The immune system can exert both anti- and pro-tumour activity, therefore, understanding the role of immune cells in the cancer microenvironment is of critical importance. Our lab uses cutting-edge light microscopy and other techniques to investigate the dynamics of immune cells in cancer.

The immune system has been implicated in almost every stage of cancer development, from initiation and growth, to dormancy, invasion and metastasis. As the immune system primarily co-evolved with microbes to protect against infection with pathogens and as cancer cells are mutated host cells, the role of immunity in cancer is complicated. Even though immune cells can kill cancer cells and stabilise the primary tumour to help prevent its spread, they can also produce factors that suppress anti-cancer immunity and benefit tumour growth and dissemination. The immune compartment of cancer is composed of the resident immune cells of the tissue and leukocytes that infiltrate from the circulation. The development of the cancer immune environment is inherently dynamic, and the processes that regulate immune cell recruitment and function are not well understood. Recent success in directing and strengthening the immune system’s anti-cancer functions (e.g. tumour infiltrating lymphocyte (TIL) therapy and immune checkpoint inhibition) highlight the importance of homeostasis makes particular requirements for the way that immunity must function in this organ. Localisation and regulation of leukocytes within the pulmonary capillaries and liver sinusoids is not fully described or well understood.

The work of several groups has suggested that neutrophils are important in onco-immunology, and a high neutrophil-to-lymphocyte ratio is associated with poorer prognosis in many advanced cancers. Neutrophils are crucial in many anti-microbial and tissue damage inflammatory programmes at the end of acute inflammatory responses. Additionally, the accumulation of apoptotic neutrophils and their subsequent clearance is thought to directly contribute to anti-inflammatory programmes. The 2020 discovery of NETosis, neutrophils can consume chemokines, cytokines and growth factors and can modify the extracellular matrix. Neutrophils can produce and consume chemokines, cytokines and growth factors and can modulate the extracellular matrix. Neutrophils outside of the bone-marrow niche is associated with several pathologies including cancer, so this knowledge will help us to further understand how neutrophil regulation is modified by the presence of a tumour and potentially how to target these changes more specifically without affecting the protective roles of neutrophils.

Using a combination of flow cytometry, transcriptional profiling and proteomics, we have extended our understanding of fundamental neutrophil biology by uncovering important differences in neutrophils that originate from the bone marrow and the spleen (Figure 1 – from Mackey et al., 2021, bioRxiv). Production of neutrophils outside of the bone-marrow niche is associated with several pathologies including cancer, so this knowledge will help us to further understand how neutrophil regulation is modified by the presence of a tumour and potentially how to target these changes more specifically without affecting the protective roles of neutrophils.

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