Immunity to COVID-19

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Cell

Article

Targets of T cell responses to SARS-CoV-2 coronavirus in humans with COVID-19 disease and unexposed individuals

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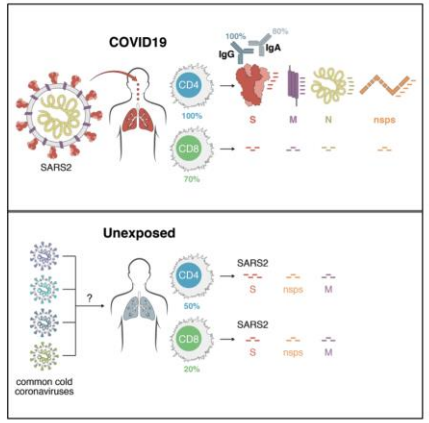
GRAPHICAL ABSTRACT



SUMMARY

Understanding adaptive immunity to SARS-CoV-2 is important for vaccine development, interpreting coronavirus disease 2019 (COVID-19) pathogenesis, and 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.

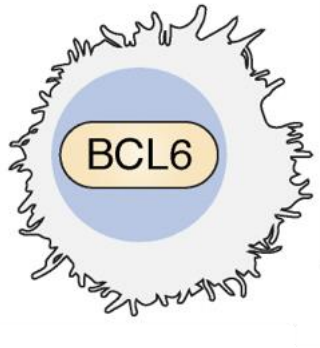
Major knowledge gaps in understanding immunity to SARS-CoV-2

- **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

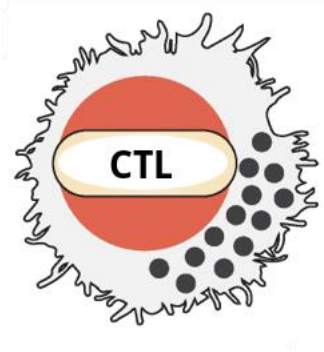
Do people develop immunity to COVID-19?

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

Antibodies (from B cells)

