Potent Neutralizing Antibody Cocktail for Prevention and Treatment of COVID-19

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Abstract

The virus responsible for the coronavirus disease 2019 (COVID-19) pandemic, SARS-CoV-2, has necessitated major adjustments in our daily lives and caused great uncertainty worldwide. One promising approach to fight the virus is the use of neutralizing antibodies that reduce the viral load to protect from disease progression and speed patient recovery. We generated 152 novel mAbs with high reactivity and specificity against SARS-CoV-2: 38 against RBD, 20 against S1, 52 against S2, and 42 against NP. Among the anti-RBD mAbs, 17 showed high neutralizing activity. We successfully developed 12 chimeric antibodies (chAbs) using genetic engineering, six of which exhibit highly potent neutralization activities with $PRNT_{50}$ values between 6.71 and 35.51 ng/ml. We then used site-directed mutagenesis to replace ACE2-binding residues within the RBD and found that the key residues, Y453, F486, and N501, were respectively recognized by neutralizing chAbs, RBD-chAb-28, -45/-51, and -25. Molecular docking studies predicted that these antibodies target three different sites in the receptor binding motif (RBM) within the RBD of SARS-CoV-2 S protein. We developed several chAbs with high neutralizing potency. These novel therapeutic antibodies have high potential for the prevention and treatment of COVID-19. A cocktail of therapeutic chAbs that target three separate epitopes on the RBM of SARS-CoV-2 spike protein may increase therapeutic efficacy and decrease the potential for virus escape mutants, serving to benefit a wide range of COVID-19 patients.