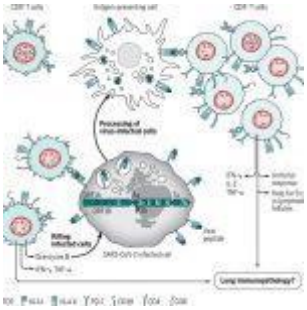
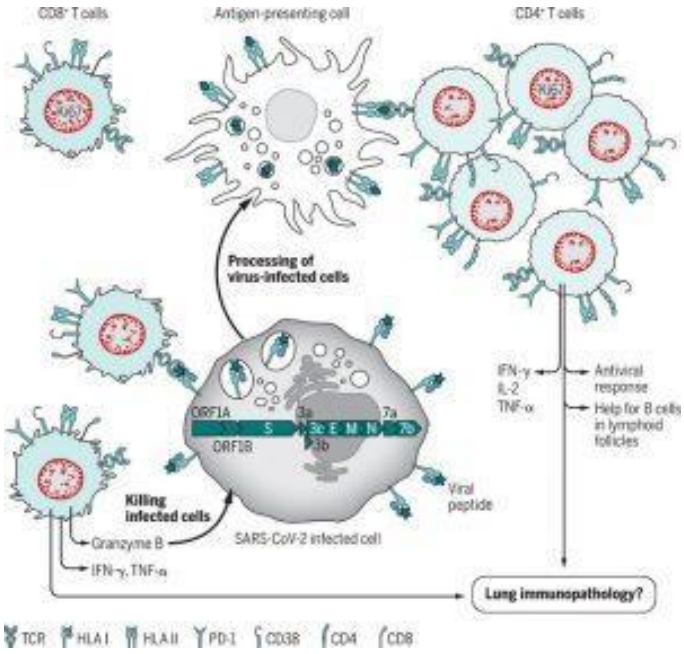
Is there a role of T cells in immune protection to SARS-CoV-2 infection and COVID-19?





Hypothetical interactions between SARS-CoV-2 infected cells, antigen-presenting cells, CD4 and CD8 T cells. Viral peptides (shown in dark green) will be processed from all parts of the SARS-CoV-2 proteome and presented to the TCR repertoire in the grooves of HLA I molecules on the infected cell, and by HLA II molecules of antigen-presenting

cells that have taken up debris from infected cells. SARS-CoV-2-reactive CD4 cells appear to be largely Th1-like, secreting IFN-γ, TNF-α and IL-2. CD8 cells can secrete a similar cytokine profile but also lyse infected target cells. We are unaware of data at present clearly indicating a role of CD4 or CD8 T cells in lung immunopathology, but illustrate here the hypothetical likelihood of this. (Source: Altman & Boyton 2020)

There are a number of studies emerging that show people infected with SARS-CoV-2 make robust T cell responses that target the spike protein, membrane antigens and nucleocapsid, with immunodominant responses against spike (See table below). With recent findings that neutralising antibodies to SARS-CoV-2 wane rapidly after peak symptoms, is there evidence that T cell memory responses linger for longer? A recent perspective article in Science poses this question and provides evidence about the type and duration of T cell responses. An intriguing question is whether the asymptomatic nature of infection in children is possibly due to cross-reactive T cell responses from other Coronaviruses in circulation. There are currently no answers to any of these questions and represents a fertile ground for research. It will also be important to assess whether pending vaccine-induced responses are antibody-mediated or due to the elicitation of a T cell response. In other words, would vaccine-induced T cell immunity represent a mechanism of protection and antibodies a correlate of protection?

