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Article

Targets of T Cell Responses to SARS-CoV-2 Coronavirus in Humans with COVID-19 Disease and Unexposed Individuals

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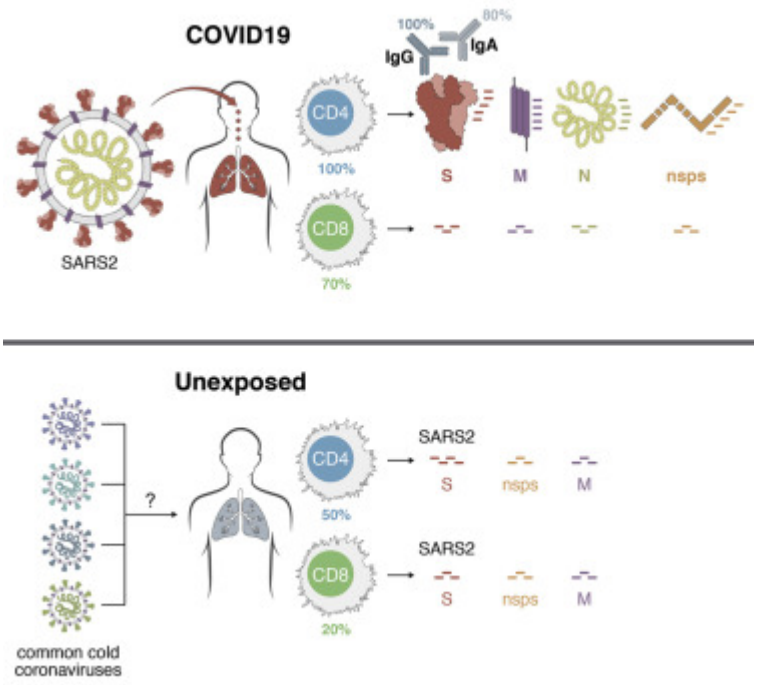
Highlights

- Measuring immunity to SARS-CoV-2 is key for understanding COVID-19 and vaccine development
- Epitope pools detect $CD4^+$ and $CD8^+$ T cells in 100% and 70% of convalescent COVID patients
- T cell responses are focused not only on spike but also on M, N, and other ORFs
- T cell reactivity to SARS-CoV-2 epitopes is also detected in non-exposed individuals

Summary

Understanding adaptive immunity to SARS-CoV-2 is important for vaccine development, interpreting coronavirus disease 2019 (COVID-19) pathogenesis, and calibration of pandemic control measures. Using HLA class I and II predicted peptide "megapools," circulating SARS-CoV-2-specific $CD8^+$ and $CD4^+$ T cells were identified in ~70% and 100% of COVID-19 convalescent patients, respectively. $CD4^+$ T cell responses to spike, the main target of most **vaccine efforts, were robust and correlated with** the magnitude of the anti-SARS-CoV-2 IgG and IgA titers. The M, spike, and N proteins each accounted for 11%–27% of the total $CD4^+$ response, with additional responses commonly targeting nsp3, nsp4, ORF3a, and ORF8, among others. For $CD8^+$ T cells, spike and M were recognized, with at least eight SARS-CoV-2 ORFs targeted. Importantly, we detected SARS-CoV-2-reactive $CD4^+$ T cells in ~40%–60% of unexposed individuals, suggesting cross-reactive T cell recognition between circulating "common cold" coronaviruses and SARS-CoV-2.

Graphical Abstract



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Keywords

COVID-19; CD4; CD8; T cells; epitopes; coronavirus; SARS-CoV-2; cross-reactivity

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