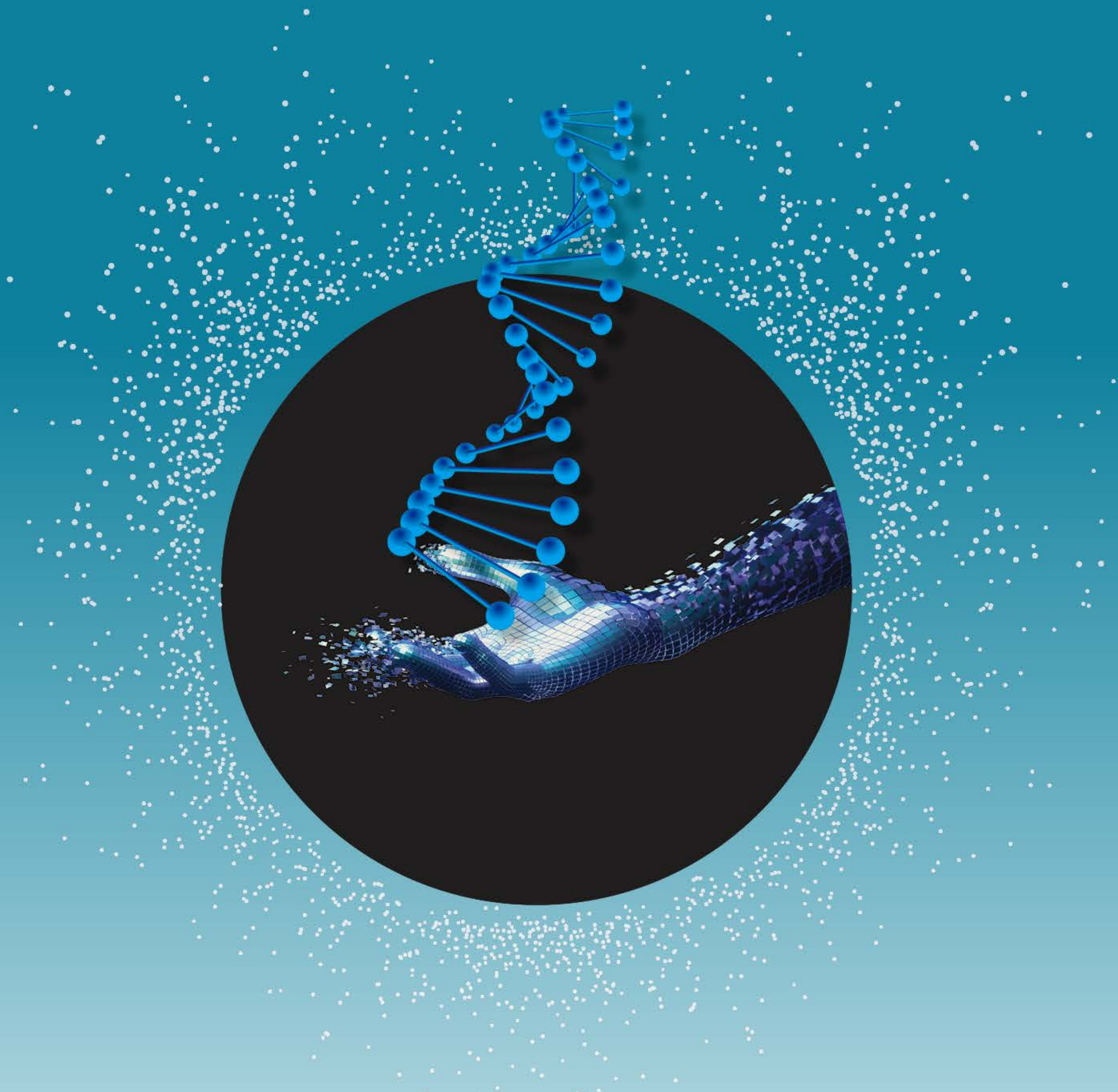
Digital Biotech
Transforming People's Lives in the Age of Biotech Digital Transformation

The Nobel Prize in Physiology or Medicine in 2023 was awarded to Professor Katalin Karikó of the University of Szeged in Hungary, who paved the way for the development of COVID-19 vaccines using messenger ribonucleic acid (mRNA). She has been called a "scientific heretic." While she was at a university in the United States, she was told that if she wanted to continue her mRNA research, she would have to take a junior researcher position or leave the university, but she did not give up on her mRNA research. She took the demotion and kept working on her research, even on weekends. She ultimately identified the interaction between mRNA and the immune system, which led to the development of vaccines that were crucial to overcoming the COVID-19 pandemic.

Digital biotech, which is considered the "No. 1 contributor" to the development of new drugs and vaccines, is fast-emerging as the new strategic technology and industry for the future. New biotechnology and industry are being created by fusing biotechnology with digital technologies such as big data and artificial intelligence (AI), and digital biotech platforms and a related ecosystem are being built. Already, biotech is undergoing a major transformation through the convergence and evolution with frontier digital technologies, resulting in the creation of new technologies and industrial values that have never existed before.

Digital biotech has also emerged as a key field in the increasingly fierce battle for technological supremacy. In September 2022, the United States issued an executive order to launch the National Biotechnology and Bioanufacturing Initiative (NBBI), putting synthetic biology, a major field of digital biotech, at the forefront. Prior to this, in 2021, the United States Innovation and Competition Act (USICA) designated synthetic biology as one of the ten core technologies, and increasing investments have been made in the field ever since. China, which announced the Five-Year Plan for the Bioeconomy, has also selected synthetic biology as a priority science and technology field, in which it is making massive investments and building infrastructure.

The era of biotech digital transformation, in which biotech affects all industries, has already begun, overcoming the limitations of conventional biotech R&D including uncertainties, time-consuming process, and high cost. Today, fostering digital biotechnology and industry has become a necessity, not an option. What will the future look like with the changes brought upon by digital biotech innovation and how will it change people's lives? And what should we do now to prepare for it? What is clear is that attempts to answer these questions are already underway. We can't wait to see how the future will be shaped by digital biotech.



KRIBB
Leading Biotech Transformation with Digital Technology

What Is Included in KRIBB's Digital Biotech Strategy?

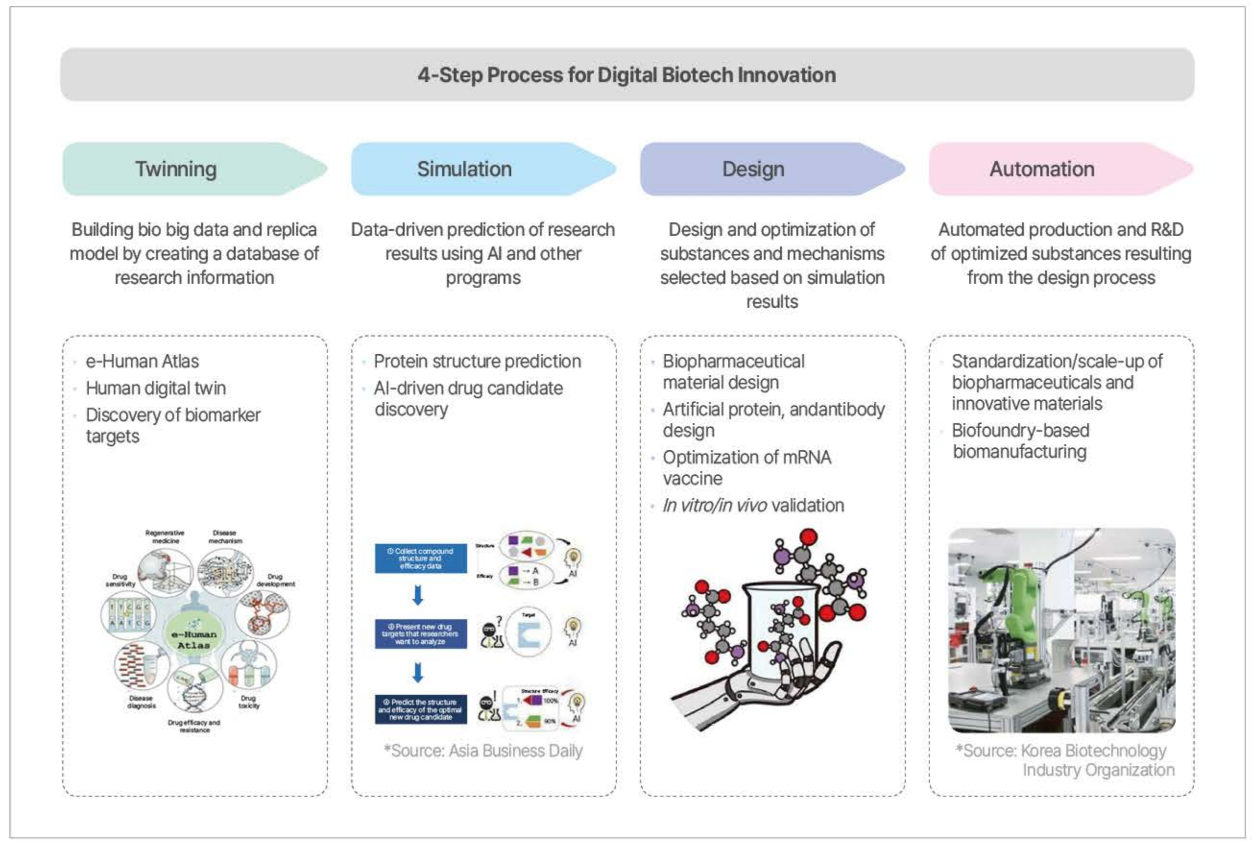
To secure data-driven cutting-edge biotechnologies and maximize the efficiency and performance of research and development (R&D) to keep in pace with the changes in the environment, KRIBB has set forth a digital biotech promotion strategy with plans to implement in full swing as soon as possible. The idea is to introduce research methods that improve research efficiency and integrity through the production, accumulation, and utilization of data in the entire range of biotech R&D such as analysis, experimentation, and production in the era of biotech transformation, through which the institute will create new technologies and new industries in the area of advanced biotech.

The reason KRIBB prepared a strategy to promote digital biotech is that the internal and external environment is rapidly changing. Externally, there is a heated global race for technological supremacy, and with aging, infectious diseases, and food shortages emerging as global issues, biotech-related markets are growing rapidly as biotechnology is expected to play a major role in tackling such issues. At the same time, high uncertainty, depletion of good candidates, and low reproducibility in biotech are creating challenges of limited productivity and efficiency. In the midst of all this, the convergence of biotech and digital technology is occurring at an accelerated rate, with new research methods using data and software applied to create new technologies and new industries in biotech and increase the speed of R&D and its likelihood of success.

In response to these external changes, KRIBB is endeavoring to secure new digital biotechnologies such as a bio foundry and the AI-driven e-Human Atlas platform to support new drug development, but there is a need to first strengthen related systems for data management as well as data collection and utilization. Moreover, with the growing importance of the biotech sector, as evidenced by the establishment of a digital bio innovation strategy by the Ministry of Science and ICT in December 2022 and the formulation of a strategy to create a new bio-health market by the Ministry of Health and Welfare in February 2023, the government has been increasing investment in basic research and commercialization in related fields. This has made it more important for KRIBB to be proactive in its response to these trends.

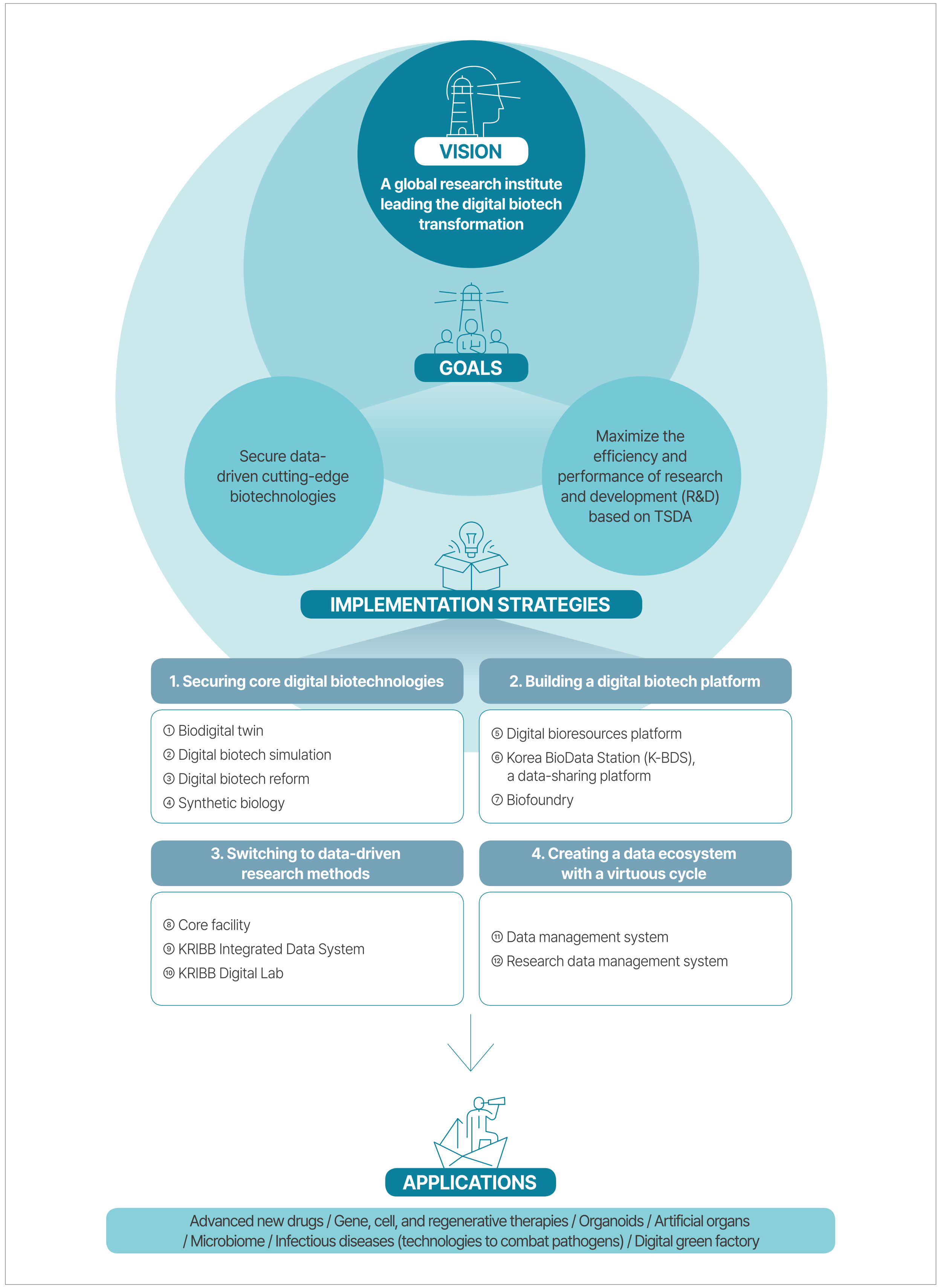
Accordingly, the digital biotech promotion strategy devised by KRIBB contain goals and detailed strategies for the institution to make technological and policy responses and lead the digital biotech field in the era of biotech transformation. Securing data-driven advanced biotechnologies as well as maximizing R&D efficiency and improving performance through TSDA[1] under the vision of becoming a global

TSDA System



1) T (Twinning): Turning research information into data and building bio big data; S (Simulation): Making data-driven predictions about research results using AI programs, etc.; D (Design): Design and optimization of substances and mechanisms selected as a result of simulation; A (Automation): Automation of production of optimized substances based on the design resluts and R&D

KRIBB Digital Biotech Strategy (Draft)



research institute leading the digital biotech transformation. Along with this, four strategies and twelve key initiatives were set forth as securing core digital biotechnologies, building a digital biotech platform, switching to data-driven research methods, and creating a data ecosystem with a virtuous cycle, with twelve tasks.

