ADVERTISEMENT FEATURE

TAKING GREAT TECHNOLOGICAL STRIDES FOR MEDICAL SCIENCE

Some Japanese immunologists took up the gauntlet to help slow the spread of the virus, while others have strived to DIGITALLY MAP HUMAN BIOLOGY.

Early in the COVID-19 pandemic, several groups of researchers in the city of Osaka made global headlines as they announced key studies that would spur the development of new vaccines; others now have an audacious plan to create detailed virtual replicas of the body to map how we respond to disease.

One group from Osaka University's Immunology Frontier Research Center (IFReC) discovered that infection by the SARS-CoV-2 virus not only produces neutralizing antibodies that protect against infection, but also antibodies that promote infectivity through enhancing the binding capacity of the SARS-CoV-2 spike protein. These results provided insights for developing vaccines that limit the production of infection-enhancing antibodies.

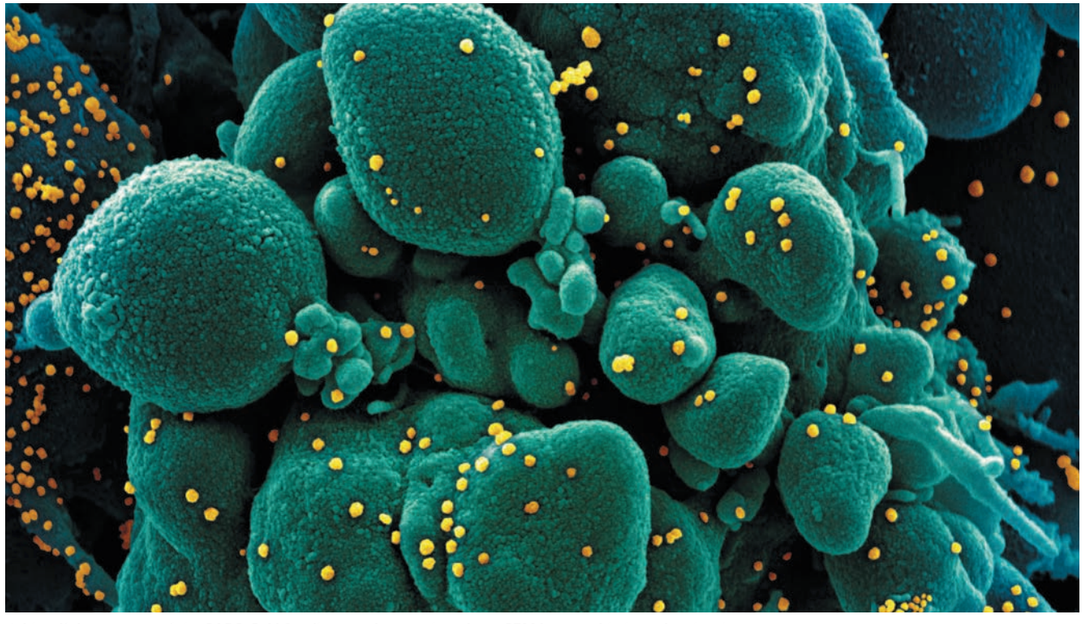
Another group at the university added to the understanding of adaptive immunity through study of particular T cell responses in healthy individuals and patients that had experienced mild symptoms of COVID-19. The IFReC team showed a specific T follicular helper cells (Tfh) was protective against COVID-19 and would be a suitable booster antigen

IFReC, since its launch in 2007, has built on Osaka University's strengths in immunology to grow into a world-class research centre. The institute was one of the first founded through the World Premier International Research Center Initiative (WPI), a prominent Japanese government scheme to support innovative research hubs.

"As the COVID-19 pandemic worsened, public interest in immunology research skyrocketed," says Kiyoshi Takeda, director of IFReC since 2019. "There was a strong feeling among IFReC researchers that we could do more to benefit society through basic research on COVID-19."

Under Takeda's leadership, researchers were quick to form a collaborative network for COVID-19 research. They also called on Osaka University's Research Institute for Microbial Diseases, as well as the Osaka University Hospital — which had been treating COVID-19 patients with severe symptoms — to expand the scope of research.

