Highly conserved, non-human-like, and cross-reactive SARS-CoV-2 T cell epitopes for COVID-19 vaccine design and validation

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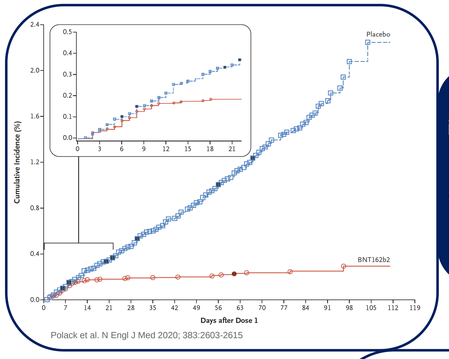
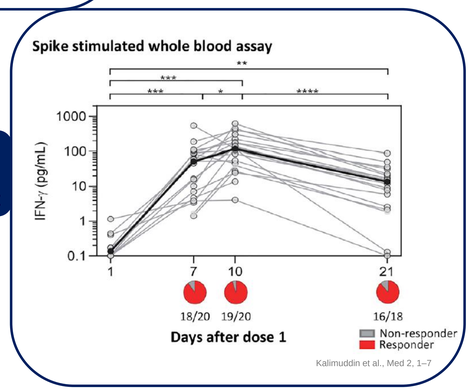
Introduction



Polack et al. N Engl J Med 2020; 383:2603-2615

Rapid induction of protective immunity following a single dose of currently approved COVID-19 vaccines points to pre-existing T cell-mediated immune memory responses that are activated by vaccination.

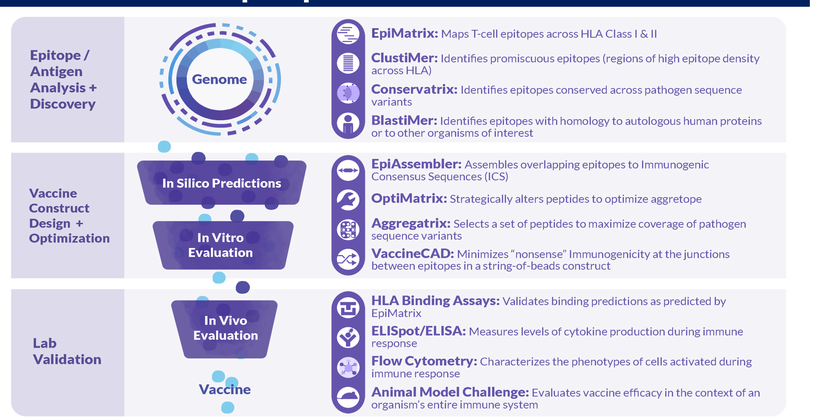


Kalimuddin et al., Med 2, 1–7

Early T cell responses are associated with COVID-19 RNA vaccine efficacy onset

T cell-directed SARS-CoV-2 Vaccine Development

Epitope Identification

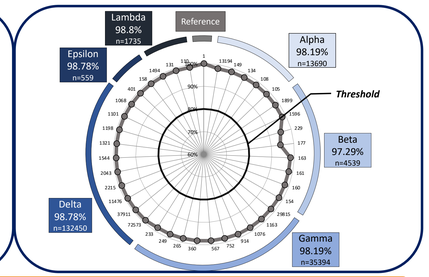


SARS-CoV-2 S/M/E sequences from GenBank

63 HLA class II epitope clusters

42 clusters with no human cross-conservation

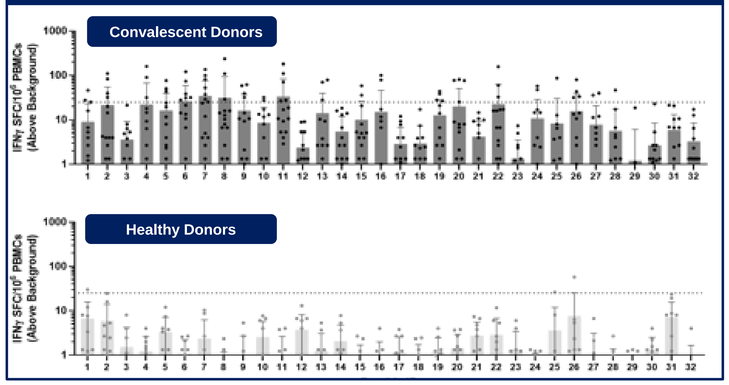
32 clusters with no peptide synthesis red flags



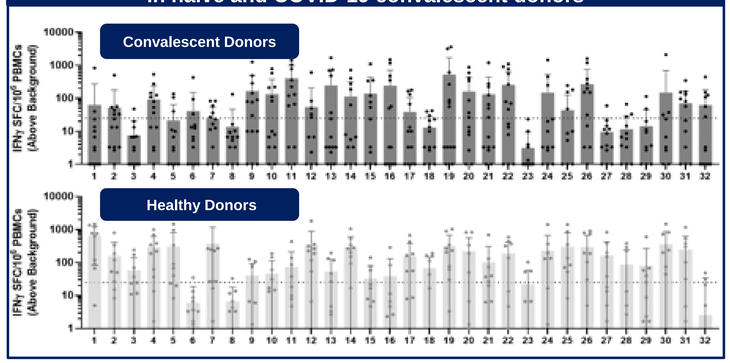
Predicted epitopes are highly conserved across SARS-CoV-2 variants

