In the news

AACR PANCREATIC
CANCER MEETING

In September 2019, *Nature Reviews Gastroenterology & Hepatology* visited Boston, USA, to attend a special conference from the American Association for Cancer Research on Pancreatic Cancer: Advances in Science and Clinical Care. This event, attended by ~500 delegates, showcased a great line-up of speakers presenting exciting research on topics such as the tumour microenvironment, immunology, early detection, novel treatment strategies and metabolism.

As a disease projected to become the second leading cause of cancer deaths in the USA, it was encouraging to see lots of hopeful new treatment strategies for pancreatic cancer. A common theme during the meeting was immunotherapy, a topic given due reverence owing to the presence of long-term survivors in the audience, who were notable for endogenous immune responses to their tumours. Despite disappointing results for checkpoint inhibitors in pancreatic cancer, data was presented on various ways to move immunotherapy forward in pancreatic cancer, including new combination approaches, new targets in macrophages and the innate immune system or the tumour microenvironment, as well as novel strategies in engineering T cells or exploiting metabolism and epigenetics.

Also at the meeting were talks suggesting the importance of not only the microbiome, but also the mycobiome, in pancreatic cancer. There were useful discussions on the relevance of mouse models and presentations on newer, potentially better models. Then there was a session devoted to prevention and early detection of pancreatic cancer, highlighting challenges but also opportunities in the form of artificial intelligence, liquid biopsies, new biomarkers and the retooling of old biomarkers to target and kill tumours. Alongside the clear talent shown by the young researchers given a platform at this meeting, these new data and the approaches on display provide hope for a dismal disease.

Iain Dickson

Unique cellular module identified in Crohn's disease

A new study in *Cell* reports a unique cellular module associated with resistance to anti-TNF treatment in a subset of patients with ileal Crohn's disease.

"We applied the latest cutting-edge technologies including single-cell mRNA sequencing, Cytotof (a technique that measures a large number of surface protein levels), and multi-parameter immunofluorescence [assays] (that allow analyses of main proteins)," explain Judy Cho, Miriam Merad and Ephraim Kenigsberg, corresponding authors.

These high-resolution analyses revealed a distinct cellular signature in inflamed versus uninfamed ileal tissue from a subset of patients with Crohn's disease, including IgG plasma cells, inflammatory mononuclear phagocytes, and activated T cells and stromal cells.

The authors coined the term 'GIMATS module' to describe this cell signature. Interestingly, presence of the GIMATS module

Multiplex immunofluorescence image highlighting foci of proliferation (yellow), as well as aggregates of T cells (red), B cells (green) and dendritic cells (magenta). Different (top versus bottom) immune cell aggregates display different cellular components, highlighting key cell-cell interactions that drive Crohn's disease. Image courtesy of J. Cho, Icahn School of Medicine at Mount Sinai, USA.

INTESTINE

Circadian neuroimmune circuits influence intestinal physiology

New research has demonstrated that circadian-controlled neuroimmune circuits regulate the function of group 3 innate lymphoid cells (ILC3s) and gut homeostasis in mice. The findings provide clues as to how environmental cues such as light can be processed and, ultimately, influence tissue physiology.

ILC3s are major regulators of inflammation, metabolism and the gut microbiota. Moreover, enteric ILC3s and neuronal cells have been shown to interact in the gut mucosa, with these neuroimmune interactions influencing mucosal defence. "However, whether [these] neuroimmune interactions operate at an organismal level, integrating environmental cues to coordinate tissue physiology was essentially unknown," explains author Henrique Veiga-Fernandes, with this question being investigated in the new study.

The researchers first demonstrated that mature intestinal ILC3s express

high levels of circadian clock genes and, by examining mice with altered expression of *Arntl* (a master circadian activator), intestinal ILC3s were shown to be controlled in a circadian manner. Moreover, ablation of *Arntl* in mice resulted in disruptions to gut ILC3 homeostasis and intestinal physiology, including increased susceptibility to infection (*Citrobacter rodentium*), a deregulated microbiota, impaired reactivity of the intestinal epithelium and disrupted lipid metabolism (increased expression of key epithelial lipid transporters).

In contrast to changes in microbiota (antibiotic treatment) and feeding regimens (food access restricted to a 12 h interval), which had only small effects, inversion of light-dark cycles had a profound effect on the circadian oscillations of enteric ILC3s — a full inversion of the acrophase (that is, the timing of the peak of the circadian cycle). Importantly, light was confirmed

“inversion of light-dark cycles had a profound effect on the circadian oscillations of enteric ILC3s”