For the strategy to secure core digital biotechnologies, four key initiatives were set forth: biodigital twin①, replicating physical organisms in the real world in the virtual world by data production to create a replica model enabling digital analysis; digital biotech simulation②, using AI and big data to improve R&D efficiency, accuracy, and speed and supporting the development of innovative technology; digital biotech reform③, using digital technology in all areas of biotech (Red, Green, and White) through the application of original technologies such as gene editing to make predictions and perform analysis to produce improved outputs; and synthetic biology④, in which engineering principles are introduced to life sciences to artificially design, manufacture, and synthesize components and systems of living organisms.

The strategy to build a digital biotech platform, which consists of tasks to be carried out at the national level, will be realized through three key initiatives: the establishment of a digital bioresources platform⑤ providing KRIBB biomaterial acquisition, information provision, distribution, and validation services; the establishment of the Korea BioData Station (K-BDS)⑥, a data-sharing platform for collecting, managing, and providing standardized domestic biotech research data and providing integrated data analysis and utilization services; and the establishment of a biofoundry⑦ for conducting automated and accelerated biotech R&D based on the convergence of synthetic biology, AI, big data, and robotics technologies and building the foundation for bio manufacturing.

Next, the strategy to switch to data-driven research methods will be implemented through three key initiatives: Core Facility⑧, a platform for integrating and sharing specialized equipment and facilities, as well as supporting research and performing research data standardization and integration with dedicated personnel; KRIBB Integrated Data System⑨, an integrated data platform that enables sharing and utilization of institutional research data through collection and analysis and improves research productivity; and KRIBB Digital Lab⑩, a collaborative research platform equipped with analytical tools and pipelines such as data-driven virtualization-based simulation based on the convergence of big data, AI, and robotics technology.

Moreover, the strategy to create a data ecosystem with a virtuous cycle will be implemented through two initiatives: a data management system⑪, where virtuous cycle system of data is created by establishing internal platforms and roles for each actor in the research data lifecycle and a research data management system⑫, aimed at preparing an institutional foundation for maintaining and strengthening the virtuous cycle system of data.

KRIBB has set specific goals for each of these four strategies and twelve key initiatives and even devised a short-term roadmap and detailed execution plans to be implemented in 2024. If everything proceeds as planned, it is expected to lay the foundation for Korea to gain a competitive edge in the digital biotech sector, where new technologies and industrial values are being created as a result of the convergence and evolution of cutting-edge digital technologies. In particular, KRIBB, as a leading government-funded research institute in the domestic biotech industry, is committed to serving as a vanguard and core force in fulfilling the government's commitment and goal to focus on bringing forth new digital biotechnologies and industries and creating a digital biotech ecosystem with the aim of becoming an advanced biotech powerhouse by 2030.

Digital Biotech

Creating an Ecosystem Is a Must to Win the Digital Biotech Supremacy Race

Interviews with experts from the industry, academia, and government on building a digital biotech ecosystem in Korea

The transition to the digital biotech era will serve as a golden opportunity for Korea, which is armed with state-of-the-art digital technology, abundant medical data, and outstanding human resources, to become a bio leader. In June 2023, the government of Korea announced the 4th Master Plan for Biotechnology Development* with the aim of becoming a leading country in biotech by 2030. The key contents of the plan include a "biofoundry" that combines digital technologies such as artificial intelligence (AI) and big data to mass-produce synthetic organic organisms, a "human digital twin" that uses big data on living organisms to design and predict genetic information, biological functions, etc., a new drug development platform using AI technology, and the training of digital tech experts. In the era of digital biotech transformation, what strategies do we need to win the race for global technological supremacy and emerge as a leading country? We sat down with Jin-Wu Nam, a professor of Life Sciences at Hanyang University; In-Suk Lee, a professor of Biotechnology at Yonsei University; Tae-Hyung Kim, a managing director at Theragen Bio; and Byung-Wook Lee, a lead researcher at KRIBB KOBIC to explore measures to create a digital biotech ecosystem in Korea and examine the role of KRIBB.

*The 4th Master Plan for Biotechnology Development: The top-level statutory plan for biotechnology jointly established by 15 government ministries and agencies under the supervision of the Ministry of Science and ICT is a long-term plan that presents the direction of biotechnology development in Korea for the next decade.

:: Why is it important to build an ecosystem for digital biotech, which is considered one of Korea's new growth engines?

A major transformation has begun in which the basic framework of biotech research and industry has shifted to digital worldwide. We look at the ecosystem components of digital bio, which has emerged as a new growth engine for Korea following semiconductors and batteries and sought expert opinions on what constitutes a sound biotech ecosystem.

In-Suk Lee — An ecosystem is essential because components cannot exist on their own. The same is true for modern biotech research. It has evolved into a very complex type of research and development (R&D) that cannot be done by an individual or a team alone. Also, biology used to be a discipline of exploring the unknown, but nowadays, countries around the world are competing against one another based on predetermined research topics, and what matters is who finds the answers faster and commercialize them faster. This is why it is necessary to establish an ecosystem with high-efficiency, high-speed, and optimized research infrastructure.

Jin-Wu Nam — Modern science, including biotech, has advanced based on the labor of laboratory researchers over the past 150 years. Digital transformation and commercialization in other fields, such as semiconductors and machinery, have occurred at a fast pace, but biotech is still a very labor-intensive and costly field due to its reliance on the labor of researchers. Accordingly, by achieving digital transformation of the biotech field in a broader and deeper sense, we must build a laboratory ecosystem that is automatory -- that is, automated and expressed. At the same time, the laboratory culture must be improved so that data can be obtained quickly and accurately.

Tae-Hyung Kim — The key to digital biotech is achieving innovation by combining information technology and biotech. In June 2000, when I was an undergraduate student, a draft of the genetic map of the Human Genome Project was published. The era of examining large amounts of digital data using computers had already begun 23 years ago. The objective in the digital biotech competition is to produce research results as quickly as possible. An example of this would be the speedy development of vaccines for COVID-19. Ultimately, the core functions of an industry ecosystem are systematic data production, collection, utilization, analysis, and recycling. That is the power of digital biotech.

Byung-Wook Lee — In June, the government announced a plan to build infrastructure for digital biotech. In order for this policy to be implemented successfully, there needs to be an institution that can pilot the mission, and I think the KRIBB, which has all the resources necessary from data to labs, should play that role experimentally. For example, by collecting cancer data, using it to create an AI model, and using the AI model in schools and hospitals, we can create an ecosystem that can enable faster and more efficient research. Then, major schools and companies will join the efforts to innovate digital biotech. As such, KRIBB should build a small ecosystem.

Tae-Hyung Kim — With the national R&D budget cut across the board, the government has announced that it will invest more than KRW 400 billion annually to develop digital biotech. Also, in June, the National Bio Big Data Project was deemed feasible based on a preliminary feasibility study. It is now difficult to carry out biological research without any data. In the past, we were able to achieve rapid advances in science and technology by employing the strategy of catching up with advanced countries, but this is not easy in the case of digital biotech because it is an interdisciplinary field, which means it requires expertise in biology, as well as IT and medicine. If infrastructure and platforms are developed as intended by the government, the research scene will change and the industry will become revitalized.

:: What should be done to build a competitive digital biotech ecosystem?

Korea failed to get a head start in the digital biotech race when compared to the United States and Europe. In order to leap forward as a biotech leader, we need creative innovation, not a chaser strategy. What are our shortcomings and how can they be addressed to build a competitive digital biotech ecosystem, in addition to fostering human resources with expertise and skills in both biotech and digital technology?

Jin-Wu Nam — The key component of digital biotech is data, followed by AI as a methodology and then automation and acceleration to build related infrastructure. Of course, human resources are also important. While the government's digital biotech project focused on building and utilizing data, new drug development and various leading projects using AI, on the other hand, are oriented toward how to efficiently utilize data and how to execute the projects faster and more accurately. Finally, in terms of automating and speeding up the processes, the biofoundry project is in the works. If these three tasks are carried out successfully, we will be able to gain an excellent ecosystem.

Tae-Hyung Kim — Europe established the General Data Protection Regulation (GDPR) in 2018, China passed a data security law last year, and the United States is rapidly mass-producing its citizens' genomic data through next-generation sequencing (NGS)* and working to protecting them. The trend now is for countries to share data only with other countries with which they have friendly ties. Korea has also established the Korea BioData Station (K-BDS), a platform for collecting, managing, and sharing research data in all areas of biology at the national level. We need to further strengthen our efforts to utilize and protect the data in K-BDS.

*Next-generation sequencing (NGS): A method of breaking down a single genome into numerous fragments, reading each fragment simultaneously, and combining them with computational technology to quickly decipher vast amounts of genomic information

In-Suk Lee — One thing we cannot leave out is human resource development. Currently, we have experts in each area making up the digital biotech ecosystem, but we lack people who understand the ecosystem as a whole and know how to integrate the different components. The Healthcare Science and Technology (HST) Program at MIT in the United States, for example, educates students on science and technology as well as medicine. Students plan their own classes and each create their own unique and special majors. We, too, need to innovate the education system to break down the barriers between departments and disciplines and provide opportunities for interdisciplinary education and training.

Jin-Wu Nam — That's right. The University of California in the United States invested in AstraZeneca to create a cancer vaccine pipeline, and this is a prime example of the importance of human resources with expertise across various fields. At the time, they conducted experimental research to automate all the equipment and optimize the pipeline between equipment, but they ultimately failed. This was because they had experts on data, experts on biotech, and experts on new drugs, but they lacked people who could interpret the data coming from the actual equipment and accurately connect the equipment to the equipment.

Byung-Wook Lee — I digress, but 19 teams participated in a biodata utilization contest last October, while 730 teams applied for an AI utilization contest held around the same time. There are more than 100 majors related to AI in Korea, but only one or two majors related to bioinformatics in Korea, and there is a significant shortage of manpower in this field. While AI-related professionals such as data scientists continue to be trained, there needs to be manpower who can contribute to the realization of digital biotech.

:: Digital biotech stems from data! How should data be produced and shared?

"Data" are the key resource when it comes to digital biotech. In December 2022, Korea launched the Korea BioData Station (K-BDS), a government-wide biotech research data sharing platform used to collect and integrate biodata produced in national R&D projects so that they can be utilized in the field. Experts recognized that data outputs are for the common benefit of society and reached a consensus on the need to create an environment where all members of the ecosystem can help one another.

Byung-Wook Lee — In order to systematically produce, collect, manage, and provide data, we must first share and accumulate data. That is why the US National Institutes of Health (NIH) began requiring researchers they fund to deposit all data from their research this year. In Korea, we are also preparing to improve the performance evaluation system so that depositing research data is used as a performance indicator. This is a move to not only recognize producing data, publishing papers, and transferring technology as research outcomes but to also evaluate researchers on the data they have accumulated and how they have deposited the data at the end of the project.

Tae-Hyung Kim — With the legislation of the Research Utilization Advancement Act, there is now a wider consensus on the need to create a data management platform (DMP) to deposit data. Plus, data are meaningful only when they are gathered in one place. Once that happens, the next step, which is utilization, starts rolling automatically. We need strategic projects to collect data and increase their utility in the next decade or two through a program like the UK Biobank (UKBB)*. K-BDS is also expected to evolve with a focus on data utilization along with its role as an archive.

*UK Biobank: The UK conducted a project to collect the genetic information of 500,000 citizens through the Biobank Project from 2006 to 2010 and provided the data to all qualified researchers across the world.

Jin-Wu Nam — With digital biotech, conditions are being created for companies to perform better research than universities. In fact, in the field of AI, the level of technological prowess of universities and companies has become reversed. Therefore, it is important for companies to have an open mind and willingness to utilize the results they've derived by using national data for the common good. In fact, Google and Microsoft have made their open AI platforms available to the public. They may be trade secrets that directly affect their profits, but this move has powered the growth of the related ecosystem. As a result, the government has been able to support the industry more aggresively.

Byung-Wook Lee — Digital biotech is transitioning from basic research to application, and progress in its industrialization is expected soon. However, it seems that different government departments such as the Ministry of Science and ICT, the Ministry of Health and Welfare, and the Ministry of Trade, Industry and Energy have slightly different ideas on how to utilize data. As you mentioned, there should be a consensus on how to give back and compensate society when companies make profits using data.

In-Suk Lee — It's hard for an ecosystem to develop if the people involved think that sharing their data will only benefit others and they won't get anything out of it. Schools and companies can create value by using data. If selling data to a company leads to the development of a new drug, it's beneficial for the entire country. So, there's no need to worry too much about whether to give them a license and if so, how much equity to ask for. The same goes for companies. If a school uses the data generated by companies and creates value, the resulting technology will eventually go to the companies. It'll take time, but the perception of opening up and sharing data has to change with a forward-looking perspective.

Tae-Hyung Kim — A good example of this is the UKBB. Drug developers invested in the UKBB in exchange for early access to the data. As a result, the UKBB had a large amount of operating funds and was able to operate with little state support, which resulted in a virtuous cycle. In Korea, there is a negative perception of companies using public data. There are people who question whether certain companies should be allowed to use data that were generated using taxpayers' money. However, when companies make good use of such data and produce excellent results, it not only raises the value of digital biotech but also the quality of life of the people. Korea can achieve something like the UKBB. It's not a matter of technological power or budget; it's a matter of perception and regulation.

:: Invigorating the digital biotech ecosystem starts with regulatory advancement

The existing regulatory framework has limitations in keeping up with the pace of technological innovation in digital biotech and responding to new industry issues in a timely manner. Above all, it is necessary to establish a consensus so that new services in digital biotech can come to fruition. What do experts think is the solution?

Tae-Hyung Kim — We need to bring forth advanced regulatory measures that take into account the data ecosystem. Companies cannot continue their business if they violate the law, so without clear guidelines, innovative R&D and commercialization are not easy to achieve. Developed countries already thought about this 30 years ago when they conducted the Human Genome Project and changed public perception by continuously holding discussions and public forums. This is how the US and UK were able to implement All of Us* and the UKBB. Korea, as a latecomer, is now just beginning to contemplate how to form a consensus. Investment is important, but it is also important to build an open ecosystem where philosophers, researchers, and citizens can come together.