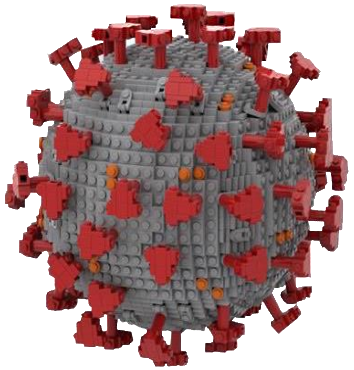


CD4 T cells
Helpers



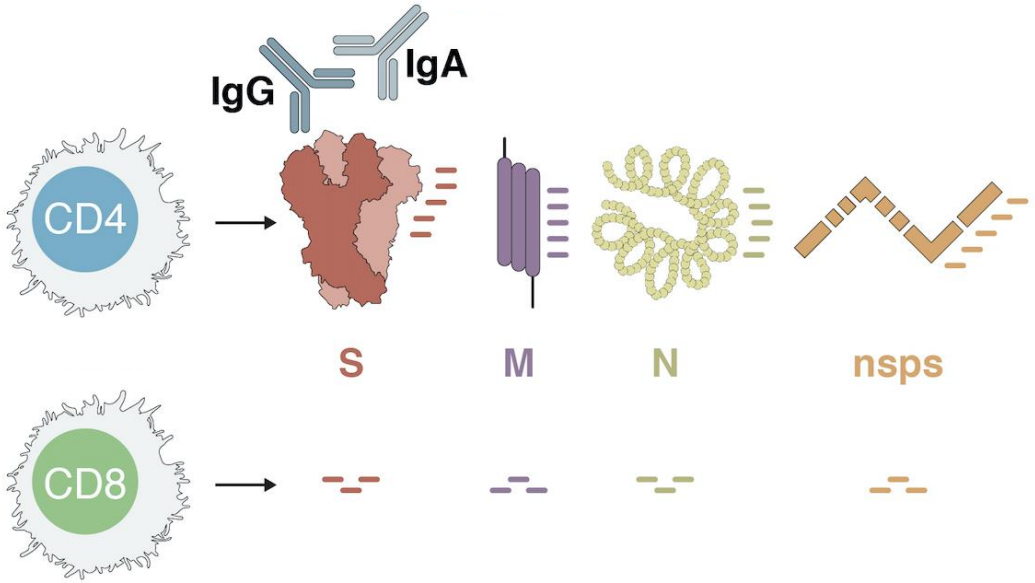
CD8 T cells
Killers

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



SARS-CoV-2

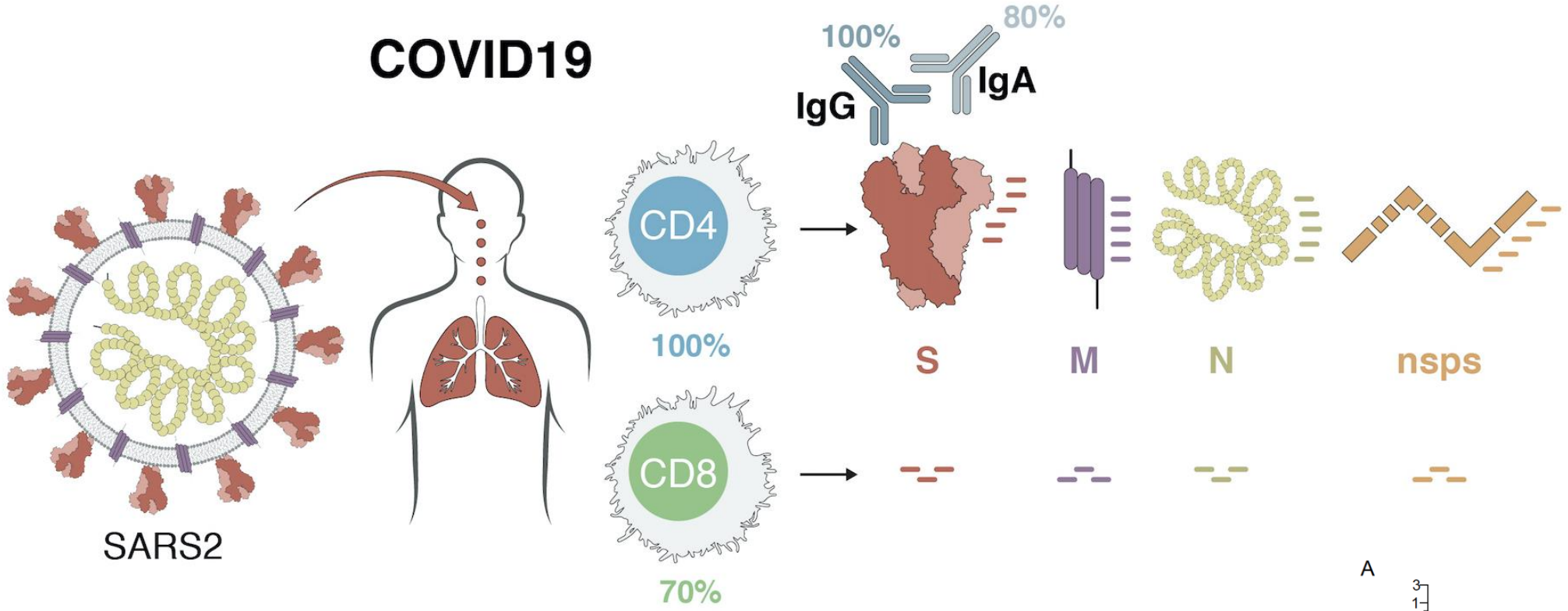
viral antigens

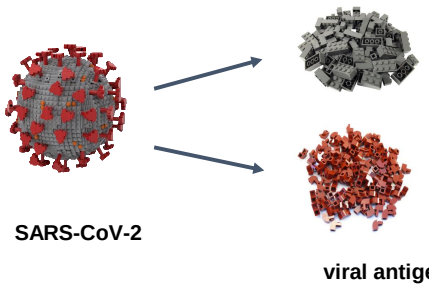


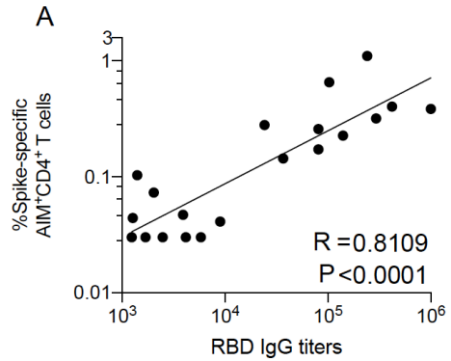
Alessandro Sette

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

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

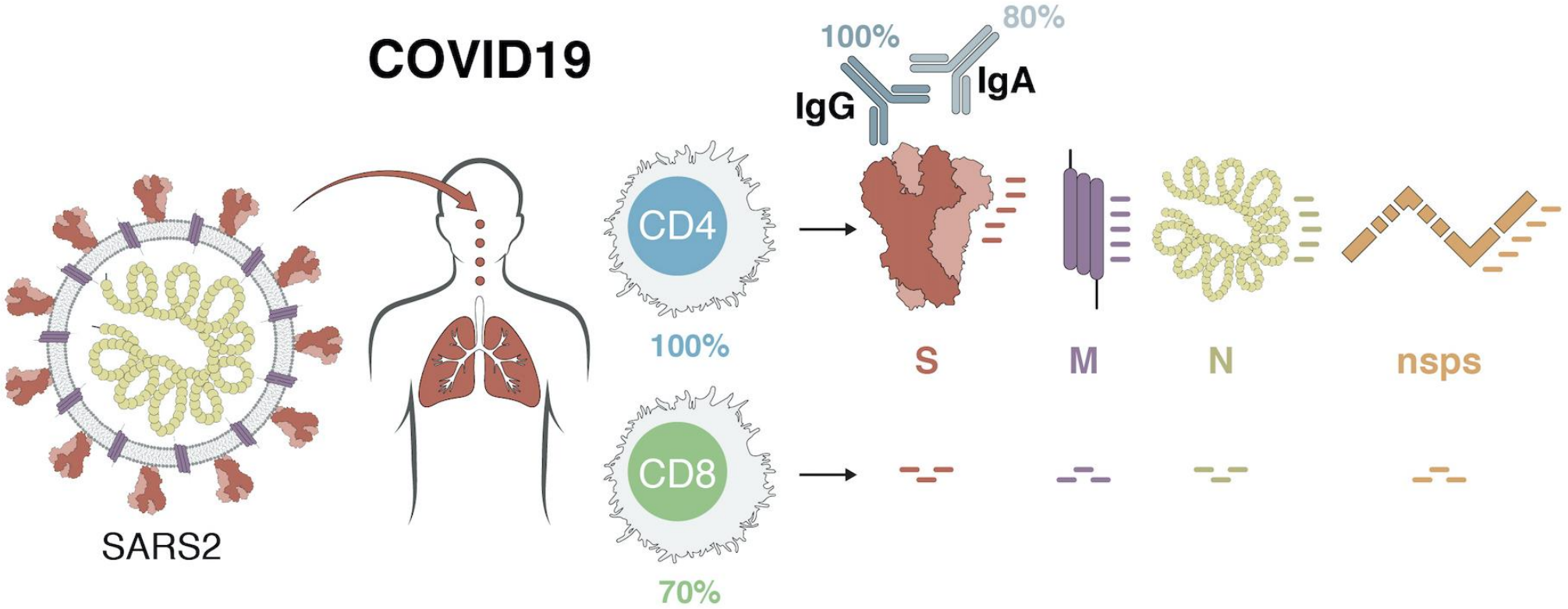






Good news!

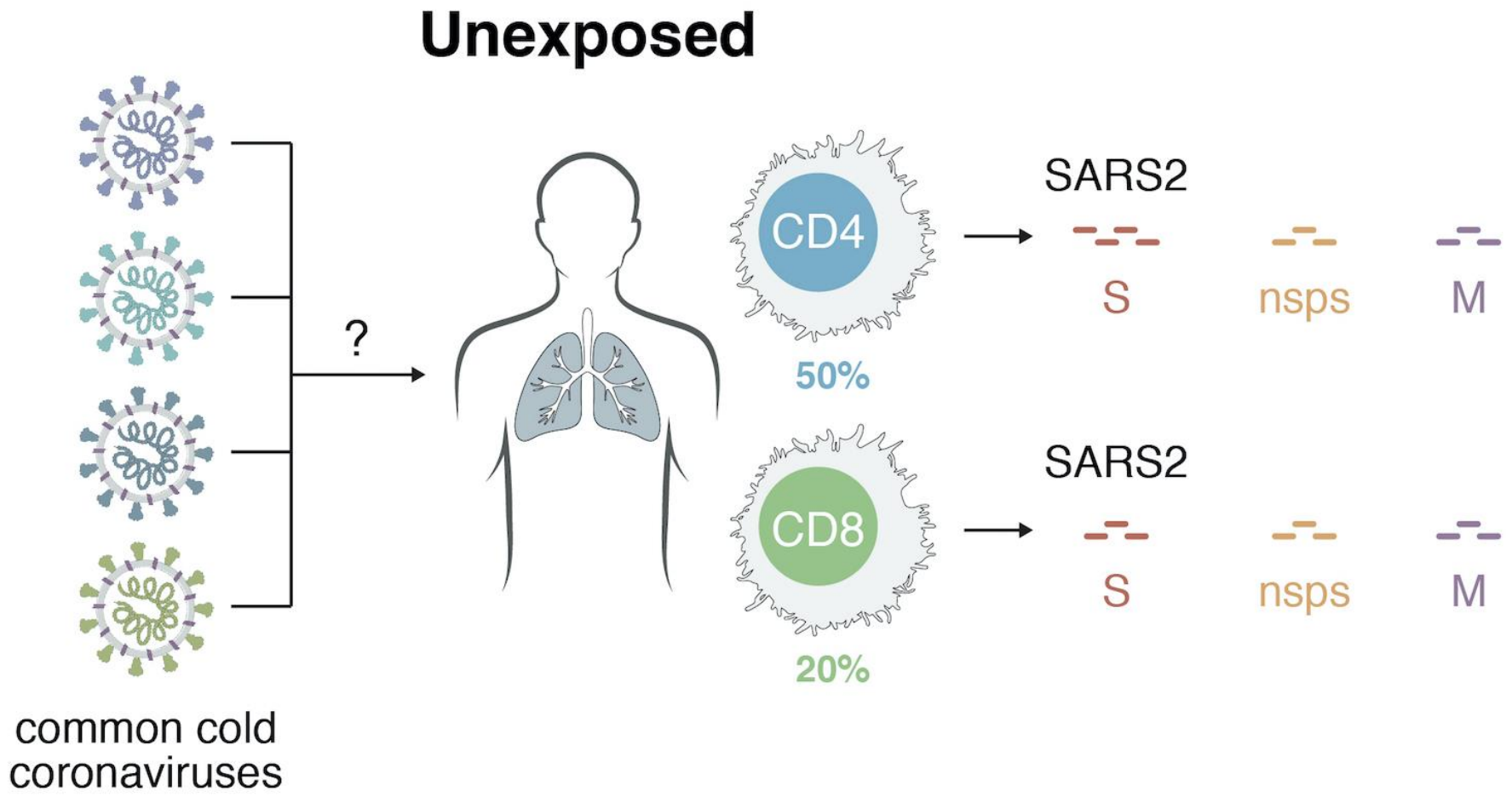
Antiviral immunity that matches expectations



