

IN BRIEF

COVID-19

SARS-CoV-2 vaccine — think globally, act locally

In this preprint, Hassan et al. show that local immunization with the ChAd-SARS-CoV-2-S vaccine, based on a chimpanzee adenovirus, confers sterilizing protection in mice engineered to express human ACE2. Intramuscular delivery of ChAd-SARS-CoV-2-S protected against lung pathology but did not clear the infection of the upper respiratory tract after SARS-CoV-2 challenge. However, when administered intranasally, it induced local neutralizing antibody and T cell responses that provided superior protection to both the upper and lower respiratory tract, with no signs of viral replication 8 days post viral challenge. The presence of tissue-resident memory T cells in the lung suggested long-lasting protection. This work illustrates the importance of the delivery route to vaccine effectivity.

ORIGINAL ARTICLE Hassan, A. O. et al. A single intranasal dose of chimpanzee adenovirus-vectored vaccine confers sterilizing immunity against SARS-CoV-2 infection. Preprint at bioRxiv <https://doi.org/10.1101/2020.07.16.205088> (2020)

COVID-19

Antibody response to SARS-CoV-2 — sustained after all?

Recent studies have indicated that antibody responses to SARS-CoV-2 drop significantly within 2 months. In this preprint, Wu et al. analysed antibody responses in 349 individuals who were among the first to become infected with SARS-CoV-2. All antiviral antibody titres significantly increased in the first weeks after disease onset, followed by a contraction phase, where IgM became undetectable at around week 10–13. Importantly, although Spike-targeted IgG (IgG-S) declined over time, it remained detectable at relatively high levels until the end of the 6-month study period. IgG-S titres correlated closely with neutralizing capacity, although exact correlates of protection for SARS-CoV-2 are still elusive. These results suggest that antibody responses in symptomatic patients with COVID-19 follow a prototypical progression and result in a sustained memory response, suggesting long-term protective immunity.

ORIGINAL ARTICLE Wu, J. et al. SARS-CoV-2 infection induces sustained humoral immune responses in convalescent patients following symptomatic COVID-19. Preprint at medRxiv <https://doi.org/10.1101/2020.07.21.20159178> (2020)

COVID-19

Getting to the (germinal) centre of SARS-CoV-2

Robust antibody responses rely on affinity maturation, which predominantly occurs in germinal centres (GCs) located in secondary lymphoid organs (SLOs). This preprint describes the absence of GCs in patients with fatal COVID-19, suggesting that SARS-CoV-2 might impair humoral immune responses by disrupting SLO architecture. The authors report a specific block in BCL-6⁺ T follicular helper (T_{FH}) cell differentiation and an increase in T helper 1 (T_H1) cells, as well as aberrant TNF production, at the site of T_{FH} cell differentiation. Increased levels of SARS-CoV-2-specific circulating plasmablasts, likely of extrafollicular origin, were found to correlate with systemic inflammation. It remains unclear whether the loss of GCs also occurs in COVID-19 survivors and whether this may cause an inefficient and short-lived antibody response.

ORIGINAL ARTICLE Kaneko, N. et al. The loss of Bcl-6 expressing T follicular helper cells and the absence of germinal centers in COVID-19. Preprint at SSRN <https://doi.org/10.2139/ssrn.3652322> (2020)

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INFLAMMATION

Highs and lows of the LPS response

The histone deacetylase activity of HDAC3 is associated with transcriptional repression, but there is also evidence that HDAC3 has non-enzymatic functions in transcriptional activation, such as the inflammatory response to lipopolysaccharide (LPS). A report in *Nature* describes a mechanism by which HDAC3 can fine-tune the LPS response by balancing transcriptional activation and repression.

Using *Hdac3*-knockout bone marrow-derived macrophages transduced to express wild-type HDAC3 or a catalytically inactive mutant, Nguyen et al. investigated the transcriptional response to LPS in vitro. One-third of the genes that were differentially expressed after LPS stimulation of wild-type cells were not differentially expressed by *Hdac3*-knockout macrophages. Of these HDAC3-dependent,

LPS-responsive genes, the differential expression of more than half could be rescued by inactive HDAC3 (referred to as deacetylase (DA)-independent genes). These were mainly pro-inflammatory genes that were upregulated by LPS. HDAC3-dependent genes that were downregulated by LPS stimulation could not be rescued by inactive HDAC3 (DA-dependent genes) and were mainly involved in regulating Toll-like receptor signalling.

LPS stimulation increased the occupancy of HDAC3 close to the transcription start sites of the DA-independent genes but not the DA-dependent genes, associated with increased enhancer activity at the DA-independent genes. Conversely, enhancer activity proximal to DA-dependent genes was decreased by LPS stimulation but increased in the absence of HDAC3, consistent with the known

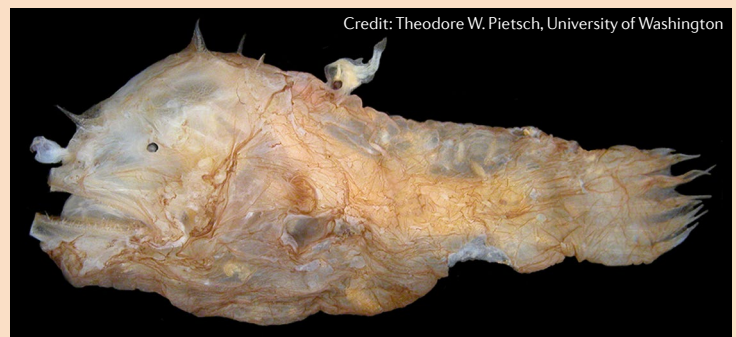
EVOLUTIONARY IMMUNOLOGY

Loss of immunity lets a sexual parasite hold on tight

Certain species of deep-sea anglerfish employ a unique reproduction strategy (sexual parasitism) that involves the permanent joining of males to females. Thomas Boehm and colleagues now report that these Ceratioidei fish have lost key components of adaptive immunity.

During mating, the tiny male deep-sea anglerfish attach themselves to relatively gigantic females. In some species,

there is fusion of epidermal and dermal tissues and joining of circulatory systems, with the male becoming permanently dependent on the female for nutrients. Swann et al. set out to explore how this naturally occurring form of parasitism can occur between non-identical individuals without provoking allogeneic rejection. They generated whole genome sequences for ten species of Ceratioidei that mate through temporary



Credit: Theodore W. Pietsch, University of Washington