*All of Us: A program led by the US NIH to build a voluntary cohort of more than one million people to explore how an individual's lifestyle, environment, and biological makeup influence their health and medical conditions with the aim of advancing precision medicine

In-Suk Lee — As mentioned, it's crucial to change the perception. In Korea, targeted therapy based genome sequencing for cancer is quite advanced, and patients are willing to share their data because of the high mortality rate, but for other general diseases, it's not easy to get patients to cooperate. On the other hand, people in the UK joined in the efforts to build the UKBB because they thought that even if they don't have a critical illness, testing and sharing their genomes to find new treatments will eventually benefit society as a whole, as well as future generations. In Korea, most patients go to the big five hospitals in Seoul, and the data that they have are comparable to a national database. We also has an excellent national health insurance system, so we have a lot of opportunities to catch up with the developed countries if we just combine everything together software-wise.

Byung-Wook Lee — Once a consensus is reached on the importance of people providing their data, and if researchers make more proactive efforts, there will come a time when patients make tangible contributions to public health. In order for a new ecosystem to grow, there must be regulations that clearly state what is prohibited in the form of "You can do whatever you want except for this," but the current regulations say, "You can't do this and that." And there is still no place to ask, "Well, can I do this then?" Deregulation and consensus in society are as important as government research funding.

Jin-Wu Nam — Tada is a good example of the importance of regulatory frameworks. It was a very innovative business into which a huge amount of money and technology were invested, but it disappeared due to regulation. The same holds true for biotech. There are many opportunities to create innovative businesses, but they are hampered by regulations. If the vested interests, including those in the medical community, are not eliminated, no matter how much the government invests and how much technology advances, the industry will not grow. KRIBB was involved in drafting the Advancement Act, and it is now time for the whole community to come together to raise public awareness of it. I believe it is most important for the government to relax the related regulations to start a virtuous cycle in the digital biotech ecosystem.

:: Recommendations by experts from industry, academia, and research field on how to build a sound digital biotech ecosystem

In order to pioneer new technologies and markets at the intersection of digital and bio technologies, government policies, participation of the industry, academia, and research institutes, and public interest and support are now more important than ever. Experts from the industry, academia, and research field recommend ways to build a digital biotech ecosystem where researchers, companies, the government, and the public can be organically connected.

Jin-Wu Nam — Digital biotech can be achieved faster only if there is a change in the perception of the value and importance of data. To achieve digital biotech, we need to know how data move in the ecosystem. First of all, people need to recognize that data are valuable. Also, data ownership and the movement, processing, and valuation of original data – that is, data licensing or copyright (DOI) issues - must also be reflected in the ecosystem through policy and legal considerations.

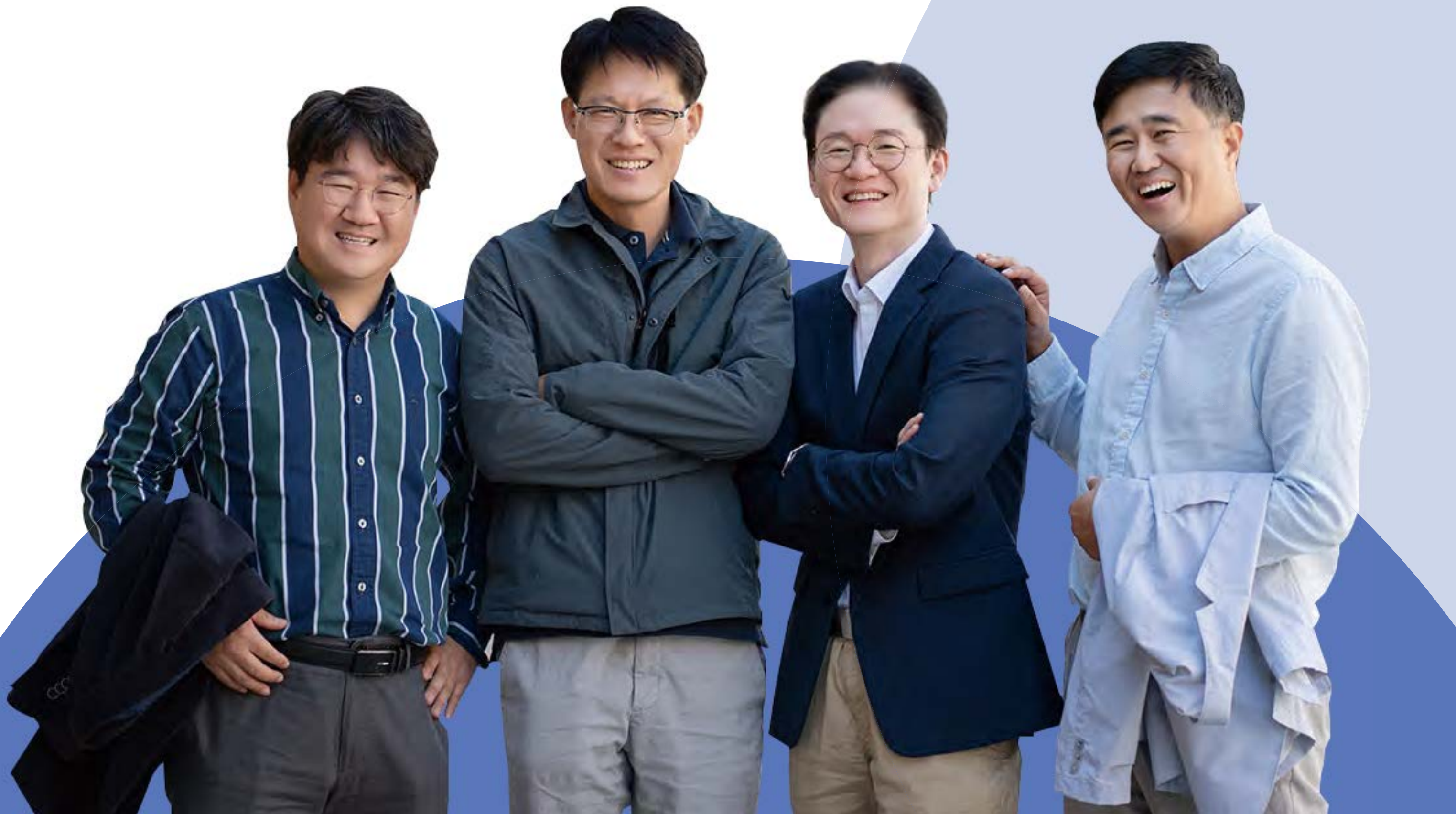
In-Suk Lee — The success of data-driven research is ultimately dependent on managing and recycling data to find value. In the future, the process of producing data will become more and more automated, and more people will be needed to analyze data and make them valuable. However, the number of people in charge of that process at KOBIC is relatively small. Of course, we have gained more people than in the past, but our goal is to catch up with the research power of the United States and Europe, so we need to grow our size accordingly. Qualitative growth is possible only with quantitative growth.

Tae-Hyung Kim — There are three things I expect from KRIBB, and KOBIC in particular. With the arrival of the digital biotech era, the speed at which R&D and industrialization proceed has become very fast. Decisions need to be made quickly, but the content needs to be creative and innovative. Given these conditions, I would like to see KRIBB become a testbed that boldly takes on new challenges. The second is education. Digital biotech is an interdisciplinary field, and it undergoes rapid changes. I believe KRIBB is capable of creating an advanced education system for digital bitotech. Finally, I would like to ask KRIBB to spearhead the efforts to set forth regulations and guidelines that can help create an environment where researchers can pursue groundbreaking research at ease.

Byung-Wook Lee — Strategic international cooperation is important for digital biotech to lead to industry innovation and advancement. We need to have our own competitive edge and know-how to promote international cooperation not only with developed countries but also with other Asian countries. I hope Koreans will take an interest and encourage KRIBB to play its role in strengthening the capabilities of the data-driven biotech ecosystem.

KRIBB **Special Interview**

The nearly two-hour interview confirmed that data, human resources, and consensus are the basic elements for the development of the digital biotech ecosystem and the source of competitiveness. We hope that Korea's digital biotech ecosystem will be more firmly rooted for remarkable growth in the future, based on the recommendations of the four experts from the industry, academia, and research field.



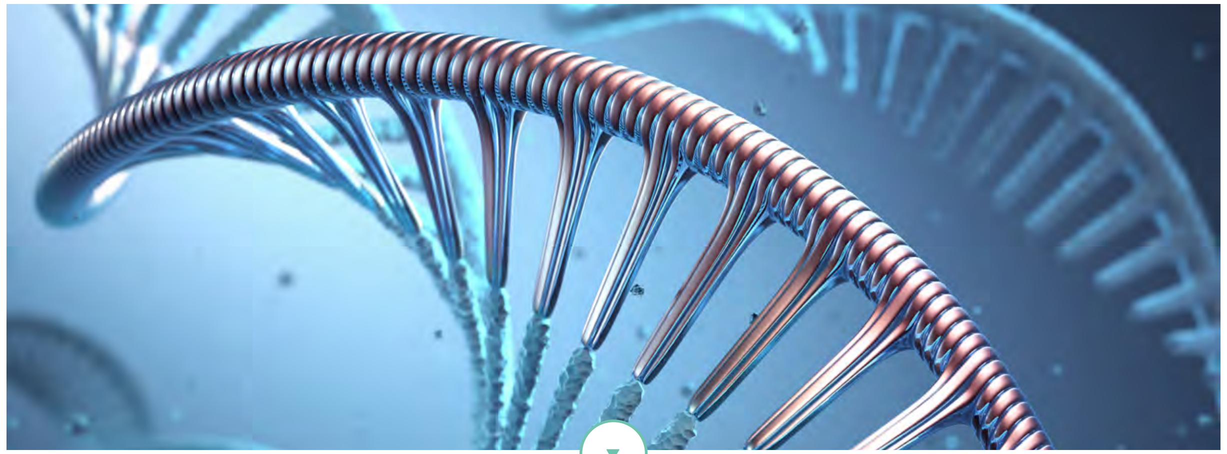
Digital+Bio Convergence
Shifting the Paradigm of Technology and Industry

Digital Biotech Leading the Biotech Digital Transformation

From ancient times to modern times, discussions and research on life have undergone ceaseless changes and advances. The spontaneous generation theory first proposed by Aristotle remained prominent until the 18th century. Due to the unclear boundary between theology and science and the lack of understanding of living organisms, it was believed that "living things come into existence naturally." This was the era of naturalistic observation. Then, the 19th century ushered in the era of microbial research pioneered by Louis Pasteur. The discovery of the existence of microorganisms and how they cause decay and disease laid the foundation for scientific biological research.

In the 20th century, the discovery of the double helix structure of DNA by James Watson and Francis Crick led to the study of genes in full swing and the development of molecular biology, which studies RNA and proteins as molecular units. This marked the beginning of the age of genetics. In the 21st century, bioinformatics began with the completion of a draft of a genetic map of the human genome. Also, synthetic biology, which is aimed at creating and utilizing artificial cells, has developed, and artificial intelligence (AI) and big data have been used for advanced analysis and prediction of biological phenomena. The digital convergence era has begun.

Then, how about the present and future of biotechnology? The keyword is "digital bio," which combines digital technology and biotechnology. With the ongoing biotech digital transformation, which is characterized by the integration of cutting-edge digital technologies such as AI and robotics, as well as data as the core research resource, we have entered the digital biotech era in which research is carried out using data and software. AI technology used to analyze a large number of data quickly to derive optimal results has dramatically sped up drug development and made it possible to develop gene therapeutics. The development of a vaccine in just one year, which contributed decisively to humanity's victory in the fight against the COVID-19 pandemic, was also made possible thanks to the power of digital biotechnology.



Synthetic biology overcoming the limitations and challenges of conventional biology

As seen in the case of the COVID-19 vaccine development, the representative field of digital biotech is "synthetic biology." Synthetic biology presents a new paradigm of biology through the convergence of biological knowledge revealed in molecular, cellular, and systems biology with other sciences and engineering such as chemistry, electronics, and mathematics. While traditional molecular and cellular biology aims to understand the components that make up biological systems and reveal how they work, synthetic biology focuses on modifying or creating new biological systems. That is, compared to traditional biology, which is based on "understanding through discovery," synthetic biology seeks "progress through invention."

"Although the biotech sector has been highlighted as a national growth engine and core technology, it has been difficult to achieve remarkable results because it involves tacit knowledge, reproducibility is low, and uncertainty is high," said Jeong Il-young, head of the Future Innovation Strategy Research Center at the Science and Technology Policy Institute (STEPI), in *"Science and Technology Policy Outlook 2023."* He added,"Synthetic biology has the potential to overcome these challenges. [...] It has high potential to realize faster, larger-scale, and lower-cost biological research and to be applied to a variety of future industries, including pharmaceuticals, energy, chemicals, and agriculture."

Synthetic biology has proven potential in the development of COVID-19 messenger ribonucleic acid (mRNA) vaccines. mRNA vaccines, when inside the human body, help strengthen the immune system by exposing mRNA that contains the information to make the target virus' spike protein*. The development of mRNA vaccines began immediately after the outbreak of COVID-19, and it took less than a year for the first doses to be administered in the United Kingdom. The speed at which the mRNA vaccine was developed can only be described as "super-fast," considering that vaccines and other medicines typically take more than a decade to develop. The secret was the accumulation of research results on mRNA and combined application of digital and synthetic biology technologies in the vaccine design and synthesis process.

*Spike protein: A protruding protein on the outer part of the virus that the virus uses to bind to the host cell's receptor.

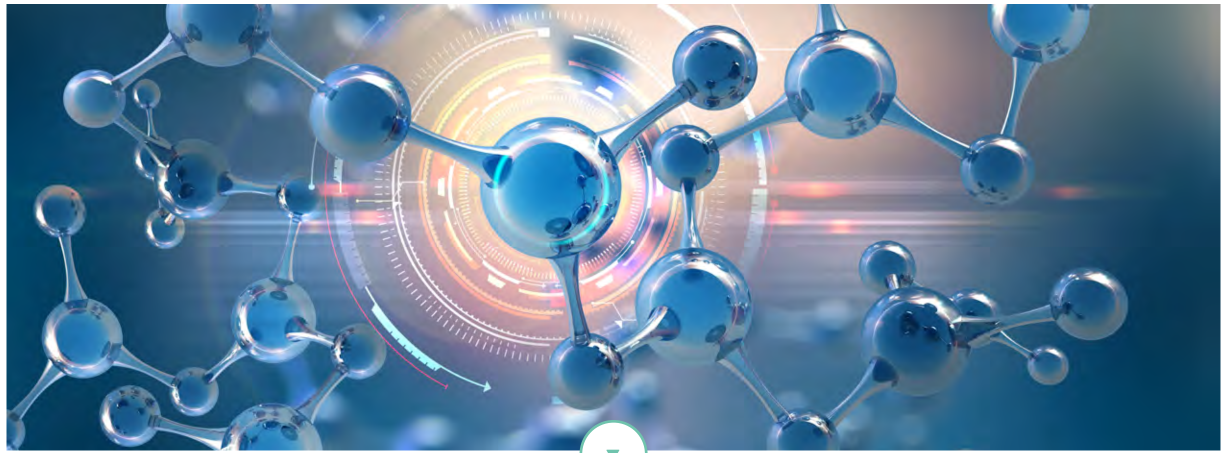
Synthetic biology uses genome editing to redesign genetic systems by cutting or synthesizing cells. This makes it useful for developing new drugs, such as anticancer agents and treatments for incurable diseases. It can also be used to create male mosquitoes with controlled fertility to prevent the spread of malaria and Zika, or to create microorganisms that can mass-produce natural rubber to be used as a raw material. It is also possible to create drug-secreting microorganisms that can be used treat genetic diseases or solid tumors.

