

CD8+ T cell responses and SARS-CoV-2 variants

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Background:

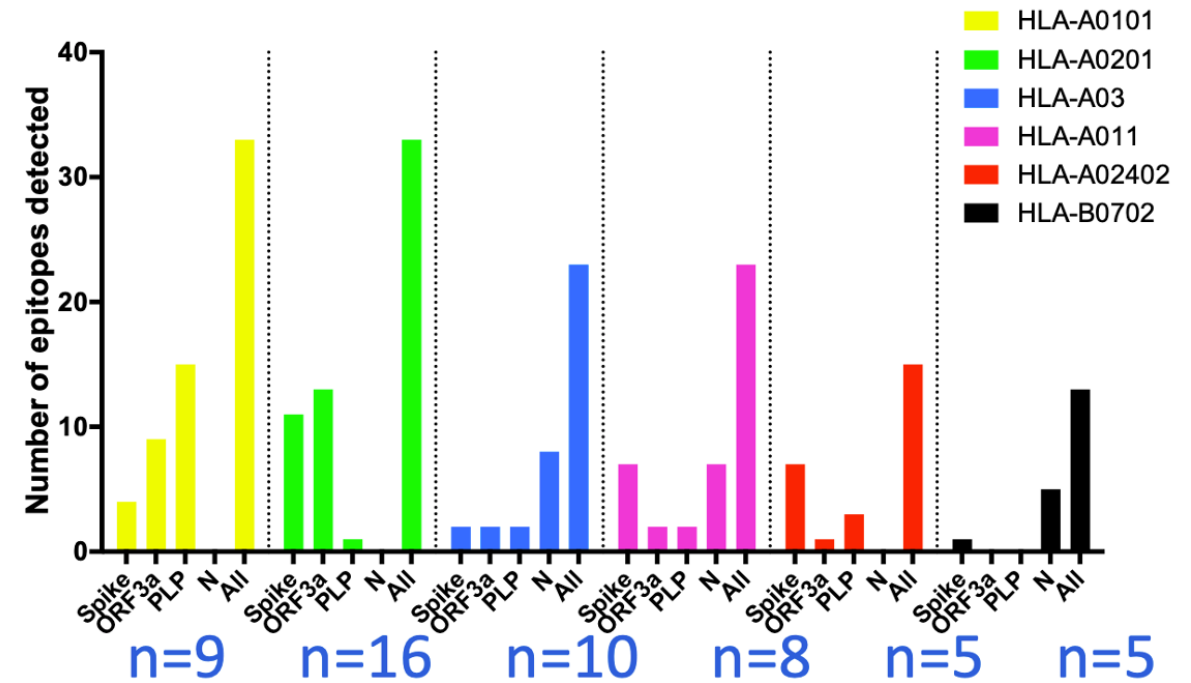
- CD8+ T cells, or cytotoxic T lymphocytes (CTL), identify and kill cells infected with intracellular pathogens.
- Mediated by interactions with MHC-class I molecules (HLA) expressing epitopes of the target antigen
- CTL help clear SARS-CoV-2 infected cells and helps prevent progression of disease
- Several studies have shown robust and broad CD4+ and CD8+ T cell responses in previously infected individuals and vaccinees

Methods:

- Study Population: PBMC from convalescent plasma donors in the U.S. (n=30)
- Donors were randomly selected from tertiles according to IgG antibody titer, and checked for proper HLA type (n=10 for each tertile)
- Total T cell (28-markers) and CTL populations (408 target epitopes) examined via CyTOF analysis
 - *Kared et al. 2020, JCI*

Anti-SARS-CoV-2 CD8+ T cell response

- 52 unique epitopes identified
- All patients with sufficient cell populations had CD8+ T cell response
- Structural and non-structural proteins targeted
- T cell response matures overtime and was associated with NAb response



Impact of SARS-CoV-2 α, β, γ variants:

