T-Cell Response in Public Health Interventions and Vaccine Trials

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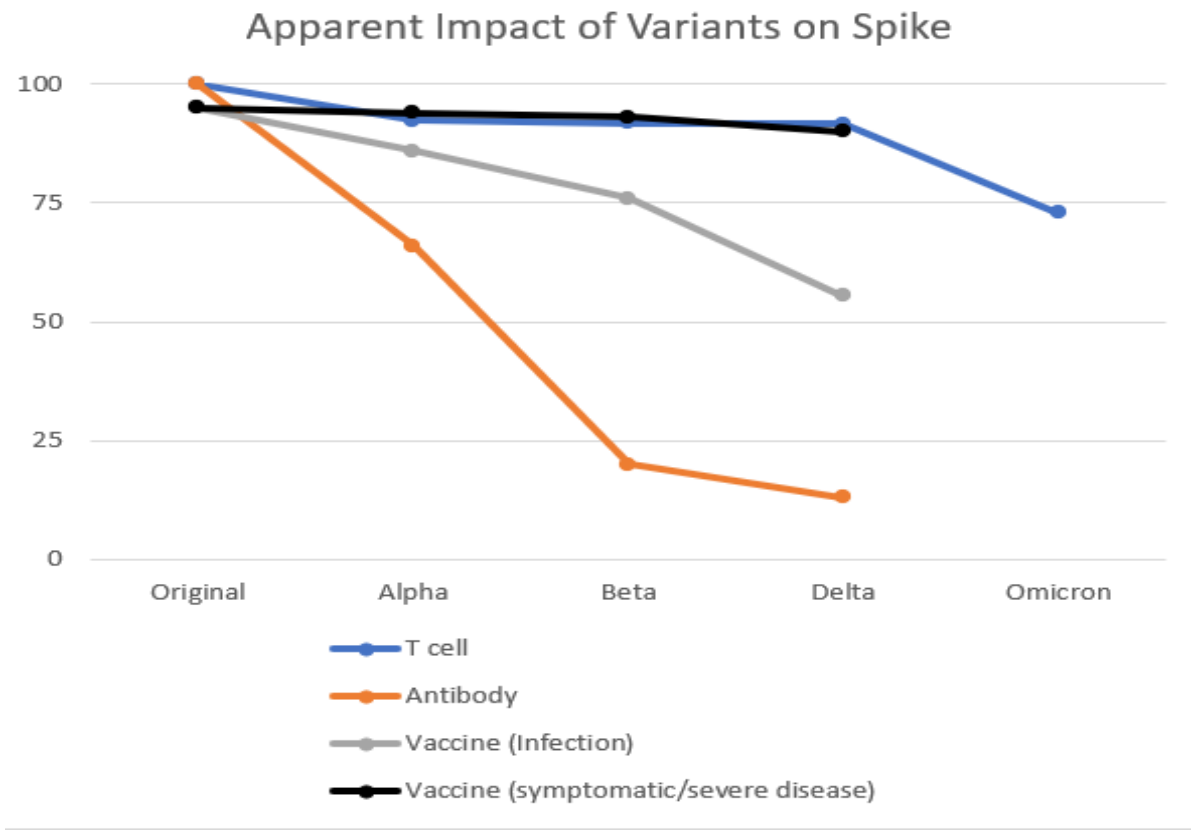
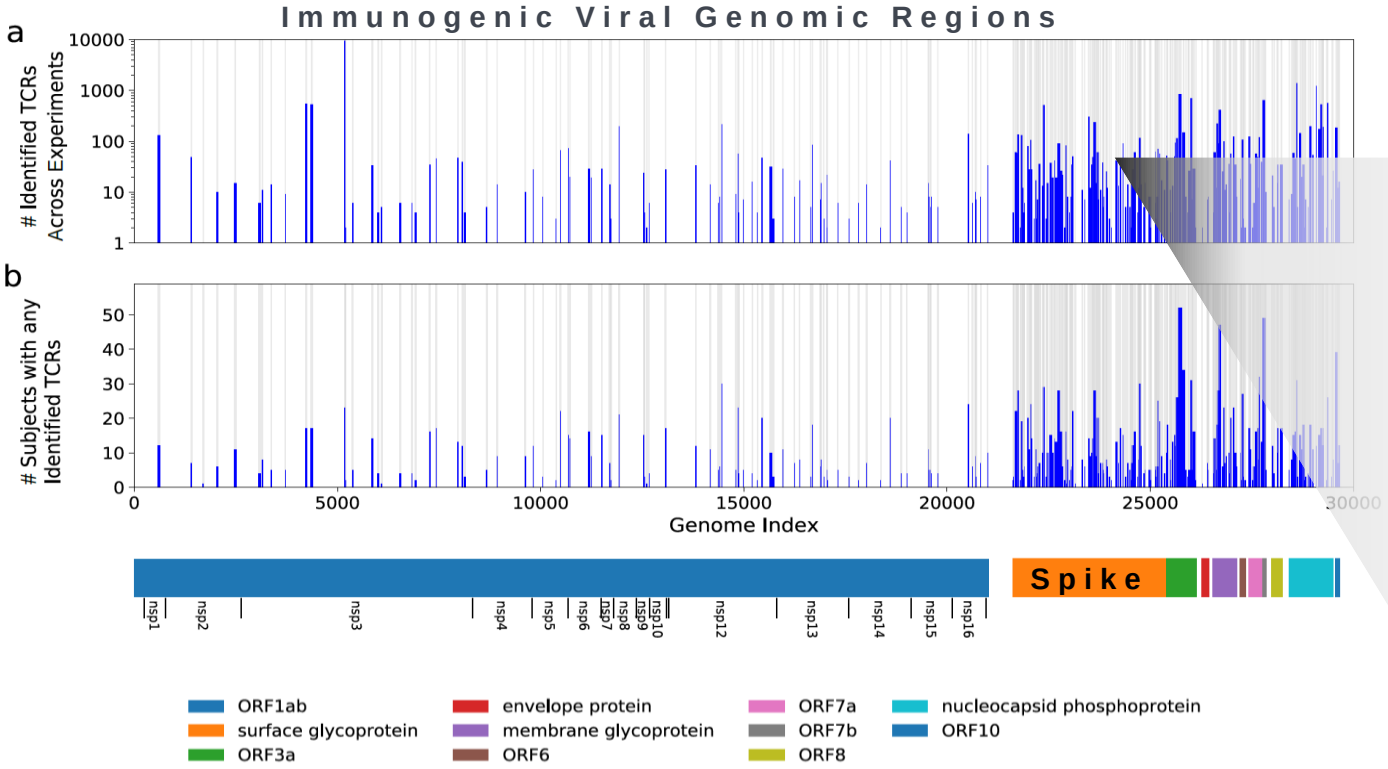
At a population level, SARS-CoV-2 specific T cell response correlates with protection from severe disease