Major countries in the race for biotech supremacy are **building biofoundries**

With the advancement of digital technology and genomic technology, biofoundries, which use AI and robotics to automate the entire process of synthetic biology, are in the spotlight. In October last year, Lee Jong-ho, Minister of Science and ICT, reported at the 11th Emergency Meeting on Economic Affairs that "Korea's biotech market share is only about 2%, but we will strive to increase it to a double-digit figure within the next decade. [...] To this end, we need a facility where swift design and production is possible for new vaccines and new drugs, and that is a biofoundry." He emphasized that there is an urgent need for biofoundries in order to turn biotechnology and industry a key growth engine of Korea through digital biotech.

A biofoundry, which basically uses microorganisms as factories, is a platform that dramatically speeds up biotech research and development (R&D) by applying AI and robotics to synthetic biology. It is a facility that outsources the entire process of designing, building, testing, and learning new biological systems or synthetic biology. It is similar to a semiconductor foundry, but the process is quite different. Unlike semiconductor production, which is subdivided into design, manufacturing, testing, and packaging, biofoundries have standardized, automated, and high-speed processes occurring in one place. As a result, the repetitive tasks required for the biotech R&D can be automated and the throughput can be maximized, thereby enabling R&D on a much larger scale than it is possible using conventional technologies.

Biotech powerhouses are already working to build biofoundries at the government level. The United States, which began researching synthetic biology in earnest in the early 2000s, launched the National Science Foundation (NSF) in 2006 and the Defense Advanced Research Projects Agency (DARPA) in 2013 to support synthetic biology and biofoundries. The National Biotechnology and Biomanufacturing Initiative (NBBI) executive order signed by President Joe Biden in 2022 also focuses on new concepts of biomanufacturing, including biofoundries. The United Kingdom, the first country in the world to establish a national synthetic biology roadmap in 2012, has since built seven synthetic biology centers and three biofoundries. In May last year, China announced its 14th Five-Year Bioeconomy Development Plan with the aim of enhancing its comprehensive bioeconomy capabilities to the level of advanced countries and invested KRW 720 billion to build and operate the world's largest large-scale biofoundry in Shenzhen. Other countries such as Japan, Denmark, Canada, and Singapore are also showing great interest in biofoundries.



Leading the biotech digital transformation with a digital biotech innovation strategy

Digital biotech is not just about technology and industry transformation. It has actually become a major factor in the race for dominance in the increasingly fierce global competition for technological supremacy. The COVID-19 pandemic, in particular, has shown that biotechnology is not only a means of achieving economic development and tackling social issues, but also a major shield to protect people's health and survival and an important tool for national defense and security. When it comes to the global biotech supply chain, only a small number of countries account for 93% of total exports and 80% of export volumes in the case of vaccines. For this reason, major countries around the world have designated synthetic biology as a strategic technology to be fostered at the national level and are striving to achieve hegemony in this field by building biofoundries as core infrastructure.

Korea, too, has recognized these changes in the times and plans to focus on developing digital biotechnology and industry. In November last year, the government announced the National Synthetic Biology Initiative to foster synthetic biology by pursuing state-led establishment of biofoundries as core infrastructure and selecting and supporting six super-gap strategy areas. With the vision of "accelerating national biomanufacturing innovation by promoting synthetic biology," the National Synthetic Biology Initiative proposed a number of goals such as achieving 90% of the world's top synthetic biology technology level by 2030, achieving 30% biotech digital transformation of the manufacturing industry in the next decade, building a world-class national biofoundry, and intensively fostering six strategic areas of synthetic biology.

In December, the Digital Bio Innovation Strategy was announced to accelerate technological innovation by combining advanced digital technologies such as AI and big data with biotech research. The objective of the strategy is to raise the level of domestic technology to 85% of the world's top technology by 2030 by investing around KRW 400 billion in R&D investment each year. It also describes the vision to lead a new biotech R&D paradigm by spreading data-based biotech research and creating an ecosystem to foster digital biotech. To this end, five major areas of related infrastructure such as biofoundries, DNA-encoded compound libraries, and human digital twins, as well as 12 key technologies related to third-generation therapeutics such as electronic and digital therapeutics, AI-based new drug development, artificial organ and organoid production, and precision gene editing and control were selected as key areas to be fostered. In June, the Ministry of Science and ICT reaffirmed its commitment by announcing a plan to build digital biotech infrastructure at the Global Cluster Strategy Conference for High-Tech Industries, chaired by President Yoon Seok-yeol.

KRIBB preparing to become a digital biotech hub and a base for related ecosystem

The Korea Research Institute of Bioscience and Biotechnology (KRIBB) has been busy preparing for the biotech digital transformation. Expectations that it will serve as a hub for fostering digital biotechnology and industry and as a base for the industry ecosystem are at their all-time high. "The government has prepared the top seven strategies and drawn a big picture to foster digital biotechnology. To strive for it successfully, there needs to be an institution that acts as a pilot, and KRIBB, which has all necessary infrastructure ranging from databases to laboratories should take on that role," said Dr. Lee Byeong-uk from the Korean Bioinformation Center (KOBIC).

In response to these expectations, KRIBB underwent an organizational reform last year to lead the biotech digital transformation and strengthen its excellence-driven group research system. The main directions of the reorganization were to expand the collective research system in core areas, establish a response system to lead the biotech digital transformation, and upgrade the national biotech infrastructure operating system. For this purpose, the existing system of four specialized research centers was converted into a system of one specialized research center (Synthetic Biology Research Center) and one specialized research group (Personalized Genomic Medicine Research Center). In particular, the specialized research group in the field of synthetic biology was expanded into a research center, and the Digital Biotech Innovation Center was established under the vice president to respond to changes in the three paradigms of biotech digital transformation: digitization, platformization, and strategic technologicalization.

For more than a decade, KRIBB has been operating a specialized research organization in the field of synthetic biology and securing related technologies. It has successfully developed smart microorganisms for detecting inflammation in the intestines and artificial microorganisms that convert methane, a greenhouse gas, into a high-value eco-friendly material. In addition, the institute is operating a pilot biofoundry and participating in the Global Biofoundry Alliance (GBA), a collaborative platform for synthetic biology infrastructure around the world, to spearhead related R&D efforts. Above all, with the ever-increasing importance of biodata, KRIBB is running the Korea BioData Station (K-BDS) platform to collect and manage data produced from national R&D projects and make them available to researchers.

The biotech digital transformation that will be brought upon by digital biotechnology is referred to as the Fifth Industrial Revolution. The Fifth Industrial Revolution is expected to focus on the organic combination of humans and engineering and the convergence of digital technology and biotechnology. McKinsey, a global consulting firm, reported that the market size of synthetic biology, one of the main fields of digital biotechnology, will reach USD 28.8 billion (approx. KRW 38.6 trillion) in 2026 and up to USD 3.6 trillion (approx. KRW 4,800 trillion) in 2040. The U.S. government has also predicted that the bioindustry will grow to USD 30 trillion (approx. KRW 40 quadrillion) in size thanks to synthetic biology. Using its excellent digital capabilities and abundant medical data and collaborating with biotech powerhouses, Korea has a golden opportunity to become a biotech leader. Efforts by domestic industry, academia, research institutes, and government, along with KRIBB, have already begun to seize this opportunity.

Global Biodata Center Extending Its Reach Across the World

Korea Bioinformation Center(KOBIC)

Korea's first national bioinformation management platform can be traced back to some two decades ago. In 2001, the National Genome Information Center was established, and as a result of the expansion of the organization in 2006, the National Bioresource Information Management Center opened its doors. Then, in 2010, the current Korea Bioinformation Center (KOBIC) was officially launched as a cross-ministerial national center for the overall management of domestic biological research resource information and specialized research in the field of bioinformatics. Kim Seon-young, the head of KOBIC from 2020 to the end of 2023, says that the government's full-fledged investment over the past three years helped reaffirm the role and potential of KOBIC. In the past three years, KOBIC has successfully implemented the Korea BioData Station (K-BDS) project and also completed the Korea Biotech Big Data Pilot Project. The center is also cultivating its global competitiveness by engaging in exchanges with the US National Center for Biotechnology Information (NCBI), the European Bioinformatics Institute (EBI), the DNA Data Bank of Japan (DDBJ), and the National Genomics Data Center (NGDC) of China.

Building K-BDS tailored to domestic conditions

In 2020, the government planned to build the Korea BioData Station (K-BDS) to collect, manage, and utilize all research data produced in national biotech research and development (R&D) projects. KOBIC joined the project in early 2021 and played a major role in building the database alongside the Korea Institute of Science and Technology Information (KISTI).

"It was necessary to specify what kinds of data were needed and what kinds of data needed to be organized according to each field. Over the past three years, KOBIC, related ministries, and experts from industry, academia, and research institutes have created an action plan and laid the foundation for systematic collection and utilization of various data in a way that suits the situation in Korea," said Kim Seon-young. Kim says that in the early stages of building the K-BDS, it was important to learn how biodata centers in major developed countries operate. They thus examined what kinds of biodata the NCBI, EBI, and DDBJ have been collecting and how they have been building their databases. Based on the information they acquired, KOBIC selected and prioritized the main domains of data according to the circumstances in Korea and established a system by determining the management entity for each area.

As a result, KOBIC is in charge of data related to genomic differentiation, which is a core field, and large-scale data in increasingly important fields such as proteomics, metabolomics, compounds, and imaging will be collected and quality controlled by experts from domestic industry, academia, and research institutes. However, KOBIC will manage the hardware and software infrastructure required for data storage so that the data handled by the experts can be retained as national assets. Currently, KOBIC and the Proteome Quality Leadership Center, Metabolome Quality Leadership Center, Compound Quality Leadership Center, and Image Quality Leadership Center are jointly undertaking software development, data collection, and quality control, and a data standard registration form is being updated annually since it was first created in 2020. There are still a number of research fields where standardization is difficult, so KOBIC and the four quality leadership centers will work together to create a more effective standard registration form in consideration of those fields.

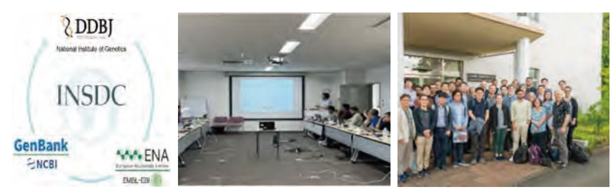
K-BDS extending its reach across the world through international collaborations

The government of Korea recognized the need for K-BDS based on an understanding of the international trends in regard to biodata. The intensification of biodata supremacy of a small group of developed countries, resulting in a movement toward tighter restrictions on data disclosure, was perceived as a threat. Under these circumstances, K-BDS, which began to be operated in full swing in December 2022, is now comparable to world-class biodata centers.

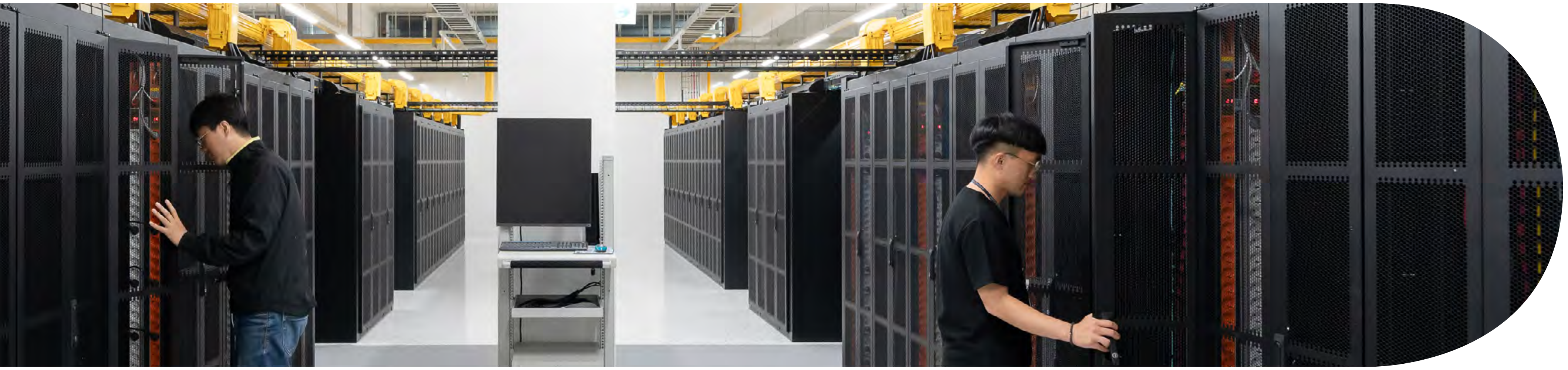
On October 12, 2023, KOBIC held a symposium on Global Bio Data Resources at the 32nd International Korea Genome Organization (KOGO) Annual Conference in the presence of the EBI and DDBJ, which are members of the International Nucleotide Sequence Database Collaboration (INSDC), and NGDC and KOBIC shared the current status of their respective organizations. KOBIC is also currently discussing data exchange and quality control with DDBJ and NCBI. Through such international collaborations, KOBIC is preparing to join the INSDC.

The INSDC is important global infrastructure for sharing the latest data in real time in the nucleic acid field and is currently composed of three centers: NCBI, EBI, and DDBJ. The three centers share data on a daily basis and have established a system allowing data to be registered by any of the centers and viewed by the others. If and when KOBIC joins the INSDC, Korean researchers will be able to keep pace with the international trend of sharing and utilizing biodata.

In order for KOBIC to join the INSDC, it will require not only the approval of the members but also the understanding of domestic researchers, according to Lee Cheon-mu of the Policy Planning Division. "KOBIC needs to maintain membership with the international organization, INSDC, to provide a convenient research environment for domestic researchers. Currently, Korean researchers have to upload their data to both K-BDS and INSDC, but if KOBIC joins INSDC, it will be fine to just upload the data to K-BDS."



