Project Title: "Characterising the Immune Response to Immunotherapy in Malignant and Healthy Tissue"
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Research Group: Cancer Inflammation and Immunity

Immunotherapies based on antibodies that target T cell-immune checkpoints have transformed the landscape of cancer treatment across multiple tumour types. These immune checkpoint blockade (ICB) therapies can elicit remarkable and long-lasting responses in both patients with late-stage cancers and in (neo)adjuvant settings. However, most patients experience only transient or no benefit, and many suffer harmful side effects. Solutions to these clinical problems require improved fundamental understanding of the principles that govern anti-cancer immune responses.

Our group at the Cancer Research UK Manchester Institute investigates the signals and pathways that dictate the establishment of tumour inflammatory environments which either promote or restrain the anti-tumour function of the immune system. In close collaboration with the Cancer Research UK National Biomarker Centre, led by Caroline Dive, we have established a pioneering patient-derived tumour fragment (PDTF) platform, expanding on the groundbreaking work of collaborators at The Netherlands Cancer Institute (Voabil et al 2021, Nature Medicine, Roelofsen et al START Protocols, 2023). PDTFs are generated from freshly resected tumours and retain the architecture and microenvironment, including resident immune cells. Crucially, the immune response measured in these PDTFs following PD-1 blockade ex vivo is highly concordant with the clinical response to ICB in the corresponding donor patient.

Building on our previous findings uncovering pro-tumourigenic inflammatory mediators as major drivers of immune evasion (Zelenay et al Cell 2015, Bonavita et al Immunity 2020, Pelly et al Cancer Discovery 2021, Bell et at Nature communications 2022), and leveraging this pioneering platform using both human and mouse tissue, this project will investigate the signals that regulate the establishment of tumour inflammatory environments that either stimulate or hinder immune-mediated tumour control. A central aim of the project is to evaluate the responses of malignant and healthy tissue to standard-of-care ICB and to combination treatments with anti-inflammatory drugs, with implications for therapeutic response and the prevention of adverse side effects. We welcome applications from individuals with a strong academic track record and previous laboratory research experience.

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