T-cell receptor responses mapped across the entire SARS-CoV-2 genome



Unique TCRs Viral Region Specific Antigen

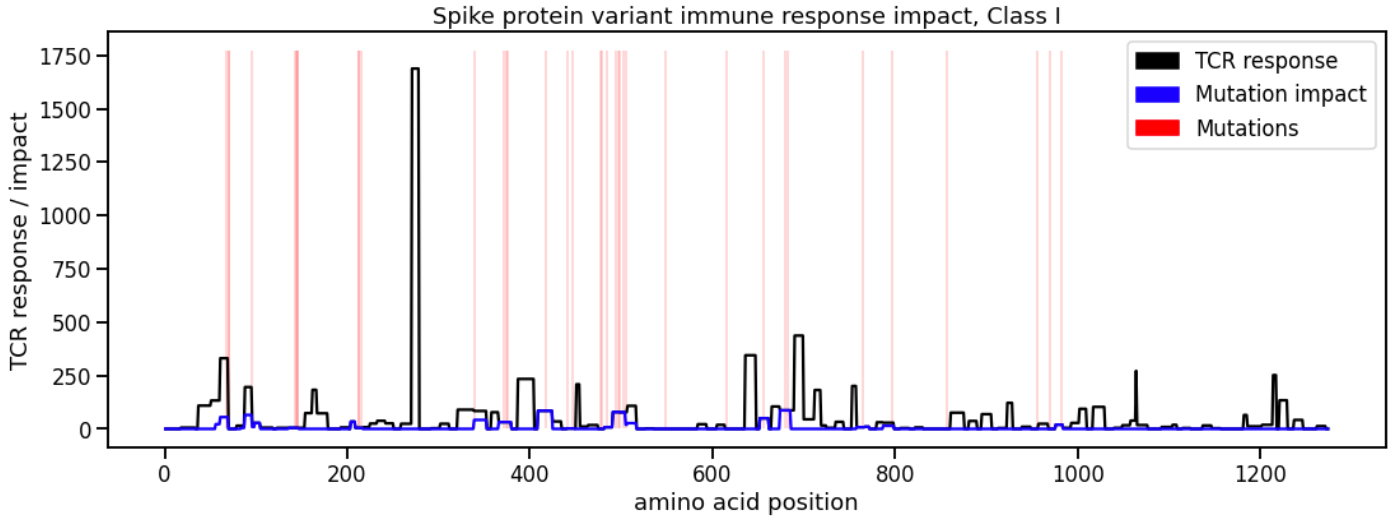
TCR Nucleotide Sequence	ORF	Viral Amino Acid Sequence
NTGAAGATCCAGCCCTCAGAA	surface glycoprotein	FASTEKSNIIRGWIFGTTLDSKTQSL
CTGGAGTTGGCTGCTCCCTCC	surface glycoprotein	KVCEFQFCNDPFLGVYYHKNNKSW
GTGACCAGTGCCCATCCTGAA	surface glycoprotein	KVCEFQFCNDPFLGVYYHKNNKSW
ACCAGTGCCCATCCTGAAGAC	ORF3a	ATIPIQASLPFGWLIVGVALLAVFQ
NTGTCGGCTGCTCCCTCCCAG	ORF3a	ATIPIQASLPFGWLIVGVALLAVFQ
CAGCCCTCAGAACCCAGGGAC	membrane glycoprotein	MADSNGTITVEELKKLLEQWNLVI
CAGCAGGTAGTGCGAGGAGA	membrane glycoprotein	MADSNGTITVEELKKLLEQWNLVI

