

Immune response to SARS-CoV-2 variants investigated

August 16 2021

A
T-CoV Delta Q478K.V1 (B.1.617.2+AY.1+AY.2) CD8 epitopes CD4 epitopes

Summary
This strain contains 18 protein-level mutations:

- 5 mutations in Spike protein: L452R, T478K, D614G, P681R, D950N
- 3 mutations in N protein: D63G, R203M, G219C
- 1 mutation in M protein: I82T
- 1 mutation in NS3 protein: S26L
- 2 mutations in NS7a protein: V82A, T120I
- 1 mutation in NS9b protein: T60A
- 1 mutation in NS9c protein: G50W
- 2 mutations in NSP3 protein: A488S, P1469S
- 1 mutation in NSP12 protein: P323L
- 1 mutation in NSP14 protein: 413-415 GCD->LNY

We identified all possible linear viral peptides affected by these mutations. Whenever it was possible, we matched the reference peptide with the mutated one. For example, D->L mutation transformed S**D**NGPQNGR to S**L**NGPQNGR. Cases when it was not meaningful included deletions and insertions at the flanks of the peptide, e.g., HV deletion in NVT**Y**FW**H**WV peptide.

Then, we predicted binding affinities between the selected peptides and frequent HLA alleles. Predictions were made with NetMHCpan-4.1 and NetMHCIIpan-4.0. The binding affinities were classified into three groups:

- Tight binding** (IC_{50} affinity < 50 nM)
- Moderate binding** (50 nM < IC_{50} affinity < 500 nM)
- Weaker binding** (IC_{50} affinity > 500 nM)

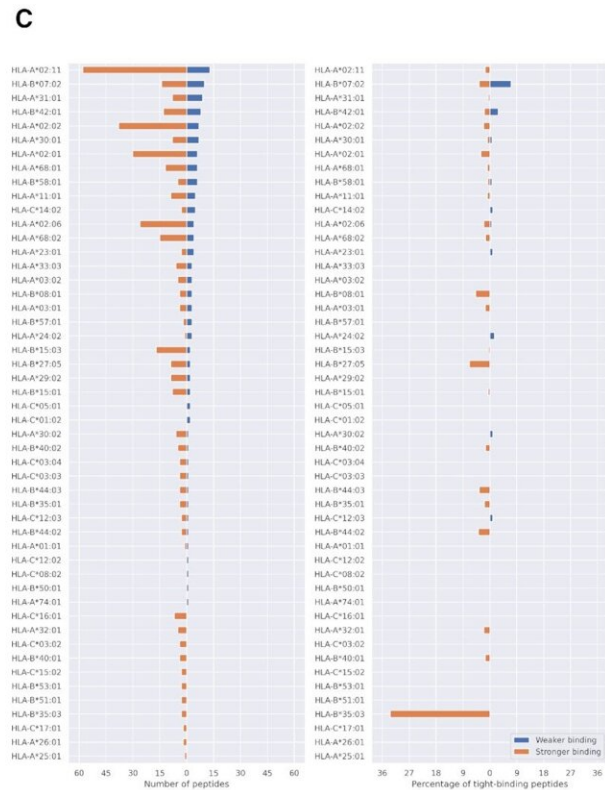
Here we report HLA-peptide interactions whose affinity was altered by at least two folds. Note that mutations with empty set of altered interactions are not showed.

B
T-CoV Delta Q478K.V1 (B.1.617.2+AY.1+AY.2) CD8 epitopes CD4 epitopes

D614G

Reference: PCSFGGVSIVTPGNTNINQWAVLYQDFVNCETVPVAIHAGDLTPFWVYSTG
 Mutated: PCSFGGVSIVTPGNTNINQWAVLYQDFVNCETVPVAIHAGDLTPFWVYSTG