Also Read: **Rapid decay of IgG to SARS-CoV-2 in people with mild COVID-19**

Journal Article: Altman & Boyton. 2020. [SARS-CoV-2 T cell immunity: Specificity, function, durability, and role in protection.] Science Immunology

Summary by Clive Gray

Manuscript	Methods	Cohort	T cell subsets, features	Antigen hierarchy	Epitope data	Cytokine/Effector function	Cross-reactivity evidence
Braun et al (10)	Spike peptide panel, ELISA	Mild, severe, ICU COVID-19	CD38+HLA-DR+ activated T cells	Analysis limited to Spike	nd	nd	Few, a third of HC responded to C-terminal peptides from Spike
Thieme et al. (7)	Peptide panels, ICS	Moderate, severe, ICU COVID-19	- CD4 response detected in 95% - CD8 response in 77%	M>S>N	nd	CD4 response: IFN-γ, IL-2, TNF-α. Higher frequency of polyfunctional cells in patients with greater severity	nd
Sekine et al. (8)	Peptide panels; ICS; AIM; tetramers.	Moderate to severe COVID-19; exposed family members	+ CD4: CD38+CD69+ 4-1BB+ PD-1+ + CD8: CD38+ CD39+ CD69+ CTLA-4+ HLA-DR+ 4-1BB+ LAG-3+ TIM-3+ 'activated-cycling' phenotype	M>N	Several predicted HLA-A and HLA-B predicted binders from the full proteome used to make tetramers	CD4 response: IFN-γ, IL-2, TNF-α; Th1-skewed response. CD8 response: IFN-γ, TNF-α, CD107a	Yes: cross-reactive recognition of Spike and M
Peng et al. (9)	Peptide pools (not ORF1); ICS; ELISpot; pentamers; T cell lines	Recovered from mild to severe COVID-19	Higher magnitude and broader breadth of T cell responses in severe cases in comparison with mild cases	S>M>ORF3a	Spike: 19 peptides M: 18 peptides M: 6 peptides ORF3a: 6 peptides ORF3a: 3 peptides	IFNγ, IL-2, and TNF-α polyfunctional response in both CD4 and CD8, mild and severe cases	No: none observed in n=19
Grifoni et al. (9)	Mega-pools; AIM; ICS	Mild to severe COVID-19, and pre-2019 samples	Patients were convalescent and showed no evidence of lymphopenia	S>M>N	Antigen mega-pools not resolved to the level of individual epitopes	CD4 response mainly IFN-γ; CD8 is IFN-γ, TNF-α, and granzyme B	Half of HC showed cross-reactivity with RBD from HCoV-OC43 or NL63

Lebert et al. (75)	Peptide pools from N, ORF3 NSP-7 and NSP-13	Mild to severe COVID-19 convalescent	Response in 100% to N epitopes	Study focus on N	N: 7 peptides	nd	All SARS-CoV patients showed cross-reactive response to SARS-CoV-2 NP. Half of HC show cross-reactivity with epitopes in ORF-1 NSP-7 and -13
Gallais et al. (4)	Peptide pools; ELISpot.	Household contacts of 7 PCR+ cases	Response in 100% of index cases and in seronegative contacts	S=M=N co-dominant	nd	nd	nd
Weiskopf et al. (73)	Mega-pools; AIM	ICU ARDS including fatal cases	↑ T cell lymphopenia - Majority of responder cells were Tcm based on CD45RA and CCR7 expression	S>remainder of proteome mega-pool'	Antigen mega-pools not resolved to the level of individual epitopes	T cell culture supernatants contained: IFN-γ, TNF-α, IL-2, IL-5, IL-13, IL-10, IL-9, IL-17A, IL-17F and IL-22	Cross-reactivity in 2/10 HC.
Oja et al. (2)	Peptide pools; AIM; ICS; used PBMC and BAL	Mild, severe, ICU COVID-19	↑ T cell lymphopenia ↑ PD-1 highest in most severe	S>N>M>ORF3a. Spike response seen in BAL. Reduced response to Spike and N in ICU cases	nd	Mainly IFN-γ and TNF-α. IFN-γ response significantly lower in ICU cases	No cross-reactivity found to Spike peptides from S229E, S-OC43

Source: Altman & Boyton 2020