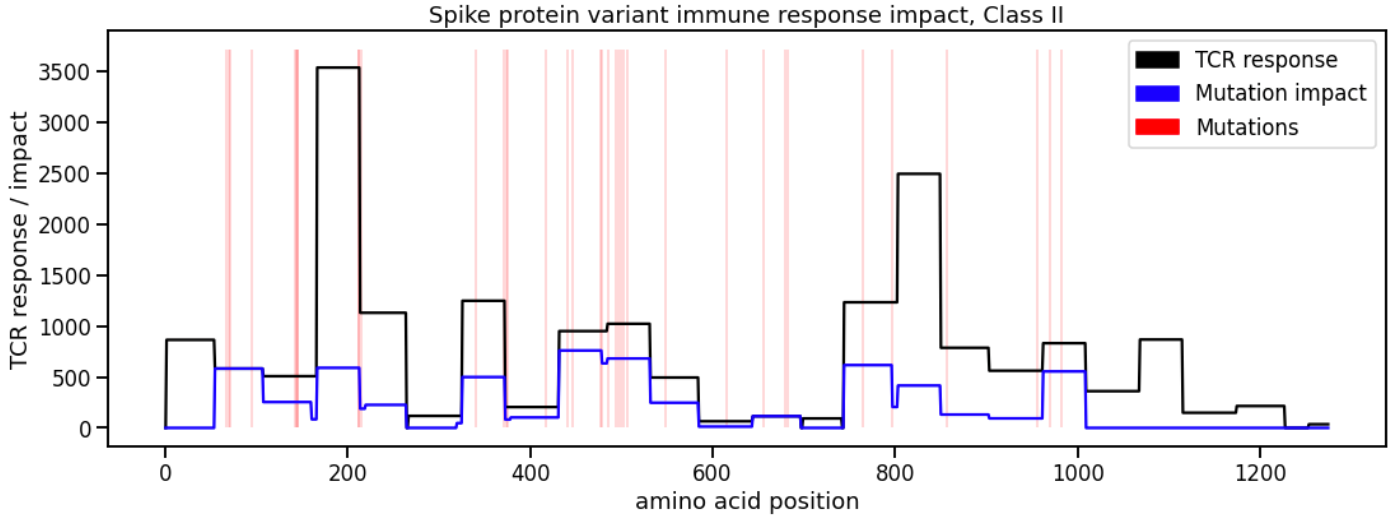
- 135,000+ T cells have been mapped to SARS-CoV-2 antigens; 6,500+ have been validated by biological response assay
- These data identify “hotspots” of the virus, which display stronger T-cell response than other locations
- We have identified antigens that are much more common to see across subjects in the population
- Growing database of patient COVID-19 specific antigen and TCR sequences, continually increasing TCR ‘library’

View of Omicron projected impact on spike (both CD4 and CD8)

- Results from combining our high-resolution map of TCRs to antigens, with new omicron mutational data*
- Assume (as upper bound) that any mutation will affect prior TCR response to original strain/vaccine if within a presented antigen

- CD8 T cell response estimates:
  - Omicron = 79% unaffected
  - Compare to Delta = 94% unaffected
- CD4 T cell response estimates:
  - Omicron = 67% unaffected
  - Compare to Delta = 89% unaffected

