PDAC led to increased pancreatic infiltration of cDCs and reduced tumour lesions; this was associated with a decreased T<sub>reg</sub>-17-type response and an increase in T<sub>H</sub>1 cell and cytotoxic CD8<sup>+</sup> T cell responses in the pancreas. FLT3L treatment alone or in combination with anti-CD40 did not lead to regression of established pancreatic tumours; however, the authors found that a triple combination therapy of FLT3L, anti-CD40 and radiotherapy led to regression of established tumours in most KPC-OG mice.

These findings suggest that cDC number and function can determine whether adaptive immune responses to tumour neoantigens are protective or detrimental in PDAC. Importantly, targeting cDCs may be crucial for effective therapies for PDAC, a disease that has been notoriously difficult to treat.

**Yvonne Bordon**

**IN BRIEF**

**COVID-19**

**Dysregulation of lung myeloid cells in COVID-19**

Acute respiratory distress syndrome (ARDS) and robust cytokine storm are the hallmark of severe COVID-19 cases. Using single-cell RNA sequencing of bronchoalveolar lavage fluid, this preprint study from Liao et al. found that the depletion of tissue-resident alveolar macrophages and the accumulation of monocyte-derived inflammatory macrophages associate with disease severity. Inflammatory macrophages adopted interferon-signalling and monocyte-recruiting chemokine programmes that may drive ARDS. Increased clonal expansion of CD8<sup>+</sup> T cells was found in mild cases; this may reflect viral clearance due to the induction of virus-specific cytotoxic T cells, as is seen in influenza virus infection. Overall, these data support therapeutic strategies that target the myeloid cell compartment, such as IL-6 inhibitors, to treat COVID-19-associated inflammation.

**ORIGINAL ARTICLE** Liao, M. et al. The landscape of lung bronchoalveolar immune cells in COVID-19 revealed by single-cell RNA sequencing. Preprint at medRxiv https://doi.org/10.1101/2020.02.23.20026690 (2020)

**COVID-19**

**Fighting COVID-19 exhausts T cells**

Lymphopenia is seen in severe cases of COVID-19, but the functional state of T cells in these patients is not known. Based on the retrospective study of 522 patients with COVID-19 and 40 healthy controls from Wuhan, China, this preprint study found that the age-dependent and clinical severity-dependent reduction in T cell numbers inversely correlates with serum levels of TNF, IL-6 and IL-10. The expression of T cell exhaustion markers (PD1 and TIM3) was assessed in peripheral blood cells from 14 patients with COVID-19 and 3 controls. CD8<sup>+</sup> T cells from patients in intensive care units (ICUs) showed increased expression of PD1 compared with patients not in ICUs and healthy controls. This suggests that as disease severity progresses in patients with COVID-19, a concomitant rise in inflammatory cytokine levels may drive the depletion and exhaustion of T cell populations.

**ORIGINAL ARTICLE** Diao, B. et al. Reduction and functional exhaustion of T cells in patients with coronavirus disease 2019 (COVID-19). Preprint at medRxiv https://doi.org/10.1101/2020.02.18.20026364 (2020)

**COVID-19**

**In the eye of the COVID-19 cytokine storm**

Not all patients with COVID-19 develop the same symptoms, but the immunological determinants of a poor prognosis are unknown. In this preprint article, Yang, Y et al. followed a cohort of 53 clinically moderate and severe patients; they conducted a multiplex screen for 48 cytokines and correlated these results with lab tests, clinical characteristics and viral loads. They found a marked increase of 14 cytokines in patients with COVID-19 compared with healthy controls. Continuously high levels of three of these cytokines (CXCL10, CCL7 and IL-1 receptor antagonist) were associated with increased viral load, loss of lung function, lung injury and a fatal outcome. These observations offer key insights into the immunopathology of COVID-19 and provide new avenues for prognosis and therapy.

**ORIGINAL ARTICLE** Yang, Y et al. Exuberant elevation of IF-10, MCP-3 and IL-1ra during SARS-CoV-2 infection is associated with disease severity and fatal outcome. Preprint at medRxiv https://doi.org/10.1101/2020.03.02.20029975 (2020)

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