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
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 (GVYFAS\textsubscript{I}EK)
  • 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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