Immunity to COVID-19

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GRAPHICAL ABSTRACT

SUMMARY
Understanding adaptive immunity to SARS-CoV-2 is important for vaccine development, interpreting coronavirus disease 2019 (COVID-19) pathogenesis, and calibrating pandemic control measures. Using HLA class I and II presented 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.
Major knowledge gaps in understanding immunity to SARS-CoV-2

- How much of an adaptive immune response is there to COVID-19?
  - Important for vaccine design
  - Important for predictions of herd immunity and future social distancing policies

- How long does immunological memory to COVID-19 last?

- What kind of immunity is important against COVID-19?
  - Important for vaccine design
Do people develop immunity to COVID-19?

- COVID-19 is an acute infection that resolves/cures in most humans.
- What kind of immunity is important against COVID-19?

Antibodies (from B cells)

CD4 T cells (Helpers)

CD8 T cells (Killers)
Study of immune responses of ‘average’ COVID-19 cases

SARS-CoV-2 → viral antigens

IgG → IgA

CD4 → S, M, N, nsps

CD8
Study of immune responses of ‘average’ COVID-19 cases

To establish a benchmark of COVID-19 T cell and antibody responses
Good news!

Antiviral immunity that matches expectations
What about immunity to “common cold” coronaviruses?

Is there potential for any cross protection to SARS-CoV-2 from exposure to “common cold” coronaviruses?
SARS2 reactive T cells in unexposed, normal healthy donors

Blood samples collected 2015-2018
What's next?

❖ Understanding SARS-CoV-2 reactivity seen in unexposed donors
❖ Working with vaccine developers
❖ Studying the immune responses in acute COVID-19

❖ Studying the immune responses across the spectrum of disease severity
  ❖ What types of immune responses are protective?
  ❖ What types of immune responses are potentially pathogenic?
THE TEAM

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CD4\(^+\) T cells respond to multiple SARS-CoV-2 antigens
Antibody responses to SARS-CoV-2 Spike protein

![Graphs showing antibody responses to SARS-CoV-2 Spike protein](image-url)
CD4+ T cell responses to SARS-CoV-2
CD8⁺ T cell responses to SARS-CoV-2
Cross reactive CD4⁺ T cells to SARS-CoV-2 after exposure to “common cold” HCoV.
Cytokine responses of immune cells to COVID-19

TH1 cytokine response
The main focus of current SARS-CoV-2 vaccine candidates

SARS-CoV-2 Spike Protein

Wrapp et al., 2020 Science
Coronaviruses (CoV)

- Enveloped, single-stranded (+) RNA viruses with large genome (20-30 kb)
  - Structural proteins: Spike (S), Membrane (M), Envelope (E), Nucleocapsid (N)
  - Non-structural proteins (nsps)
  - Accessory proteins

Inside: RNA, N, nsps, accessory proteins

Outside: S, M, E
CD8⁺ T cells respond to multiple SARS-CoV-2 antigens
T cell responses correlate with viral protein abundance

SARS-CoV-2

CD4$^+$ response

CD8$^+$ response
Diseases caused by coronaviruses

• Cause disease in mammals and birds
  • 4 groups (alpha-delta)
    • alpha and beta CoV cause disease in humans

• Cause a wide range of illness:
  • upper and lower respiratory tract infections
    • asymptomatic disease to severe pneumonia
    • acute respiratory distress syndrome (ARDS)
  • COVID-19
  • other sites of disease outside lungs
## Human Coronaviruses (HCoV)

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