- Identified the prominent mutations and indels from three major variants of “concern” (n=45)
- Mapped the mutations and the 52 unique epitopes identified in earlier study
- Any identified cross-over was assessed for estimated effect on putative HLA binding
- Only one mutation found within 1/52 unique epitopes in one patient
 - *Redd et al. OFID, 2021*
- Repeated analysis with mutations associated with Omicron

Epitope/Omicron cross-over for Spike

Spike

MFVFLVLLPLVSSQCVNITTRTQLPPAYTNSFTRGVYYPDKVFRSSVLHSTQDLFLPFFSNVTWFHAIHVSGTN
GTKRFDNPVLPFNDGVYFASTEKSNIRGWIFGTTLDSTQSLIVNNATNVVIKVFCEFCNDPFLGVVYHK
NNKSWMESEFRVYSSANNCTFEYVSQPFLMDLEGKQGNFKNLREFVFKNIDGYFKIYSKHTPINLVRDLPQG
FSALEPLVDLPIGINITRFQTLALHRSYLTGDDSSSGWTAGAAAYVGYLQPRTFLLKYNENGTITDAVDCALDP
LSEKCTLKSFTVEKGIYQTSNFRVQPTESIVRFPNITNLCPFGEVFNATRFASVYAWNRKRISNCVADYSVLYNS
ASFSSTFKCYGVSPTKLNDLCFTNVYADSFVIRGDEVQRQIAPGQTGKIADYNYKLPDDFTGCVIAWNSNLDLSDK
VGGNYNYLYRLFRKSNLKPFERDISTEIYQAGSTPCNGVEGFNCYFPLQSYGFQPTNGVGYQPYRVVLSFEL
LHAPATVCGPKKSTNLVKNKCVNFNFNGLTGTGVLTESNKKFLPFQQFGRDIADTTDAVRDPQTLEILDITPCSF
GGVSVITPGTNTSNQVAVLYQDVNCTEVPVAIHADQLTPTWRVYSTGSNVFQTRAGCLIGAEHVNNNSYECDI
PIGAGICASYQTQTNSPRRARSVASQSIIAYTMSLGAENSVAYSNNSIAIPTNFTISVTTEILPVSMTKTSVDCTM
YICGDSTECSNLLLQYGSFCTQLNRALTGIAVEQDKNTQEVFAQVKQIYKTPPIKDFGGFNFSQILPDPSKPSKR
SFIEDLLFNKVTLADAGFIKQYGDCLGDIAARDLICAQKFNGLTVLPPLTDEMIQYTSALLAGTITSGWTFGA
GAALQIPFAMQMAYRFNGIGVTQNVLYENQKLIANQFNSAIGKIQDSLSSTASALGKLQDVVNQNAQALNTL
VKQLSSNFGAISSVLNDILSRLDKVEAEVQIDRLITGRLQSLQTYVTQQLIRAAEIRASANLAATKMSECVLGQS
KRVDFCGKGYHLMSFPQSAPHGVVFLHVTYVPAQEKNTTAPAICHGKAHFPREGVFNSTGTHWVFVTRN
FYEPQIITDNTFVSGNCDVVIGIVNNTVYDPLQPELDSFKEELDKYFKNHTSPDVDLGDISGINASVVNIQKEI
DRLNEVAKNLNESLIDLQELGKYEQYIKWPWYIWLGFIAGLIAIVMVTIMLCCMTSCCCLKGCCSCGSCCKFD
EDDSEPVKGVKLHYT

Impact of SARS-CoV-2 Omicron variant:

- Repeated same analysis with Omicron associated mutations
- Only one mutation (T95I) found within 1/52 unique epitopes in two patients
 - Mutated epitope located in Spike (GVYFASTIEK)
 - Non-dominant and 1/5 and 1/13 epitopes targeted, respectively
- No apparent accumulation of T cell escape mutations
 - Previously identified T cell mutation in Beta is not found in Omicron
- CD8+ T cell response should be largely intact
 - Current vaccinees and convalescent patients should maintain protection from disease caused by variants
- T cell escape should be monitored as SARS-CoV-2 is now endemic in the human population

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