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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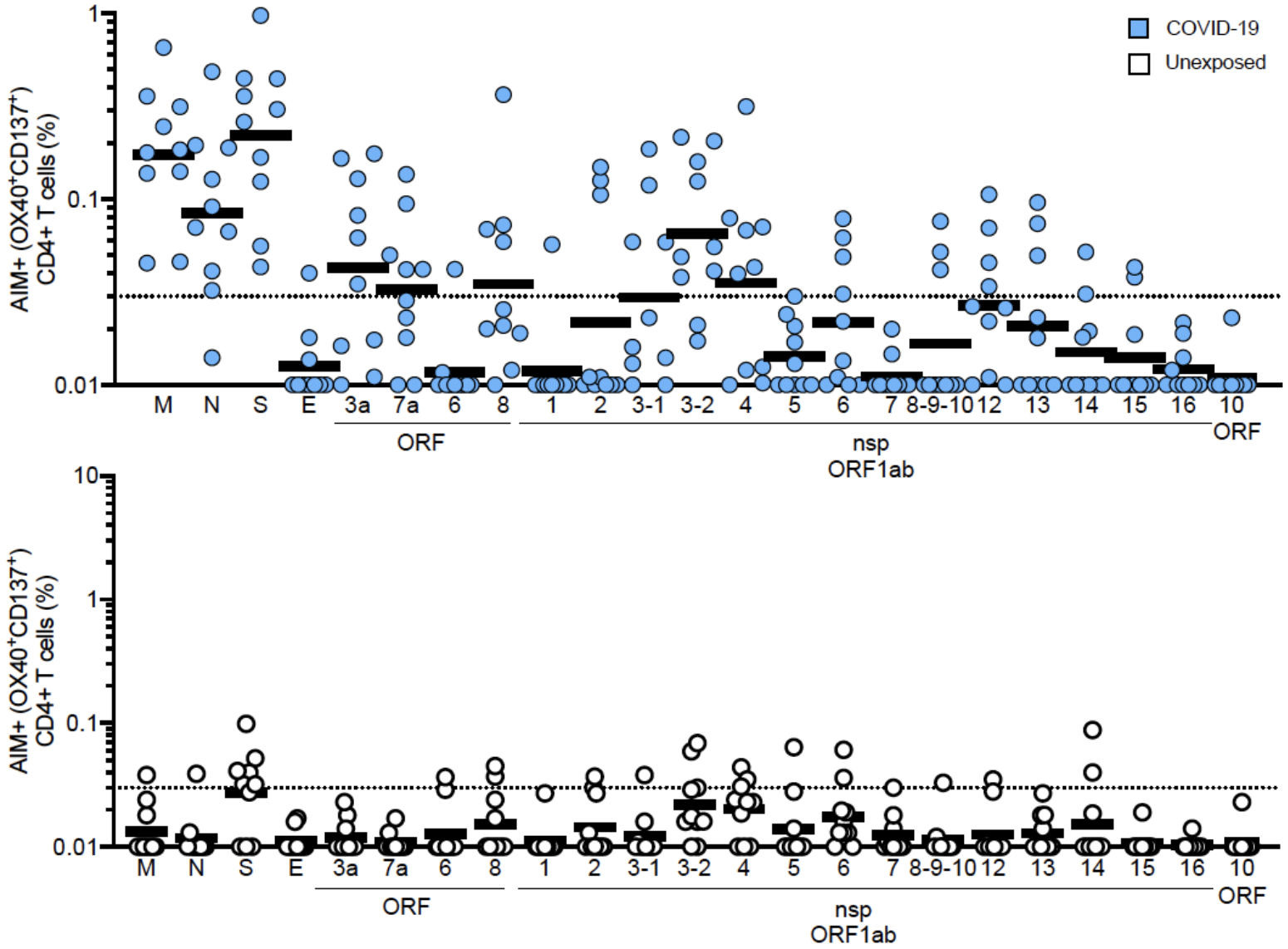
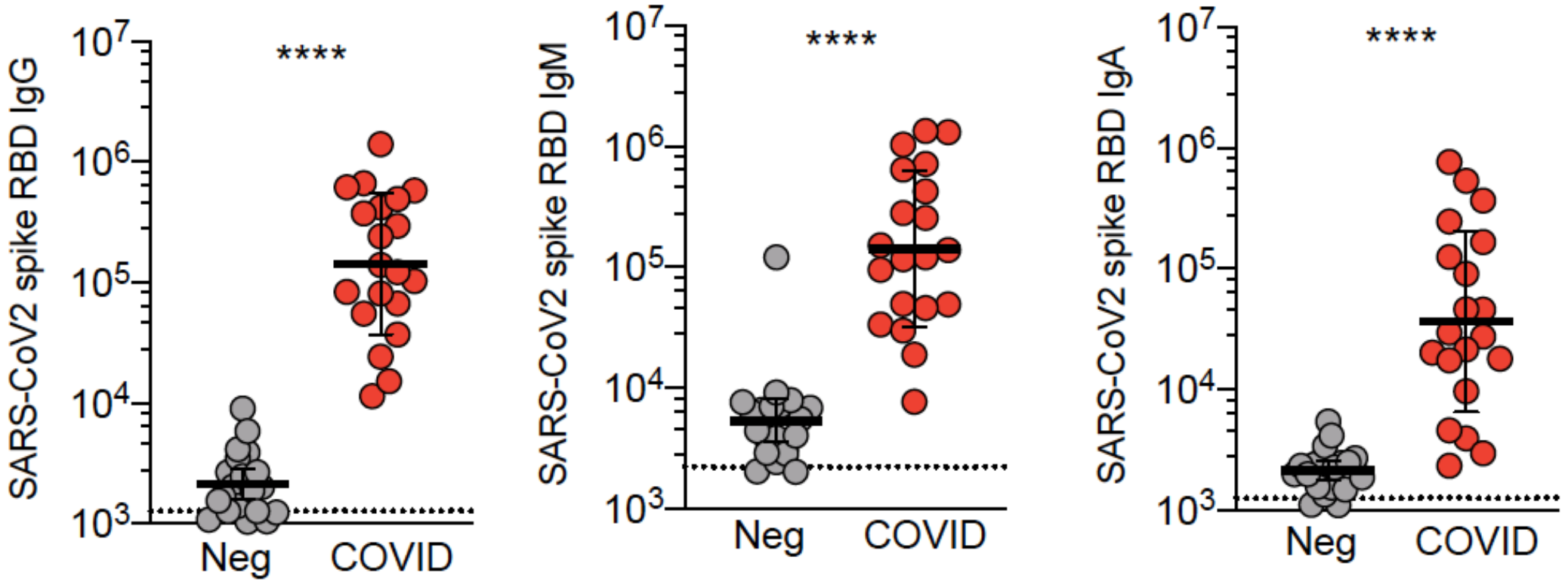
CORONAVIRUS TASK FORCE

