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MEDIA RELEASE

CRITICAL ANTIBODY TARGET SITES IN THE SARS-COV-2 VIRUS IDENTIFIED FROM PATIENTS IN SINGAPORE WHO RECOVERED FROM COVID-19

Known as epitopes, these are the specific sites on the virus' surface to which antibodies produced during infection are able to bind and neutralise the virus

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- *Results from two scientific studies in Singapore have shown that **antibodies from patients who have recovered from COVID-19 bind to four epitopes (S14P5, S21P2, S20P2, N4P5) of SARS-CoV-2** and effectively neutralise the virus.*

- *Antibodies produced during infection attach to many parts of the virus, but **only some antibodies are capable of eliminating the virus or offering protection against infection**. This depends on the specific target of the antibody – the binding site which is also known as an epitope.*

- *All four epitopes can be used for **diagnostic testing, as therapeutic targets, and as measures of immunity after vaccination or infection**. A*STAR's Singapore Immunology Network (SIgN) will be using these epitopes in a multi-centre collaborative study for the development of the World Health Organization's (WHO) International Standard for COVID-19 antibody and Reference Panel.*

1. The National Centre for Infectious Diseases (NCID) and A*STAR's Singapore Immunology Network (SIgN) today announced research findings that antibodies found in recovered COVID-19 patients are able to limit the spread of SARS-CoV-2 in the body by counteracting ("neutralising") four linear amino acid sequences ("epitopes") **S14P5, S21P2, S20P2,** and **N4P5**.

2. Epitopes are specific parts of the virus that are recognised by our immune systems' antibodies and bind to them. Epitopes are located on the spike proteins of the "crown" surrounding the coronavirus' body. Of the four epitopes, **N4P5** achieved the highest level of specificity (100%) and sensitivity (>96%) against SARS-CoV-2.

3. The two studies were published in international scientific journals *Nature Communications*[1] and *EBioMedicine*[2] by The Lancet. NCID formulated the clinical

[1] Two linear epitopes on the SARS-CoV-2 spike protein that elicit neutralising antibodies in COVID-19 patients, *Nature Communications,* https://doi.org/10.1038/s41467-020-16638-2

[2] Linear B-cell epitopes in the spike and nucleocapsid proteins as markers of SARS-CoV-2 exposure and disease severity, *EBioMedicine* by The Lancet, https://dx.doi.org/10.2139/ssrn.3605114

studies, recruited patients, and collected samples and clinical data, while A*STAR's SIgN conceptualised the scientific studies and performed the experiments. The studies were funded by various schemes, including the COVID-19 Research Fund, which is supported by the National Research Foundation Singapore (NRF) and Ministry of Health (MOH), administered by the National Medical Research Council, as well as through A*STAR's core research grants and A*ccelerate's GAP-funding.

4. "SARS-CoV-2 is the novel causative agent of COVID-19. This seventh human coronavirus has challenged the entire scientific world with numerous unresolved questions awaiting scientists to unravel. Antibodies are key to our bodies' defence mechanisms against viruses. We are pleased to share this internationally leading work by the local research team which focuses on a powerful aspect of finding out how humans can generate specific antibodies targeted against SARS-CoV-2. The implications are manifold as explained by the studies," said Professor Leo Yee Sin, Executive Director, NCID.

5. Key findings of the two studies are as follows:

- Tests on more than 100 convalescent COVID-19 patients showed **evidence that S14P5, S21P2, S20P2 and N4P5 are recognised** in COVID-19 patients. This means that these epitopes are good detection markers to identify patients who have been exposed to SARS-CoV-2.

- COVID-19 patients' sera demonstrated the ability to neutralise more than 50 per cent of SARS-CoV-2 pseudovirus[3] entry, while SARS patients did not. This is a significant finding, implying that **COVID-19 patients' sera**, which contains antibodies, **are able to prevent SARS-CoV-2 entry into the human body by counteracting S14P5 and S21P2**.

- Using the epitopes to measure antibody responses (Immunoglobulin G, the most common antibody in our blood) can serve as useful indicators for the degree of immunopathology in COVID-19 patients, and function as highly specific and sensitive sero-immunosurveillance tools for recent or past SARS-CoV-2 infections. The **flexibility of these epitopes** to be used alone or in combination **will allow for the development of improved point-of-care-tests (POCTs)**.

6. The findings of these studies demonstrated that epitopes S14P5, S21P2, S20P2 and N4P5 can be deployed for the following purposes:

    a. *To **diagnose SARS-CoV-2 in individuals** by using blood samples (serology studies) to identify these epitopes in individuals who might have had negative results with the PCR test.*

    b. *To refine existing studies on the nature of SARS-CoV-2's behaviour after 14 days **by narrowing their focus to the antibodies that counter these epitopes.***

    c. *To provide an estimate of the community's immunity to COVID-19 infection by **surveying the degree to which the population carries antibodies that can counteract these epitopes.***

[3] Pseudovirus: refers to synthetic viruses used to inject genetic material into cells, but are unable to replicate.

d. *To **support the development of therapeutics and vaccines** – these findings can support development of monoclonal or polyclonal antibodies targeting the neutralising epitopes.*

7. These epitopes will be used by A*STAR in a multi-centre collaborative study for the development of the WHO International Standard for COVID-19 antibody and Reference Panel.

8. "The identification of these specific targets on the virus is a crucial advance in the development of better diagnostics and treatments for COVID-19. There is also potential to use these targets against similar coronaviruses to address other viral outbreaks," said Professor Lisa Ng, Senior Principal Investigator, Singapore Immunology Network (SIgN), A*STAR. "We are pleased to have leveraged our immunological experience in this research, in collaboration with renowned infectious disease and healthcare agencies in Singapore," she added.

9. Further studies will be conducted to enable the design of diagnostic tools and the development of vaccines and therapeutics.

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For media enquiries, please contact:

Hioe Zhi Hui Joanna
Senior Executive, Group Corporate Communications
National Healthcare Group
For Corporate Communications Department, Executive Director's Office
National Centre for Infectious Diseases
DID: +65 6511 5073 / HP: +65 9720 6841
Email: joanna_zh_hioe@nhg.com.sg

Mr Robin Chan
Head, Corporate Communications
Agency for Science, Technology and Research (A*STAR)
Tel: +65 6826 6281
HP: +65 9830 2610
Email: robin_chan@hq.a-star.edu.sg

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