Press Release

学校法人 北里研究所 THE KITASATO INSTITUTE

北里大学 KITASATO UNIVERSITY

May 7, 2020

A research group led by Prof. Kazuhiko Katayama at the Ōmura Satoshi Memorial Institute of Kitasato University has discovered SARS-Coronavirus-2 neutralizing VHH antibodies with therapeutic potential against COVID-19

Summary

A research group led by Prof. Kazuhiko Katayama and including researchers from Laboratory of Viral Infection I at the Ōmura Satoshi Memorial Institute at Kitasato University, Epsilon Molecular Engineering, Inc. and Safety Science Research Laboratory of Kao Corporation announced today that they have discovered VHH antibodies[*1] that neutralize severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (Figure1). Coronavirus disease 2019 (COVID-19) is an infectious disease caused by SARS-CoV-2. The antibodies have the potential to be developed as a new therapy and diagnostic tools for COVID-19 (Figure 2).

*1; VHH antibodies: The heavy-chain single-domain antibodies. The antibodies were originally discovered from camelids, a group that includes camels and llamas. A key feature of the antibodies is their size. They are only one-tenth the size of a conventional antibody. They are also very stable and can be produced at low cost by using microorganisms.

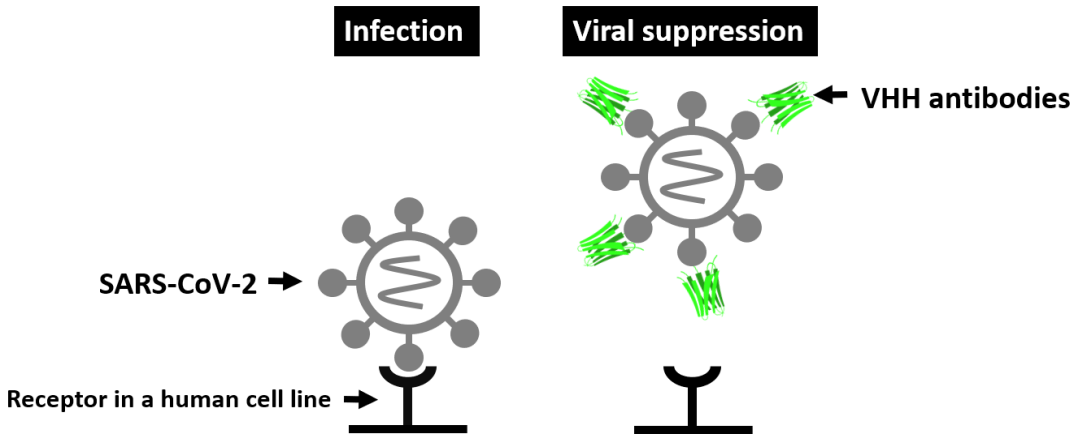

Fig. 1 Inhibition of SARS-CoV-2 binding to the receptor by VHH antibodies

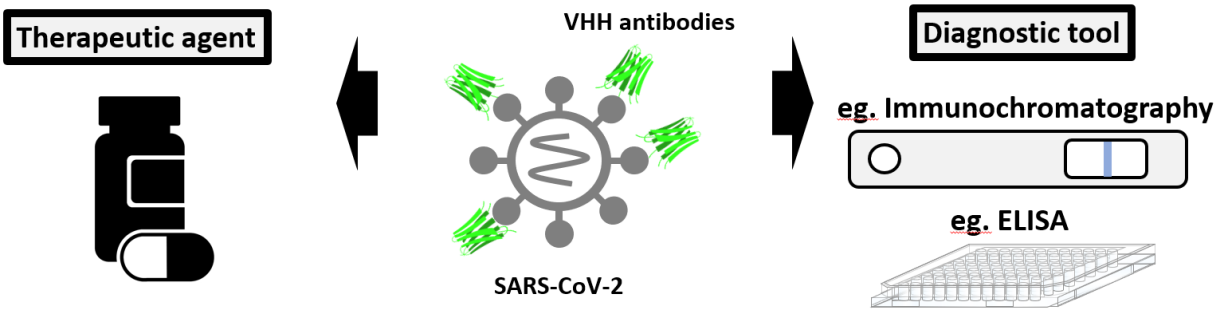

Fig.2 Applications of VHH antibodies

Background

Currently, SARS-CoV-2 is a global pandemic. More than 200,000 have died, and that number continues to increase. The pandemic has overwhelmed medical resources and disrupted national economies. Researchers are scrambling to develop COVID-19 therapies by repurposing existing, approved drugs and other antiviral agents to treat SARS-CoV-2. To stop the COVID-19 epidemic, we need effective therapeutic agents and highly accurate, sensitive and rapid diagnostic methods to prevent the transmission of SARS-CoV-2. In recent years, antibody drugs and antibody conjugates, which utilize monoclonal antibodies for treatment, have been put into practical use. Antibodies recognize and bind specific antigens. Monoclonal antibodies that bind specifically to SARS-CoV-2 are expected to be used as therapeutic and diagnostic agents. Kitasato University, Epsilon Molecular Engineering, and Kao have established collaborative relationships to discover VHH antibodies that specifically inhibit SARS-CoV-2.