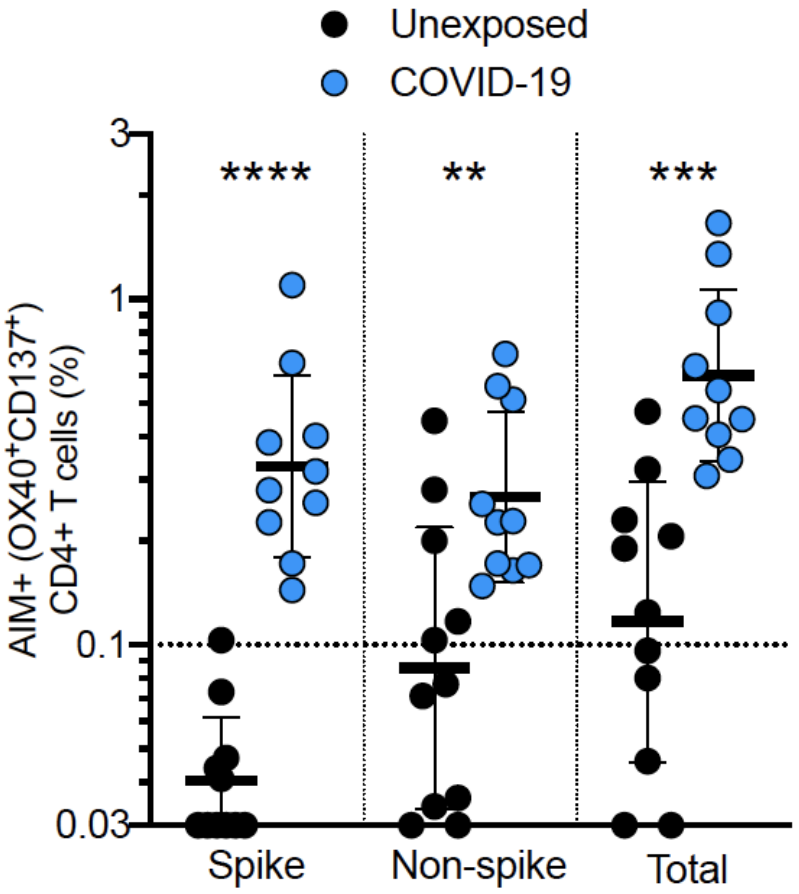
CD4$^+$ T cells respond to multiple SARS-CoV-2 antigens

