T follicular helper cells and the germinal centre are required for memory B cell formation and humoral immunity after ChAdOx1 nCoV-19 vaccination.

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Abstract

Emergence from the SARS-CoV-2 pandemic has been facilitated by the fast rollout of multiple effective COVID-19 vaccines. Robust serum SARS-CoV-2-specific antibody serves as an excellent correlate of protection; thus, successful vaccines produce high affinity antibody producing plasmablasts and long-lived memory B cells to provide protection from infection. The contribution of the germinal centre to SARS-CoV-2 humoral immunity is unclear. Here, we show a requirement for T follicular helper (Tfh) cells and the germinal centre (GC) reaction for optimal serum antibody and memory B cell formation after ChAdOx1 nCoV-19 vaccination in both mice and humans. We found that Tfh cells and the GC play an important role in the amplification of antigen specific B cells, while identifying Tfh cell dependent and independent subsets of memory B cells. Upon booster vaccination, GC B cells generated during primary immunisations can be recalled in secondary responses as either GC B cells again, or as other effector cell types. Likewise, GC-Tfh cells generated during a primary immunisation can be recalled as both Tfh and Th1 cells upon recall immunisation, highlighting the pluripotent nature of Tfh cell memory. This study demonstrates that vaccine induced germinal centres are a critical source of humoral immunity following ChAdOx1 nCoV-19 vaccination.