Structures of antibodies in complex with spike recognize 23 distinct epitopic sites (ES) on the receptor binding domain (RBD)

Jiansheng Jiang1, Christopher T. Boughter2, Javeed Ahmad1, Lisa F. Boyd1, Kannan Natarajan1, Martin Meier-Schellersheim2, David H. Margulies1

1Molecular Biology Section, and 2Computation Biology Section, Laboratory of Immune System Biology, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD 20892, USA
jiangji@niaid.nih.gov

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Thousands of structures related to SARS-CoV-2 have been rapidly determined, either by X-ray crystallography or CryoEM and deposited in the Protein Data Bank (PDB) since the COVID-19 outbreak. We systematically investigated the structures of 340 antibodies and 83 nanobodies in complex with spike protein or the receptor binding domain (RBD) of SARS-CoV-2. Most of these antibodies are from patients or vaccinee (Cov-AbDab1) and reportedly have high neutralizing potency to SARS-CoV-2 or variants of concern (VOC). Instead of looking at each structure, we present a general overview of how antibodies recognize the epitope sites on RBD. We identified 23 distinct epitopic sites (ES) on the RBD surface (Figure 1) and revealed the vital role of the complementarity-determining Region (CDR) loops in recognizing these epitopes. The 23 ES possesses the secondary structure feature and a large accessible surface area. About 75% of the total surface of RBD areas is accessible by the elicited antibodies, while the CDR3 loops occupied 50% of the contact surface. Most variants of concern escape mutations, including Omicron, occur within these 23 ES. We also present a clustering method for analyzing ES similarities and reveal many binding motifs. The characterizations of CDR loops, the usage of amino acids, and the profiling epitope-paratope interactions (EPI) not only provide rich structural information for AI training and prediction but also offer insights for enhanced vaccine, therapy, and drug design against the future virus and diseases.

Figure 1. 23 Epitope Sites are illustrated by a color map of the RBD surface area


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