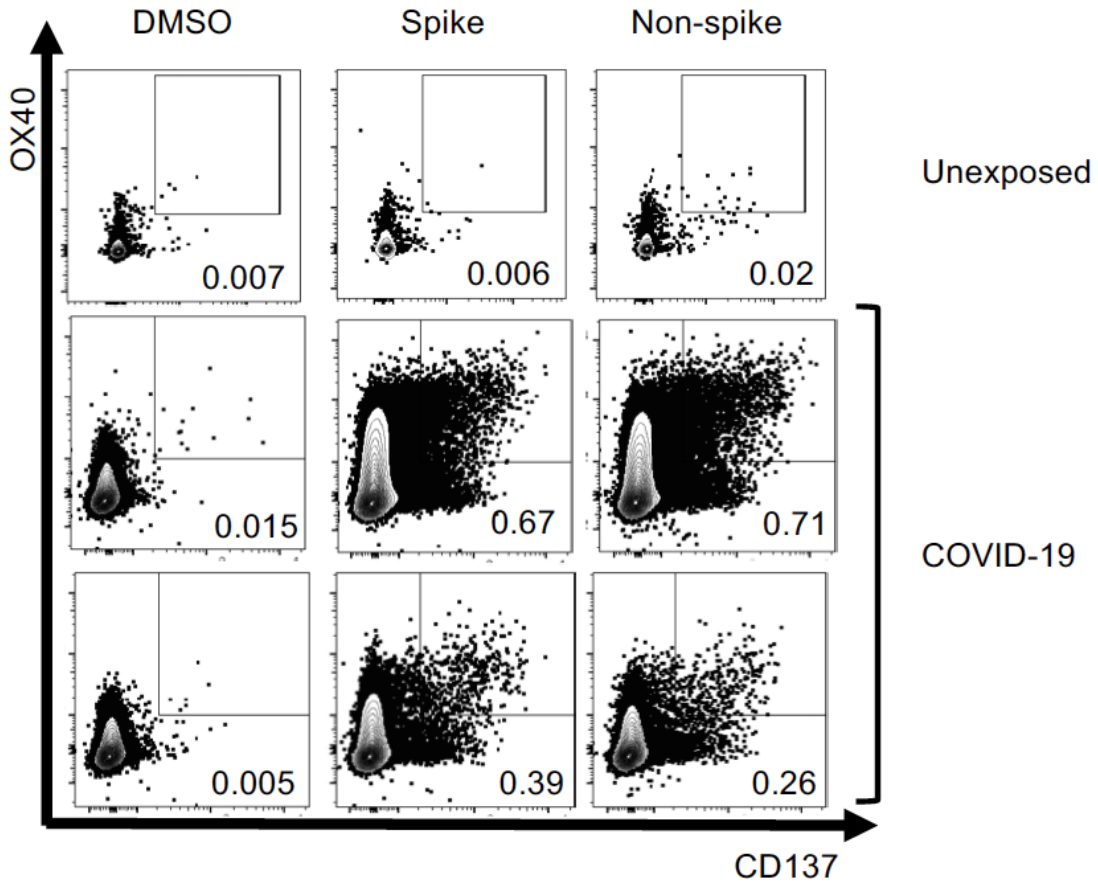


Antibody responses to SARS-CoV-2 Spike protein

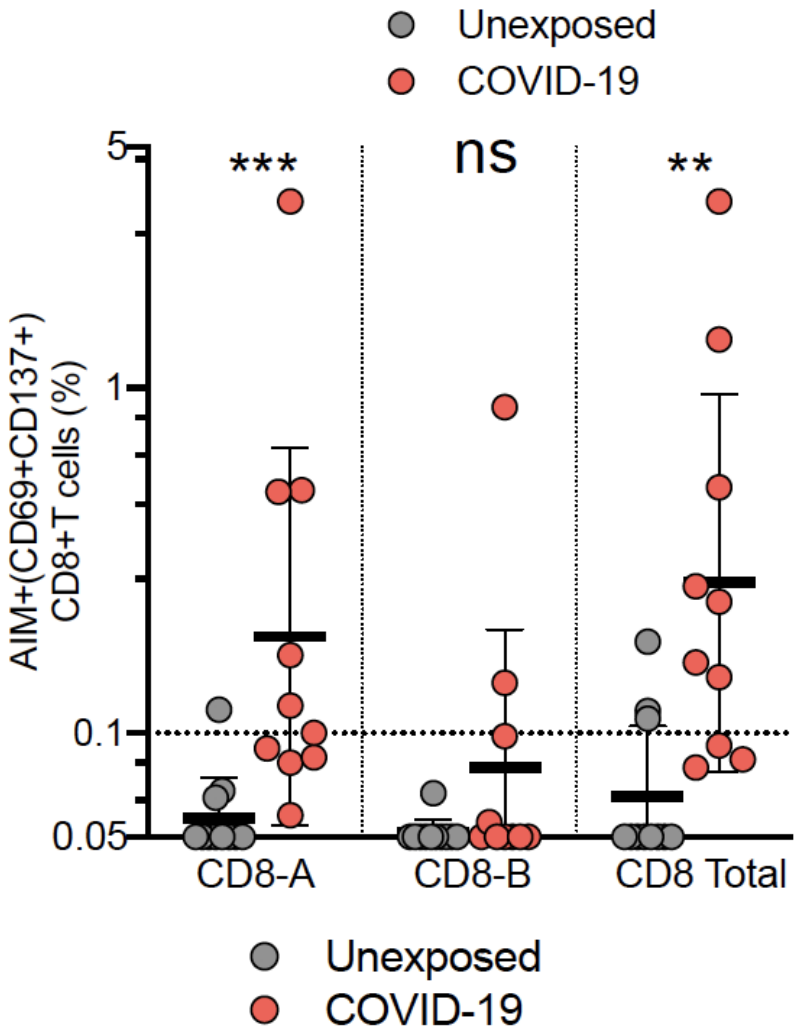


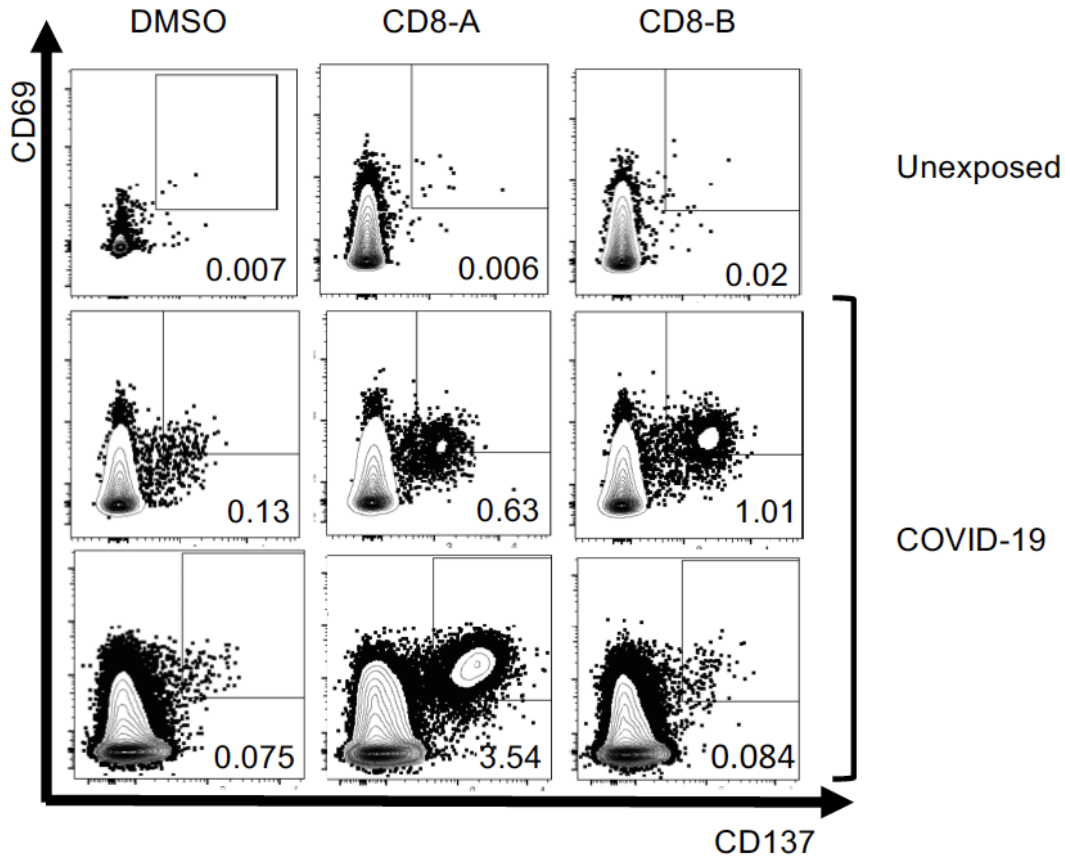
