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Successful Treatment for Coronavirus Disease 2019 in Hamster Models: A Significant Advancement for Clinical Use of VHH Antibodies Administered Nasally

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In May 2020, a research group consisting of researchers from The Kitasato Institute, Epsilon Molecular Engineering, Inc., and Kao Corporation announced that they had discovered VHH antibodies[*1] that neutralize severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

The group was then joined by researchers from the Department of Organoid Medicine, Sakaguchi Laboratory, Keio University School of Medicine, the Department of Pulmonary Medicine, Keio University School of Medicine, and the National Institute for Physiological Sciences, National Institutes of Natural Sciences. A subsequent study showed that nasal delivery[*2] of VHH antibodies inhibited replication of SARS-CoV-2 in infected lungs of hamster models. This effect was also demonstrated in an experiment using human lung–derived alveolar organoids, also called micro-organs. In addition, their analysis using cryo-electron microscopy[*3] revealed the binding pattern between SARS-CoV-2 spike proteins and VHH antibodies.

These results showed that the aforementioned VHH antibodies are a potential therapeutic agent for coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2. The results also suggested the possibility of nasal delivery of drugs for the treatment of COVID-19, which is a new administration route for COVID-19 treatment that may expand the available treatment options for COVID-19.

These findings were reported in the American scientific journal *PLOS Pathogens* (https://doi.org/10.1371/journal.ppat.1009542)[*4]

Major achievements of this research:

- Nasal delivery of the discovered VHH antibodies inhibited replication of SARS-CoV-2 in infected lungs of hamster models.
- VHH antibodies are a potential therapeutic agent for COVID-19.
- Nasal delivery as a new administration route for a COVID-19 treatment with potential to expand the available treatment options.

*1. VHH antibody: Variable domain of Heavy chain antibody in camelids. A VHH antibody is one-tenth the size of general antibodies. It has recently drawn attention because it is highly stable and can be manufactured at low cost using microorganisms.

*2. Nasal delivery: A drug administration route in which drugs are absorbed from the nasal mucosa when sprayed into the nostril. It is highly advantageous in terms of ease of administration.

*3. Whereas specimens that have been dried in a vacuum are used in conventional transmission electron microscopy, specimens that have been flash-frozen in solution are used in cryo-electron microscopy. Therefore, cryo-electron microscopy can visualize the natural morphology of specimens that include water molecules.

*4. Nasal delivery of single-domain antibody improves symptoms of SARS-CoV-2 infection in an animal model

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