A Bioinformatics Analysis Exploring the Impact of SARS-CoV- 2 Alpha Variant B.1.1.7 on CD8+ T cell Epitope Diversity

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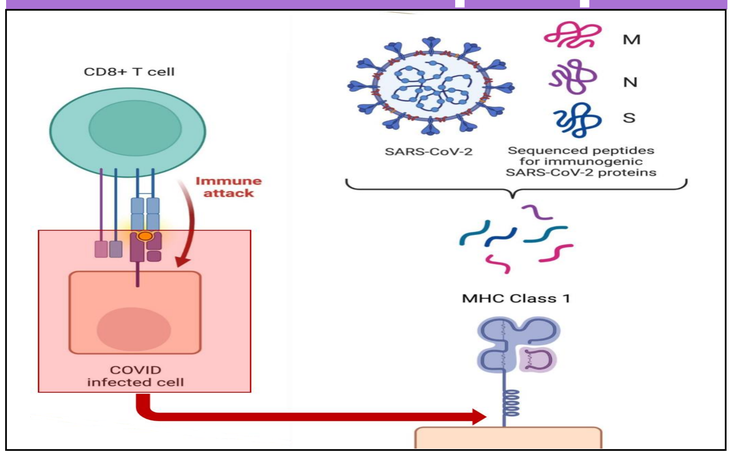
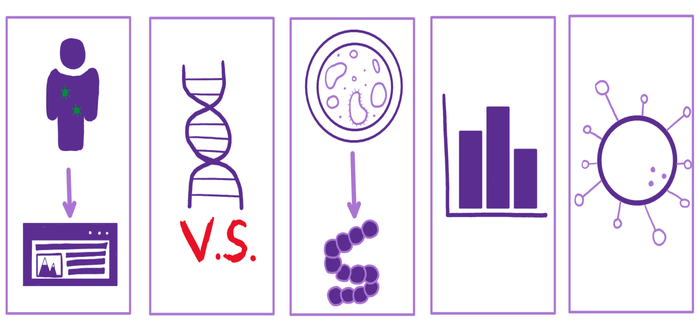
Introduction

- CD8+ T cell activation is crucial component of the immune defense against intracellular pathogens, such as SARS-CoV-2.
- T cell epitopes, which are specific targets recognized by CD8+ T cells, are essential in ensuring long-term immunity. It consists of two components: the viral protein fragment and the major histocompatibility complex (MHC).
- The MHC class I genes exhibit high polymorphism.
- 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.
- 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.

What is an Epitope?



Methods



Generate FASTA for each variant.

Blast variants against original Wuhan Strain with Ensembl-Covid 19

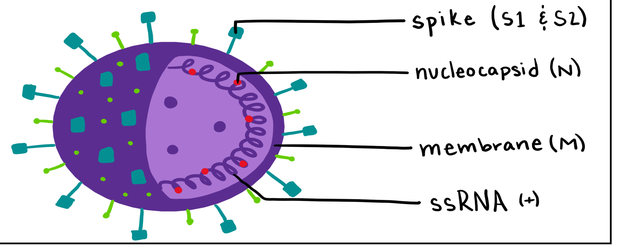
Generate variant specific amino acid sequence for S, N, and M using EXPASY

IEDB TepiTools Analysis (concise results)

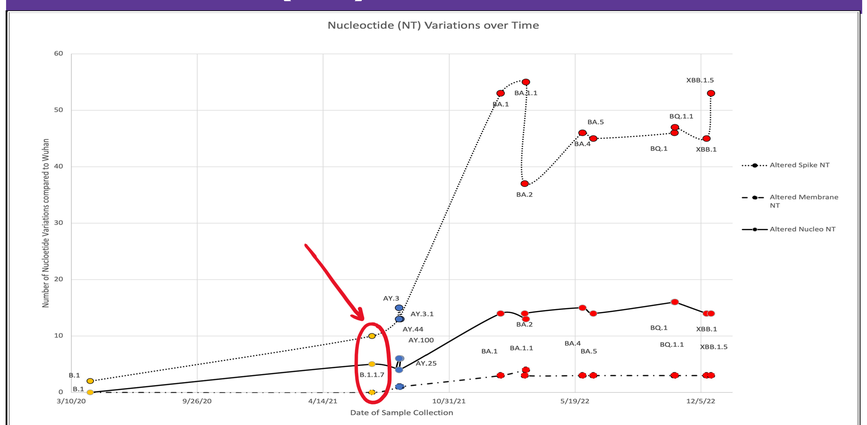
Covid Epitope cross comparison analysis

SARS-CoV-2 Pathogen

- SARS-CoV-2 pathogen is a virus that causes the disease known as COVID-19.
- The virus is mostly spread from person to person via droplets from coughing, sneezing or talking.
- Highlighted symptoms include fever, cough, loss of taste/smell, and tiredness



Nucleotide (NT) Variations Over Time



This graph illustrates the number of NT variations compared to the original Wuhan variant over time. The yellow dots symbolize the Alpha variant, while the blue and red dots signify the Delta and Omicron variants. Over time, the number of nucleotide variations has increased. After only 13 months, there were NT alterations in spike and nucleocapsid between the B.1 and the B.1.1.7 variants.

Wuhan Epitope Data

S Epitopes	Alpha		Delta					Omicron								
Variant of Interest	B.1	B.1.1.7	AY.100	AY.25	AY.3	AY.3.1	AY.44	BA.1	BA.1.1	BA.2	BA.4	BA.5	BQ.1	BQ.1.1	XBB.1	XBB.1.5
Comparison Variant	Wuhan (NCBI: NC_045512.2)															
↓ Immunogenicity	1	453	24	24	5	81	6	101	222	224	122	168	702	717	720	609
Lost	2	37	40	40	42	38	41	93	96	103	113	114	133	138	111	131
↑ Immunogenicity	1	27	3	3	4	11	4	72	80	16	18	16	20	32	37	39
Gained	2	2	30	30	39	30	39	91	92	79	93	94	135	90	111	103
Total epitopes	1081	1095	1084	1084	1077	1084	1077	1084	1088	1102	1098	1099	1110	1115	1109	1109

This table illustrates the comparison of spike epitopes between the variants of interest and the Wuhan variant. We analyzed the epitope diversity of the 27 most common HLA-A and HLA-B alleles in North America. We predicted that Alpha B.1.1.7 variant had 453 epitopes (41.1%) that experienced decrease in immunogenicity compared to Alpha B.1 variant that had 1 epitope affected. B.1.1.7 experienced a loss of 18.5x more epitopes than B.1.

Results

- 41.4% of B.1.1.7 (alpha) spike CD8+ T cell epitopes experienced a decrease in immunogenicity, with 453/1095 epitopes affected.
- 27 B.1.1.7 (alpha) spike CD8+ T cell epitopes experienced an increase in immunogenicity.
- 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.
- The Omicron VOC 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 evasion, compared to the precedent B.1 alpha strain.
- This may be a result of the changes of CD8+ T cell epitopes experienced by viral mutation.
- Furthermore, the two gained epitopes in this variant offer significant potential for enhanced monitoring of viral evolution and immune response. This insight can effectively guide personalized treatments and increase our preparedness for future pandemics.