Allele	Reference peptide	Mutated peptide	Reference affinity (IC_{50} , nM)	Mutated affinity (IC_{50} , nM)
HLA-C*08:01	YQDVNCTEV	YQDVNCTEV	82	8597
HLA-C*08:02	YQDVNCTEV	YQDVNCTEV	89	8066
HLA-A*02:11	DVNCETVPV	GVNCTEVPV	2140	72
HLA-A*02:02	DVNCETVPV	GVNCTEVPV	4099	213
HLA-A*08:02	DVNCETVPV	GVNCTEVPV	36	659
HLA-A*02:06	DVNCETVPV	GVNCTEVPV	3807	208
HLA-A*08:02	QWAVLYQDV	QWAVLYQDV	183	13
HLA-A*08:02	NQWAVLYQDV	NQWAVLYQDV	650	82
HLA-A*02:06	QWAVLYQDV	QWAVLYQDV	1312	148



The web interface of T-CoV. (A) Top part of the page contains SARS-CoV-2 variant name, list of protein-level mutations, short introduction and two navigation panels: through viral proteins and different HLA alleles. (B) A single mutation analysis includes a fragment of pairwise sequence alignment (the reference variant and the variant of consideration) and a table with HLA-peptide interactions significantly affected by the analyzed mutation. (C) Allele-specific differences between numbers of T-cell epitopes from the reference virus and the variant of consideration (plot was constructed for the Delta variant). Left panel

stands for the absolute number of peptides, while the right panel represents percentage of tight HLA-peptide interactions (absolute number relative to the number of tight-binders in the reference immunopeptidome). Credit: DOI: 10.1093/nar/gkab701

HSE University researchers assessed the effectiveness of the T-cell immune response to 11 variants of SARS-CoV-2. The researchers used their results to develop the T-cell COVID-19 Atlas portal (T-CoV). The findings have been published in *Nucleic Acids Research*.

The continuing emergence of new SARS-CoV-2 mutations allows the [virus](#) to spread more effectively and evade antibodies. However, it is unclear whether new strains are capable of evading T-cell immunity—one of the body's main lines of defense against COVID-19.

The development of a T-cell [immune response](#) is largely governed by [genetic factors](#), including variations in the genes of the major histocompatibility complex (also known as HLA). Each HLA gene variant has a corresponding molecule that identifies a specific set of peptides (protein) of a virus. There are a huge number of such gene variations, and each person has a unique set of them.

The effectiveness of the development of T-cell immunity to COVID-19 strains varies from person to person. Depending on the set of HLA molecules, some people's immune systems will identify and destroy a mutated virus with the same efficacy as they would the base form of the virus. In others, the response is less effective.

The research was carried out by a group of scientists from HSE University's Faculty of Biology and Biotechnology and the Institute of Bioorganic Chemistry of the Russian Academy of Sciences, including

Stepan Nersisyan, Anton Zhiyanov, Maxim Shkurnikov, and Alexander Tonevitsky. They assessed the genetic features of the development of T-cell immunity to 11 main SARS-CoV-2 variants by analyzing the most common HLA gene variants. The researchers used their results to develop the T-cell COVID-19 Atlas portal (T-CoV, <https://t-cov.hse.ru>).

The researchers used bioinformatics to assess the binding affinities of hundreds of HLA molecule variations and tens of thousands of virus peptides of the main SARS-CoV-2 variants (Alpha, Beta, Gamma, Delta, Epsilon, Zeta, Eta, Theta, Iota, Kappa and Lambda). The team identified the HLA alleles that displayed the most significantly changed set of identified virus peptides. According to the scientists, mutated variants may pose a higher risk to people with these alleles.

"T-cell immunity works such that the variation in HLA molecules and T-cell receptors prevents viruses from evading the immune response. Our research did not find a single HLA genotype [variant](#) that is negatively affected by viral mutations in a significant way. This means that even in conditions of reduced antibody effectiveness, T-cell immunity continues to operate effectively," said Aleksander Tonevitsky, Dean of the Faculty of Biology and Biotechnology at HSE University.

More information: Stepan Nersisyan et al, T-CoV: a comprehensive portal of HLA-peptide interactions affected by SARS-CoV-2 mutations, *Nucleic Acids Research* (2021). [DOI: 10.1093/nar/gkab701](https://doi.org/10.1093/nar/gkab701)

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