Result

1. Isolation of the cDNAs for VHHs obtained by the cDNA display screening in collaboration with EME and Kao

EME has developed a powerful cDNA display library technology[*2] and a high-throughput screening method. Kao prepared a recombinant S1 protein[*3] of COVID-19 from human cells as the target molecule the cDNA display screening and obtained several VHH candidates that bound to the S1 protein.

*2; cDNA display: cDNA display is a robust and versatile in vitro protein selection tool. To make this tool, a protein is covalently linked with its coding cDNA via a specially designed, puromycin linker. By using this technology, it is possible to efficiently identify a protein that binds to a target molecule from among innumerable proteins.

*3; S1 protein: a surface protein of the coronavirus particle.

2. Preparation of VHH candidates

Kao prepared recombinant VHH candidates using an expression system with microorganism, and, after purification, determined their binding affinities to the target S1 protein with a BioLayer Interferometry[*4] (Fig. 3).

*4. BioLayer Interferometry : a label-free technology for measuring biomolecular interactions.

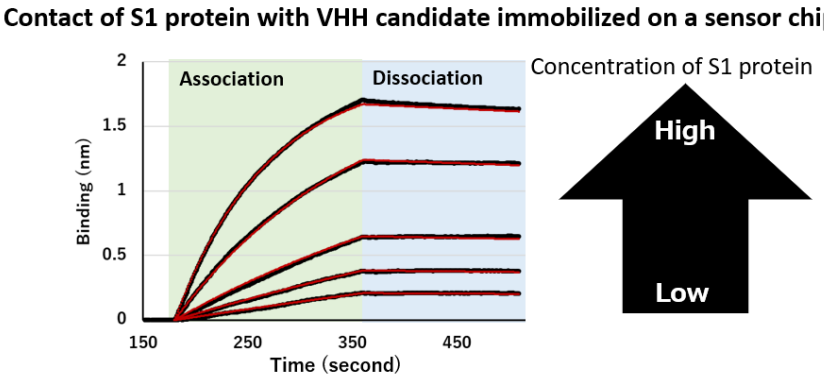

Fig.3 Binding affinities measurement with a BioLayer Interferometry

3. Evaluation of inhibitory activities of VHHs against SARS-CoV-2 infection in collaboration with Kitasato University and Kao

Prof. Kazuhiko Katayama of the Laboratory I of Viral Infection at the Ōmura Satoshi Memorial Institute of Kitasato University developed a novel assay method to evaluate the drug for its ability to inactivate SARS-CoV-2. They confirmed that VHH not only binds to SARS-CoV-2, but also suppress viral infection.

Future Direction

The research group succeeded in discovering VHH antibodies that inhibit infection by SARS-CoV-2. This research suggests the possibility of using VHH to develop therapeutic agents and diagnostic medicines. In future work, the research group will assist other groups in leveraging this discovery to defeat the coronavirus pandemic.

About Kao

Kao creates high-value-added products that enrich the lives of consumers around the world. Through its portfolio of over 20 leading brands such as Attack, Bioré, Goldwell, Jergens, John Frieda, Kanebo, Laurier, Merries and Molton Brown, Kao is part of the

everyday lives of people in Asia, Oceania, North America and Europe. Combined with its chemical division, which contributes to a wide range of industries, Kao generates about 1,500 billion yen in annual sales. Kao employs about 33,000 people worldwide and has 130 years of history in innovation. Please visit the Kao Group website for updated information.

Company Name: Kao Corporation
Address: Tokyo Japan
Representative: Michitaka Sawada, President and CEO
Founded: June 1887
Contact Information: pr@kao.co.jp
Website: https://www.kao.com/global/en/

About Epsilon Molecular Engineering Inc.

Epsilon Molecular Engineering (EME) Inc. is an evolutionary molecular engineering-based biopharmaceutical drug discovery company. EME was established in 2016 as a biotech startup incubated by Saitama University in Japan, and has proprietary technologies, unique cDNA display libraries of the heavy-chain single-domain antibodies (VHH), cyclic peptides of great diversity ($10^{13\text{-}14}$), and high-throughput screening methods using next-generation sequence, FACS and machine learning (Bioinformatics). EME is, currently, conducting several joint research projects, including COVID-19 and 17 other ongoing inhouse projects in the areas of cancer, inflammation, and Alzheimer's disease.

Company Name: Epsilon Molecular Engineering, Inc.
Address: Saitama Japan
Representative: Naoto Nemoto, CEO and CSO
Founded: August 2016
Contact Information: info@epsilon-mol.co.jp
Website: https://www.epsilon-mol.co.jp/

Contact information for inquiries

About the research:
Professor Kazuhiko Katayama,
Laboratory of Viral Infection I, Ōmura Satoshi Memorial Institute & Graduate School of Infection Control Sciences,
Kitasato University

Media Contact Information:
The Kitasato Institute
Public Relations section, Office of General Affairs
5-9-1 Shirokane, Minato-ku, Tokyo 108-8641, Japan
e-mail : kohoh@kitasato-u.ac.jp