



Project Title: “Inducing leukaemic differentiation to prevent post-transplant relapse”
Group Leader: Mark Williams
Research Group: Leukaemia Immunology & Transplantation

Allogeneic haematopoietic stem cell transplantation is the only curative therapy for many patients with acute myeloid leukaemia (AML) and other poor-risk haematological malignancies. Recipients are ‘conditioned’ with chemo/radiotherapy before receiving blood-forming stem cells harvested from a donor. These stem cells repopulate the bone marrow and provide a new immune system which eliminates the cancer. However, disease relapse remains the most common cause of death and is due to failure of donor T cells to eradicate residual leukaemia in some cases. Donor T cells are often dysfunctional at relapse, and leukaemic cells frequently exhibit reduced immunogenicity. Determining the major drivers of donor T-cell dysfunction and leukaemic immunogenicity is critical to inform strategies that re-establish anti-leukaemic T-cell responses and prevent relapse.

AML is a cancer of bone marrow progenitors and is characterised by a block to differentiation. Several emerging classes of small molecular inhibitor can release this block, leading to the production of leukaemia-derived myeloid immune cells. A current focus of our lab is determining the way in which different leukaemic differentiation states interact with donor immune cells, with the aim of manipulating leukaemic differentiation to augment donor immune responses and prevent relapse. This is a particularly appealing strategy in the context of stem cell transplantation, where immunotherapies that target immune cells directly tend to cause severe immunotoxicity.

We are looking for a hard-working, focused, ambitious person to join our excellent, friendly and interactive team. Our laboratory makes use of a broad range of *in vitro* and *in vivo* techniques to study interactions between leukaemia and donor immune cells, with the aim of developing novel therapies for patients. Our approach spans cutting-edge single cell sequencing and epigenetics, through to murine models, biomarker development and clinical trials. We would be particularly happy to receive applications from individuals with a strong academic track record and Masters-level and/or other laboratory research experience in leukaemia, cancer biology or immunology.

This project would enable the successful candidate to work in the world-leading research environment of the CRUK Manchester Institute, whilst applying cutting-edge techniques to address a critical clinical problem. Students would gain broad exposure to immunology, haematology, oncology and transplantation. Upon completion, candidates would be well positioned to pursue a career in the fascinating and expanding field of cellular immunotherapy for cancer.

University of Manchester entry: September 2024