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## “A Bioinformatics Analysis Exploring the Impact of Alpha Variant B.1.1.7 Spike CD8+ T cell Epitope Diversity”

**Introduction:** The activation of CD8+ T cells plays a vital role in strengthening the immune defense against intracellular pathogens like SARS-CoV-2. A T cell epitope is a specific target recognized by CD8+ T cells. It consists of two components: the viral protein fragment and the major histocompatibility complex (MHC). The MHC class I genes exhibit high polymorphism and can be used to analyze the intensity of COVID-19 variants. The mutations present in the SARS-CoV-2 variants of concern (VOC) have the potential to impact the binding affinity and immunogenicity of T cell epitopes. T cell epitopes are essential in ensuring long-term immunity. Therefore, distinguishing SARS-CoV-2 epitopes that are gained, lost, or reduced in immunogenicity between variants of concern can serve as a predictive indicator of COVID disease severity and progression.

**Methods:** This study used Ensembl's SARS-CoV-2 genome browser to compare the genomic sequences of different SARS-CoV-2 variants with the original Wuhan strain (INSDC accession CGA\_009858895.3). This comparison resulted in the generation of variant-specific cDNA sequences for transcripts, focusing on spike, membrane, and nucleocapsid proteins. To convert these cDNA sequences into amino acid (protein) sequences, the Expasy translate tool was used. The prediction of MHC-I epitope binding to the gene products specific to each variant was performed using the Immune Epitope Database and Analysis Resource, specifically the TepiTool with the default prediction recommended by IEDB. For the analysis of MHC-I epitope binding, a set of 27 frequently observed A and B alleles were utilized.

**Results:** B.1.1.7 VOC was sequenced on July 1, 2021. There was a very large amount of B.1.1.7 (alpha) spike CD8+ T cell epitopes that experienced a decrease in immunogenicity, with 453/1095 epitopes experiencing a reduction in immunogenicity. Conversely, 27 B.1.1.7 (alpha) spike CD8+ T cell epitopes experienced an increase in immunogenicity. Additionally, the variant suffered a loss of 37 epitopes while gaining 2 new epitopes. Over time, B.1.1.7 underwent alterations in nucleotide variations, specifically affecting 10 spike nucleotides, 0 membrane nucleotides, and approximately 4 nucleotides. Comparatively, the Omicron variant of concern demonstrated a significantly higher number of altered spike nucleotides when compared to both the alpha and delta variants.

**Conclusion:** These findings indicate that the spike protein of the B.1.1.7 (alpha) variant may display heightened immune resistance, compared to the precedent B.1 alpha strain. This may be a result of the diminished presence of CD8+ T cell epitopes within its viral proteins. Furthermore, the two gained epitopes in this variant hold promise for informing the development of vaccines that can effectively enhance CD8+ T cell immunity against SARS-CoV-2.