Project Title: Investigating the role of MYB in Burkitt lymphoma
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Lymphoma is a cancer of white blood cells, mature lymphocytes. Among lymphomas, Burkitt lymphoma (BL) is an aggressive B cell lymphoma, which is currently treated only with intensive chemotherapy with high toxicities. There is thus an unmet clinical need for the development of new targeted therapies with less toxicities. This project is built on our preliminary results identifying novel roles for the MYB oncogene in BL. The overarching hypothesis is that a transcription factor MYB plays crucial roles in the initiation and maintenance of mature B cell lymphomas, particularly BL, through dysregulated transcriptional programs in GC B cells.

Aim 1. Investigate the consequences of overexpression of Myb in GC B cell development and B cell transformation.
Aim 2. Investigate the effect of pharmacological inactivation of Myb in transformed B cells.

With the Cancer Council ACT support, we have initiated Aim 2, which test the effect of potential MYB inhibitors, such as celastrol, plumbagin, and toyocamycin. We optimised growth assay for three mouse B cell lines that were transformed with Myb expression, together with human BL cell lines, Jiyoye (sensitive to MYB knock-down) and Raji (resistant to MYB knock-down). Toyocamycin, but not the other two inhibitors, suppressed the proliferation/survival of MYB-dependent Jiyoye cells at a lower concentration compared to MYB-independent Raji cells. For Aim 1, retrovirus vectors expressing Myb variants have been constructed in different backbones. We have been optimising gene delivery and analysis systems to investigate the effect of MYB overexpression on activated B cells in the next six months. We expect that the findings will define the role of Myb in the development of normal GC B cells and malignant B cells.