Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

transform 4-androstenedione (AD) to1,4-androstadiene-3,17-dione (ADD). in this study, we investigated how the active site of KstD211 affected substrate specificity by protein modeling and site-directed mutagenesis. We found that Tyr116 played an important role in recognizing steroid substrates. The mutation of Tyr116 to Ile enhanced the conversion rate of 4AD from 54% to 87%, compared with KstD211. in a pilot-scale reaction, the productivity of ADD by converting 4-AD reached 3.32 g/L/h. Furthermore, our data also revealed that different F116 mutants exhibited distinct specificity for a variety of steroidal substrates. Therefore, our work has provided the potential application of to KstD211 to dehydrogenize steroids in pharmaceutical industry.

98-Pos

Predicting the Ability of SARS-CoV-2 to Utilize the ACE2 Receptor for Cell Entry in North American Rodents

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SARS-CoV-2, the virus responsible for the ongoing COVID-19 pandemic, was first discovered in a human population in 2019, likely the result of cross-species transmission from bats to humans. While it is widely accepted that SARS-CoV-2 originated from an animal host, little is currently known about the role animal hosts play in the transmission of the disease. Due to the serious nature of the pandemic, there is an urgent need to identify potential animal host species of the virus. in order to gain entry into host cells, the receptor binding domain(RBD) on the spike protein of the virus must be able to dock to angiotensin converting enzyme 2(ACE2), a membrane protein found in the cells of many organisms. Therefore, a calculation of the binding affinity of the RBD with the ACE2receptor of an organism can allow us to predict the susceptibility of an organism toSARS-CoV-2. in this study, we developed a computational pipeline to predict the binding affinity of the RBD with the ACE2receptor of animal species, with a focus on North American rodents. Sequences of the ACE2protein for more than100North American rodent species were obtained, and homology modeling was used to generate structures of the ACE2receptor for each sequence, using available humanACE2structures as a template. Protein-protein docking tools were then used to dock the RBD against the snapshots, generated using molecular dynamics simulations, of each ACE2homology model. The docking score for eachRBD-ACE2docked complex was used to compile a short list of North American rodents for empirical testing. We expect our data to be vital in the identification of potentially susceptible animal species, in understanding the cross-species transmission of CoVs, animal surveillance, and the development of animal therapies and vaccines.

99-Pos

Rationally Designed Chimeric Antibodies for COVID-19 and Future Coronavirus Variants

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Most of the antibody treatments targeting the ACE2 receptor binding motif (RBM) on SARS-COV-2 spike glycoprotein are vulnerable to virus evasion through the occurrence of mutations in RBM. To circumvent this issue, a chimeric antibody composed of an IgG1 framework with ''ACE2-units'' grafted on complementarity-determining regions (CDRs) was developed to act as a decoy for virus binding and neutralization. ACE2-units were composed of spike-interacting regions of ACE2 that are then connected by Rosetta-designed linker peptides. Such a chimeric construct is designed to neutralize SARS-COV-2 by binding spike RBM and is expected to be tolerant to mutations, as long as ACE2 recognition is required for infection. The ACE2-units' binding free energy to the spike RBM were assessed by molecular dynamics simulation. in total, the free energy of 8 ACE2 units, with their size ranging from 69 to 259 amino acids, and whole ACE2 was assessed. The computation result surprisingly showed that some ACE2-units had similar or even stronger RBM binding than the whole ACE2. For example, two ACE2-units consisting of 17% and 43% the size of ACE2 maintained 78% and 123% binding free energy, respectively. A similar strategy using the whole ACE2 fused with the Fc region of IgG1 was proposed recently that claimed mutation resistance [1]. Our chimeric antibody offers the additional benefit of ACE2-units that not only have similar or even higher binding affinity, but can also be grafted on multiple CDRs due to their small size to increase the avidity. Additionally, the whole IgG1 construct should have a longer lifetime than the Fc-fusion protein.

1. Lei, Changhai, et al. ''Neutralization of SARS-CoV-2 spike pseudotyped virus by recombinant ACE2-Ig.'' *Nature communications* 11.1 (2020): 1-5.

100-Pos

Combining Computational Modeling with Library Screening to Adapt SARS-CoV-Neutralizing Antibody 80R to SARS-CoV-2

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The worldwide COVID-19 pandemic has had enormous consequences in terms of lives lost, economic impact, and in affecting the quality of life in nearly every country around the globe. It has revealed the urgent need for generating therapeutics to mitigate the effects of novel viruses on a shorter timescale than that required to generate a vaccine. As one potential avenue to address this need, we report a new method for adapting antibodies to related virus types and subtypes. by combining computational modeling with targeted large-scale library generation and high-throughput screening, we successfully mutated theSARS-CoV-neutralizing antibody80R to bind to the homologous epitope on the spike protein (S) of SARS-CoV-2. The designed library generated 77 unique sequences that bound strongly to S of SARS-CoV-2, with an average of 6.5 mutations per sequence. Virus neutralization was demonstrated by plaque reduction using a VSV-SARS-CoV-2 pseudovirus. The combined approach mitigates the limitations of each when applied separately and provides a very powerful synergism able to meet the challenging demands of repurposing antibodies to related virus types and subtypes. We will report on the efficacy of this method, the timescale required, and suggest avenues for further improvements.

101-Pos

Automated Computational Technique to Improve the Quality of SARS-CoV-2 Proteins

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The COVID-19 pandemic caused by SARS-CoV-2 is a global health emergency. in order to develop an effective drug or a preventative vaccine, it is critical for research and development teams to have access to high-resolution and accurate viral protein structures. Current COVID-19 proteins available on the Protein Data Bank contain some moderate- to low-resolution structures. in order to improve the quality of the structures, we used a torsional optimization protocol that combines Protein Data Bank-based torsional optimization with real-space refinement against the electron density derived from crystallography or cryo-electron microscopy. Our automated method converts moderate- to low-resolution protein structures at initial (e.g. backbone trace only) or late stages of refinement to structures with increased numbers of hydrogen bonds, improved crystallographic R-factors, and superior backbone geometry. Application of this automated method on COVID-19 proteins has produced high-quality structures that can further aid the counter-pandemic efforts.

102-Pos

Characterizing Binding Kinetics and Thermodynamics of Computer-Designed Nanobodies Targeting SARS-CoV-2 RBD

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The pandemics caused by SARS-CoV-2 has emerged on a global scale, and no vaccines or antivirals are available to prevent or treat COVID-19. We computer-designed three Nanobodies (Nb) (Nb-72, Nb-Hum, Nb-Ab) targeting neutralizing epitopes of the SARS-CoV-2 receptor-binding domain (RBD) to neutralize viral particles. The design was based on a previously reported SARS-CoV-1 neutralizing Nb, which prevented the neutralization of SARS-CoV-2, mainly due to its substantially higher dissociation constant. The crystallographic structure of Nb-SARS-CoV-1 was used as a template to model the structure of the Nb-SARS-CoV-2 complex. These systems were used as control of successful and unsuccessful binding partners. Given the firmly established importance of high affinity and rapid binding for therapeutic settings, the designed complexes must possess favorable binding kinetics and thermodynamics. To gain insight into molecular recognition, atomistic simulations in the aqueous environment were employed to reconstruct the free energy surface of the Nbs-RBD systems by 20 ns metadynamics using the Gromacs package interfaced with the Plumed plug-in, and the association rates were obtained through the Simulation of Diffusional Association (SDA) method, based in