engineered to express Als1 could induce IgA and IgG responses. Notably, when C. albicans was isolated from monocolonized wild-type or Rag1-/- mice and then competed in naive wild-type or Rag1-/- mice, fungi retrieved from wild-type mice showed a significant competitive advantage in both recipient groups. Therefore, the adaptive immune response to C. albicans increases the fitness of the fungus. This advantage was lost if the experiments were repeated using a yeast-locked strain of C. albicans, indicating that immune-mediated selection depends on the yeast-to-hyphal transition.

Candida species including C. albicans are associated with IBD, and in a final set of experiments the authors showed that C. albicans hyphae and expression of adhesins exacerbate colonic inflammation in a chemically induced colitis model. When mice were vaccinated using the anti-Candida NDV-3A vaccine — that targets Als3 and has been shown in human clinical trials to prevent recurrent vaginal yeast infections — the animals generated Als3-reactive IgA and IgG and showed reduced C. albicans-associated damage during chemical colitis.

Therefore, T cell-dependent IgA responses can select for fungi that are less pathogenic and more fit, thereby mutually benefitting the host and the commensal. The authors suggest that vaccinating to enhance these beneficial adaptive immune responses against commensal fungi could limit human IBD.

Yvonne Bordon

ORIGINAL ARTICLE Ost, K. S. et al. Adaptive immunity induces mutualization between commensal eukaryotes. Nature https://doi.org/10.1038/s41586-021-03722-w (2021)

COVID-19

Pan-sarbecovirus mAb protects from variants

Current vaccines for COVID-19 induce immune responses to immunodominant but highly variable SARS-CoV-2 epitopes. Given the continuing emergence of variants of concern and threat of zoonotic spillovers, pan-protective monoclonal antibodies (mAbs) are highly desirable. A report in Nature by Tortorici et al. now describes a human mAb (S2X259) that binds a highly conserved cryptic receptor-binding domain epitope of SARS-CoV-2. S2X259 cross-reacts with spike proteins from all four sarbecovirus clades and protected Syrian hamsters from challenge with prototypic SARS-CoV-2 and with the SARS-CoV-2 beta variant. Apart from identifying S2X259 as a promising candidate for clinical development, the discovery of a target site for broadly neutralizing antibodies may also guide efforts to develop pan-sarbecovirus vaccines that protect against SARS-CoV-2 variants and future cross-species transmission.

ORIGINAL ARTICLE Tortorici, M. et al. Broad sarbecovirus neutralization by a human monoclonal antibody. Nature https://doi.org/10.1038/s41586-021-03817-6 (2021)

COVID-19

Poor nasal immunity can lead to severe COVID-19

The clinical picture of COVID-19 varies widely. Many SARS-CoV-2-infected individuals have upper respiratory symptoms only, indicating that local immunity can constrain viral pathologic to the nasopharynx. A study in Cell by Ziegler et al. investigated early intrinsic immune responses by single-cell RNA-seq of nasopharyngeal swabs from 58 individuals, including 35 who were recently diagnosed with COVID-19. In patients with mild-to-moderate disease, epithelial cells expressed antiviral and interferon-responsive genes. These responses were muted in individuals with severe COVID-19, despite equivalent viral loads. Severe disease was also characterized by the mucosal recruitment of highly inflammatory myeloid populations. The authors mapped viral tropism to specific epithelial cell subsets and defined host pathways that were linked with susceptibility or resistance. Overall, their study suggests that failed nasal epithelial antiviral immunity underlies severe COVID-19 and that host responses in the nasal mucosa are an essential determinant of the overall disease trajectory.

ORIGINAL ARTICLE Ziegler, C. G. K. et al. Impaired local intrinsic immunity to SARS-CoV-2 infection in severe COVID-19. Cell https://doi.org/10.1016/j.cell.2021.07.021 (2021)

COVID-19

Detecting future coronavirus pandemics

The past two decades saw several spillovers of animal coronaviruses (aCoVs) to humans. Reporting in Science Immunology, Klompus et al. investigated antibody cross-reactivity between human coronaviruses (hCoVs) and aCoVs by probing the antibody repertoires of 269 individuals who had recovered from COVID-19 against a library of ~13,000 peptides derived from all seven hCoVs and 49 aCoVs. Several broadly reactive monoclonal antibodies showed marked interspecies cross-reactivity. The authors demonstrated that antibody binding data combined with machine learning allows to accurately distinguish between individuals who had been exposed to SARS-CoV-2 and those who had not, even when SARS-CoV-2-specific peptides were excluded from the library. This suggests a potential application of similar antigen libraries for the rapid serological detection of future zoonotic spillovers.

ORIGINAL ARTICLE Klompus, S. et al. Cross-reactive antibodies against human coronaviruses and the animal coronavirome suggest diagnostics for future zoonotic spillovers. Sci. Immunol. https://doi.org/10.1126/sciimmunol.abf950 (2021)