Press Release

NIBIOHN 国立研究開発法人 医薬基盤・健康・栄養研究所 National Institutes of Biomedical Innovation, Health and Nutrition

研究成果

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National Institutes of Biomedical Innovation, Health and Nutrition

Field: Life Sciences / Medicine

Keywords: Coronavirus disease (COVID-19), Broad-spectrum antiviral antibody, SARS-CoV2-variants, ADCC activity

Host Immune-dependent Novel Anti-coronavirus Antibody

Potential Candidate as Broad-spectrum Therapeutic Agent for Coronavirus Diseases Caused by Different Coronaviruses, including Variants

The National Institutes of Biomedical Innovation, Health and Nutrition (NIBIOHN; Ibaraki-shi, Osaka; Director-general: Yoshihiro Yoneda), in partnership with Shionogi & Co., Ltd. (Chuo-ku, Osaka; President and CEO: Isao Teshirogi), has successfully identified a novel antiviral antibody for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), its variants, and closely associated coronavirus species.

The newly identified antibody binds to virus spike proteins displayed on the infected cell surface. The bound antibody supports the immune response of infected individuals to attack the infected cells via antibody-dependent cell-mediated cytotoxicity (ADCC). Unlike many other antibody drugs, the newly identified antibody's binding site (epitope) resides in a specific part of the spike structure poorly susceptible to mutation. Therefore, the antibody reacts with various virus variants, including the Omicron variant. Moreover, because the epitope structure with few mutations is common among many other related coronaviruses, the newly identified antiviral antibody is expected to show efficacy against a broad spectrum of coronaviruses, including potential variants in the future.

In current clinical use, antibody cocktails and other neutralizing antibodies target individuals with mild infection. In contrast, the newly identified antibody may be suitable to treat patients at high risk of disease of greater severity. In addition, a "broad-spectrum antiviral antibody" should be ideal for emergency use in the event of a probable new coronavirus pandemic in the future. NIBIOHN will conduct further research.

❖ **Contacts for related inquiries**

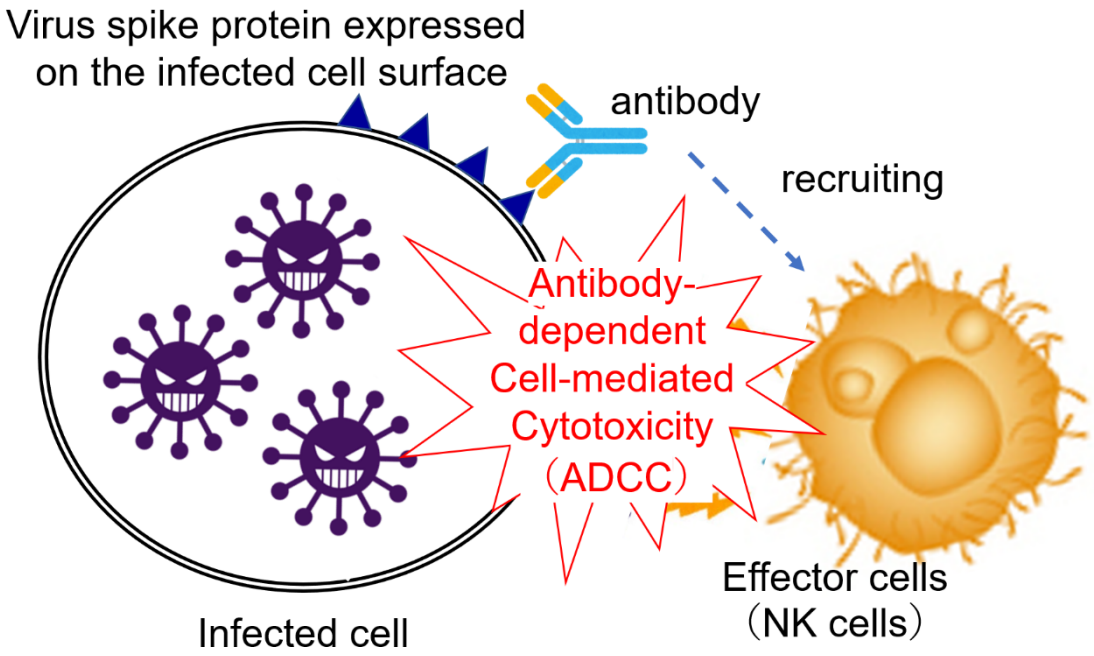
News-related matters:
Department of Strategic Planning, National Institutes of Biomedical Innovation, Health and Nutrition
(Attn: SASAKI Masahiro/ TAGUCHI Soichi/ FUJITA Ritsuko)
E-mail: kikaku[at]nibiohn.go.jp

