The contribution of immune cells to cancer progression and metastasis is now well established. Our lab is focused on a particular type of immune cell, called a gamma delta (γδ) T cell. We are exploring the involvement of γδ T cells in breast, colon and pancreatic cancers. γδ T cell is actually an umbrella term that encompasses a variety of cell subsets with distinct properties and anatomical locations. There are εγδ T cell subsets that kill cancer cells and other subsets that promote cancer progression. Our lab has ongoing projects aimed at understanding when and where these diverse γδ T cell subsets are important.

In 2021, our lab contributed to three scientific papers. Two lab members (Wilma and Rob) gave oral presentations at the 9th International γδ T Cell Conference, which was held virtually from Edinburgh. Anna was recognised for her exceptional contribution to research during the pandemic. We were also happy to receive funding from the Cancer Research Institute (New York) and Worldwide Cancer Research. 

Breast cancer

In previous years, we generated a single cell RNA sequencing (scRNAseq) dataset of γδ T cells isolated from the lungs of tumour-free and tumour-bearing mice. This analysis has yielded a number of new targets for pro-metastatic γδ T cells, including co-inhibitory and co-stimulatory molecules expressed on the surface of these cells. We have found that a subset of lung γδ T cells expressed constitutively levels of PD-1 and TIM-3, suggesting that increased IL-17A after immune checkpoint inhibitor treatment may contribute to resistance mechanisms. We are currently testing the impact of these drugs on metastasis progression and resistance to immunotherapy.

Another project in the lab is investigating the anti-tumour functions of γδ T cells. We have identified a subset of cells with cancer-killing functions (Figure 1A). We are testing different methods to increase their killing ability to use in adoptive cell transfer experiments to target primary and secondary tumours.

Colorectal cancer

We have continued our collaboration with Owen Sansom and Adrian Hayday (Francis Crick Institute) to investigate the role γδ T cells in mouse models of bowel cancer. We are particularly interested in the gut-resident γδ T cell population that express the Vγ7 chain γδ T cell receptor chain and their role in cancer progression. We have found that these cells counteract intestinal adenoma formation and kill transformed enterocytes in mice. When tumours develop, however, these cells are largely excluded from the tumour microenvironment. We have found that Butyrophilin-like 1 (BTN1) and BTN2 proteins are now using the organoid system in vitro to study the molecular link between Apc deletion and γδ T cell exclusion in tumours.

Pancreatic cancer

We have found that γδ T cells drive metastasis in the KrasG12D;Trp53R172H;Pdx1-Cre(IRC) mouse model of pancreatic cancer, and our work over the past three years has been focused on uncovering the mechanism by which γδ T cells promote metastasis. During lockdown, we discovered that macrophages and fibroblasts are responsible for reprogramming γδ T cell-deficient mice, indicating that γδ T cells regulate these cells in some way to support metastasis. Currently, we are investigating the mechanisms by which this occurs.

Publications listed on page 104