Project Title: Investigating the role of MYB in Burkitt lymphoma
Grant Awarded: $65,000
Principal Investigator: Dr Keisuke Horikawa, The John Curtin School of Medical Research, The Australian National University

September 2020 – September 2021

Lymphoma is a cancer of white blood cells, mature lymphocytes. Burkitt lymphoma (BL) is an aggressive B cell lymphoma currently treated only with intensive chemotherapy with high toxicities. There is thus an unmet clinical need for the development of new targeted therapies with fewer toxicities. This project is built on our preliminary results identifying novel roles for the *MYB* oncogene in the development of BL. We hypothesise that a transcription factor, MYB, change the gene expression program in mature B cells, leading to the initiation and maintenance of Burkitt lymphoma cells.

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

With the Cancer Council ACT support, we first initiated Aim 2 to test the effect of potential MYB inhibitors, such as celastrol, plumbagin, and toyocamycin. We optimised growth assay for three mouse B cell lines transformed by Myb, together with human BL cell lines, one sensitive to MYB knock-down and the other resistant to MYB knock-down. Toyocamycin, but not the other two inhibitors, suppressed the proliferation/survival of MYB-dependent cells at a lower concentration compared to MYB-independent cells. This result indicated that Toyocamycin might inhibit BL cell proliferation through MYB inhibition. For Aim 1, we constructed retrovirus vectors to introduce Myb and its variants into mouse B cells. We confirmed the expression of two transcription factors (Myb and Myc) transformed mature activated B cells. In addition, the transformed cells expressed a differentiation marker called CD93, indicating that Myb regulated its expression. These findings suggest that a transcription factor, Myb plays an essential role in a particular type of Burkitt lymphoma cells.