International Nucleotide Sequence Database Collaboration (INSDC)



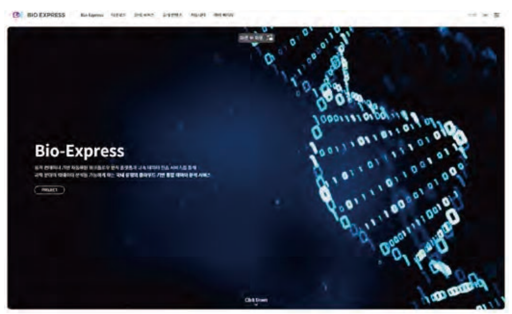
Reliable infrastructure supporting our society

KOBIC, a key player in the establishment of K-BDS, is also responsible for managing various resources related to it. Among them, the Korean Nucleotide Archive (KoNA) is a data registration system for nucleic acid data. Currently, KOBIC is developing portals for proteome, metabolome, and other types of data, and it is expected that by 2024, advanced functions will be created and organized into separate pages within K-BDS. At this time, Bio-Express (a cloud service for large-scale genome analysis) will play a key role as a resource that provides analysis tools and conditions to utilize specialized data.

KOBIC also operates BioData, a bioinformatics research output registration system, and KOBIS, a cross-ministerial bioinformatics resource information portal site, and provides not only primary data but also secondary database services. The secondary database contains the secondary data generated and provided in the process of analyzing and integrating primary data with domestic industry, academia, and research institutes.

Among KOBIC's resources, the COVID-19 research information portal played a crucial role during the pandemic. Research data on the genome, epidemiology, and mutations of the SARS-CoV-2 virus were collected, and a wide range of up-to-date data and news, including research trends, papers, and analysis tools was provided. Since then, the COVID-19 research information portal has been expanded into an infectious disease research information portal, and additional areas of data are being added to prepare for the future. Kim Seon-young, the head of KOBIC, explains that preparing for unexpected situations is one of the reasons KOBIC exists.

"Data infrastructure is usually out of the limelight, but in a crisis situation like the COVID-19 pandemic, it can play a crucial role. As we did during the pandemic, KOBIC will continue to serve as reliable infrastructure to support our society based on science," said Kim. At the end of 2023, Kim will step down from the position as the head of KOBIC and return to the Personalized Genomic Medicine Research Center. He says that it has been a rewarding experience to lead and watch KOBIC grow with its members in the last three years. "KOBIC has more than doubled in size since I took office. One of the most rewarding experiences has been seeing the new senior and full-time researchers join the center and undergo personal growth as they do their jobs."



Bio-Express

COVID-19 Research Information Portal

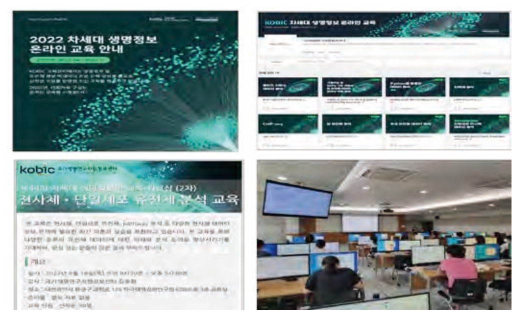
Building consensus on the importance of data collection and utilization remains critical

One of the important services provided by KOBIC is bioinformatics education. How the vast amount of data collected by KOBIC gets utilized is also an important matter, so training is provided on utilization measures. The classroom on the third floor of the KOBIC building is where theoretical education and practices take place. Many of the professionals who received the training expressed satisfaction and said they would like the center to provide up-to-date training in the future.

Creating an understanding and empathy within the research community about data collection and utilization is another task undertaken by KOBIC. According to Lee Cheon-mu, it is important to change the perception of researchers with respect to this issue.

"Research data do not belong to the researcher alone. I hope researchers pay more attention to the quality and completeness of their data so that they can be shared and utilized, based on the awareness that they are public goods created with national R&D funding. KOBIC will also continue to improve related systems with the government to protect the rights of data producers and offer incentives for data providers."

KOBIC has been serving as general support organization for biomaterial research and development since 2021. The 274 material banks previously managed by different ministries were organized into 14 material clusters, including human derivatives, stem cells, pathogens, cultured cells, animal models, microorganisms, brain, natural materials, synthetic compounds, livestock, seeds, marine life, fishery life, and wildlife, by clustering similar types of materials in terms of preservation and distribution methods and related regulations. KOBIC provides overall support by linking the data collected and produced in each cluster to the platform and establishing a cooperation network. KOBIC is in charge of not only bioinformation but also biomaterials, and it is expected to play an increasingly important role in the future.



Bioinformatics Education

Biomaterials General Support Group

Working Toward **Digital Biotech Innovation**

Digital Biotech Innovation Center

The digital transformation of the biotech sector has become inevitable. Major countries around the world are working to strengthen their biotech capabilities by building big data. In 2020, the Korean government established the Strategy for Building Big Data for Bio Research Resources along with the Korea BioData Station (K-BDS) Establishment Plan. Then, in 2022, the Digital Biotech Innovation Strategy with the aim of becoming an advanced biotech country by 2030 was announced. As for the National Integrated Biotech Big Data Project, planned as a cross-ministry project, the preliminary feasibility study has been carried out, and it is scheduled to kick off in 2024. Under these circumstances, changes within KRIBB became essential. In response to the changes in the three paradigms of biotech digital transformation, i.e., digitization, platformization, and strategic technologization, and in order to promote the digital transformation within the organization, the Digital Biotech Innovation Center was established under the Vice President of KRIBB.

Digital biotech innovation in line with global trends

The Digital Biotech Innovation Center is staffed with a total of seven staff members, including Kim Dae-soo, the head of the center, and their areas of expertise include biotech big data, genomic diagnostics, synthetic biology, and protein structure-based research. The seven researchers, who have conducted research as principal investigators in their respective fields, are leveraging their expertise to maximize research efficiency and productivity. Dr. Kim Dae-soo, in particular, oversees the affairs of the center based on years of experience in communicating with researchers from various fields while conducting bioinformatics research.

"In the case of biotech research, high costs, long research and development periods, and a high probability of failure have been pointed out as chronic problems. To overcome these problems, the KRIBB Digital Biotech Innovation Center is endeavoring to develop digital transformation technologies for the bioindustry as a new research paradigm that is data-based."

Dr. Kim Dae-soo introduced TSDA, which is necessary to secure advanced biotech strategic technologies based on data. “T” stands for twinning technology to create and utilize virtual models of the human body using biodata, and there are plans to create a database of research information and build big data. “S” stands for simulation technology, as there are plans to predict research outcomes based on data using programs such as AI. “D” stands for design, and in this process, actual verification and optimization of the substances and mechanisms selected based on the simulation results will be carried out. “A” stands for automation, which is the process of automating the production of materials that were optimized by design as well as the R&D processes.

"We want to revolutionize R&D research methods by fusing digital technologies such as biotech, artificial intelligence, digital twin, and big data together. By incorporating digital technologies, we will strive to perform research that was not possible in the past and create a platform that can give rise to new industries and maximize research efficiency and productivity."

Building an integrated system within the organization and the e-Human Atlas

The Digital Biotech Innovation Center's most important task at hand is to build an integrated system within KRIBB. The center is building a platform for integrating and managing high-quality biodata held by the organization and for sharing and utilizing it in a researcher-friendly manner. To this end, the center has identified the current status of data inside the organization and is engaging in discussions regarding the introduction of a system to link the research data infrastructure in the form of a network for the research divisions and centers. The center is also considering ways to incorporate data history management technology to track and manage the research data security settings and utilization.

The establishment of the e-Human Atlas system is another important task. The e-Human Atlas is a human organ map that will help provide a comprehensive understanding of the functions of the cells and organs that make up the human body and the process of disease onset and progression by using big data. The e-Human Atlas system will provide researchers with data on genomic changes at different stages of disease progression and allow them to predict outcomes by simulating the effects of drug candidates in advance. The system will serve as a bridge to KOBIC's K-BDS, and a system will be built within the e-Human Atlas to collect and share KRIBB's internal data.

"We're at 60 to 70% of the level of the best platforms in the world. By December this year, the beta version will be available for researchers to utilize within KRIBB, and once we have built enough data, we will open the system to researchers from industry, academia, research institutes, and hospitals." Internal collaboration was essential to building an integrated system for KRIBB and the e-Human Atlas system, and the Digital Biotech Innovation Center successfully built consensus among researchers at the institute on the need for digital biotech. "We needed to convince researchers who hadn't had much experience with digital biotech. We explained what digital biotech is and what could be achieved by big data mining. We provided researchers who hadn't experienced any great deal of trouble while applying conventional research methods with an experience of conducting research with greater ease using AI technology, and that was a major feat."

Establishing an integrated internal system

Establishing an e-Human Atlas

Realizing the vision to build an advanced biotech industry by 2030 based on convergence

The Digital Biotech Innovation Center is currently working on building a system for evaluating standard diagnostics and therapeutic potential based on simulation in the development of treatments for rare diseases. It has completed the initial concept paper and plans to proceed with full-scale planning in 2024. When the national integrated bio big data project kicks off in 2024, it will be possible to utilize genomic and clinical information related to rare diseases.

"Research on new synthetic drugs has been carried out for decades, but successful drug development has been rare. Now that biotechnology has enabled fundamental gene therapy, I think it is possible to develop treatments for rare diseases at this point."

The center hopes to tackle problems that are difficult to handle internally by collaborating with other government-funded research institutes. Together with the Korea Institute of Science and Technology Information (KISTI), displaying particular strength in the field of artificial intelligence, and the Electronics and Telecommunications Research Institute (ETRI), which specializes in hardware construction, KRIBB plans to build a platform for utilizing big data in the biotech area through convergence research.

"The increasing amount of data will be an issue, and we plan to mitigate that based on hardware. There are many tasks will need to be undertaken by AI in the future. We plan to create AI models that can solve not only drug development issues but also other challenges. Researchers will be able to receive partially processed information from these models and carry out their research."

The work of the Digital Biotech Innovation Center will play an important role in making Korea a biotech powerhouse. Kim Dae-soo, the head of the Digital Biotech Innovation Center, predicts that by 2030, it will be possible to develop treatments for rare diseases at a much faster rate than today.

Playing a leading role in the field of precision medicine in Korea

"The past year was spent on explaining the concept of digital biotech to the researchers at KRIBB and convincing them of how AI technology helps them improve their research efficiency. Through this process, I was able to reaffirm the operational mission of the Digital Biotech Innovation Center."

For Mr. Kim, the past year has also been a time when he needed to exhibit his leadership as the head of the Digital Biotech Innovation Center. He had to prepare for research-based innovations at KRIBB by combining his own biotech knowledge with the professional skills of the members of the center.

"I think the most important thing is to recognize the capabilities and expertise of the Ph.D.-level researchers at the center and assign them a mission in consideration of their capabilities and expertise. To do this, I make very effort to communicate with them at all times."

Going forward, the Digital Biotech Innovation Center will continue to promote communication among its members and collaborate within other members of KRIBB and other research institutes on research. Once the platforms currently being developed by the Digital Biotech Innovation Center get established, KRIBB will be able to play a leading role in the field of precision medicine in Korea.

"The goal of the Digital Biotech Innovation Center is to lead innovation in biotechnology and medicine by fusing together the latest technologies and research data and to help solve social issues. We want to develop innovative solutions for the medical sector and develop a platform that enables patient diagnosis, treatment, and health monitoring using biotechology and healthcare technology so that we can become a leading center in the field of precision medicine in Korea."

The Purpose of and Reason for Research Is All About "**People**"

Dr. Jun-Gi Jeong

Throughout the interview, Dr. Jeong shared his story with a gentle smile and his trademark humor, but those who worked with him at KRIBB remember him as a "charismatic" person. At a time when he was pouring everything into his research, Dr. Jeong was quite strict and rigid, as he fully understood the importance of the task he was assigned. Dr. Jeong worked on bioindustrialization research for about 25 years, from 1994 when KRIBB first created a pilot plant infrastructure organization until his retirement in 2018. He bore witness to the launch of the Bio Industry Venture and Startup Support Group in 1999, Technology Commercialization Promotion Group in 2006, Bio Industrialization Process Development Center in 2008, Bio Commercialization Center in 2010, and Bio Commercialization Support Center in 2016. Now, as he continues his research activities at a biotech company, he shared his memories of his research career and his plans for the future.

What Dr. Jeong Gained While Studying in Germany

Known for Strong Commitment and Excellent Experiments and Practices

Q1 What made you decide to leave your job as a chemical engineer for a large corporation and study abroad in Germany?

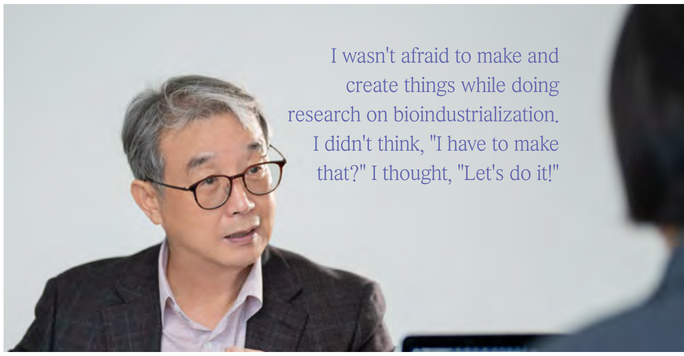
I majored in chemical engineering in college, and after graduating, I joined GS Caltex (then Honam Oil Refinery) and worked as an engineer. While I was there, I met a college alumnus who graduated earlier than I did and we became close. He went to Germany study and recommended that I study there as well. I actually yearned to study abroad because back when I was a college, my resolve to study abroad was frustrated due to a health issue. This was after my child was born though, so I was faced with many practical problems. After watching me contemplate for some time, my wife said, "If you're going to go anyway, let's go." After about six months of preparation, I went to Germany with my wife and child. I was admitted to the Technical University of Darmstadt (TU Darmstadt, Technische Universität Darmstadt), where I switched my major to biotechnology and earned my master's and Ph.D.

Q2 It must have taken a major determination to change your major. Did you have any difficulties getting your master's and doctoral degrees as an international student?

The Technical University of Darmstadt offered only master's and Ph.D. programs, without any undergraduate programs. After entering the university, I had to study analytical chemistry, organic chemistry, inorganic chemistry, and chemical engineering, and while doing so, I found organic chemistry much more interesting than chemical engineering. Also, in my third year, when I had to choose a major, there was a new course in genetic engineering, and I took the course and enjoyed it. I studied genetic engineering for two more years and got my master's degree. When I was doing experiments for my master's thesis, I got the opportunity to enter a Ph.D. program. One day, I was doing experiments until 2 or 3 in the morning, and the professor who founded the Darmstadt Institute for Biochemistry came up to the fifth floor, where I was, and he saw that the lights were on. He asked me what I was doing, and I told him that I was staying up late because my experiment wasn't going well. Other students there usually cleaned up and left at 5:00 p.m., regardless of whether their experiments went well or not, so I was worried that working until late hours would be seen as a sign of incompetence. Not long after that, he caught me doing experiments in the middle of the night again. He asked to speak with me the next day, and when I went to see him, he asked me to report on my progress. I thought I was going to get kicked out, but when he saw my report, he told me to continue with the experiment for about six weeks and then write my thesis. He asked me if I had decided where I wanted to do my Ph.D., and I told him that I hadn't, and he said, "Do you want to join my lab?" Looking back, I realize that he appreciated my willingness to work until dawn. That's how I started my Ph.D. program, a process that usually takes five or six years, but I finished in just three and a half years.

