**Molecular Mechanisms in Leukaemia Lab**

The Unnikrishnan lab investigates the molecular programs that go awry in haematological cancers. We primarily study two forms of leukaemia, Myelodysplastic Syndrome (MDS) and Acute Myeloid Leukaemia (AML), which are both diseases of increasing prevalence in rapidly ageing, developed societies like Australia’s.

We use a combination of genomics, epigenomics, molecular biology and haematopoietic stem cell biology techniques to understand the mechanisms driving leukaemia, as well as those underpinning resistance to therapy. A main focus of our group is in performing translational research, with the aim of improving treatment options for patients.

**Areas of Research:**

* **Investigating RNA splicing aberrations in leukemia**

This is a major focus of the lab. Somatic mutations in RNA splicing factors are frequently observed in MDS patients and occur early in the development of the disease. Yet, neither role in the aetiology of the disease nor their effect on the biology of leukaemic stem cells remains well understood.

A number of ongoing projects in the lab are addressing these questions in the MDS and AML.

* **Understanding the biological effects of epigenetic therapy in MDS**

The DNA demethylating agent, 5-Azacitidine (AZA) is the most effective pharmacological treatment option for MDS patients. Yet, only ~50% of patients who are treated with AZA will ever respond to therapy, and drug treatment has to be continued upon response. However, a significant fraction of patients

In studying patients who showed a complete response to AZA treatment, we have previously discovered that AZA fails to eradicate dysplastic cells, including those bearing pernicious driver mutations that existed at the presentation of disease (<https://doi.org/10.1016/j.celrep.2017.06.067>). However, AZA alters the functional properties of cells, facilitating the restoration of effective haematopoiesis in patients, without eradicating diseased cells.

We seek to understand the molecular mechanisms underpinning this. We are also collaboratively developing new technologies, including multi-modal single cell sequencing, to enable us to answer these questions.

**Opportunities:**

We are recruiting at all levels – postdoctoral, graduate students and undergrads! Potential projects include:

* Wet-lab focused (in translational biology, involving applying a variety of genomics and molecular biology techniques on human haematopoietic stem cells),
* Bioinformatics (involving analyses of genomic, transcriptomic and epigenomic data from patients)
* Or, a combination of both

If you are interested, please get in touch by email: Ashwin.unnikrishnan (at) unsw.edu.au