De novo design of anti-variant COVID-19 Vaccine

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Abstract

Recent studies have demonstrated the effectiveness of hybrid SARS-CoV-2 vaccines that combine the wild-type nucleocapsid (N) and Spike (S) proteins. Based on this strategy, we have further enhanced the idea by incorporating the spike protein with mutations from delta and post-delta omicron variants of concern (VOC). Both delta and omicron mark the transition of vaccine driven viral immunity and resistance, so their mutations are highly crucial for future viral variants also. Additionally, we have included certain nucleocapsid peptides, which have clinically shown superior T-cell immunity being similar to homologous sequences from other Human Coronaviruses (HuCoV). We have also carefully selected an envelope peptide that elicits strong T-cell immune response. These peptides are clustered in the hybrid spike's cytoplasmic region with non-immunogenic helical linkers, enabling systematic arrangement. Through AlphaFold analysis, we have determined that the resulting domain folds more efficiently when the construct lacks the transmembrane domain. The AlphaFold designs were validated using the molecular dynamics (MD) simulations and assessed various parameters of root mean square deviation (RMSD), root mean square fluctuation (RMSF), radius of gyration (Rg) and weighed the structural stability and conformational dynamics. Interestingly, the dynamics revealed more insights into the conformational changes in the structure overtime, more flexibility in the C-terminus region, and overall compactness of the structures in a time-based gradient indicating less fluctuation and transition in terms of structure mobility and maintained a relatively compact fold conformation throughout the simulation. Our proposed approach may provide option for incorporating diverse anti-viral T-cell peptides, similar to HuCoV, into linker regions, offering a versatile solution to address outbreaks and challenges posed by various viruses, thereby enabling effective management through multiepitope strategies in this era of innovative vaccines.

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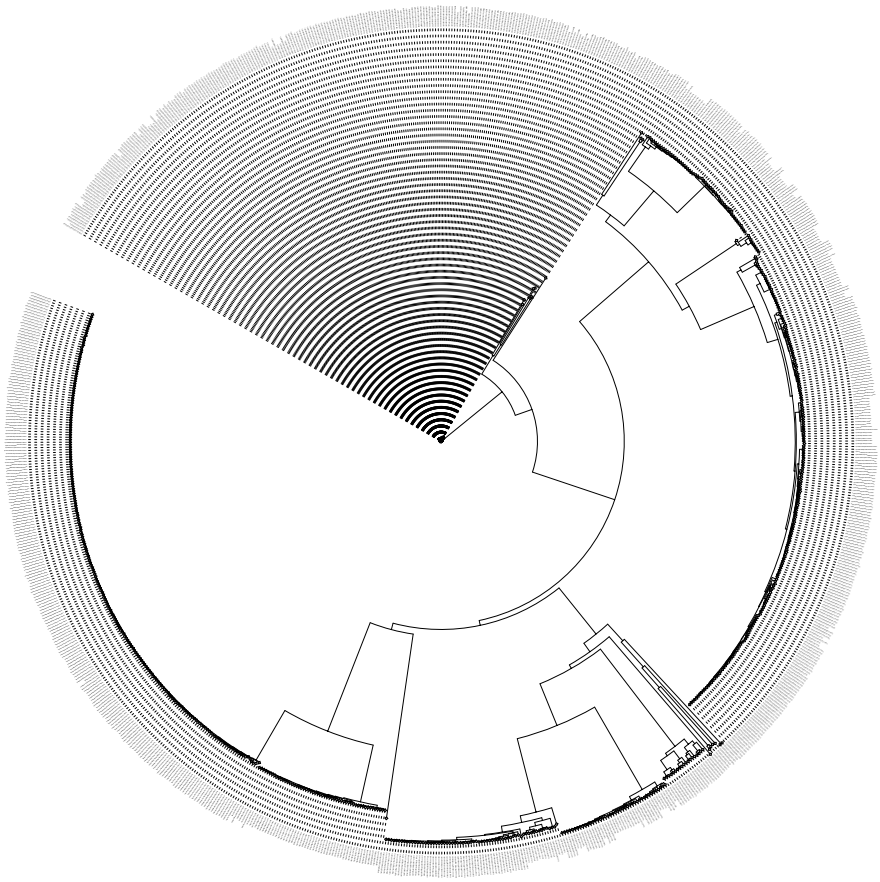

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Supplemental Table 1.xlsx available at https://authorea.com/users/630911/articles/650502-de-novo-design-of-anti-variant-covid-19-vaccine