

IN BRIEF

COVID-19

Does asthma make COVID-19 worse?

There is active interest in reconciling the tremendous variation observed in COVID-19 outcomes with host immunity. In this preprint, Sajuthi et al. analyse nasal airway epithelial transcripts from a large cohort of healthy and asthmatic subjects to distinguish relative contributions of host immune networks to coronavirus susceptibility. They use network co-expression analyses and transcriptomics on mucociliary cultures to show that genes implicated in SARS-CoV-2 infectivity, specifically *TMPRSS2* and *ACE2*, are significantly influenced by type 2 cytokine-driven inflammation and interferon signalling, respectively. Although SARS-CoV-2-specific analysis and experiments are lacking, the study provides a rationale for why type 2 responses, which are aggravated in patients with asthma, might increase susceptibility to severe COVID-19.

ORIGINAL ARTICLE Sajuthi, S. P. et al. Type 2 and interferon inflammation strongly regulate SARS-CoV-2 related gene expression in the airway epithelium. Preprint at bioRxiv <https://doi.org/10.1101/2020.04.09.034454> (2020)

COVID-19

Neutralizing antibody response in mild COVID-19

This preprint reports robust induction of SARS-CoV-2-specific neutralizing antibodies in 94% of 175 patients with clinically mild COVID-19 within 2 weeks of symptom onset. Compared with young patients, middle-aged and older patients in this cohort had higher titres of neutralizing and binding antibodies. As older patients are generally considered at greater risk of severe disease, the robust humoral responses in this cohort may explain their apparent protection. Of note, 10 of 175 patients recovered without developing detectable neutralizing antibody titres, suggesting that antiviral binding antibodies and cellular immune responses can both result in convalescence. Longitudinal observations in addition to stringent clinical and immunological characterization are needed to further assess the specificity and relative contribution to protection of neutralizing antibodies against SARS-CoV-2.

ORIGINAL ARTICLE Wu, F. et al. Neutralizing antibody responses to SARS-CoV-2 in a COVID-19 recovered patient cohort and their implications. Preprint at medRxiv <https://doi.org/10.1101/2020.03.30.20047365> (2020)

COVID-19

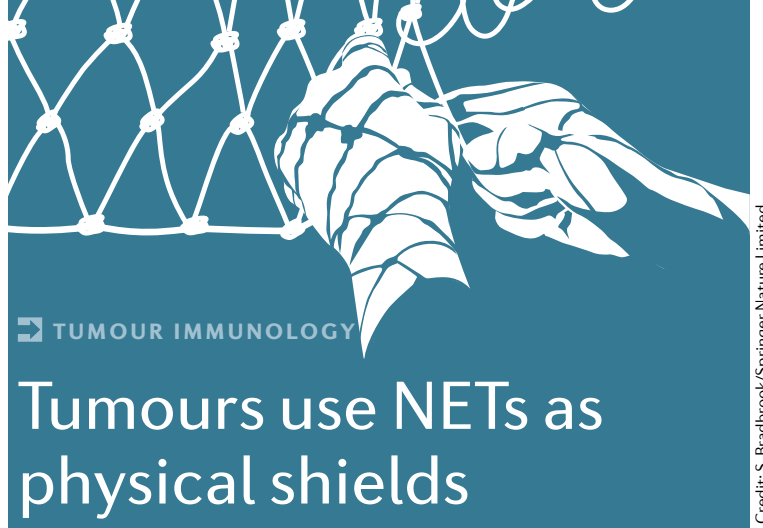
Cancer therapy tool informs COVID-19 vaccines

T cell vaccines against SARS-CoV-2 are being developed at a rapid pace, but it is imperative that the proteins or peptides they deliver bind to a large variety of HLA haplotypes in the global population. Using a computational tool designed to predict candidate neoantigens for cancer vaccines, this preprint identifies 1,103 unique 9-mer antigens from the SARS-CoV-2 peptidome, each of which binds to a median of 3 of 1,022 HLA class I alleles. This resulted in 6,748 peptide-MHC pairs with high binding affinity. Up to 684 peptides were derived from each viral protein tested. Furthermore, 12 of the identified SARS-CoV-2 epitopes match SARS-CoV-2 epitopes that were previously shown to generate T cell responses *ex vivo* and *in vitro*. This publicly available dataset will be an important resource to guide vaccine development.

ORIGINAL ARTICLE Campbell, K. M. et al. Prediction of SARS-CoV-2 epitopes across 9360 HLA class I alleles. Preprint at bioRxiv <https://doi.org/10.1101/2020.03.30.016931> (2020)

Samarth Hegde, Verena van der Heide and Miriam Saffern
Sinai Immunology Review Project,
Icahn School of Medicine at Mount Sinai, New York, NY, USA
e-mail: sinai.immunology@gmail.com

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TUMOUR IMMUNOLOGY

Tumours use NETs as physical shields

An expansion of neutrophils in patients with cancer is usually associated with a poor prognosis. This is thought to be due to the ability of neutrophils to induce angiogenesis and mediate immunosuppression. Reporting in *Immunity*, Teijeira et al. now show that cancer cells can also subvert neutrophil functions by inducing the formation of neutrophil extracellular traps (NETs), which wrap around the tumour cells and protect them from T cell- or natural killer (NK) cell-mediated toxicity.

NETosis is a peculiar form of cell death that is unique to neutrophils and results in the extrusion of

DNA-protein complexes. It is induced by various stimuli, including chemotactic cues. The authors show that a number of chemokines that are secreted by tumour cells readily induce NETosis in human neutrophils. This was dependent on the chemokine receptors CXCR1 and CXCR2 as inhibitors of these receptors, such as reparixin and pertussis toxin, or blocking antibodies against CXCR1 prevented NETosis induction.

To investigate the effects of NETs on tumour cells the authors created tumour spheroids from a colon carcinoma cell line and filmed their interactions with healthy donor

IMMUNE REGULATION

MDSC metabolite stuns T cells

Myeloid-derived suppressor cells (MDSCs) accumulate in tumours and inflamed tissues and block immune cell effector functions. But how they do this remains an issue of debate. New research published in *Nature Immunology* shows that MDSCs have a repressed metabolic state that they transfer to nearby T cells through the metabolite methylglyoxal, which paralyzes T cell effector functions.

Transcriptome analysis comparing monocytes and MDSCs revealed that MDSCs have a marked downregulation of genes encoding glycolysis-related enzymes and show reduced glucose uptake. Similarly repressed glycolysis, as well as lower mitochondrial membrane potential and mitochondrial respiration, was also observed in MDSCs isolated from human tumours. This led the authors to investigate whether this

metabolic dormancy is involved in their suppression of T cells.

T cell activation by monocytes is associated with increased glucose uptake and glycolysis, which supports their effector function. However, when CD8⁺ T cells were activated in the presence of MDSCs, they failed to increase glycolysis, produce cytokines and proliferate. This suppression depended on T cell contact with MDSCs. Using fluorescence-labelled MDSCs, the authors showed that cytoplasmic material is transferred to T cells from MDSCs on cell-cell contact and is required for suppression.

To understand what factor might be transferred between the cells, the authors carried out a highly sensitive screen for metabolites and identified an accumulation of methylglyoxal in MDSCs but not in monocytes or other immune