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Keio University School of Medicine

**Development of a Simple, Highly Reliable Kit for Measuring COVID-19
Neutralizing Antibodies**
**— Kit allows for the understanding of patient’s immune status,
promotes evaluation of vaccine performance —**

A research team at Keio University, through joint research with JSR subsidiary Medical & Biological Laboratories Co., Ltd., has succeeded in developing a kit for measuring novel coronavirus (SARS-CoV-2) neutralizing antibodies. The group was led by Professor Tsutomu Takeuchi and Project Assistant Professor Masaru Takeshita of the Division of Rheumatology, Department of Internal Medicine together with Professor Hideyuki Saya of the Division of Gene Regulation, Institute for Advanced Medical Research. This simple kit can produce results in less than two hours, and performance tests showed a high correlation with the results of neutralization tests using an infectious virus.

In general, when the patient has an infection, the immune system produces protective factors called antibodies. These antibodies recognize and bind to specific parts of a pathogen, but their ability to defend against infection varies by antibody. Antibodies that have the ability to bind to the critical sites of a virus, inhibit its function, and inactivate the virus are called “neutralizing antibodies.” Measurement of the neutralizing antibodies to SARS-CoV-2 has required the experiments using an infectious authentic virus in a biosafety level (BSL) 3 facility that is capable of pathogen containment. In this joint research project, the team generated the receptor-binding site of the spike protein, which is important for the virus entry into the human cells, and the ACE2 protein, which is a receptor of human cells. Using these proteins, they reproduced the process of virus entry. The kit enables the measurement of neutralizing antibodies by quantifying the extent to which neutralizing antibodies in serum inhibit the process. And because the kit is virus-free, it can be used in normal BSL-1 laboratories.

It is currently being prepared for practical use as a research reagent by Medical & Biological Laboratories Co., Ltd. and is expected to greatly enhance understanding of a patient’s immune status and promote evaluation of the performance of vaccines currently being developed.

1. Research Background

COVID-19 cases continue to increase, however at the same time, many studies have been conducted around the world, and scientists are beginning to understand the mechanism of infection. It has already been clarified that the novel coronavirus (SARS-Cov-2) begins to invade the human host when the spike protein on the surface of the virus binds to the ACE2 protein on the cell membrane. (See Fig. 1) It is thought that if this binding can be blocked then the virus can be prevented from invading the host cell. Scientists around the world are currently seeking a substance with such properties as a therapeutic drug candidate.

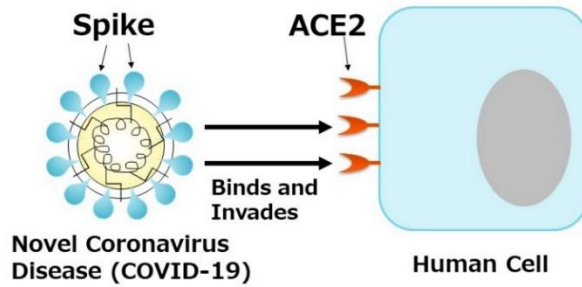


Fig. 1: How SARS-CoV-2 Invades the Body

Generally, when a patient is infected with a virus, their immune system begins working, producing protective factors called antibodies. Antibodies work by binding to various parts of the pathogens, inhibiting the activity of pathogens and eliminating them from the body. It is now known that antibodies are produced by patients even after being infected with SARS-CoV-2. To measure such antibodies, patient serum is incubated with a viral antigen to determine if it contains antibodies that can bind to the virus. However, because antibodies are made to protect against various parts of a virus, their action depends on which part of the virus the antibody can bind to.

Antibodies that bind to the spike protein of SARS-CoV-2 and inhibit the binding to ACE2 are called neutralizing antibodies, which are different from general antibodies. Neutralizing antibodies are thought to be directly involved in infection defense, and high doses are considered to be highly effective against infection. These neutralizing antibody tests are different from PCR and antigen tests that are used to detect the presence of the virus itself.

2. Research Findings

The research team first generated a receptor-binding domain (RBD), a particularly important part of the spike protein, which is used by SARS-CoV-2 to invade a host cell. By reacting RBD with the patients' serum and ACE2 in turn, they created a kit that reproduces the process of the virus invading the cells. This allowed us to quantify the extent to which neutralizing antibodies in the patients' serum inhibit the binding of RBD to ACE2. (See Fig. 2) Because this kit does not contain the infectious SARS-CoV-2 virus, it can be used in a normal laboratory.