This was even more successful than they could have predicted, says Takeda. "As this grew into a university-wide initiative, we gathered support from the university headquarters and the Nippon Foundations. By April 2021, we established the Center for Infectious Disease Education and Research, a dedicated unit which brings together knowledge and talent to address the current pandemic and future infectious diseases."



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▲ **Identifying aspects of the SARS-CoV-2 spike protein, seen here in an SEM image, aided vaccine development.**

NEW OPPORTUNITIES

A novel collaborative framework implemented by IFReC is expected to drive research impact even further. In 2017, IFReC began a collaboration with Otsuka Pharmaceutical and Chugai Pharmaceutical, whereby the companies fund IFReC research and get early access to pre-published data but have no direct input into the direction of research.

The first collaboration of its kind in Japan, this partnership provides "a way for us and pharmaceutical companies to find openings for new drugs at an early research stage. It's an effective method for translating basic research into real-world impact in Japan, where spinning off startups from university research is less common," says Takeda.

"Once we have a drug in the market from this collaboration, we anticipate more companies to follow suit. For that, we need to continue being a world-class research centre," he adds.

Through IFReC, Takeda also stresses training for early-career researchers, with a focus on international exchange. Plans are underway for postdoc exchanges and double-degree programmes with institutions abroad. "The International School of Advanced Immunology, which we offer jointly with the University of Bonn, is an excellent start," suggests Takeda. "We're keen to prepare more international research experiences for young researchers and students."

VIRTUAL REALITY PIONEERS

In late 2022, Osaka University announced the selection of a second WPI centre that is striving to improve human health, the Premium Research Institute for Human Metaverse Medicine (PRIMe). By developing a digital replica of a person — or bio digital twin — the centre is pioneering a new method of medicine in which disease onset and pathology for an individual can be modelled virtually on a computer.

Its director, Kohji Nishida, says that bio digital twins will be made possible by combining informatics with data from patient samples, and using organoids, miniaturized 3-D organ models that allow study of biological processes.

▲ **Kohji Nishida (at centre) of Osaka University's Premium Research Institute for Human Metaverse Medicine is helping push the limits of medical technology.**

AN EFFECTIVE METHOD FOR TRANSLATING BASIC RESEARCH INTO REAL-WORLD IMPACT

The ultimate result, he envisions, is super-precision medicine and a disease model unique to each person that "not only helps understand how genes and the environment interact, but how variations in each single nucleotide polymorphism, and each type of environmental factor, affects each individual."

"Medicine has conquered many diseases that arise from a single factor. For these, animal studies have played a significant role," he says. "However, we need more precise models based on humans to address diseases that arise from a complex interaction of genetic and environmental factors. At the same time, we must move beyond how we use human data in research, as it only captures a snapshot of the individual at a given point in time."

Research at PRIMe focuses on chronic, age-related diseases, with an initial focus on six target organs and systems: the brain, eyes, joints, ovaries and heart, as well as the hepatobiliary and pancreatic systems. These relate to common chronic diseases linked to age, including dementia, stroke, and osteoarthritis.

There are plans to extend the scope of the research to the entire body and refine models to a level of precision that could "offer personalized preventative care for people that appear healthy," Nishida explains.

METAVERSE MEDICINE

Key to developing these virtual models of our bodies will be the development of more advanced organoids and a better ability to replicate the ageing process.

"There is surprisingly little evidence on the types of stressors that cause ageing in the human body. It could vary between organs, but there may also be stressors that all organs have in common, and we need to apply those stressors in organoids to create a model for ageing," Nishida says.

Previous work by PRIMe researchers lay a solid foundation for developing the virtual models, says Nishida. In a world first achievement, his team has already generated organoids of the entire eye: a basis from which to create bio digital twins for retinal and optic nerve degeneration.

"Human Metaverse Medicine will be a new scientific field that prompts a paradigm shift in both biomedical research and health care. Pioneering the field is a great challenge, but great strides are needed if we truly want to replicate phenomena inside a real human," Nishida says. ■

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