Project Title:
Unravelling mechanisms of acquired immunomodulatory drug resistance in myeloma

Primary Supervisors:
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Project Summary:
Multiple myeloma remains incurable despite advances in therapy. Immunomodulatory drugs (IMiDs) are the current backbone of standard and experimental combination therapies at all stages of disease. Understanding IMiD refractory states is therefore imperative to help us improve patient outcomes. IMiD activity against myeloma cells results from their ability to bind to the CRL4^{CRBN} E3-ligase and alter its substrate specificity. We have developed and characterised models of acquired IMiD resistance as a consequence of low cereblon (CRBN) expression, mirroring findings in patient samples. This project will focus on identifying mechanisms that modulate the changes in CRBN levels as well as identifying synthetic lethal vulnerabilities in this context. These observations will be correlated with primary samples from patients with acquired IMiD resistance. Furthermore the student will be part of a larger team working on novel CRBN modulators being developed at The Institute of Cancer Research and during the later stages of the thesis compounds will be available for studies to identify additional pathways associated with myeloma resistance. The student will learn a broad range of molecular and cell biology techniques in the laboratory including tissue culture, molecular cloning, use of CRISPR libraries and protein biology including TMT proteomics. There will also be training in computational and bioinformatics approaches. In addition they will be part of a multidisciplinary team with a focus of team science and shared learning.

Clinical Specialties:
Haematology