Computational Analysis of SARS-CoV-2 Variants' Binding With Vertebrate ACE2

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This study explored the effect of changes in the spike protein across SARS-CoV-2 variants (wild-type, Alpha, Beta, Gamma, and Omicron) on the initial binding interactions with American mink (Neovison vison), brown rat (Rattus norvegicus), and domestic cat (Felis catus) ACE2 receptors. For cell infection to occur, the viral spike protein binds to the cellular angiotensin-converting enzyme II (ACE2) receptor-binding domain (RBD). This study used the HADDOCK 2.4, PRODIGY, and PDBePISA webservers to calculate the protein docking, Gibbs free energy, and interfacial contacts, respectively. Tertiary structural alignment of the spike protein RBDs suggests that the Beta variant most closely resembles the wild-type while there was a large difference between the wild-type and Omicron variants. An amino acid sequence percent-identity-matrix of the variant RBDs suggests that the Alpha variant is most similar to the wild-type at 97.30% while there are large differences between the wild-type and Omicron variant (91.30% similar). These differences in sequence similarity are also reflected in the binding affinity results. In all cases, receptors' binding with the Alpha variant had a more favorable Gibbs free energy than binding with wild-type, likely due to the additional interfacial contacts involved. Neovison vison had the most favorable binding interaction (Gibbs free energy) for each variant compared to other mammals studied, suggesting it is more susceptible to these variants than other animals studied. This study's binding favorability results match up with in vivo testing of animals, indicating that this study's methods are a resource-effective way to predict susceptibility.

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