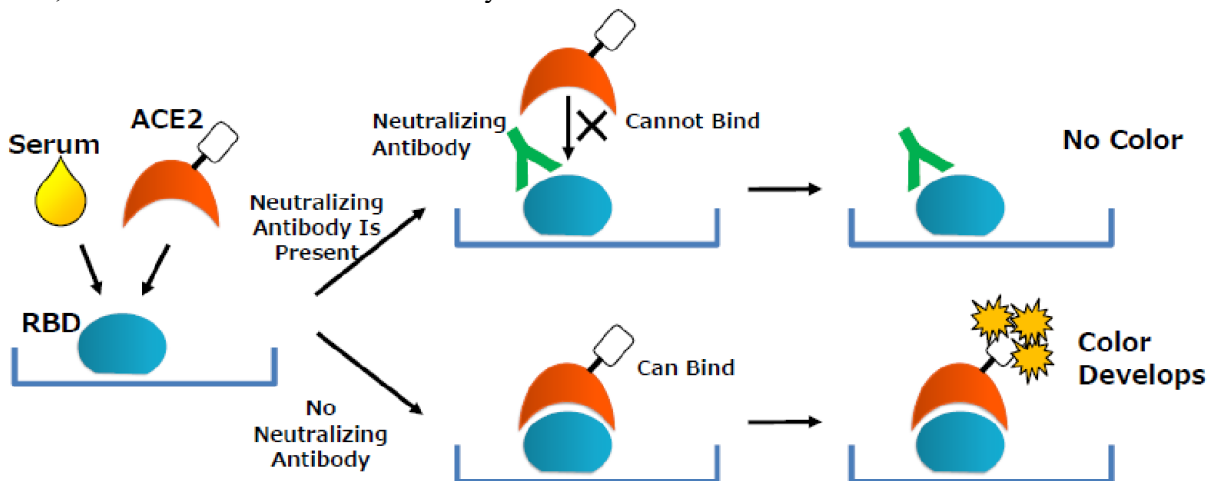


Fig. 2: Measurement Principle of the Neutralizing Antibody

The research team compared the results from the newly developed kit with the results from authentic virus neutralization tests in accordance with protocol established by the National Institute of Infectious Diseases using sera from convalescent patients. Results using the kit were well correlated to authentic virus neutralization tests, showing that the kit can properly measure neutralizing antibodies. (See Fig. 3)

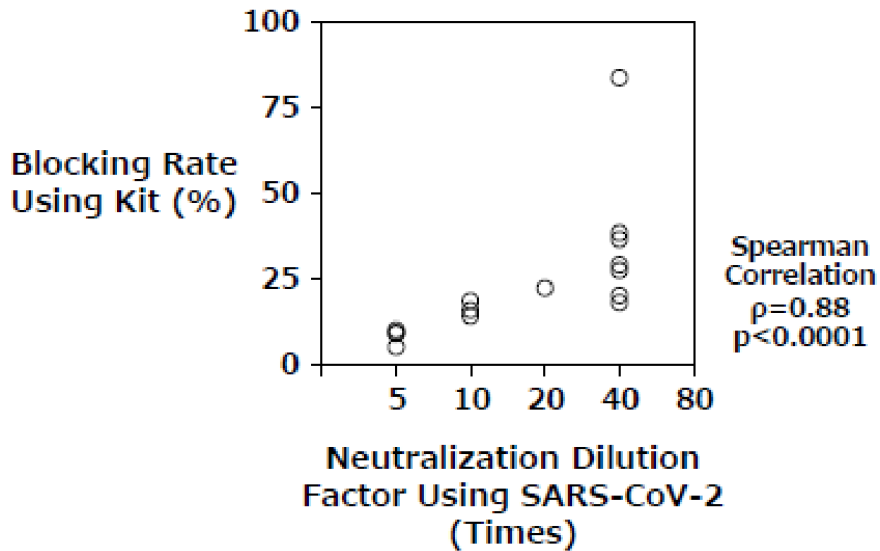


Fig. 3: Measurements Made Using the Kit

3. Research Significance and Future Development

This kit enables the measurement of neutralizing antibodies that have the ability to defend against infection. The kit is expected to be useful in the evaluation of each patient’s immunity to defend against infection as well as the effectiveness of convalescent plasma therapy being performed in the United States and China.¹ The kit will also be useful in evaluating the performance of vaccines currently being developed.

[Glossary]

¹ Convalescent plasma therapy being performed in the United States and China

A treatment method in which patients are injected with plasma containing antibodies donated by people who have recovered from COVID-19. Neutralizing antibodies found in the plasma are thought to have therapeutic effects.

*Please direct any requests or inquiries for coverage to the contact information provided below in advance.

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