Delving into the microbiome to identify specific organisms that might mediate the protective effect, the authors honed in on a group of 28 Clostridiales. Remarkably, colonization of antibiotic-treated mice with one of these, *Clostridium scindens*, reduced CHIKV infection in the serum and restored type I IFN levels to those detected in vehicle-treated mice. Colonization with *C. scindens* also prevented transmission of the virus back to mosquitoes after exposing them to the blood of treated mice. *C. scindens* encodes an enzyme that converts primary bile acid into secondary bile acids. Oral administration of secondary bile acid to antibiotic-treated mice prior to CHIKV infection resulted in reduced virus titres and restored type I IFN responses. Thus, the microbiome provides antiviral protection through a bile acid–pDC–IFN signalling axis.

**IN BRIEF**

**COVID-19**

Preventing escape from neutralizing antibodies

Convalescent plasma (CP) and monoclonal antibodies (mAbs), two approaches being evaluated for COVID-19 therapy, are vulnerable to antibody-resistance mutations in SARS-CoV-2 that maintain viral fitness. This preprint describes the use of replication-competent chimeric viruses to generate spike protein escape mutants to four CP samples and three mAbs. Viral RNA from resistant cultures was used to identify shared and treatment-specific escape mutations. The mutations identified in this study are currently found at low frequencies in sequencing databases, but this methodology could be used to monitor emerging virus variants and predict their impact on mAb treatments. These findings support the use of combination mAb regimens and the design of vaccines targeting conserved B cell and T cell epitopes to prevent mutational escape.

*ORIGINAL ARTICLE* Weiskuhl, Y. et al. Escape from neutralizing antibodies by SARS-CoV-2 spike protein variants. Preprint at bioRxiv https://doi.org/10.1101/2020.07.21.214799 (2020)

**COVID-19**

IgGs drive COVID-19 myeloid hyperinflammation

Recent studies have identified an aberrant myeloid cell activation programme in patients with COVID-19. In this preprint, Hoepel et al. elucidate a mechanism by which alveolar macrophages facilitate hyperinflammation. Serum IgGs, in complex with spike protein, from patients with severe COVID-19 were shown to induce a potent pro-inflammatory response in human macrophages through multiple FcyRs, but mainly through FcγRII. Blockade of this pathway using an inhibitor of the kinase SYK counteracted the pathological production of IL-6, IL-1β and TNF. Interestingly, in vitro exposure of endothelial cells to serum IgGs from these patients resulted in loss of barrier integrity and increased coagulopathy. These results improve our understanding of the abnormal myeloid response in COVID-19 and identify a potential therapeutic target.

*ORIGINAL ARTICLE* Hoepel, W. et al. Anti-SARS-CoV-2 IgG from severely ill COVID-19 patients promotes macrophage hyper-inflammatory responses. Preprint at bioRxiv https://doi.org/10.1101/2020.07.13.190140 (2020)

**COVID-19**

ACE2 is not induced by interferon

Interferon (IFN) is emerging as a promising therapeutic for COVID-19. Yet it was also proposed that IFN induces transcription of the SARS-CoV-2 entry receptor ACE2, potentially increasing viral infectivity. In this preprint, Onabajo et al. show that it is actually a shorter transcript of ACE2, coined dACE2, that was previously detected by RNA sequencing upon IFN exposure. Expression of dACE2, but not the canonical ACE2, is induced by viral infection as well as treatment with type I, II and III IFNs. dACE2 is also highly expressed in several tumour tissues, owing to an inflamed microenvironment that resembles virus-infected tissues. Importantly, dACE2 cannot bind to the SARS-CoV-2 spike protein receptor-binding domain and lacks carboxypeptidase activity, dispensing concerns that IFN treatment might enhance viral infection.

*ORIGINAL ARTICLE* Onabajo, O. O. et al. Interferons and viruses induce a novel primate-specific isoform dACE2 and not the SARS-CoV-2 receptor ACE2. Preprint at bioRxiv https://doi.org/10.1101/2020.07.19.210955 (2020)

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