Q3 How did your experience of studying in Germany influence your subsequent bioindustrialization research?

I think the practical and realistic perspective I gained in Germany had a positive impact on my later work. At TU Darmstadt, exams were carried out orally, and the questions started with real-life objects, like for example, "Mr. Jeong, what do you see through the window?" "I see trees and buildings." "What is the window made of?" "It is made of silicate." Then comes the important question. "Isn't silicate a metal? How can they turn metal into that shape?" To answer this question, you have to analyze the structure of silicate, and if you are unable to answer correctly, it means you have to study more. Also, the strength of the tech or engineering universities in Germany lies their labs and practice exercises. At the beginning of the semester, the first thing you do is get a spot in the lab, and then you make time to go to the lectures. This is to learn the theories behind the experiments and practice exercises. Because I studied in this kind of environment, I wasn't afraid to make and create things while doing research on bioindustrialization. I didn't think, "I have to make that?" I thought, "Let's do it!"



KRIBB, the center of bioindustrialization research in Korea

Q4 You joined KRIBB in 1994. What was the impetus?

When I was in Germany, I used to get calls from my mother in Korea and my heart would drop because I was afraid I'd receive terrible news. Then, one night, I got a call that my father had passed away. I knew that moment would come someday, but I thought my mother would wait until I came back home to tell me, so it broke my heart. I'm their only son, so I came to Korea and hosted the funeral. Then, I tried to take my mother to Germany, but then I realized that for her, staying in Germany would be like being in prison. I was supposed to work for a company founded by my professor, but I asked for his understanding and came back to Korea. This was when KRIBB was building a pilot plant for bioindustrialization research, and they were looking for people who had studied both chemical engineering and DNA. Someone introduced me and I was given a job offer. It was a great opportunity for me, given that it had been just two months since I returned to the country.

Q5 What was the situation with and the level of bioindustrialization research in Korea at the time?

Bioindustrialization research was almost nonexistent. We were operating the pilot plant for the first time as well, so we spent our first year trying to understand the mechanical equipment in the plant, instead of hiring any new employees. About 70% of the mechanical equipment had been imported at the time, and most of them were made in Germany. I remember translating and teaching the staff how to use the equipment. I also redesigned the factory using the knowledge I had gained as a chemical engineering major. The preparation process was quite long. We worked even on weekends, and it was a major learning process for me.

Q6 For what needs and purposes did KRIBB start operating the pilot plant?

I think Dr. Park Young-hoon, who was the vice president at the time, felt the need after seeing and studying pilot plants in other countries. The purpose was to build facilities for bioindustrialization research and to help biotech companies with the know-how gained from our research. Back then, large corporation had the manpower, capital, and equipment, but small and medium-sized enterprises (SMEs) did not. We provided commercialization support mainly to SMEs, and many of them were able to launch their products onto the market as a result.

Q7 It's been about 30 years since the establishment of the first pilot plant. What are the achievements that have been made since then?

One of the notable achievements that we made was the construction of a new large-scale pilot plant in Ochang in 2014. In the initial pilot plant, we only dealt with microorganisms, but since then, we have expanded into the area of animal cells and now have a building for microorganisms and animal cells each. Another accomplishment worth noting is the human resources development for bioindustrialization. When we first started operating the pilot plant, we didn't have the manpower we needed, so we aspired to nurture our own manpower over time as we operated the plant. Based on the excellent resources of KRIBB, we initiated a program to train bioindustrialization researchers and produced related professionals. Those who have worked at the pilot plant have gone on to work for biotech companies and for the bioindustry promotion agencies across the country. Meanwhile, we provided training to not only Koreans but also Malaysians, as the Minister of Science, Technology and Innovation of Malaysia personally requested the training after seeing our facilities and training programs.

Q8 It must have been a rewarding experience to see the companies you assisted launch their products onto the market.

I've seen a company that was going downhill come back to life after a technology transfer from KRIBB, and I've also helped a company that wanted to build a factory increase their project scale tenfold so that they could perform original equipment manufacturing (OEM) elsewhere. I did everything I could to assist such companies, seeing it as my job, my mission, rather than to seek a sense of fulfillment. To reduce the burden on the companies, we allocated a research budget with 70% funded by KRIBB and 30% by the government.

Practical Bioindustrialization Research Experiences at a Company

Q9 What is it like to conduct bioindustrialization research at a company?

I am currently conducting bioindustrialization research and research for practical market entry at the request of a biotech company. Commercialization research at a biotech company seems to be completely different from what I experienced at KRIBB. Companies need to generate revenue and launch their products onto the market as soon as possible to be competitive. Industrialization research is thus conducted from the perspectives of price competitiveness, technological superiority, market entry, and product excellence, which are completely different from I was used to at KRIBB.

Q10 What is the current level of bioindustrialization research of Korean companies?

In the past, the expertise of national research institutes was clearly pronounced, but the conditions for bioindustrialization research at biotech companies have also improved significantly. Excellent research infrastructure and researchers have been secured by making enorous investments in research.

"Commercialization research at a biotech company seems to be completely different from what I experienced at KRIBB. Companies need to generate revenue and launch their products onto the market as soon as possible to be competitive."

The Need for Joint Research with Biotech Companies

Q11 What suggestions do you have for KRIBB in regard to the direction of bioindustrialization research?

I'd like to suggest not neglecting to work with companies. In the past, when companies lacked technology, they received considerable support from research institutes, but now they only learn what they need to learn from research institutes. The network between research institutes and companies has shrunk quite a bit. On the other hand, national research institutes cover quite a wide range of research areas, although research is somewhat concentrated in basic science. Back in the day, biotech companies did not have any basic research experts, who mainly worked for universities and research institutes. Therefore, the conditions for researchers to collaborate with biotech companies in areas of basic research weren't there, but now the situation has changed, and biotech companies also have competitiveness in basic research. Under these circumstances, it's time for KRIBB to offer more support for basic research collaborations with biotech companies. Biotech companies still need KRIBB's excellent research capabilities and commercialization equipment (infrastructure). I think we need to create a symbiotic relationship.

Q12 It seems that strengthening joint research and networks will help enhance Korea's bioindustrialization research capabilities.

If KRIBB actively pursues human resource exchanges through joint research with biotech companies, it will be possible for excellent researchers to find jobs at biotech companies after retirement. This in turn will help strengthen the bioindustrialization research capabilities of the private sector. To talk about a more realistic issue, the retirement age for researchers at national research institutes is currently 61. They say it will be extended to 65, but the thing is, researchers can continue their research activities even after the age of 65. From my own experience, there are many advantages to working in a biotech company after retirement and unleashing your research capabilities.

Determined to Live for the Marginalized When the Time Comes

Q13 When you look back on your long research career at KRIBB, you must have had both regretful and rewarding experiences.

Because I was so focused on research, I often wasn't as considerate of my subordinates as I should've been. I regret that I didn't embrace them as much as I should have. They still followed me as their leader though, and I'm grateful to them for that. I haven't attended as much since I retired, but on the center's Homecoming Day, about 70 to 80 staff members gather together. I find it meaningful to speak with those who come with their children to see how they are doing, and even if I don't see them face-to-face, whenever they tell me how they are doing, like they got a degree or they found a job at a company, I feel happy for them.

Q14 How do you feel when you visit KRIBB these days?

Nowadays, there are more unfamiliar faces than familiar faces. It's always a great pleasure to see people I used to work with. They've all been assigned important positions, which makes me realize that a lot of time has passed since I left and I also feel proud of them.

Q15 What advice would you give to younger researchers based on your own experience?

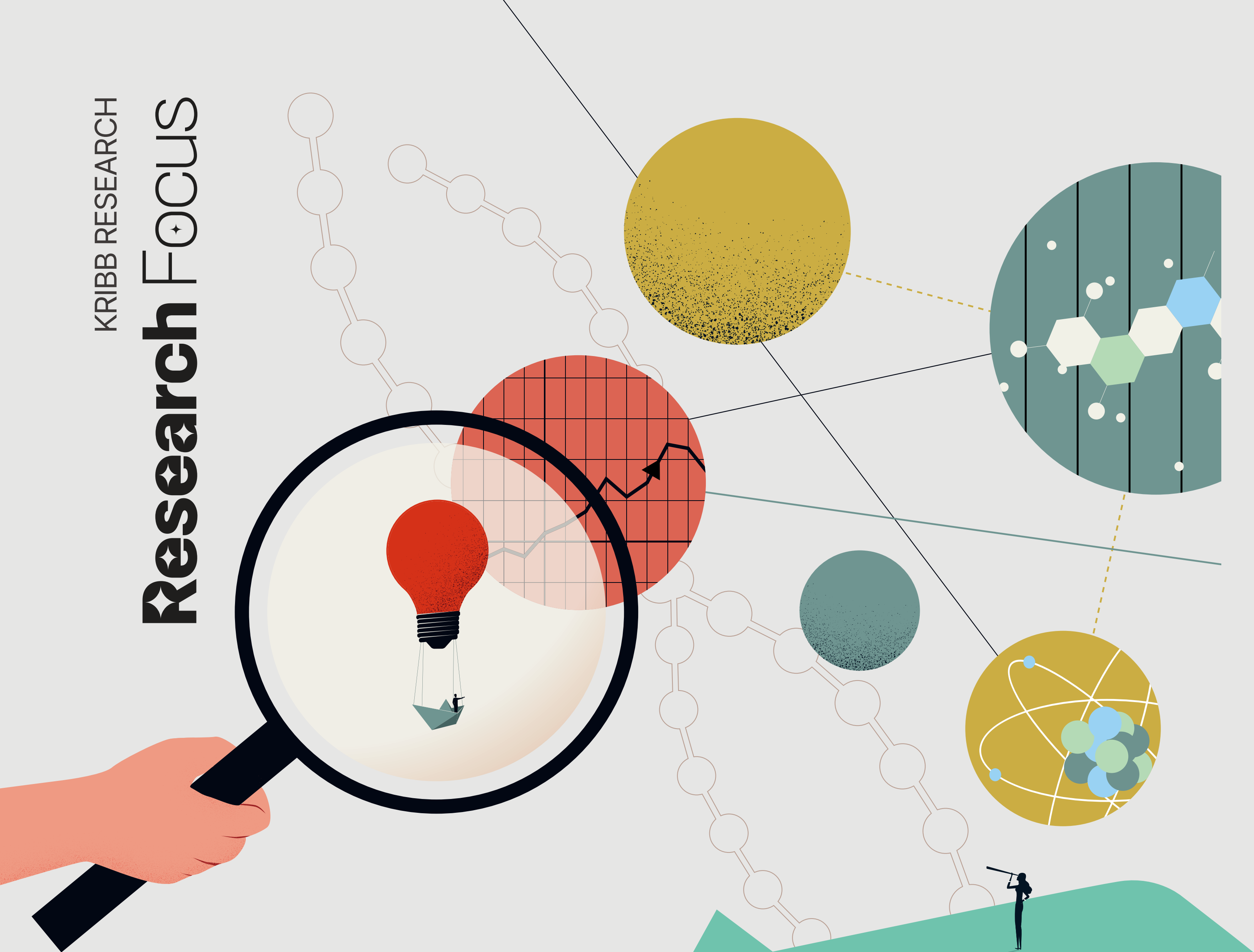
Research is important, but I'd like them to form and develop a wide range of human relationships with biotech companies and researchers. By being considerate of others, rather than prioritizing your own interests, you will be able to grow together with those around you. Nowadays, I often have the opportunity to meet and talk with new employees at my company, and when I ask them what kind of person they want to be: someone who is professionally competent but is only focused on their job or someone who is not professionally competent but helps many people. They all say they want to be the latter. They know what's more desirable, but it's hard to put it into action. I'm sure you'll find your research life more rewarding if you take care of the people next to you, like your fellow researchers and people from biotech companies. Speaking of the life aspect, I hope you take time to look at the sky and relax every now and then. I didn't, and in hindsight, I don't think the results you produce won't be that much different regardless of whether you are entirely focused on research or living a relaxed life. I hope you relax a little more and enjoy doing research.

Q16 What are your future plans as a researcher?

When I worked at KRIBB, I was able to conduct research in an excellent environment. Looking back, I realize that I had it all. I'm grateful that I was provided with that environment and those conditions. I've made a promise to myself that when the time comes, I will live for the marginalized, and I'm currently trying to fulfill that promise. I'm working on developing a cure for a rare disease based on my research experience. Right now, three experts in the field are working on the project, with plans to raise funds. I don't know whether the project will be successful, but I'm devoting myself to it because I think it's my last chance to serve others. If there's one concern, it's probably my physical condition. As I get older, I often realize that I'm not as fit as I used to be. I believe that the maximum number of years that I'll be able to focus on research from now on will be around two or three years, but for now, I want to do the best I can.

KRIBB RESEARCH

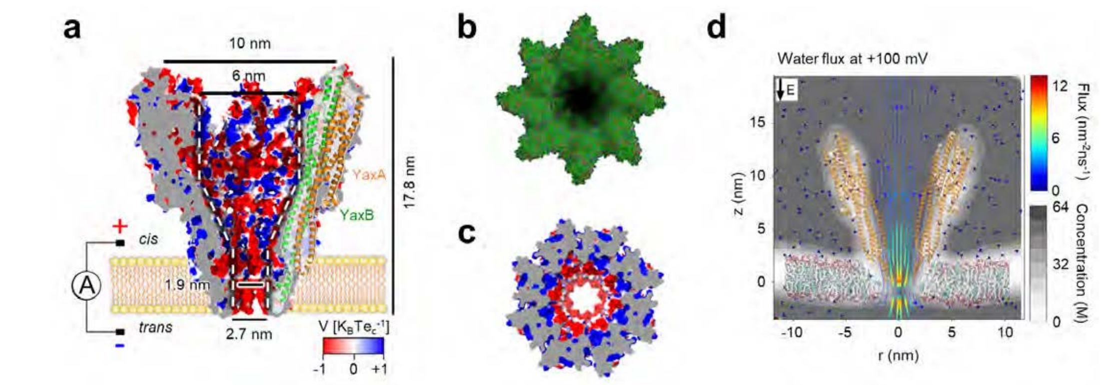
Research Focus



Relentless Efforts to Develop Biotechnology **to Serve as Driving Force Behind Korea's Bioindustry**

Medicinal products tend to have a long life. While smartphones and computers typically need to be replaced after two to five years of use, aspirin has been in use for 110 years since it started being marketed in 1899 and erythropoietin (EPO), a muscle endurance enhancement drug, for 30 years since 1989. There are cases where antibiotic resistance and tolerance to the drugs used in chemotherapy occur, and when this happens, a new drug or approach is necessary. Drug development helps to identify resistant strains and transmission routes and develop new therapies that can "bypass" resistance. KRIBB strives to develop new drugs by applying new scientific technologies such as novel proteins and genetic recombination.