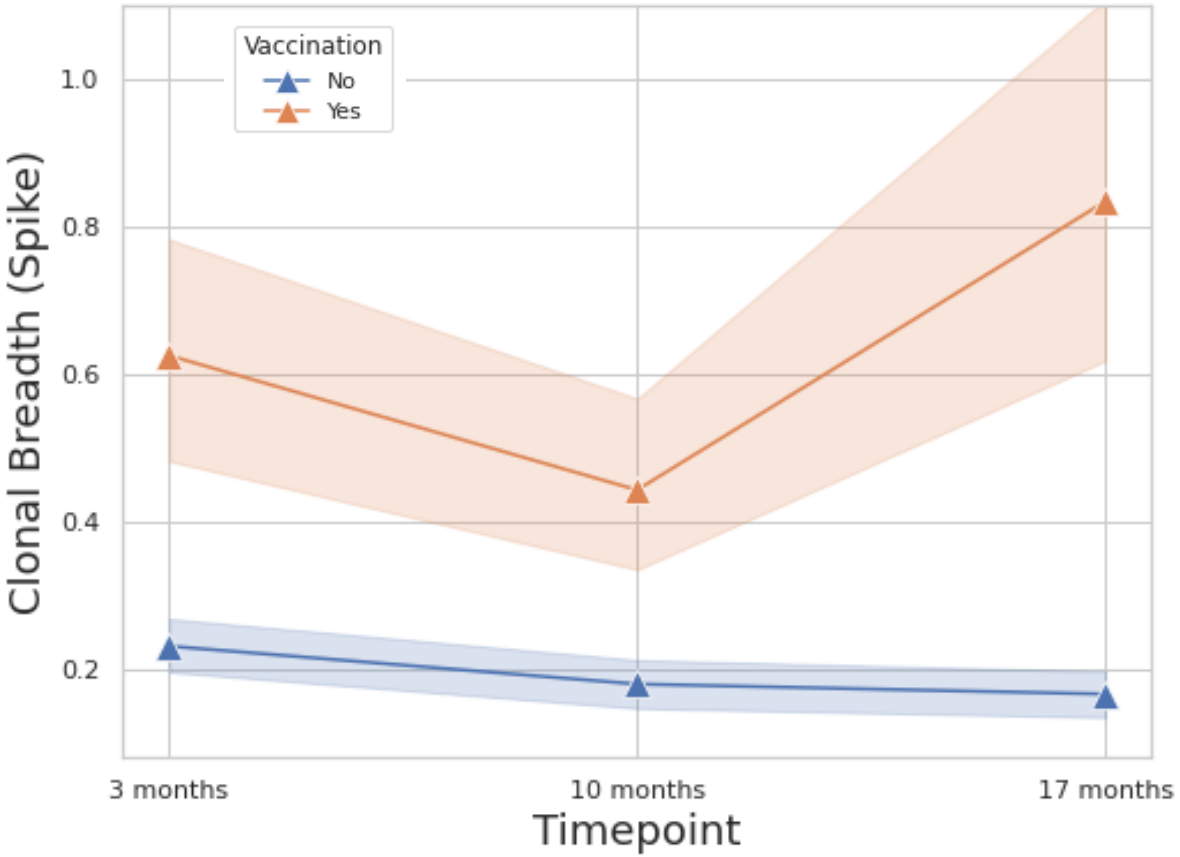


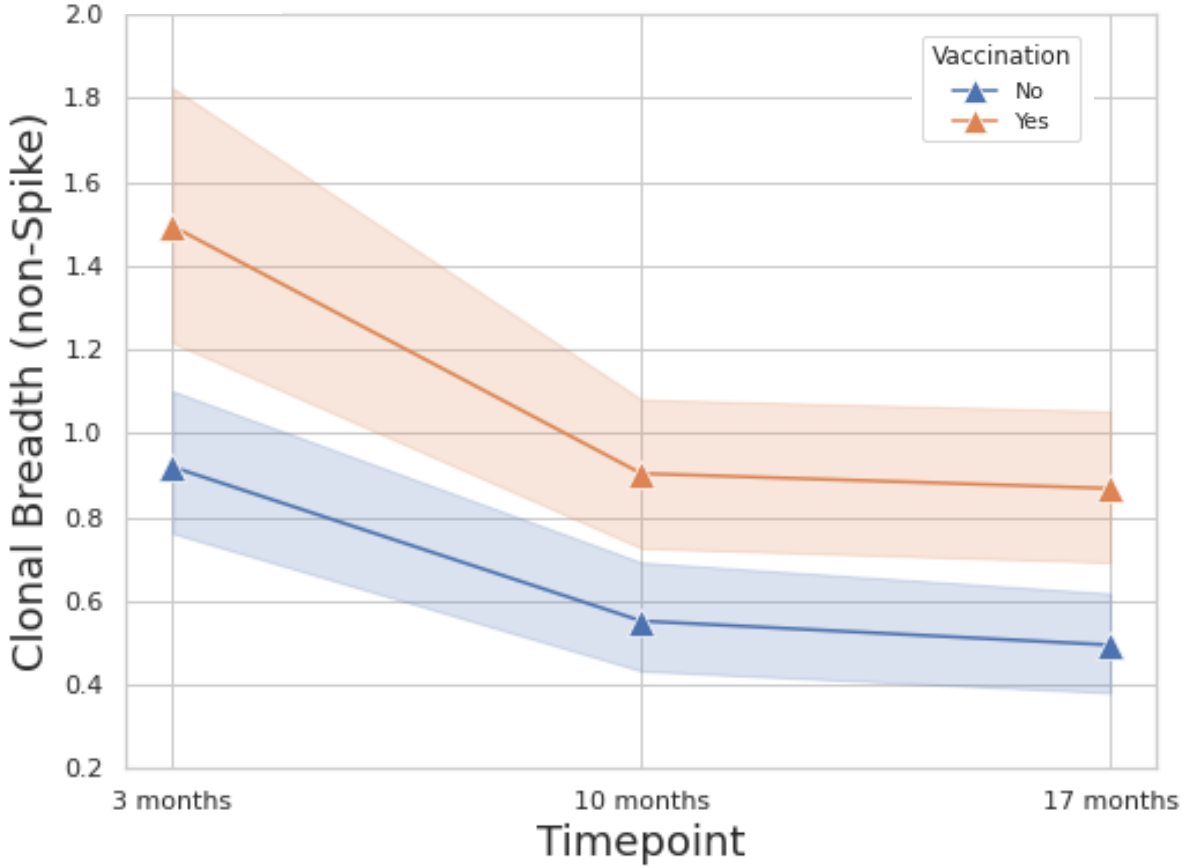


*Omicron mutations calculated by aggregating 75%+ common mutations from over 172 sequences available in GISAID

Long term persistence of T cells and impact of vaccines on spike-associated T cells

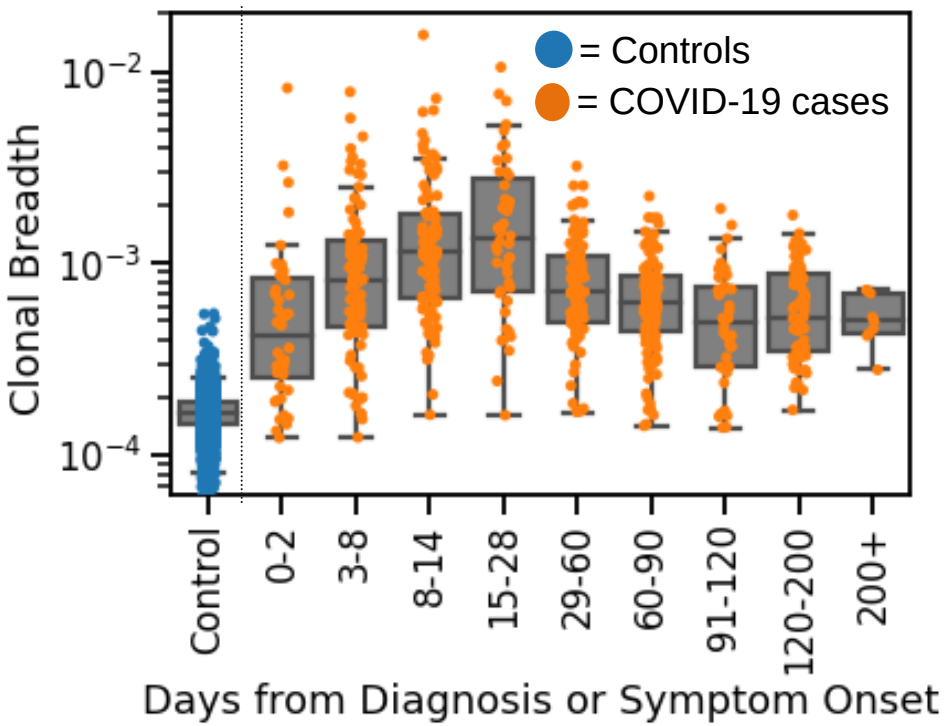
- Data from 72 subjects with prior infection, where 43 were vaccinated around 15-17 months
- Vaccination leads to increase in spike signal only
- Consistent decrease in non-spike signal in both vaccinated and unvaccinated cases



