Our lab focuses on a type of immune cell, called gamma delta (γδ) T cell. γδ T cell refers to a variety of cell subsets with distinct properties and anatomical locations. There are γδ 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. We are exploring the involvement of γδ T cells in breast, colon, liver, and pancreatic cancers.

In 2022, our lab contributed to six scientific papers; two of these publications highlighted our work on IL-17A-producing γδ T cells. We deposited data from other studies as preprints on BioRxiv, which centre around tissue-resident subsets of γδ T cells. We attended several conferences to disseminate this work, including the 2nd International workshop on “Receiving and Transmitting Signals via the γδ TCR” in Cellu, Sicily, and the British Society for Immunology annual congress in Liverpool. Mark and Hannah successfully completed their PhD studies. We welcomed three new members of the group: Kyi Lai, Federico, and Anna.

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 uncovered two new avenues of research in the lab. First, we found that subsets of IL-17A-producing γδ T cells expressed different co-inhibitory molecules on their surface. One subset (Vγδ6+) expressed constitutive levels of PD-1, while Ly6C+ γδ T cells did not. Future efforts will focus on the endogenous role of these cells in breast cancer progression.

Colorectal cancer
We have continued our collaboration with Owen Sansom and Adrian Hayday (Francis Crick Institute) to investigate the role of 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 T cell receptor chain and their role in cancer immunotherapy. We have found that Btynl1 mRNA using organoids derived from our data in breast cancer, T cells were maintained by the cytokine, IL-27, which amplified their cancer-killing ability. In adoptive transfer experiments, Ly6C+ γδ T cells delayed mammary tumour growth, while Ly6C− γδ T cells did not. Future efforts will focus on understanding these pathways.

Immunotherapy resistance
Liver cancer
Together with Tom Bird’s lab, we have started to address the role of γδ T cells in hepatocellular carcinoma. We have discovered that γδ T cells promoted cancer progression in mouse models driven by oncogenic β-catenin and MYC. Unlike our data in breast cancer, γδ T cells in the liver failed to express IL-17A. For the future, we will undertake a deep phenotypic analysis of these γδ T cells in the liver and perform experiments to understand how they perpetuate tumour growth.

Pancreatic cancer
We have found that γδ T cells drive metastasis in the KrasG12D+/+;Tgf53CreERT2;Pdx1-Cre (KPC) 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 were reduced in pancreatic tumours from γδ T cell-deficient mice, indicating that γδ T cells regulated these cells in some way to support metastasis. Currently, we were investigating the mechanisms by which this occurs.

Publications listed on page 103