CD4⁺ T cell responses to SARS-CoV-2



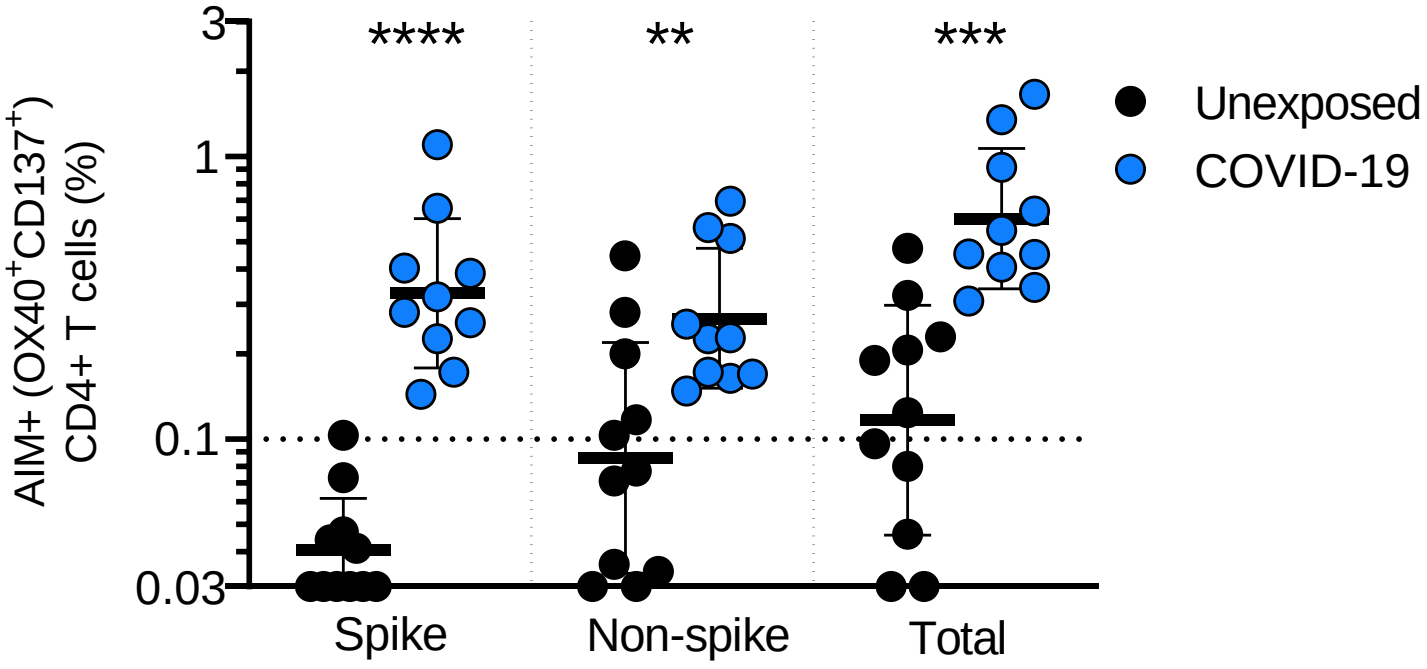


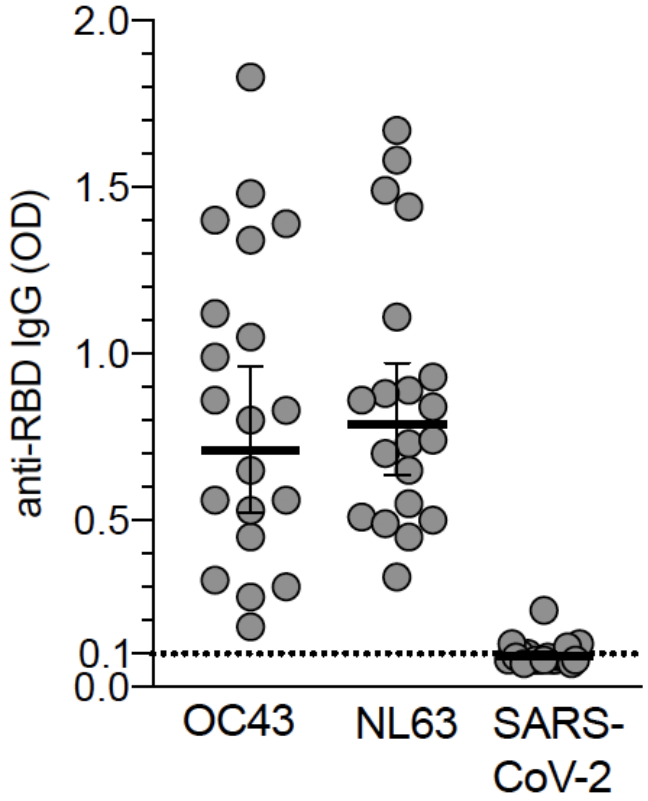
CD8⁺ T cell responses to SARS-CoV-2



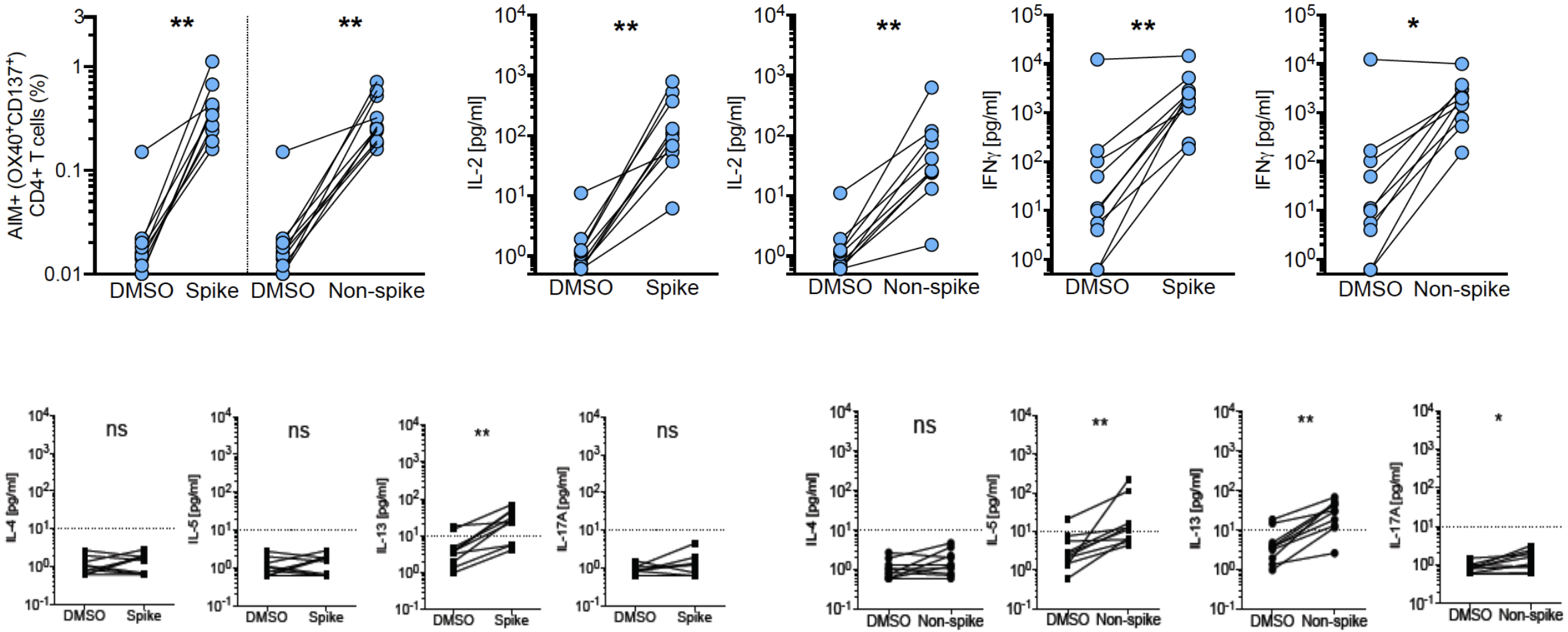


