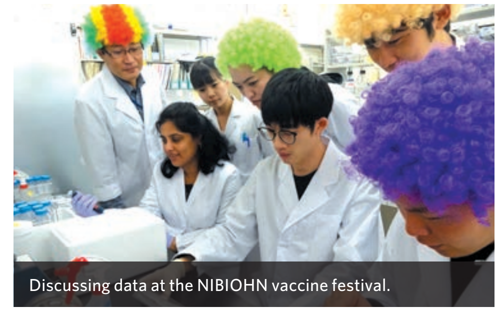
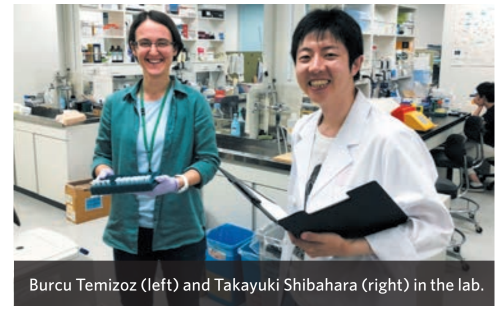
The best ingredients make the best vaccines

NIBIOHN SCIENTISTS ARE HELPING RESEARCHERS PICK **THE RIGHT ADJUVANT** FOR THEIR VACCINES.

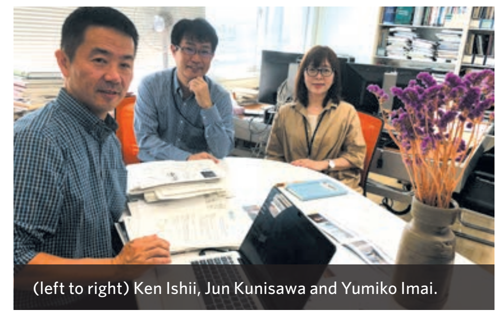
NIBIOHN scientists participate in an outreach programme for elementary and junior high school students.



Discussing data at the NIBIOHN vaccine festival.



Burcu Temizoz (left) and Takayuki Shibahara (right) in the lab.



(left to right) Ken Ishii, Jun Kunisawa and Yumiko Imai.

Of all the medical innovations in modern times, vaccines have probably saved the most lives. Diseases that used to claim the lives of around one in three children have now been eradicated from large parts of the world. Now, a new wave of vaccines is tackling not only emerging infectious diseases, but also cancer, obesity and metabolic diseases, and even smoking.

THE UNSUNG HERO OF VACCINES IS A COMPONENT CALLED THE ADJUVANT

By focusing on making cheaper, more effective and faster-acting vaccines to target a range of diseases and infections, the Center for Vaccine and Adjuvant Research at the National Institutes of Biomedical Innovation, Health and Nutrition (NIBIOHN) in Japan, is at the forefront of this vaccine revolution.

Building more effective vaccines

The unsung hero of vaccines is a component called the adjuvant. It puts a 'red flag' on the antigenic component of the vaccine — an inactivated whole or part of a virus or bacteria — and instructs the immune system to mount a defence against that antigen whenever it is encountered. Without adjuvants, vaccines would be ineffective, because the immune system would not be primed enough to recognize and react to the pathogenic threat.

One adjuvant might work well in a vaccine against influenza, but cause an immune over-reaction in a different vaccine. This is because adjuvants are like spices, explains Ken Ishii, director of the Center for Vaccine and Adjuvant Research. "Every spice has a different taste, but you can't compare which is the best or worst — for each disease, you need a different adjuvant."

To help researchers choose the best adjuvant for their vaccine, the Center established the Adjuvant Database Project 7 years ago. The database now has over 30 vaccine adjuvants listed, all of which are either approved for use or are under development in clinical trials.

Choosing the right adjuvant may be the key to expanding the reach of vaccines well beyond the traditional model of infectious disease prevention.

Take smoking, for example. The ingredient that makes cigarettes so addictive is nicotine, because it causes cravings that can only be relieved by more nicotine. But what if you could immunize the body against nicotine, so there was no reward gained from inhaling nicotine into the lungs?

The problem is that if you simply inject nicotine into the body, the immune system doesn't recognize the chemical as a threat. But administer nicotine along with the right adjuvant, and the adjuvant will flag the nicotine to the immune system, marking it as a threat that needs to be neutralized. Suddenly, nicotine becomes an antigen, the immune system learns to recognize it, and you have a vaccine that can help smokers to quit the habit.

The same principle could apply to recreational drugs, and possibly, over-eating. "Some people are working on an anti-obesity vaccine, or a vaccine against ghrelin, which is the hormone that makes you feel hungry," Ishii explains.

Faster and cheaper using DNA

In the traditional method of manufacturing some vaccines, such as influenza, the virus is injected into chicken eggs to incubate, then harvested, inactivated and purified to extract the viral antigen for vaccine manufacturing. It's a complex process that can take 6 to 12 months.

Researchers at the Center for Vaccine and Adjuvant Research are looking at ways to make this both faster and cheaper, by using messenger RNA — the genetic material that transmits the instructions from DNA to the protein-manufacturing facilities in the cells.

Instead of injecting an antigenic protein into the body for the immune system to recognize and react to, researchers are instead introducing the genetic material that codes for that antigenic protein — messenger RNA or rings of DNA called plasmids — into the body, encapsulated in a nanoparticle coating to protect it from degradation by the immune system. This coating also makes the package look like a virus, so it will be picked by immune cells called macrophages.

"We inject the messenger RNA, then macrophages take up the RNA, and transcribe and translate it into the protein," Ishii says. "But then the host cell says 'oops, we are making someone else's protein', the immune system comes and recognizes this protein as foreign, and produces antibodies to recognize and attack it."

Another advantage of using messenger RNA or plasmids as the basis of vaccines is that they are much tougher than viruses. This means that not only will these vaccines be able to survive without refrigeration, they can be administered by various methods, including nasal spray.

Cooperation and collaboration

The Center for Vaccine and Adjuvant Research is trailblazing its way through vaccine research, thanks in no small part to its principal investigators, Jun Kunisawa, Yumiko Imai, Yasuhiro Yasutomi and Teruhito Yasui. But Ishii is also particularly proud of its role in cultivating collaboration among scientists across the Asian region through initiatives such as the Japanese Vaccine Adjuvant Research Consortium, which in 2018 held its 11th meeting in Osaka, and the Asia Vaccine and Immunotherapeutic Workshop. "Peace comes not from politicians but from people like us, working without borders to help people who suffer from disease around the world," he says. ■

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