Department of Pathology

2020 Seminar Programme presents

Sai Shyam & Ben Halliday

Friday 9 October, 1-2 PM, D'Ath Lecture Theatre, Hercus Building

Sai Shyam – Developing circulating tumour cells as a model to identify tumour-specific epigenetic signatures of colorectal cancer metastasis

New Zealand currently has the highest incidence and death rate for Colorectal Cancer (CRC) accounting for 4 deaths/day. Metastasis is responsible for 90% of cancer related deaths, but if detected early, the prognosis improves substantially. Circulating Tumour Cells (CTC) are tumour seeds that arise from solid tumours, responsible for metastatic dissemination and can be detected in patient blood. Hence, CTCs possess great potential to improve CRC management. However, their role in metastasis is largely unknown due to the lack of genome-wide methylation and expression profiles of CTCs, particularly in colorectal cancer patients. A major challenge for studying epigenetics of CTCs is their low number in patient blood and lack of user-friendly, yet robust methods to isolate or enrich for CTCs in a standard laboratory setting. We are employing a well validated size-based isolation method (MetaCell) to enrich for CTCs in CRC patients. MetaCell based enrichment is fast, easy to use, relatively inexpensive and could be deployed in laboratory and clinical settings. The isolated CTCs will be cultured and characterised and used for generating the first DNA methylomes and transcriptomes of circulating tumour cells, to identify the methylomic and transcriptomic signatures/markers for CTCs, to facilitate exploring the role of these markers in CRC metastasis.

Ben Halliday – Building a Brain – *From Phenotypes to Genes, and Back Again*

Cortical malformations arise from *in utero* disruption of neurogenesis, the process of proliferation, differentiation, and migration of neurons in the developing brain. Finding attributable genetic causes for these malformations will sharpen diagnosis and prognostication for patients. However, the heterogeneous nature of these abnormalities creates challenges for assigning pathogenicity. The aim of this study is to apply high-throughput sequencing methods to a cohort of 200 patients with periventricular nodular heterotopia (PVNH), a cortical malformation characterised by grey matter nodules abutting the lateral ventricles of the brain due to a failure in neural migration. Sequence data from patients was processed using a range of custom pipelines designed to capture damaging genetic variation. Disease-causing variants were identified in 30 patients, as well as 15 patients with candidate variants. The primary finding of this analysis was the association of *SON* variants with PVNH ($n = 5$, $P < 0.001$, binomial), a gene previously attributed to ZTTK syndrome, a severe multisystemic developmental disorder. Deep phenotyping revealed a set of consistent neuroradiological features in *SON* patients, providing a potential diagnostic marker. Further accurate phenotyping of patients with cortical malformations can help disentangle the complexity of these heterogeneous disorders, and provide tangible benefits for these patients.