Project Title: “Detection and targeting of protein homeostasis in multiple myeloma”

Project Supervisors: Dr David Millrine, Translational Immunology Team Lead [CBC], Dr Emma Searle, Christie NHS Foundation Trust

Research Group: Translational Immunology, Cancer Biomarker Centre

Hosted in the CRUK Cancer Biomarker Centre (CBC), University of Manchester directed by Professor Caroline Dive

Multiple Myeloma (MM) is a devastating plasma B-cell (PBC) malignancy characterized by high levels of circulating monoclonal immunoglobulin, PBC bone marrow infiltration, bone destruction, and organ failure. Due their high secretory load malignant PBCs are acutely dependent on mechanisms that maintain protein homeostasis in the endoplasmic reticulum (ER). This project will explore the significance of a ubiquitin-like post-translational modification (PTM) responsible for ribosome quality control (RQC) and ER-turnover. The student will apply cutting edge cellular biochemistry to deplete pathway critical proteins from cell lines and evaluate the consequence to immunoglobulin secretion and cell survival, whilst also performing mechanistic studies to understand the biological function of this enigmatic PTM. We will consider whether the pharmacological targeting of this pathway is likely to show synergy with current frontline therapies using degron approaches.

We hypothesize that perturbed protein homeostasis may correlate with disease stage and therefore, have biomarker utility. Here the project will also have a bioinformatic component that seeks to identify relevant phenotypes from bulk transcriptomic data. This project is an exciting opportunity to study an important emerging cellular pathway and may inspire future drug discovery efforts or methods for patient stratification. The project is jointly supervised by Dr David Millrine (Translational Immunology Team Lead) and Consultant Haematologist Dr Emma Searle, a specialist in the treatment of Multiple Myeloma based at the Christie NHS Foundation Trust.

We are looking for a motivated, focussed and ambitious student to join our team and would be particularly happy to receive applications from individuals with a strong academic track record and Masters-level and/or other laboratory research experience.

University of Manchester entry: September 2024