Cross reactive CD4$^+$ T cells to SARS-CoV-2 after exposure to “common cold” HCoV





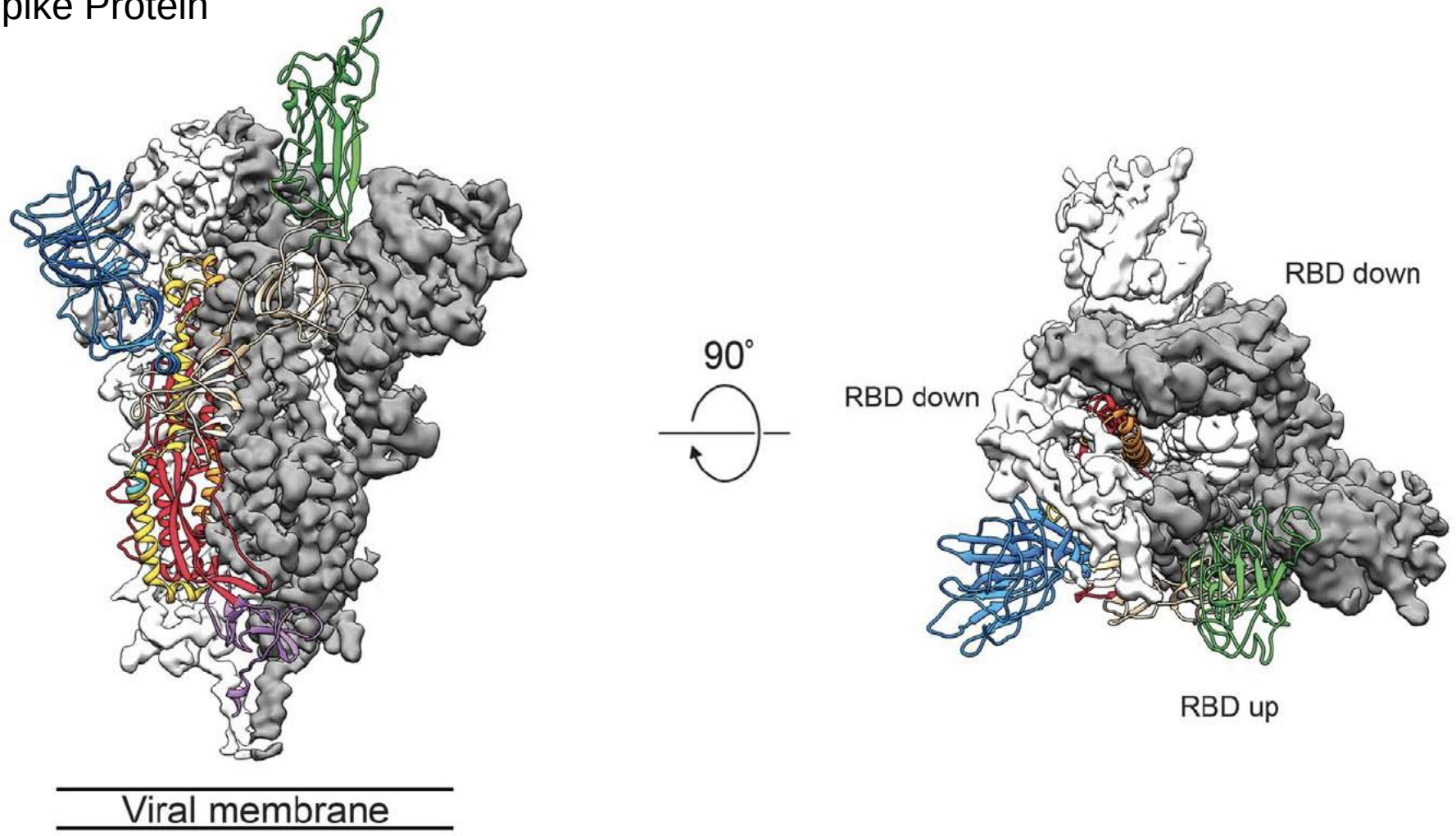
Cytokine responses of immune cells to COVID-19