01 Development of the world's first highly efficient drug discovery sensor



Tertiary structure of protein and nanofluidic properties detected by the nanopore sensor

The first step to developing a new drug is the discovery of candidate substances. The key is to analyze the binding between the drug and the target proteins associated with the disease. However, drug candidate discovery has been costly and time-consuming due to the inefficiency of existing analytical technologies. Current assays require costly equipment or involve taking an average of the signals measured from multiple molecules in an ensemble. Such methods have low sensitivity and require a large amount of sample, and some target proteins and drugs have low solubility in the sample, making it new drug development difficult.

Recently, domestic researchers have mitigated the problems with existing analytical technologies. They have developed a drug discovery sensor that can dramatically reduce the time and money spent on drug development. The research team led by Dr. Chi Seung-uk from the KRIBB Division of Biomedical Research developed the world's first high-efficiency nanopore sensor for drug discovery that can measure ultra-trace amounts of the target substance at the level of single molecules with high sensitivity.

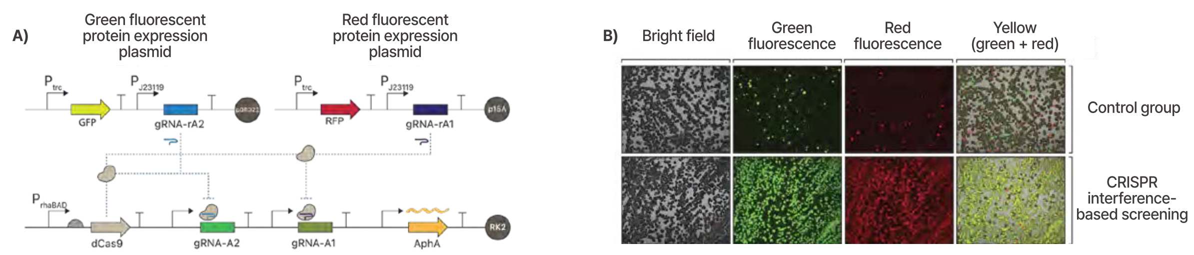
A nanopore sensor is a system that electrically measures the flow of ions through a hole measuring just a few nanometers (nm; one billionth of a meter). By measuring the electrical signals generated by biomolecules as they pass through the nanopore, single molecules can be characterized. However, existing nanopore sensors had limitations in that it was difficult to measure proteins of different sizes and charges and had low sensitivity in determining whether the drug bound to the target protein. With this in mind, Dr. Ji's research team developed a highly efficient nanopore sensor for drug discovery that can analyze target protein-drug binding at the single molecule level.

Using protein engineering techniques, the research team designed a funnel structure with a nanometer-sized hole to capture only one target protein. Based on the principles of electro-osmosis, multiple target proteins can be measured individually, enabling drug screening with extremely small samples at the picomole (one trillionth of a mole) level.

This technology is highly cost-effective as it reduces sample volume by about 4,500 times compared to nuclear magnetic resonance spectroscopy (NMR), a conventional drug screening technique, and can significantly reduce the time and cost to prepare target protein and drug samples. It is also possible to analyze protein-protein interaction and the efficacy of the drug that inhibits it, thereby enabling a new approach to drug development for targets for which it has been difficult to develop drugs as well as insoluble targets. "Our success in developing a new ultra-sensitive nanopore sensor that can measure target protein-drug binding with just a single molecule will enable highly efficient drug development using only trace amounts of sample," said Dr. Ji, the principal investigator in the project.

*References: Jeong, Ki-Baek, et al. "Single-molecule fingerprinting of protein-drug interaction using a funneled biological nanopore." *Nature Communications* 14.1 (2023): 1461.

02 No more worries about antibiotic resistance!



Effectiveness of Crisper Interference-based Multiplasmid Screening

Dr. Kim Seong-keun of the KRIBB Synthetic Biology and Bioengineering Research Center has developed a highly efficient system that can select recombinant plasmids for use in biomanufacturing processes without the need for antibiotics.

Genetic recombination is one of the technologies that powered the growth of the bioindustry. It is a technology in which a new gene, created by changing the sequence of a particular gene or combining it with another gene, is placed in a self-replicating DNA carrier called a plasmid and placed into a suitable host cell to mass-produce a useful substance.

The first biopharmaceutical to be produced using genetic recombination technology was insulin in *E. coli*, and the technology is now widely used to produce a variety of biological raw materials, including biocompounds, enzymes, protein drugs, and DNA vaccines.

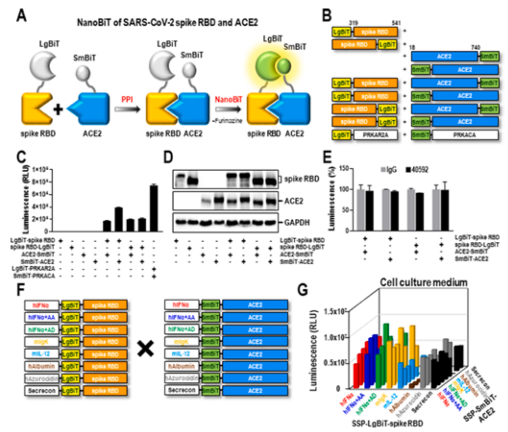
In order to develop a manufacturing process for the mass production of biological products using these recombinant technologies, it is important to select plasmids that can survive in host cells. The most common way to do this is by antibiotic screening.

Antibiotic screening involves treating a host cell with an antibiotic and selecting cells that survive as they are resistant to the antibiotic. However, antibiotic screening can lead to the emergence of antibiotic resistance by mutation, allergic reactions, and increased manufacturing costs. An alternative method is to use nutrient-requiring strains, but strain production is difficult in this case, the screening ability is poor, and the number of genes available for screening is limited. Especially for biopharmaceuticals such as DNA vaccines, the smaller the plasmid size, the higher the delivery efficiency in the body and the more antigens that get expressed, so it is necessary to develop a platform to select small plasmids.

The research team developed an intelligent gene circuit based on synthetic biology to select cells with plasmids. Once it is applied to an antibiotic-free biomanufacturing process, it is expected to have a broad range of applications in the future.

*References: Kim, Seong Keun, et al. "CRISPRi-based programmable logic inverter cascade for antibiotic-free selection and maintenance of multiple plasmids." *Nucleic acids research* 50.22 (2022): 13155-13171.

03 Biosensor technology to analyze variant viruses quickly and easily



Development of a secreted NanoBiT-based biosensor for detection of the spike RBD-ACE2 interaction

In the case of SARS-CoV-2, the coronavirus that caused the COVID-19 pandemic, it was difficult to prevent and treat as new variants emerged one after another. In the future, however, we won't have to worry about the difficulty of dealing with variants. This is because Dr. Cho Sung-chan, head of the KRIBB Nucleic Acid Therapeutics Research Center, has developed a biosensor technology for analyzing the interactions that occur in the early stages of coronavirus infection.

Dr. Cho's team has developed a biosensor technology for quantitative analysis of the binding between the spike protein, which plays a key role in the coronavirus entering the human host cell, and the receptor protein (ACE2) in cell culture, and the technology can be used in various ways.

First, it can facilitate the discovery of antiviral drug substances that can inhibit spike-ACE2 protein binding, which is formed between the spike protein on the viral envelope and the ACE2 protein on human cells.

The formation of spike protein-neutralizing antibodies in coronavirus-infected patients or vaccine recipients can then be analyzed. Spike protein-neutralizing antibodies are antibodies against the spike proteins of the coronavirus that have the ability to neutralize the virus. They bind to the spike proteins to prevent the virus from entering the body or neutralize it.

The technology can also be used to analyze the cross-reactivity of antiviral drugs and neutralizing antibodies by applying diverse variants of the virus.

This platform technology has wide applications, as it can be used for rapid antibody diagnosis of new variants as they emerge and for the development of new drugs that target interactions between cell membrane proteins. A patent application has recently been filed in Korea, and there are plans to transfer the technology to companies that are interested.

*References: Ham, Youngwook, et al. "The SpACE-CCM: A facile and versatile cell culture medium-based biosensor for detection of SARS-CoV-2 spike-ACE2 interaction." *Biosensors and Bioelectronics* 227 (2023): 115169.

KRIBB ENTREPRENEUR

Desire to Help Restore **Muscles for Elderly People to Regain Their Youth**

Ki-Sun Kwon, CEO of Aventi Inc.

Decreased muscle mass can lead to motor disorders and geriatric diseases in seniors. In the past, age-related sarcopenia was simply regarded as a natural phenomenon, but now it is recognized as a disease. The World Health Organization (WHO) and the US Centers for Disease Control and Prevention (CDC) classified sarcopenia as a disease and assigned a disease code in 2016 and Korea followed suit in 2021. However, there is no FDA-approved drug for the condition, and health supplements are used in place of therapeutic drugs. Aventi Inc. aims to satisfy the unmet demand for FDA-approved drugs by developing a cutting-edge new drug. Aventi was founded in 2020 by a former KRIBB researcher, Kwon Ki-sun, who had served as the head of the KRIBB Longevity Science Research Center, Aging Research Center, and Aging Control Research Group.

Using KRIBB's research achievements as a driving force

"Just ten years ago, 'aging' was not accepted as a major theme in biology, but the executive department of KRIBB recognized the importance of aging research early on, and the senior personnel at KRIBB guided me toward aging research."

Kwon recalls that he got into aging research around 2007, thanks to the insights of the organization's executive department. Back then, KRIBB formed a network with the very few researchers and societies specializing in aging research in Korea, and in 2008, it established the Longevity Science Research Center, the predecessor to the subsequently established Aging Research Center, Aging Control Research Group, and Convergence Research Group for Aging.

While studying aging, Mr. Kwon paid special attention to muscle. He recognized the importance of studying muscle aging while conducting research to discover target factors for aging control, as a project of the Ministry of Science, ICT and Future Planning, in 2014. The research was recognized for its excellence and was selected as one of the 50 best basic research projects by the Korea Research Foundation in 2014 and one of the 100 best national research and development (R&B) projects by the Ministry of Science and ICT. While Kwon was conducting his research, the research community also recognized the criticality of muscle aging and its impact on the body.

"The importance of muscle has grown to the point that it is no longer considered as just a motor organ, but it is described as an endocrine organ that secretes various substances responsible for physical vitality. When muscles age, it doesn't just cause problems with physical activity. It can lead to a broad range of conditions, including diabetes, cardiovascular disease, depression, and dementia."

Muscle begins to gradually shrink in young adulthood, and people start losing 1 to 2% of their muscle mass each year when they reach their 50s. The condition in which physiological changes of aging lead to muscle loss is known as age-related sarcopenia, which can lead to difficulties with daily activities. Sarcopenia affects more than 20% of men and 10% of women in their 60s and about 40% of both men and women in their 70s. As such, a large portion of the elderly population suffers from sarcopenia, but there are currently no licensed drugs for the condition and drug intervention is thus impossible. Recognizing this situation, Mr. Kwon decided to start his own company to develop a treatment for age-related sarcopenia. In March 2020, he founded Aventi to commercialize the outcomes of his research at KRIBB, and he received assistance from the KRIBB SME Support Center and Technology Transfer Center in the process.

Aventi, is Italian for "to twenty." It embodies the commitment to restoring muscles and health, like those of a 20-year-old, for seniors.

The company name, Aventi, is Italian for "to twenty." It embodies the commitment to restoring muscles and health, like those of a 20-year-old, for seniors.

Toward faster development of therapeutics

Aventi is currently developing four drugs: AVTR101, AVTN301, AVTM201, and AVTP401. Among them, AVTR101 is a new drug that has been recreated from a drug used for other indications to be applied to sarcopenia, and it has been approved for clinical trials by the Ministry of Food and Drug Safety after successful completion of an animal study. A clinical trial has been conducted at four hospitals in Korea since the end of 2022, and it is currently in Phase II clinical trials.

Aventi is competing with global biotech companies in the development of sarcopenia treatment. In the world, there are about ten companies that have initiated Phase 2 clinical trials and one company that has completed a Phase 2 clinical trial. In the face of increasing competition, Aventi is striving to become the first company in the world to have a therapeutic agent approved for sarcopenia, and the R&D team is confident that AVTR101 is a viable sarcopenia treatment.

"Safety is what gives AVTR101 its competitive advantage. It has been used for other indications and many people have already used it. There have been very few side effects, so there's no need to worry about safety. Plus, we have excellent researchers from this particular field, who have gained recognition in the academic circles, as the investigators in the clinical trial, so I believe we will succeed in drug development without any significant difficulties," said Mr. Kwon.

Aventi CEO Kwon Ki-sun explains that networking with physician scientists is absolutely crucial, as they are the ones who will explain the purpose and process of the clinical trial and the efficacy of the drug among other things to the people participating in the trial. Aventi's journey has been accompanied by key opinionators in the field with whom Mr. Kwon has been networking while conducting basic research at Biotech.

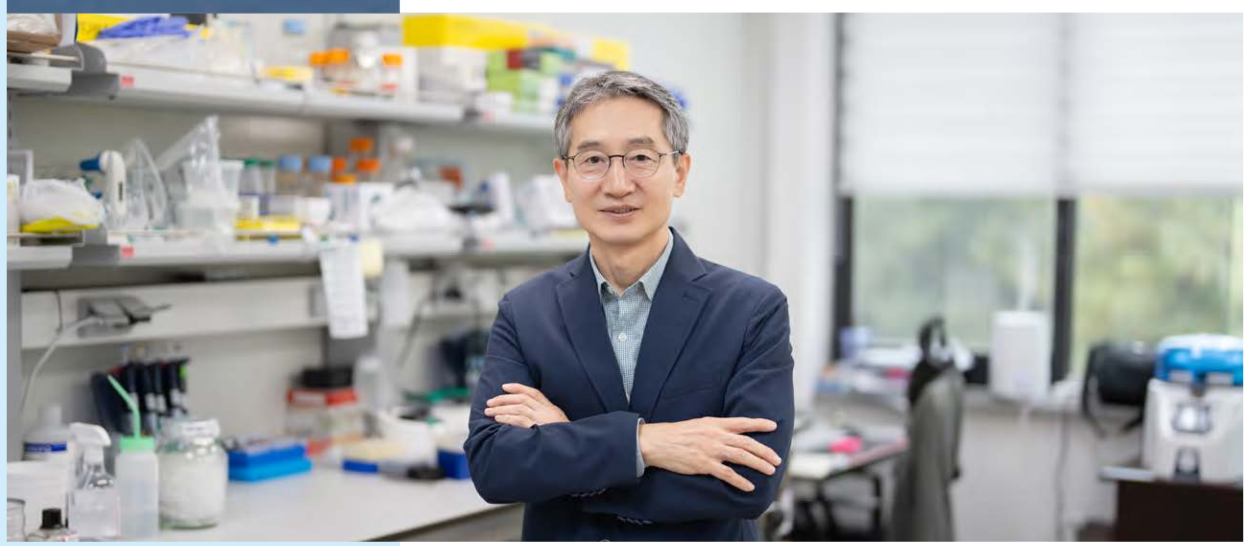
By September 2024, the results of the Phase 2 clinical trial of AVTR101 will be out. If it meets the necessary criteria a Phase 3 study will be carried out, and if all goes well, the company may potentially launch a treatment for sarcopenia onto the market by 2027.

