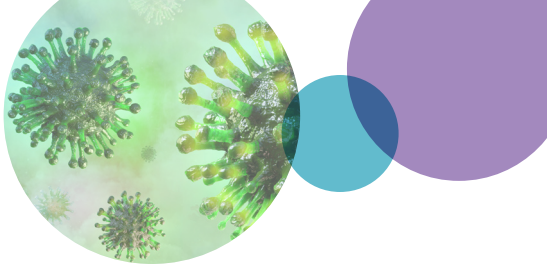
FORTÉBIO



Recent insights into COVID-19 binding epitopes

The novel coronavirus, COVID-19, has been declared a pandemic by the world health organization (WHO). As it spreads, researchers are mobilizing to understand the virus's binding mechanisms as a first step in the development of a vaccine. Below are examples of recent publications highlighting insights into these binding mechanisms.

CASE 1

Just two weeks after receiving the genome sequence of the virus from Chinese researchers, a team from the University of Texas at Austin and the National Institutes of Health made a critical breakthrough by creating the 3-D atomic scale map of the virus that binds to and infects human cells. The paper was published in the journal Science[1].

Bio-Layer Interferometry (BLI) played a vital role, allowing scientist to rapidly determine virus binding mechanisms. The Octet RED96e system was utilized in this research as well as the Anti-Human Capture (AHC) biosensors.

Two experiments, one to determine binding affinity and the other to check for cross-reactivity were quickly performed using Fc-tagged 2019-nCoV RBD-SD1 and ACE2 (binding affinity studies and SARS-CoV RBD-directed mAbs S230, m396 and 80R (cross-reactivity assessment). The Fc epitope binding anti-human capture (AHC) biosensors from ForteBio were used for the studies.

The scientists found that despite the relatively high degree of similarity between 2019-nCoV RBD and SARS-CoV RBD, no binding to the 2019-nCoV RBD could be detected for any of the three mAbs tested. Although the epitopes of these three antibodies represent a relatively small percentage of the surface area of the 2019-nCoV RBD, the lack of binding implies that SARS-directed mAbs may not be cross-reactive. Thus, therapeutic design utilizing 2019-nCoV S proteins as probes could show promise.

SPR data showed in the same article that ACE2 bound to 2019-nCoV S with an affinity of (K_D=14.7 nM). Both BLI and SPR demonstrated that new coronavirus and cell ACE2 affinity is much higher than SARS (K_D = 325.8 nM). The atomic-resolution structure of 2019-nCoV S should enable rapid development and evaluation of medical countermeasures to address the ongoing public health crisis.

CASE 2

Scientists from Fudan University and Wuhan Institute of Virology, Chinese Academy of Sciences identified a SARS antibody that binds to the coronavirus. The Octet RED96 system, with selected biosensors, was used to quickly determine the binding affinity of several SARS-CoV-specific neutralizing antibodies with 2019-nCoV. The binding epitope of CR3022 was confirmed by performing a short (10 min) cross-competition study.

The scientists expressed and purified 2019-nCoV RBD protein and predicted the structure. Next, they expressed and purified several representative SARS-CoV-specific antibodies that target RBD and possess potent neutralizing activities.

One SARS-CoV-specific antibody, CR3022, was found to bind potently with 2019-nCoV RBD as determined by ELISA and BLI. CR3022 demonstrated a fast-on (k_{on}=1.84×10^5 Ms^{-1}) and slow-off (k_{off}=1.16×10^{-3} s^{-1}) binding kinetics, resulting in a K_D=6.3 nM. To confirm the binding result, they further measured the binding kinetics using BLI. The whole binding kinetics assay of BLI took only 10 min. Researchers concluded that CR3022 has the potential for development into a therapeutic candidate[2].

Conclusion

Target binding characterization is an essential analytical step for the selection of high affinity and highly specific therapeutics regardless of the types of molecules. Kinetic analysis further describes the components of association and dissociation that comprise the overall affinity interaction.

BLI technology is helping to address real-world research questions and complete projects faster.

References

1 Daniel Wrapp, Nianshuang Wang, Kizzmekia S. Corbett, Jory A. Goldsmith, Ching-Lin Hsieh, Olubukola Abiona, Barney S. Graham, Jason S. McLellan, Cryo-EM structure of the 2019-nCoV spike in the prefusion conformation, *Science*, 2020 Feb 19, pii: eabb2507, 10.1126/science.abb2507, [Epub ahead of print].

2 Tian X, Li C, Huang A, Xia S, Lu S, Shi Z, Lu L, Jiang S, Yang Z, Wu Y, Ying T. Potent binding of 2019 novel coronavirus spike protein by a SARS coronavirus-specific human monoclonal antibody, *Emerg Microbes Infect.*, 2020 Dec;9(1):382-385, doi: 10.1080/22221751.2020.1729069.

FORTÉBIO

www.fortebio.com

FB_4018 Rev A