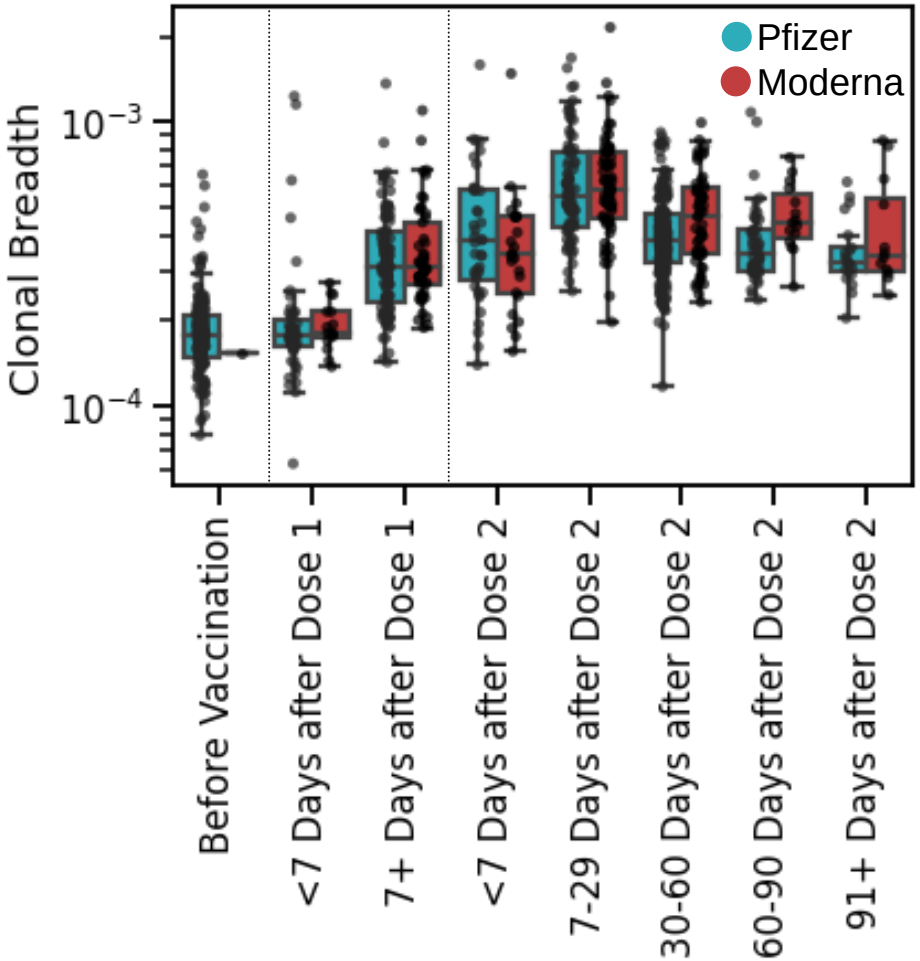


Breadth of the T-cell response during and after infection or vaccination

Infection



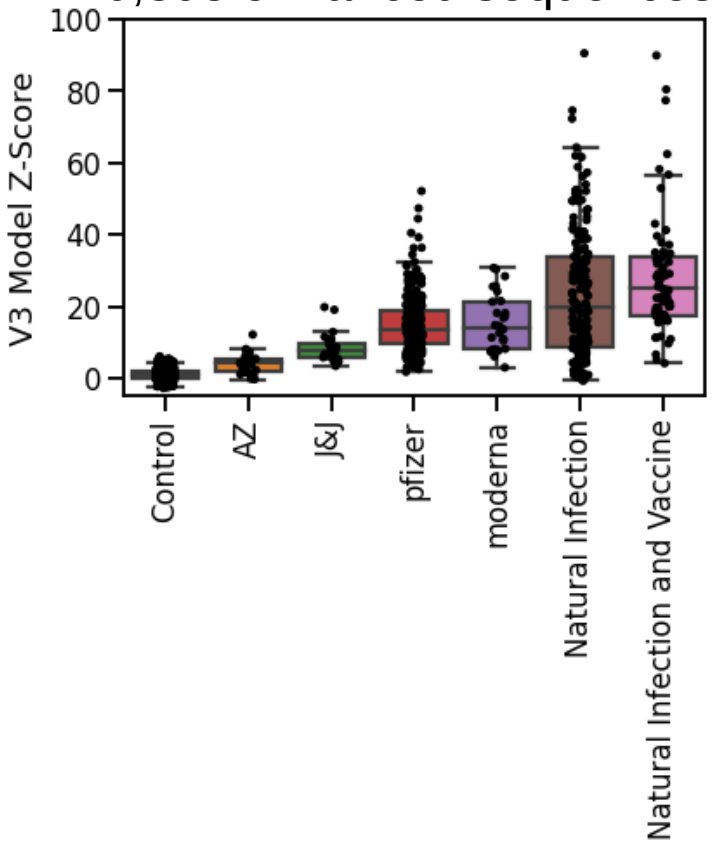
Vaccination



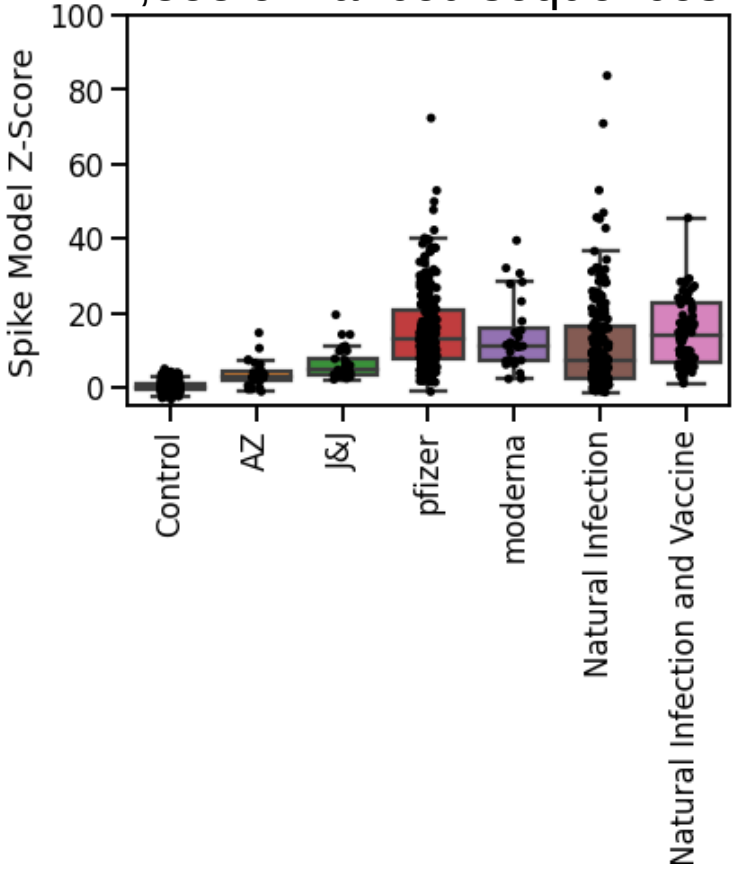
