

Cholera vaccine delivered via a cup of rice water

Integrating basic and clinical research is key to the development of safe and effective mucosal vaccines taken orally or nasally, says **HIROSHI KIYONO** of the Institute of Medical Science, the University of Tokyo.

Vaccinations against

widespread pathogens could be ingested or inhaled as oral or nasal vaccines, respectively, thanks to breakthroughs in the development of non-invasive vaccines targeting the mucous membranes. These could help combat a range of infectious diseases such as cholera, typhoid, rotavirus, norovirus, influenza and *Streptococcus pneumoniae*.

Researchers at the International Research and Development Center for Mucosal Vaccines (IMV), the Institute of Medical Science, the University of Tokyo (IMSUT) have developed a rice-based oral vaccine called MucoRice and nanogel-based nasal vaccines for immunity against intestinal

and respiratory infections caused by *Vibrio cholerae* and *S. pneumoniae*, respectively.

Most pathogens enter our bodies through mucosal surfaces in our respiratory, digestive and reproductive tracts. Mucosal vaccines, which can be delivered via many routes including oral, nasal, ocular, rectal or sublingual administration, can induce protective immunity at local mucosal sites as well as whole-body (systemic) immunity.

"If we think of our bodies as individual homes, needle-based vaccinations are similar to having a policeman inside the house, but with unlocked doors and windows," explains Hiroshi Kiyono, director of the IMV, former dean at IMSUT and adjunct professor at the

University of California San Diego (UCSD) and Chiba University. "On the other hand, with mucosal vaccination, the policeman's inside the house, and the doors and windows are locked."

Rice-inspired breakthroughs

In 2003, Kiyono's group initiated the MucoRice Project, as part of a new mucosal immunology program at IMSUT. The project led to MucoRice-CTB, the world's first genetically modified strain of rice that carries a vaccine antigen for *V. cholerae*-induced diarrhea. With support from AMED Translational Research Network Program, phase I clinical trials with healthy human volunteers have just been completed in IMSUT Hospital, Tokyo. The project is now advancing in collaboration with Astellas Pharma Inc., based in Tokyo, Japan.

"Our project arose out of a unique blend of expertise in medical science, agriculture and engineering," says Kiyono. "We were inspired by the fact that rice can be stored at room temperature for a long time. MucoRice offers a safe, cold-chain- and needle-free delivery system; it does away with the need for syringes and expensive refrigeration — an important consideration, particularly in developing countries."

International partnerships

Researchers at the IMV have also recently developed a nanogel-based pneumococcal surface protein A (PspA) nasal vaccine, through longstanding collaborations with Kyoto University and the University of Alabama at Birmingham. Headed by Yoshikazu Yuki in Kiyono's team, the project's promising preclinical results led to the establishment of a venture company, HanaVax Inc, in 2016.

Speaking as a member of the Chiba University-UCSD Center for Mucosal Immunology, Allergy and Vaccine (cMAV), Kiyono comments: "Going forward, we want to create a Pan-Pacific research platform that reaches out to other continents including Asia, Oceania, and North and South America. Diversity is key to advancing mucosal immunology and vaccinology related fundamental and translational research. We aim to facilitate borderless interaction." ■



www.ims.u-tokyo.ac.jp/mucovac/index-e.html



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Nanogel-based nasal vaccine delivery system.



MucoRice growing in a pharmaceutical greenhouse.



Hiroshi Kiyono's group in front of the IMSUT and its hospital building.