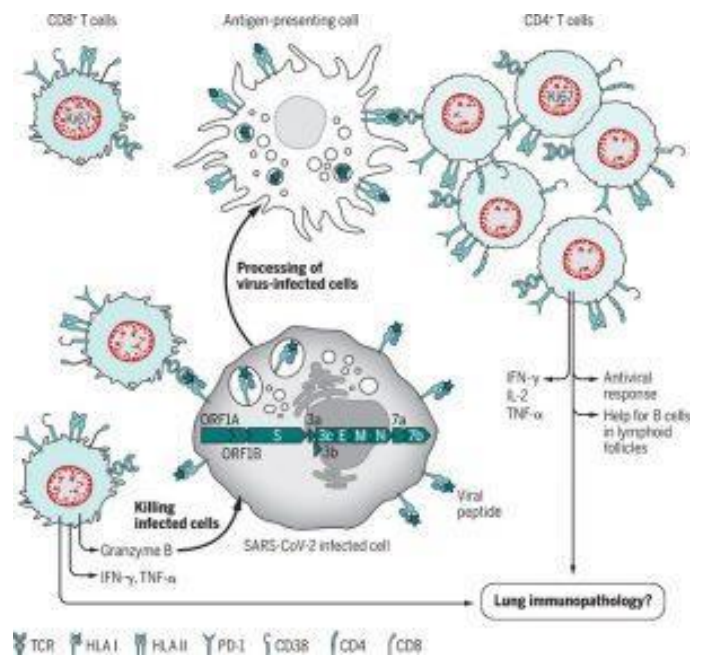
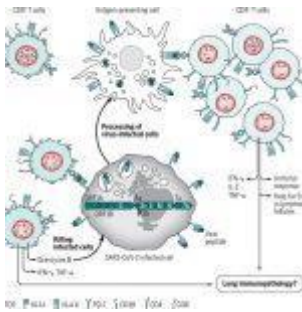


Is there a role of T cells in immune protection to SARS-CoV-2 infection and COVID-19?



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
Bevan et al (78)	Spike peptide panel, MHC	Mild, severe, ICU COVID-19	CD8 ⁺ HLA-DP ⁺ activated T cells	Analysis limited to: Spike	nd	nd	Yes: a third of HC responded to C-terminal peptides from Spike
Thieme et al (75)	Peptide panels, IC3	Moderate, severe, ICU COVID-19	- CD4 ⁺ response detected in 90% - CD8 ⁺ response in 77%	M-H-H	nd	CD4 response: IFN- γ , IL-2, TNF- α Higher frequency of polyfunctional cells in patients with greater severity	nd
Sehmi et al (8)	Peptide panels, IC3, AMI, tetramers	Moderate to severe COVID-19: exposed family members	+ CD4 ⁺ CD8 ⁺ CD45 ⁺ IL-7 ⁺ PD-1 ⁺ + CD8 ⁺ CD8 ⁺ CD45 ⁺ CD45 ⁺ CTLA-4 ⁺ HLA-DP ⁺ HLA-DR ⁺ LAG-3 ⁺ TIM-1 ⁺ "activated-cycling" phenotype	M-H	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 T _H 1-skewed response CD8 response: IFN- γ , TNF- α , CD137a	Yes: cross-reactive recognition of Spike and M
Peng et al (9)	Peptide pools (not overlapping IC3); Multipot; post-tetramers; 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-H-DP/3a	Spike: 18 peptides N: 18 peptides M: 8 peptides ORF3a: 4 peptides ORF3a: 3 peptides	IFN- γ , IL-2, and TNF- α polyfunctional response in both CD4 and CD8, mild and severe cases	No: none observed in n=16
Griffen et al (9)	Mega-pools; AMI, IC3	Mild to severe COVID-19, and pre-COVID samples	Patients were convalescent and showed no evidence of lymphopenia	S-M-H	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 MHC from HCoV OC43 or NL63

Lebert et al. (24)	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. (23)	Mega-pools; AIM	ICU ARDS including fatal cases	- T cell lymphopenia - Majority of responder cells were Tcm based on CD45RA and CD47 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-18, IL-9, IL-17A, IL-17F and IL-32	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+ORF3s. 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 S299E, S-0043

Source: Altman & Boyton 2020