mRNA vaccines effectively promote spike-focused T cell response

Median response to spike higher from mRNA vaccines; across all proteins natural infection leads to more T cells

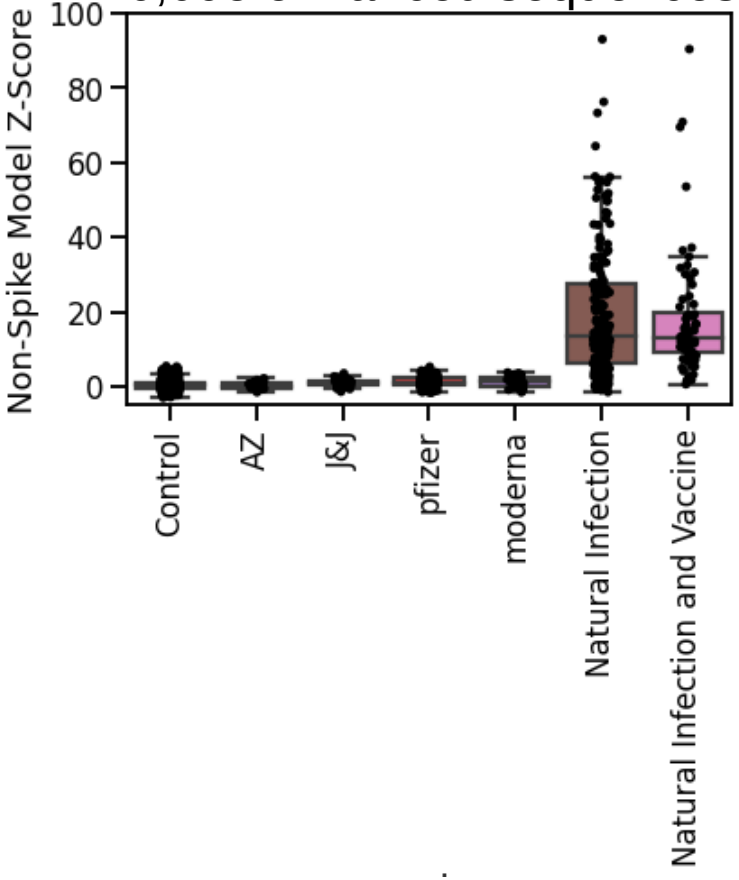
Whole virus (v3) model
10,398 enhanced sequences