"There is a huge demand for sarcopenia treatment. We often meet people who ask us when we'll develop a cure and who tell us that they hope we develop a cure soon. We're developing treatment for sarcopenia with a strong desire to help people who are suffering," said Mr. Kwon.

There is also a backup plan, just in case, and it is to develop AVTN301, which is currently under development through the synthesis of new compounds, and AVTP401, a protein drug candidate. AVTM201, a microRNA treatment for sarcopenia and cachexia, is another backup plan, even though its development is currently on hold.

Aiming to grow into an aging-related biotech company

According to the statistics on the elderly released by Statistics Korea in September 2023, the number of seniors aged 65 and over in Korea in 2023 was 9.5 million, accounting for nearly 18.4% of the total population. The United Nations defines "senior" as a "person aged 65 or older," and classifies societies as an "aging society" if the proportion of the elderly population is 7% or more of the total population, as an "aged society" if it is 14% or more, and as a "super-aged society" if it is 20% or more. Accordingly, Korea is an aged society, as of 2023, and Statistics Korea expects it to become a super-aged society by 2025. Amidst these social changes, the importance of Aventi and the development of a sarcopenia treatment is growing day by day.



Aventi is currently developing four drugs: AVTR101, AVTN301, AVTM201, and AVTP401.

"The rate of aging in Korea is one of the fastest in the world. A large proportion of the population is elderly, and if they become dependent due to mobility problems, it will lead to national issues. If the elderly can stay healthy and be economically active, it will help revitalize Korea's competitiveness." Meanwhile, according to Statistics Korea, in 2022, 34.3% of seniors reported that they were satisfied with their current life, and 31.2% were satisfied with their social and economic achievements. For seniors to be satisfied with their lives, they need to be healthy and have no problems with mobility.

"If your body doesn't do what you want it to do, your quality of life will deteriorate. Muscle aging gives rise to other medical conditions, and it can eventually lead to depression. It is the state of the body and mind that determines the quality of life, which is more important than the ability to be economically active. We want to help improve the quality of life of seniors by developing a treatment for age-related sarcopenia."

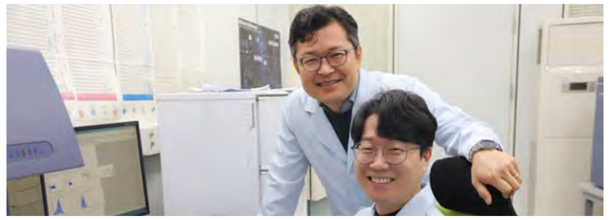
Currently, Aventi's main focus is on developing a treatment for age-related sarcopenia, but in the long run, there are plans to develop treatment for other geriatric diseases, according to CEO Kwon. AVTP401 currently under development appears to have a positive effect not only on muscles but also on other organs, so it may potentially become the seed for expansion. KRIBB is also continuing its research to discover new aging-related drugs and plans to transfer its technology for further development, if necessary.

Aventi's corporate philosophy is to value healthy life and it envisions a society where seniors are healthy and happy. The growth of Aventi will not only be a success story of a company founded by a researcher but also a driving force that will exert a positively influence when Korea turns into a super-aged society. This is why Mr. Kwon's shoulders feel heavy.

"First of all, we need to successfully complete the Phase 2 clinical trial of AVTR101. I feel a lot of pressure and a sense of responsibility. Recently, I found a phrase that was helpful. It was written at the entrance of the stadium of the US Open Tennis Championships, and it was 'Pressure is a privilege,' which was said often by tennis player Billie Jean King. Thinking that pressure is a privilege that only the chosen ones get to enjoy, I try to take it one day at a time."

Accordingly, Korea is an aged society, as of 2023, and Statistics Korea expects it to become a super-aged society by 2025. Amidst these social changes, the importance of Aventi and the development of a sarcopenia treatment is growing day by day.

Discovery of New Immune Gateway That Can Increase Effectiveness of Immunotherapy for Cancer



Researchers in Korea have discovered a new immune gateway that allows cancer cells to evade attacks by natural killer(NK) cells. A joint research team led by Dr. Kim Tae-don from the Immunotherapeutics Research Center at the Korea Research Institute of Bioscience and Biotechnology(KRIBB; President Kim Jang-seong) and Do Jun-sang, Professor of Materials Science and Engineering at Seoul National University(SNU) reportedly discovered a new immune gateway that regulates the activity of NK cells and identified its mechanism of action.

- This is expected to contribute to the development of immunotherapy agents that increase the anti-cancer activity of NK cells.

With the advances in biotechnology and medical technology, the technology to control cancer has also been evolving in various ways.

- Cancer has been mainly treated by surgery, radiotherapy, and chemotherapy, which are still useful. However, many cancer patients suffer physically and psychologically from surgery, recurrence, and development of drug tolerance, and research is being conducted heavily to develop new treatments that are different from conventional cancer treatments.

One such alternative is immunotherapy, a method of treating cancer using immune cells such as NK cells and T cells.

- When NK cells encounter pathogens such as viruses and bacteria or infected and diseased cells such as cancer cells, they directly attack them by binding to them and lysing them. NK cells create a point of contact to bind to their target, and it is called an immunological synapse(IS).
- In order for NK cells to attack infected and diseased cells, they need to be able to recognize the target cells, but cancer cells bind to immunosuppressive proteins called immune gateways to interfere with such recognition and protect themselves from immune cells.
- To prevent this, immune gateway inhibitors are used, but there are risks of side effects such as adverse reactions related to the immune system.

The research team discovered a novel immune gateway that interferes with the formation of immunological synapses on NK cells and elucidated the mechanisms concerned.

- The new immune gateway is a receptor(Nogo receptor 1(NgR1)) that recognizes an immunosuppressive protein(Nogo A) expressed in target cells, and its function is to regulate signals that control the motility of the cytoskeleton of NK cells.
- Compared to normal NK cells, NK cells with blocked NgR1 exhibit improved stability in immunological synapse formation, resulting in enhanced killing power to destroy target cells.
- In an experiment using a mouse model of solid cancer, mice injected with NgR1-blocked NK cells showed reduced cancer development and longer survival period than the control group.

The research team also found that NgR1 influences the prognosis of cancer patients.

- The more Nogo A, an immunosuppressive protein that binds to NgR1, is expressed, the worse the clinical prognosis is, and thus it may be a risk factor reducing the chance of survival.

Dr. Kim Tae-don from KRIBB who served as the principal investigator in this project said, "Our recent accomplishment was made possible by combining the knowledge of the mechanisms regulating NK cell activity discovered by KRIBB with an imaging technique for analyzing the stability of immunological synapse formation applied by Professor Do Jun-sang from Seoul National University."

- "We expect that the newly identified immune gateway will present new concepts for a better understanding of the regulation of NK cell activity and the development of anti-cancer immunotherapy drugs and that it will lead to the development of various types of convergence technologies."

The study was published in the online edition of *Nature Immunology*(IF 31.250), a world-class journal in the field of immunology, on January 9. *(Paper title: NgR1 is an NK cell inhibitory receptor that destabilizes the immunological synapse / Corresponding authors: Dr. Kim Tae-don(KRIBB) and Professor Do Jun-sang(SNU) / First author: Oh Se-chan(Doctoral Program, UST KRIBB Campus))*

- The study was conducted with the support provided through the Creative Allied Project(CAP) of the National Research Council of Science & Technology(NST), the National New Drug Development Program of the Korea Drug Development Fund(KDDF), and the Technology Development Program of the Ministry of Science and ICT.

KRIBB Spearheads Revitalization of Bio Industry Ecosystem by Innovating Technology Commercialization Platform

GenKOre, specializing in "genetic scissors" technology, signed a third-party technology transfer agreement worth up to USD 350 million(approx. KRW 450 billion) with a global pharmaceutical giant late last year.

Ingenium Therapeutics, a biotech startup, agreed to pay a total of KRW 154.5 billion to be transferred a technology related to a natural killer(NK) cell therapy in 2021.

These accomplishments were the fruits of the commercialization efforts of the Korea Research Institute of Bioscience and Biotechnology(KRIBB; President Kim Jang-seong). Through a systematic technology commercialization program, KRIBB has created a virtuous cycle of value chains that link the outcomes of basic research and development(R&D) projects to the actual bio industry.

As a result of KRIBB's efforts to revitalize the bio industry ecosystem, 31 start-up companies have been founded by researchers such as Bioneer, Genofocus, and Pharmabcine.

- The incubator that the institute has been operating since 2000 has supported 81 companies, 15 of which are listed on the Korea Exchange.
- These companies have generated KRW 636.9 billion in sales and created 1,708 jobs, as of 2022, and their market capitalization amount to KRW 2,247.2 billion in total, as of March 24, 2023.

KRIBB's technology commercialization program consists of Lab2Market, a technology commercialization platform, and 'BIO Start-up Booster, a start-up support platform.

- Lab2Market promotes technology transfers by supporting the marketing of excellent promising technologies discovered and subsequently linking them to possible business opportunities. Field utility is enhanced by bundling the necessary technologies together, rather than transferring each unit technology individually, in reflection of industry needs.
- As a result, the average number of technology transfers and total income from license fees and royalties in the last three years(2020 to 2022) increased by 38% and 61%, respectively, compared to the previous period(2017 to 2019). Also, large-scale technology transfers worth millions of dollars in advanced biotechnology fields such as NK cell therapy, gene editing, new anticancer drugs, and organoids have been arranged successfully.
- BIO Start-up Booster, on the other hand, provides support tailored to each stage, from discovery of a business idea to support for the establishment and growth of the company and investor relations. In 2020, a joint start-up system was introduced by combining the start-up ideas of KRIBB and the business expertise and capabilities of external experts, and the KRIBB Bio Start-up School, on the other hand, provides opportunities to practice attracting investors and to consult professional investment analysts.
- Through this, the period from the discovery of business ideas to the actual establishment of a start-up company has been shortened from an average of two years to one year, and seed and series A funding is received at the same time as the establishment of the business.

KRIBB is aiming to achieve large-scale technology transfers at the global level by innovating its existing technology commercialization platform.

- The plan is to build a pipeline by linking its advanced biopharmaceutical development techniques accumulated over 30 years with related businesses and improve the technical maturity of biopharmaceutical substances for new drugs.
- The institute is also making a transition from conducting R&D first and then acquiring intellectual property(IP) rights later to formulating IP strategies first and conducting R&D later. They are also supporting follow-up R&D tailored to corporate needs to shift the focus from lab-centered, supplier-based technology development to developing technology that can actually enter the market by stressing commercialization.

"By innovating the biotechnology commercialization platform, we will not only develop technology at the laboratory level, but also promote interdepartmental collaboration to further drive technological maturity to the level required by the industry, so that blockbuster-level technologies that are superior to current technologies can be commercialized," said KRIBB President Kim jang-seong.

- He also added, "I hope that this can be achieved with the government's policy support for technology commercialization along with institutional support such as increasing the pool of related professionals."

KRIBB Hosts the 2023 KRIBB Annual Conference

Advanced biomedicine, aimed at eliminating the root causes of diseases and providing personalized treatment through cell and gene therapy, and aging research, aimed at accelerating the development of anti-aging therapies by accurately calculating the biological age, are considered to be core biotechnologies that will save humanity and promising technologies that will shape the future.

In line with this trend, a conference has been organized to provide a platform for academic exchanges in the fields of high-tech biomedicine and anti-aging to lay the groundwork for solving national challenges in the bio sector and leading the bio transformation.

The Korea Research Institute of Bioscience and Biotechnology (KRIBB) announced its plans to hold the 2023 KRIBB Annual Conference on December 5 (Tuesday) at the ICC Hotel in Daejeon.

Under the slogan, "Advanced Biomedicine & Aging, Opening New Horizon of Future Biotechnology," the conference will feature a keynote lecture by KAIST Vice President for Research Lee Sang-yup, who founded the field of systems metabolic engineering, followed by a broad range of discussions among experts on advanced biomedicine and anti-aging research.

In the advanced biomedicine session, a panel discussion will be held with Kim Tae-don, a principal investigator at KRIBB, as the chair, following the keynote presentations; Shin Ui-cheol, Director of the IBS Center for Viral Immunology (professor at KAIST); Lee Mi-ok, principal investigator at KRIBB; Koo Bon-kyoung, head of the IBS Center for Genome Engineering; Lee Dae-hee, Head of the Systems Biology Research Group; Kim Geon-soo, CEO of Curocell; and Jung Hyo-young, Head of the Advanced Medicine Team at KBIOHealth.

The anti-aging session chaired by Eunsoo Kwon consisted of presentations by Kwon Ki-sun, principal investigator at KRIBB; Lee Seung-jae, professor at KAIST; Kim Jong-pil, professor at Dongguk University; Ryu Dong-yeol, professor at GIST; Ryu Ja-hyoung, professor at UNIST.

A variety of other programs will also be organized for KRIBB to share the major research achievements from the year 2023 and enable practical exchanges among the attendees.

- At the KRIBB Poster Festival, which will be held for the 15th time this year, 160 posters presented by KRIBB researchers at domestic and international conferences will be exhibited, and at the Young Speaker Presentation, 20 up-and-coming researchers who will lead the future of Korea's biotech sector will present their noteworthy research findings.
- The KRIBB Family Business Networking Day will be held as a network exchange program between family businesses of KRIBB, and a meeting will be held to present the best practices among government-funded projects (main projects).

In his opening remarks, Kim Jang-sung, President of KRIBB, said, "As biotech emerges as a game changer in the global technology landscape, competition among nations to secure advanced biotechnologies is intensifying, and amid these circumstances, the Korea Research Institute of Bioscience and Biotechnology will endeavor to secure super gap technologies by undertaking challenging and innovative R&D to serve as a leader in tackling national challenges and spearhead the bio transformation."

- He also asked for "cooperation in bringing together the capabilities of industry, academia, research institutes, and medical institutes to secure national strategic technologies, as the centerpiece of advanced biotech R&D."

KRIBB creating a better future
together with the people of Korea
based on research for life
and technology for tomorrow

To promote health and safety among citizens
and drive Korea's innovative growth,

KRIBB is embarking on a new journey
toward a more prosperous tomorrow.

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Korea Research Institute of Bioscience and Biotechnology

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www.kribb.re.kr

125 Gwahak-ro, Yuseong-gu, Daejeon 34141, Korea
Tel. +82-42-860-4114 Fax. +82-42-861-1759

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