IN BRIEF

COVID-19

Altered immune cell differentiation in the lungs of patients with critical COVID-19

This preprint from Wauters et al. analysed the single-cell transcriptome of bronchoalveolar lavages from 5 patients with mild and 26 patients with critical COVID-19, and detected important differences in immune cell functionality. In mild COVID-19, T cells assumed a resident memory $CD8^+$ or T helper 17 (T_H17) cell phenotype, whereas in critical COVID-19 they acquired an exhausted phenotype. In mild COVID-19, monocytes differentiated into macrophages with phagocytic and antigen-presenting capacity, whereas in critical COVID-19 monocytes did not differentiate and showed a pro-inflammatory phenotype. Interestingly, neutrophils showed a large capacity to phagocytose viral particles and/or infected cells. Future longitudinal analyses may show how immune cell differentiation correlates to the disease course of COVID-19.

ORIGINAL ARTICLE Wauters, E. et al. Discriminating mild from critical COVID-19 by innate and adaptive immune single-cell profiling of bronchoalveolar lavages. Preprint at *bioRxiv* https://doi.org/10.1101/2020.07.09.196519 (2020)

COVID-19

Attacking the defence: SARS-CoV-2 can infect immune cells

Lymphopenia and systemic viral dissemination are commonly found in severe COVID-19. This preprint study reports that immune cells (monocytes, $CD4^+$ T cells, $CD8^+$ T cells and B cells) are susceptible to SARS-CoV-2 infection. This was observed by in vitro infection of immune cells and by ex vivo detection of SARS-CoV-2 in peripheral blood mononuclear cells from patients with severe COVID-19. Post-mortem in situ analysis of lung tissues further confirmed the presence of infected immune cells in COVID-19. As monocytes and lymphocytes do not express ACE2, it remains to be seen whether the virus uses an alternative entry strategy and whether circulating infected immune cells contribute to viral spread and COVID-19 disease progression.

ORIGINAL ARTICLE Pontelli, M. C. et al. Infection of human lymphomononuclear cells by SARS-CoV-2. Preprint at *bioRxiv* https://doi.org/10.1101/2020.07.28.225912 (2020)

COVID-19

$CD8^+$ T cells remember same bits of SARS-CoV-2

Deciphering the epitope dominance of the natural memory responses seen in recovered patients with COVID-19 will aid vaccine development. In this preprint, Ferretti et al. used an unbiased genome-wide screen (T-Scan) to map the epitopes recognized by memory $CD8^+$ T cells from convalescent patients with COVID-19 with prevalent HLA types. SARS-CoV-2-specific memory $CD8^+$ T cells recurrently targeted a limited set of immunodominant epitopes, which were unique to SARS-CoV-2 and not from highly variable regions. Only 10% of these epitopes corresponded to the S protein, stressing the relevance of developing vaccines that promote T cell responses against other viral targets, such as ORF1ab and N protein.

ORIGINAL ARTICLE Ferretti, A. P. et al. COVID-19 patients form memory $CD8^+$ T cells that recognize a small set of shared immunodominant epitopes in SARS-CoV-2. Preprint at *medRxiv* https://doi.org/10.1101/2020.07.24.20161653 (2020)

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TYPE 2 IMMUNITY

Basophils balance ILC2s

All immune responses are subject to multiple checks and balances to minimize collateral damage, with type 2 immune responses being no exception. Now a study in *Nature Immunology* identifies a previously unappreciated regulatory role for basophils in controlling helminth-induced type 2 inflammation. Basophils confer on group 2 innate lymphoid cells (ILC2s) the ability to respond to neuron-derived signals necessary to maintain tissue integrity.

Increased basophil numbers is a hallmark of type 2 responses but the functions of helminth-induced basophils are poorly understood. Siracusa and colleagues studied mice depleted of basophils and show that, although type 2 inflammation in the gut and clearance of the nematode *Nippostrongylus brasiliensis* were unaffected by basophil depletion, the mice suffer increased immune pathology in the lungs and compromised lung function. Lung basophil responses occur 3–5 days after infection, when *N. brasiliensis* larvae have left the lungs and the innate response depends on ILC2s. Basophil-depleted mice had more ILC2s in the lungs after infection than control mice, in particular ILC2s producing IL-5 and IL-13. ILC2 numbers, mucus production and eosinophilia in the lungs returned to normal levels when basophils were restored by adoptive transfer, suggesting that basophils negatively regulate lung ILC2 responses after *N. brasiliensis* infection.

Exploring the mechanism of augmented pathology in basophil-depleted mice, the authors ruled out a role for known ILC2 activators such as IL-25, IL-33 and thymic stromal lymphopoietin. RNA sequencing and pathway analysis of lung ILC2s from infected wild-type mice revealed an upregulation of genes associated with neuropeptide signalling. ILC2s sorted from the

NK CELLS

Killing via nanotubes

During pregnancy, maternal immune cells must balance the contradictory demands of tolerating the fetus and providing protection against placental infection. A new study in *Cell* shows that natural killer (NK) cells in the placenta decidual tissue have an elegant way of achieving this balance. Instead of killing infected placental trophoblasts, decidual NK cells transfer the antimicrobial peptide granulysin through nanotubes to trophoblasts to kill intracellular bacteria, sparing the trophoblast.

Decidual NK cells are inferior killers compared with NK cells from the periphery, yet they express high levels of the cytotoxic effectors perforin, granzymes and granulysin. To better understand this conundrum and its impact on infection, Judy Lieberman and colleagues studied placental infection with *Listeria monocytogenes*, which can cause miscarriage, stillbirth and neonatal sepsis. Co-culture of human decidual or peripheral NK cells with a trophoblast-like cell line JEG-3 infected with *L. monocytogenes* significantly reduced intracellular bacteria levels but did not result in JEG-3 cell death. Bacterial killing could be inhibited by granulysin-blocking antibodies, but not by inhibitors of degranulation or perforin pore formation, and required NK cell–JEG-3 cell contact. Similar results were observed using primary

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