Spike model
1,858 enhanced sequences

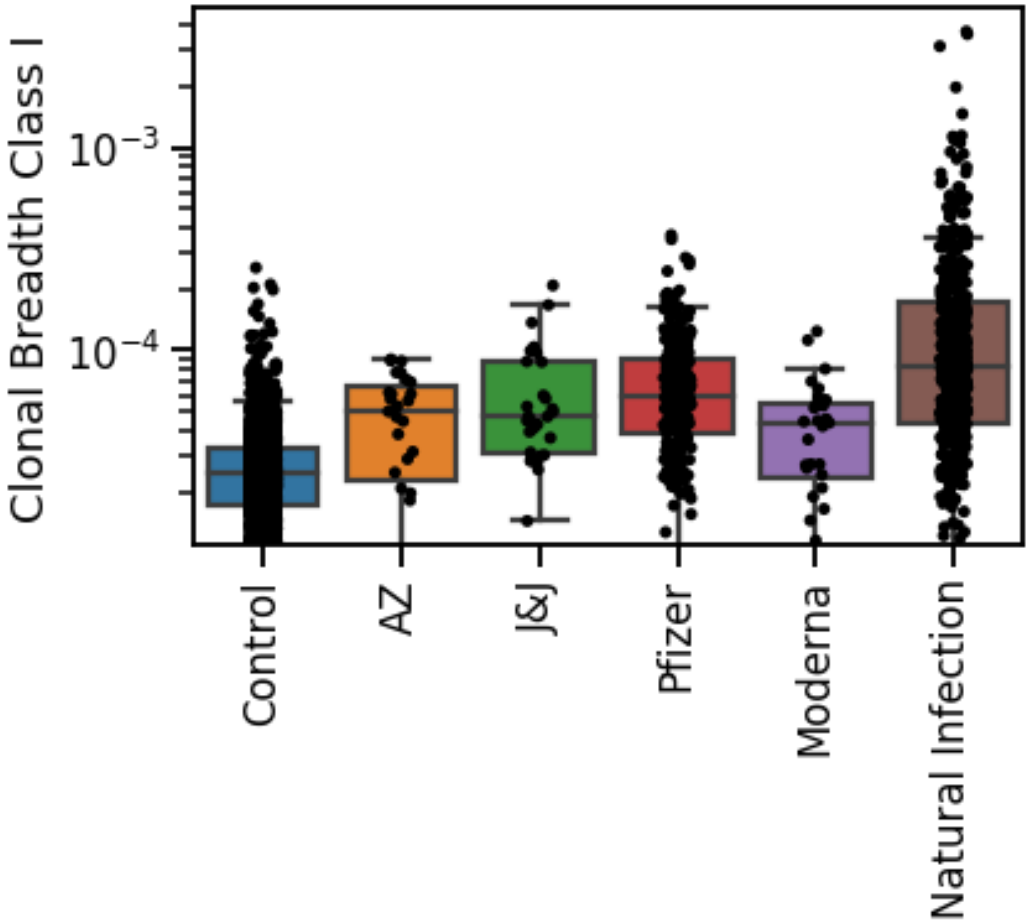


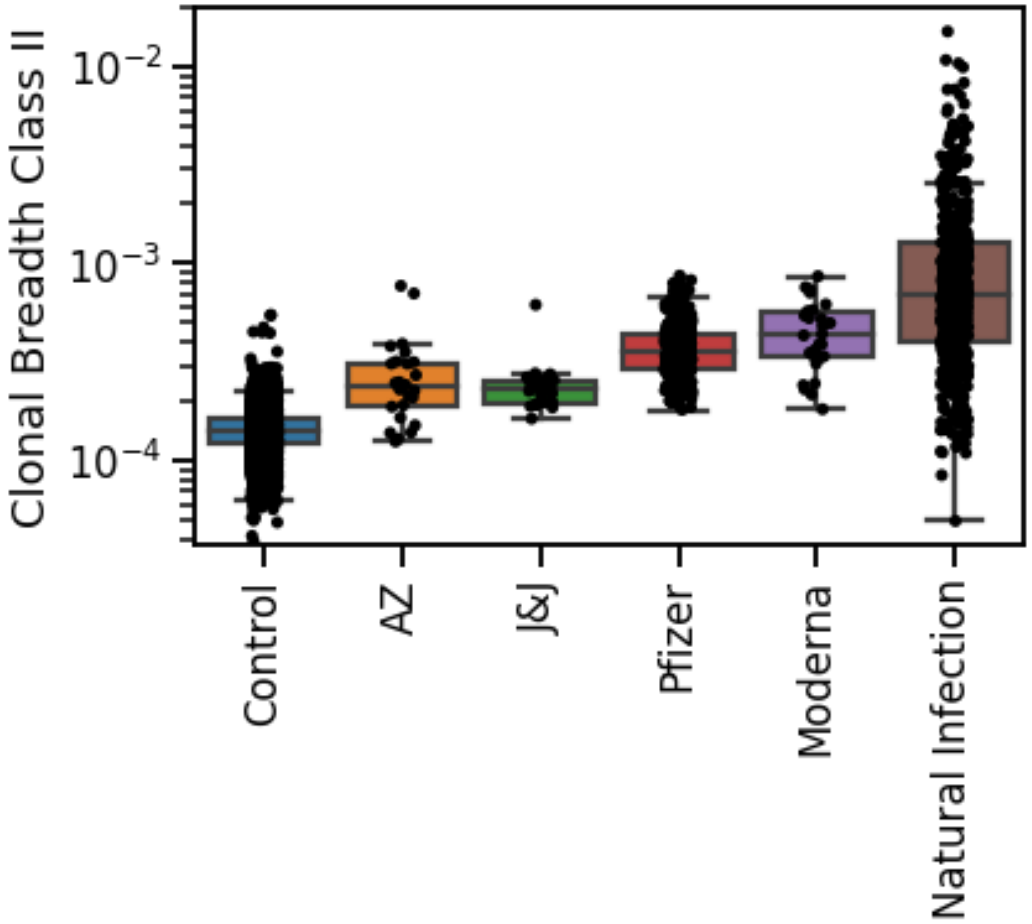
Non-Spike model
6,095 enhanced sequences



