عنوان مقاله:

Enhancement of SARS-CoV-۲ Receptor Binding Domain -CR۳۰۲۲ Human Antibody Binding Affinity via In silico Engineering Approach

محل انتشار:

مجله میکروبیولوژی پزشکی و بیماریهای عفونی, دوره 9, شماره 3 (سال: 1400)

تعداد صفحات اصل مقاله: 14

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خلاصه مقاله:

Introduction: The angiotensin-converting enzyme ۲ (ACE۲) is the effective primary receptor for SARS-CoV-۲. The interaction between ACE۲ and the spike protein of the virus is the crucial step for virus entry into the target cells. ACE۲ receptor can be blocked by neutralizing antibodies (nAbs) such as CR۳۰۲۲ which targets the virus receptor-binding site. Enhancing the binding affinity between CR۳۰۲۲ and ACE۲ would lead to a more efficient blockade of virus entry. Methods: In this regard, the amino acids with central roles in the binding affinity of CR۳۰۲۲ antibody to spike protein were substituted. The best mutations to increase the affinity of antibodies were also selected based on protein-protein docking and molecular dynamics simulations. Result: The variants ۴۵ (H:۳۰I/G, H:۵۵D/F, H: ۱۰۳S/Y, L:۵۹T/F, L:۹۸Y/A), ۶۰(H:۳۱T/D, H:۵۵D/E, H:۱۰۳S/Y, L:۵۹T/D, L:۹۸Y/F), ۶۷(H:۳۰I/G, H:۵۵D/F, H:۱۰۳S/Y, L:۵۶ W/L, L:۵۹T/Y, L:۶۱E/G), ۶۹(H: ۳۱T/D, H:۵۵D/F, H:۱۰۳S/Y, L:۵۹T/F, L:۹۸Y/A), and ۷۱(H: ۳۱T/D, H:۵۵D/F, H:۱۰۳S/Y) with respective binding affinities of -۱۶۷.۳, -۱۶۷.۵, -۱۶۱.۶, -۱۷۳.۰, and -۱۶۹.۸ Kcal/mol had higher binding affinities against the RBD of the SARS-CoV۲ spike protein compared to the wild-type Ab. Conclusion: The engineered antibodies with higher binding affinities against the target protein can improve specificity and sensitivity. Thus, a more successful blockade of the ACE۲ is achieved, resulting in a better therapeutic outcome. In silico studies can pave the way for designing these engineered molecules avoiding the economic and ethical challenges.

کلمات کلیدی:

Coronavirus, SARS-COV-۲, Antibody, Bioinformatics, Affinity maturation