Research flow

NIBIOHN and Shionogi & Co., Ltd. are engaged in joint research seeking to identify an effective therapeutic antibody drug that exhibits broad cross-reactivity against associated coronaviruses in addition to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

The research group has also pursued antibodies that show efficacy through a mechanism different than antibody neutralization[1].

Using NIBIOHN's "epitope-normalized antibody panel"[2,3] technology, the researchers have successfully identified a group of antibodies that prioritizes ADCC activity[4] and recognizes structures within the virus spike (S) protein expressed on infected cells.



❖ **Glossary**

[1] Neutralizing antibody

An antibody that inhibits the infectivity of a virus. Neutralizing antibodies bind to the receptor-binding domain (RBD) of vital spike protein and thereby block the virus entry into the cell.

[2] Epitope

A target site to which an antibody binds. Generally, an epitope is a small part of the antigen molecule. Individual antibodies bind to their specific epitope and exhibit different functions depending on the epitope.

[3] Epitope normalized antibody panel (ENAP; NIBIOHN patented technology)

ENAP is an antibody panel with a minimal number of members that encompasses all of the epitope groups on a target's accessible surface. This technology allows exploration and identification of antibody functions with a minimal number of antibodies.

Website: https://www.nibiohn.go.jp/cddr/research/project02.html

[4] Antibody-dependent cell-mediated cytotoxicity activity (ADCC activity)

When a virus infects a target cell, viral spike antigens appear on the cell surface upon virus replication. Antibodies that bind to these antigens on the infected cells recruit host effectors cells such as natural killer (NK) cells via Fc-portion of the antibody constant domains. As a result, the recruited effector cells become activated and destroy the infected cell; this sequence of events is the ADCC..

❖ **The National Institutes of Biomedical Innovation, Health and Nutrition**

The Institutes were established on April 1, 2015, integrating the National Institute of Biomedical Innovation (NIBIO) and the National Institute of Health and Nutrition (NIHN). The laboratories have expertise in a broad range of research from medicine to the health sciences and were designated a national research and development agency to ensure the most significant results for research and development in the public interest, as provided through means such as enhancements to the level of science and technology in Japan, leading to the robust growth of the national economy.

Website: https://www.nibiohn.go.jp/

❖ **Background of the Researchers**

NAGATA Satoshi: Ph.D., Science University of Tokyo 1992-. Assistant professor at Science University of Tokyo. 1996- Assistant Professor, University of Tokyo, 1999- Research Fellow at NIH (USA). 2007- Associate Scientist at Sanford Research (USA). Returned to Japan in Fall 2015, currently Project Leader, Antibody Design Project, Center for Drug Design Research, National Institute of Biomedical Innovation.

KAMADA Haruhiko: Ph.D., Graduate School and School of Pharmaceutical Sciences,

Osaka University Assistant professor at Faculty of Medicine, Mie University (2000). Guest Researcher at ETH (Eidgenössische Technische Hochschule) Zürich (2007). Invited Professor at Osaka University (2014). Collaborating Professor at Graduate School and Faculty of Pharmaceutical Sciences, Kyoto University (2020). Affiliated with National Institute of Biomedical Innovation since its founding in 2005, currently Project Leader, Laboratory of Biopharmaceutical Research.

❖ Contacts for related inquiries

Research-related:
NAGATA Satoshi, Project Leader, Laboratory of Antibody Design
KAMADA Haruhiko, Project Leader, Laboratory of Biopharmaceutical Research
Center for Drug Design Research, National Institute of Biomedical Innovation
National Institutes of Biomedical Innovation, Health and Nutrition
E-mail: cddr-office[at]nibiohn.go.jp

News-related:
Department of Strategic Planning, National Institutes of Biomedical Innovation, Health and Nutrition
(Attn: SASAKI Masahiro/ TAGUCHI Soichi/ FUJITA Ritsuko)
E-mail: kikaku[at]nibiohn.go.jp