Epitope Validation

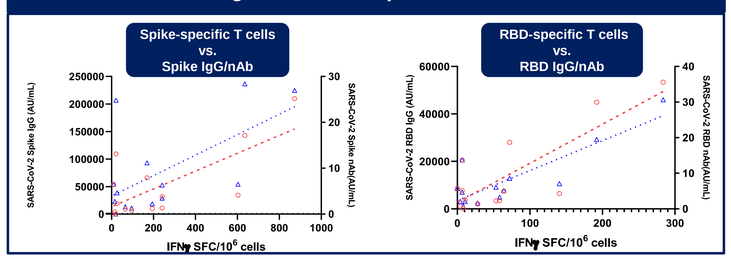
Ex vivo immune recall responses differentiate SARS-CoV-2 naïve and experienced individuals and validate several iVAX-predicted epitopes



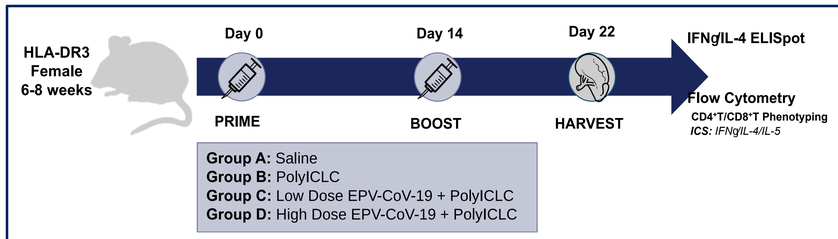
iVAX SARS-CoV-2 peptides stimulate low frequency epitope-specific T cells following expansion in culture in naïve and COVID-19 convalescent donors

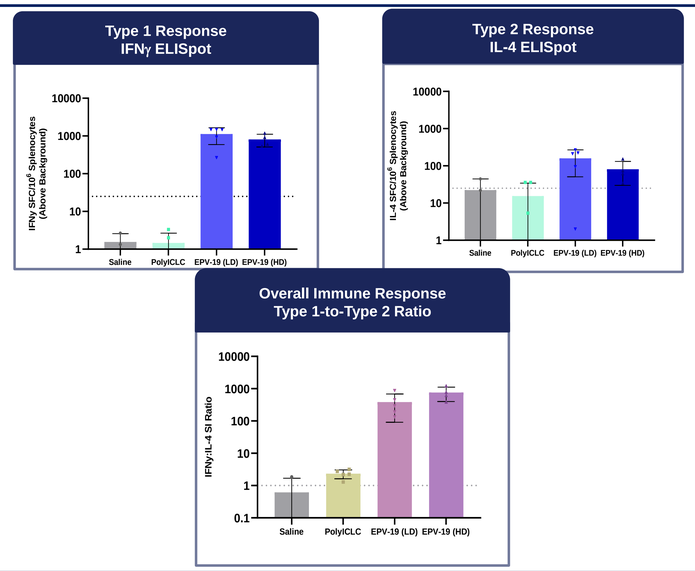


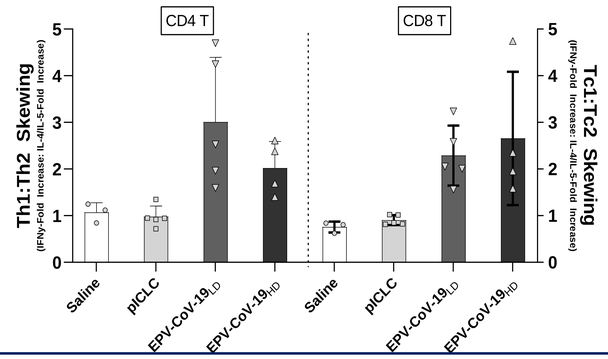
Ex vivo T cell responses to predicted T cell epitopes correlate with total IgG and nAb responses in convalescent donors



Peptide Vaccine Immunogenicity







EPV-CoV-19 peptide vaccination induces a Th1/Tc1 skewed response

Conclusions

- All predicted epitopes are recognized by immune cells generated during infection
- Our SARS-CoV-2 peptides recall a Th1 response in recovered donors
- The predicted SARS-CoV-2 peptides may stimulate pre-existing immunity to common cold coronaviruses
- Cross-reactive memory may boost immunity in infection and vaccination
- Preliminary safety studies identify no induction of the responses associated with ERD following vaccination with EPV-CoV-19
- Robust recall responses can be measured only from Th1/Tc1 cells isolated from vaccinated animals, confirming a targeted response

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