Using a multi-omics approach to investigate the reversal of proteasome inhibitor drug resistance in multiple myeloma with epigenetic inhibitors

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A thesis submitted for the degree of
Doctor of Philosophy

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Abstract

Background: Multiple myeloma (MM) is an incurable cancer of plasma cells. Novel therapeutics, including proteasome inhibitors (PI) and immunomodulatory imide drugs, have almost doubled median survival time of MM patients. However, most patients relapse and become resistant to drugs they previously have been treated with. Acquired anti-cancer drug resistance remains one of the biggest barriers in the treatment of myeloma.
Aims: PI resistance mechanisms in MM will be investigated with the aim of reversing the resistance phenotype, making MM cells sensitive to proteasome inhibition. Standardised robust wet-lab and computational single-cell workflows will be established to characterise drug-resistant MM cells and their surrounding microenvironment at different points in disease progression.
Results: Cured cancer mate

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Results: Cured cancer mate

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List of Abbreviations

RNA-Seq . . . Ribonucleic acid sequencing

scRNA-Seq . . Single cell RNA-Seq

MM . . . . . Multiple Myeloma

1 Introduction

1.1 Introduction to multiple myeloma

Multiple myeloma accounts for 1-2% of all cancers and has the second highest incidence of hematological malignancies, after non-Hodgkin's lymphoma [1].

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Historically multiple myeloma..

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References

[1] International Myeloma Working Group. “Criteria for the classification of monoclonal gammopathies, multiple myeloma and related disorders: a report of the International Myeloma Working Group”. In: *British journal of haematology* 121.5 (2003), pp. 749–757.