T_H1 cytokine response

The main focus of current SARS-CoV-2 vaccine candidates

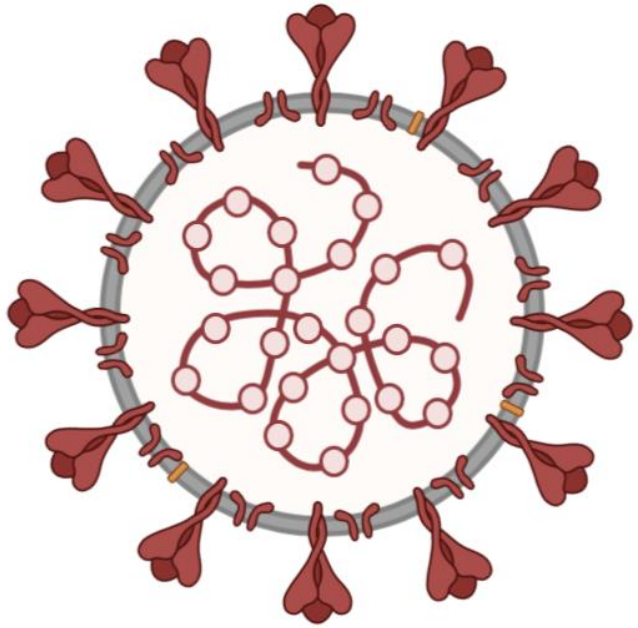
SARS-CoV-2 Spike Protein



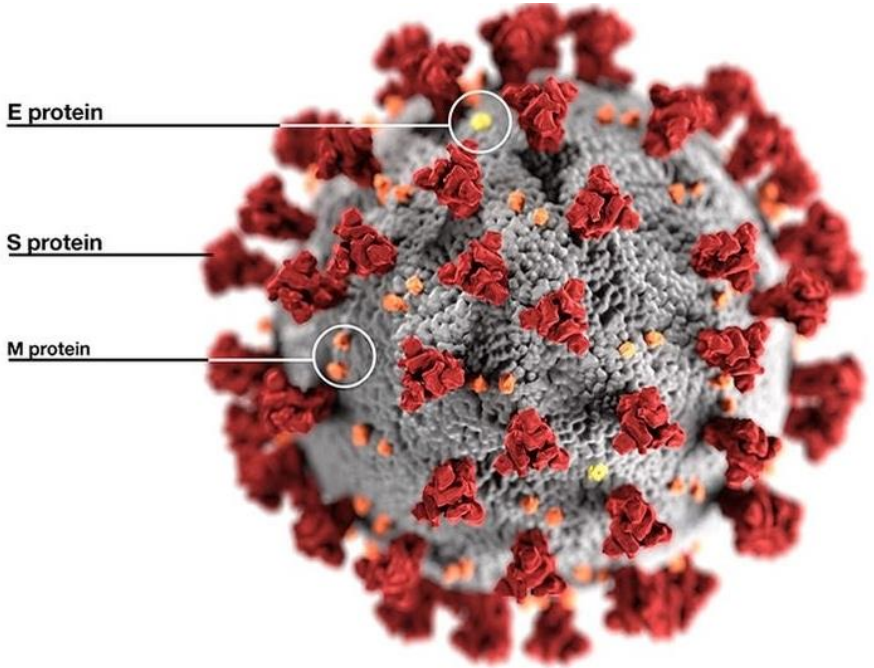
Wrapp et al., 2020 Science

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

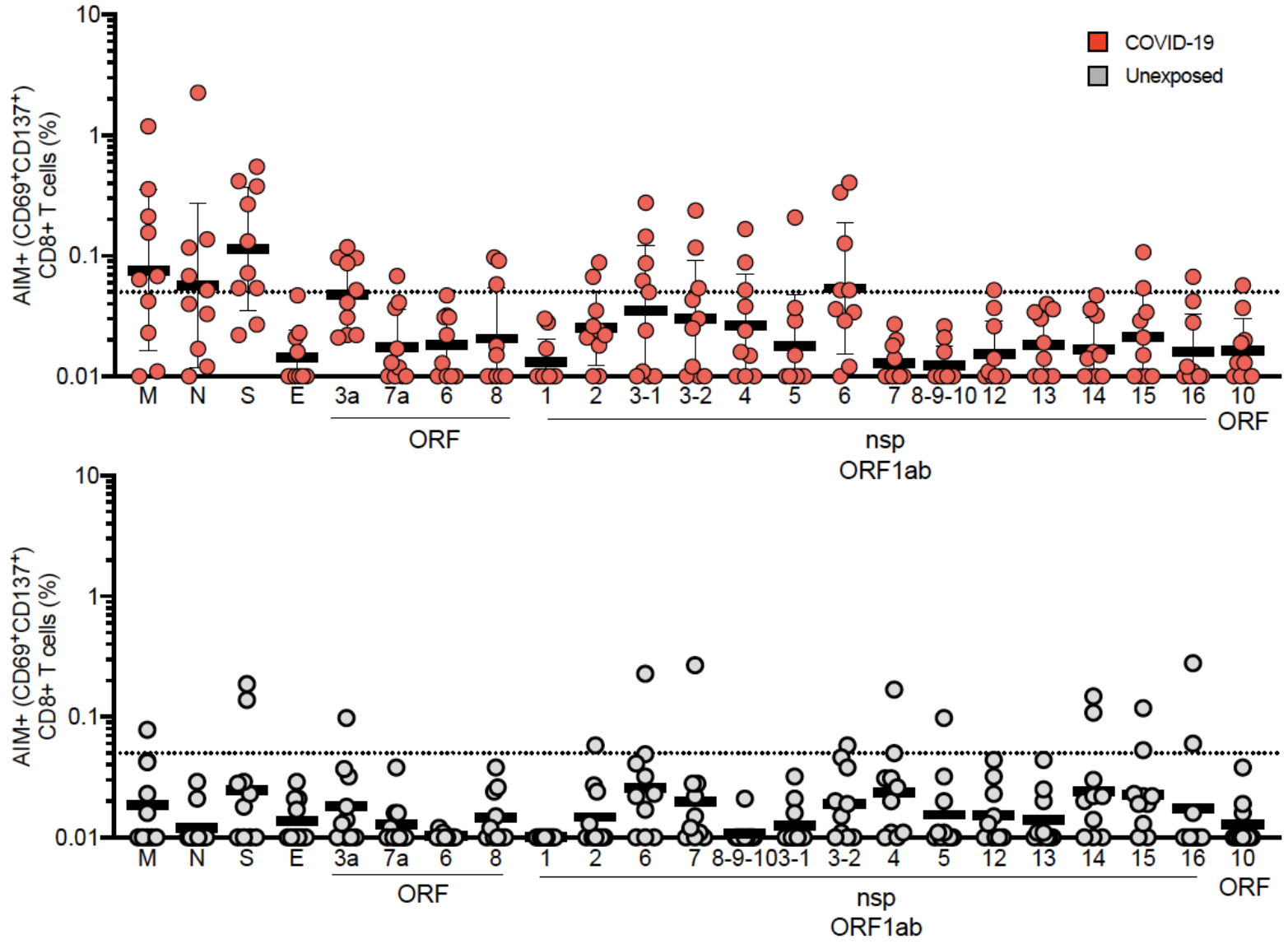


Inside: RNA, N, nsps, accessory proteins

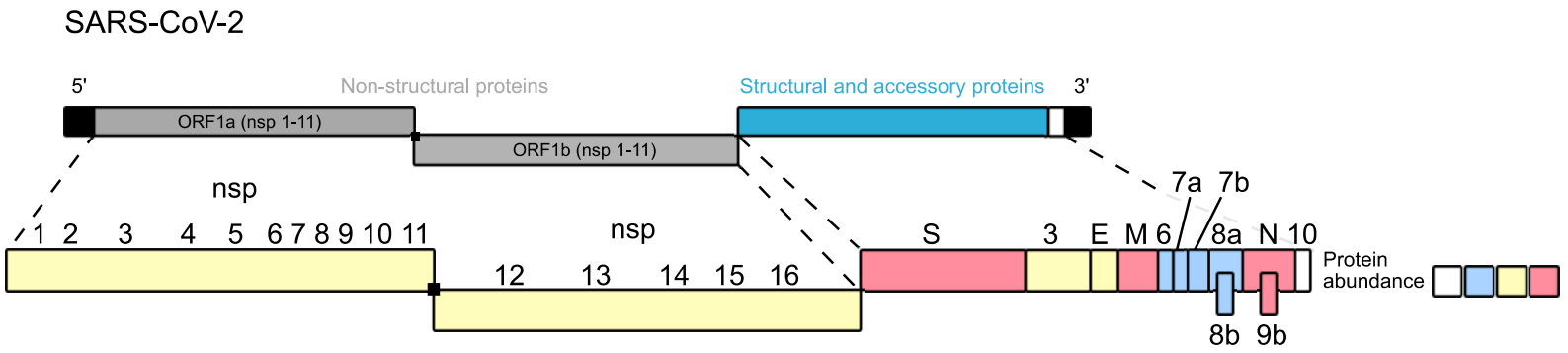


Outside: S, M, E

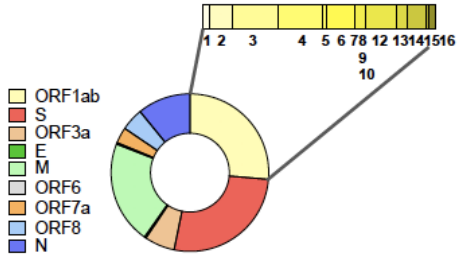
CD8$^+$ T cells respond to multiple SARS-CoV-2 antigens

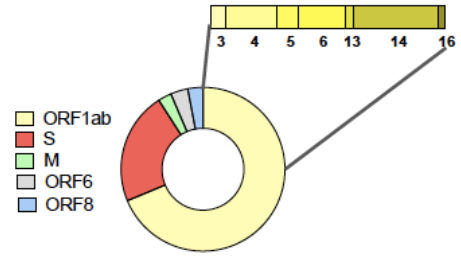


T cell responses correlate with viral protein abundance

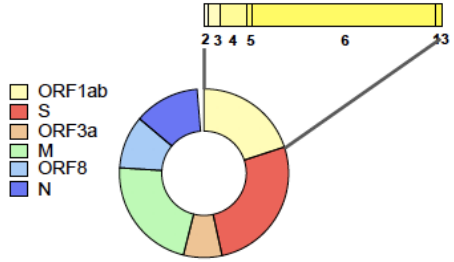


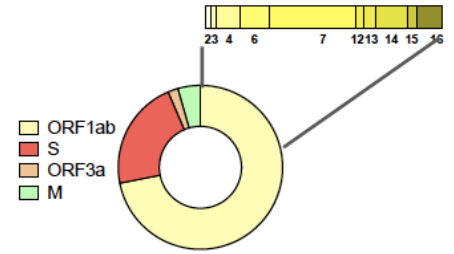
CD4+ response





CD8+ response

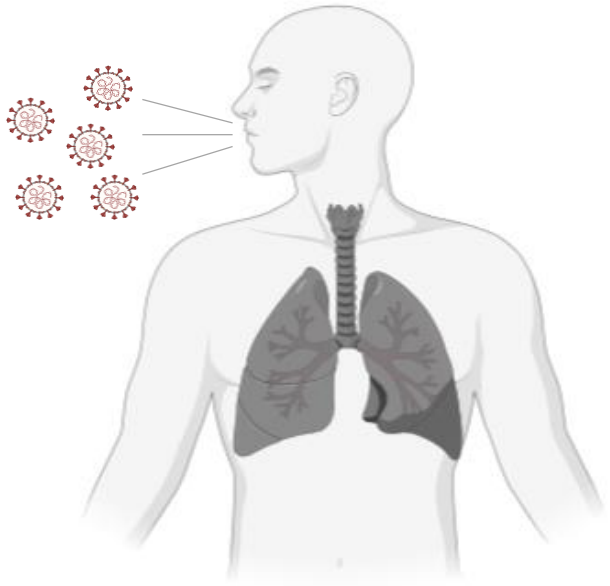




Diseases caused by coronaviruses

- 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)

Virus	Alpha/Beta	Year of Discovery	Common cold	Severe disease	Syndrome or illness	Vaccine?
OC43	beta	1960	✓			No
229E	alpha	1962	✓			No
SARS	beta	2003		✓	SARS	No
NL63	alpha	2004	✓			No
HKU1	beta	2005	✓			No
MERS	beta	2012		✓	MERS	No
SARS-CoV-2	**beta**	**2019**		✓	**COVID-19**	**No**