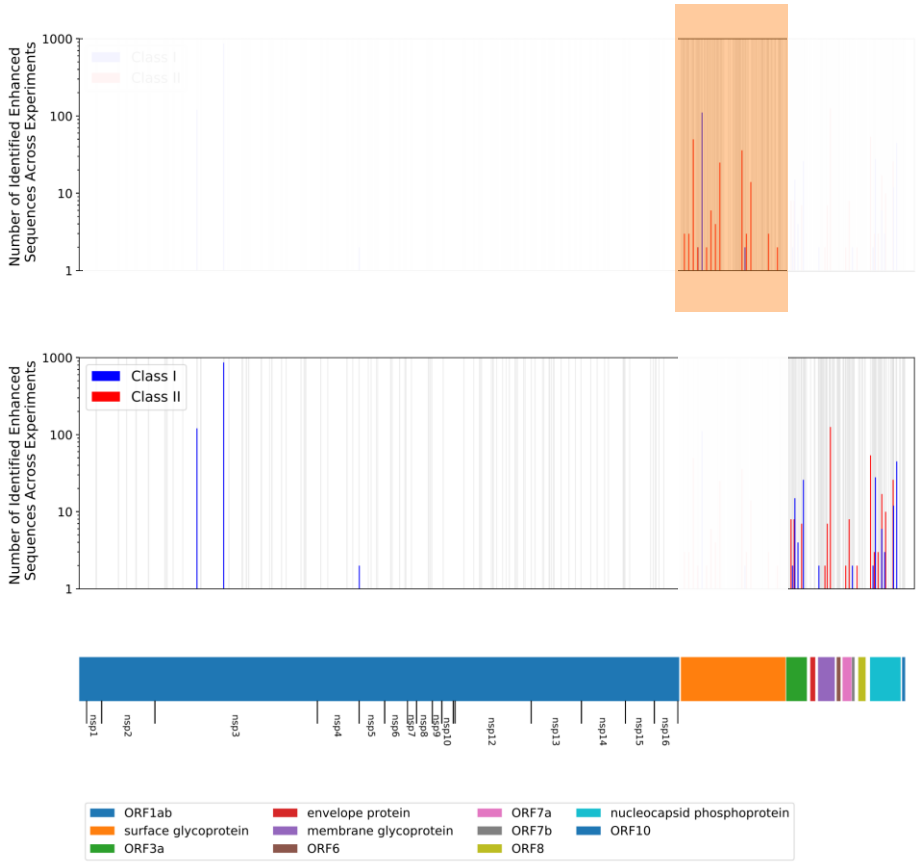
Class I and class II response across vaccines and natural infection

Across all proteins, natural infection leads to more CD4 and CD8 T cells than any vaccine

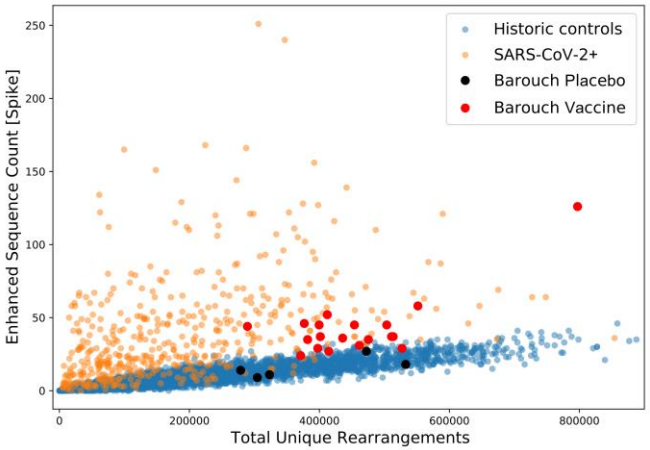




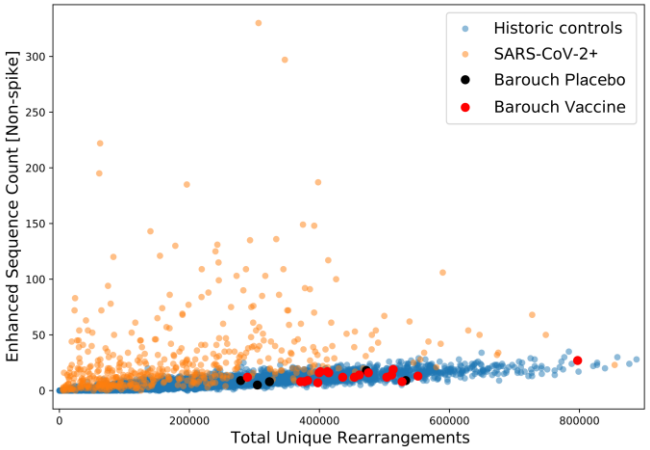
T-cell response to spike vs. non-spike can be used to distinguish infection from vaccination



Spike only sequences



Non-Spike sequences



Scalable technology now exists to measure T cell response in both the individual and at population level

March 2021:
Coronavirus (COVID-19) Update: FDA Authorizes Adaptive Biotechnologies T-Detect COVID Test

EMERGENCY USE AUTHORIZATION
(EUA GRANTED BY THE FDA)

Assessing T cells helps us answer the following critical questions

- Vaccine efficacy over time (determine booster schedules)
- Determining at-risk populations (e.g. racial disparities, elderly, immunocompromised, etc.)
- Guide design and assess efficacy of next-generation vaccines
- Individual risk assessment
- Variant impact assessment

Call to action to establish T cell response as a correlate of protection to SARS-CoV-2 vaccination

- Broad inclusion of T-cell assessment in research on immune response to COVID and COVID vaccines (and potentially other COVID research)
- Required assessment of both cellular and humoral response in COVID vaccine studies