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Covid-19 vaccines: delivering protective immunity

Evidence supports both T and B cell responses to the three leading vaccines

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Early in the covid-19 pandemic it was unclear whether and how individuals and populations would develop protective and enduring immunity against SARS-CoV-2, either after infection or vaccination. Initial focus was on defining virus neutralising antibodies from B cells after infection. Early reports indicated that such antibodies decline substantially over less than six months, raising questions about how long protective immunity might last following infection. T cells are also known to be important in protecting against many viral infections through processes known as cellular immunity. Defining the roles of T cells in covid-19 became a central focus for investigation.[1]

Both memory T cell and B cell responses specific to SARS-CoV-2[2 3] have now been found up to six months after infection. Similar T and B cell responses might be expected following vaccination, and may account for the good efficacy suggested by interim results from the three most advanced vaccine candidates.[4-6] All three vaccines—two mRNA vaccines (Pfizer-BioNTech and Moderna) and a DNA vaccine (Oxford-AstraZeneca)—encode genetic information, enabling the body to produce a viral antigen (the spike protein) that stimulates an immune response. In phase I and II trials, all three vaccines induced neutralising antibodies to the spike protein and also cellular immune responses.[7 8] Interim data from phase III trials suggest all three vaccines protect against symptomatic infection with SARS-CoV-2.

Trials of the two RNA vaccines report efficacies above 90%. The viral vector DNA vaccine trial (Oxford-AstraZeneca) reported an average of 70% efficacy, ranging from 62-90% in subgroups receiving different vaccination dosages.[5] Both the Oxford-AstraZeneca group and Pfizer-BioNTech group have published their phase III trials in peer reviewed journals (*Lancet* and *New England Journal of Medicine* respectively[5 6]), confirming efficacy claims made in earlier press releases. However, the Moderna mRNA vaccine group has so far released only limited data. Medicines regulators in the UK and US have now approved the Pfizer-BioNTech vaccine for emergency use after reviewing all the short term safety, efficacy, and quality data submitted by the manufacturer.

Cellular immunity

What role might immune cellular responses play in the development of immunity to SARS-CoV-2 and what are the implications for vaccines? As T cells recognise and respond to viral antigens they produce many protective reactions and effector molecules. One such molecule is the cytokine interferon γ, secreted by CD4+ and CD8+ T cells and their memory cells. This can be measured in laboratory tests such as the ELISpot assay as a means of documenting specific T cell responses to viral antigens.[9-11]

Individuals with high antibody levels after infection have been shown to have a high number of SARS-CoV-2 specific T cells secreting interferon γ.[10] T cells producing interferon γ have also been detected a median of 75 days after PCR confirmed covid-19 in people with undetectable SARS-CoV-2 antibodies,[10] suggesting immunity is partly mediated and maintained by memory T cells. Finally, a preprint of a recent study of 100 people with a history of asymptomatic or mild covid-19 reports T cell mediated immune responses lasting for at least six months in all participants.[11]

These studies and others[3 10 12] offer strong evidence that T cell immune responses are sustained, even in the face of declining or undetectable antibodies, implying that some immunity persists. It is possible, but as yet unconfirmed, that immunity might last even longer, as T cell responses to SARS-CoV-1 and MERS-CoV have been found several years after infection.[13] The evidence from new studies, interim results from phase III vaccine trials, and previous data from phase I and phase II trials support the notion that memory T cell responses to the vaccines, along with B cell antibody responses, should provide good and possibly enduring immunity to SARS-Cov-2. This, together with continuing public health measures, should help lay a pathway out of the pandemic.

High vaccine uptake will be critical to achieving individual and population immunity. Equitable global access to effective vaccines is also essential. Open debate and public education campaigns will be required to build trust and counter vaccine hesitancy[14] and effective pharmacovigilance[15] will be needed to monitor long term safety. Continued research and development will be needed to stay ahead of potentially consequential viral mutations,[16] which could have negative consequences for covid-19 vaccines.

The scientific achievements since SARS-CoV-2 was first identified less than year ago give grounds for optimism that within a reasonable timeframe we should, globally, be able to successfully manage this pandemic. We should also have learnt enough to prepare for—if not to avert—future epidemics and pandemics.

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