

ICM Research in Progress Seminar

Monday 17th June

Dr Jarmila Spegarova

(Prof Sophie Hambleton)

Germline TET2 loss-of-function causes childhood immunodeficiency with lymphoma predisposition

Primary immunodeficiencies are rare inherited diseases caused by aberrations in the genome, leading to functional abnormalities in the immune system. Using whole exome sequencing we identified two homozygous loss-of-function single point mutations in Tet methylcytosine dioxygenase 2 (TET2), causing an autosomal recessive syndrome of combined immunodeficiency with autoimmune lymphoproliferative syndrome features in three paediatric patients from two unrelated consanguineous families. We defined that TET2 impairment is in our patients pathogenic and leads to altered DNA methylation, B-cell maturation, skewed haematopoiesis towards myeloid lineage, and development of lymphomas.

William Reilly

(Dr Lee Borthwick, Prof Andrew Fisher, Prof Fiona Oakley)

Understanding fibroblast plasticity in idiopathic pulmonary fibrosis (IPF).

IPF is a chronic lung condition characterized by extracellular matrix deposition (ECM) within the lung interstitium, honeycombing formation and fibroblast foci accumulation. Treatment option for patients with IPF are extremely limited, only indicated in patients with mild-moderate disease and have significant side-effects. There is therefore an urgent unmet need to improve our understanding of the cellular and molecular mechanisms driving inflammation and fibrosis in the lung to identify novel therapeutic targets. While the role of the fibroblast in ECM deposition and wound repair are well established, recent studies have illuminated this as an oversimplification with fibroblasts also able to drive inflammation and regulate the switch from acute to chronic inflammation in several organs. Previous work in the lab has shown that in response to damage, lung epithelial cells release IL-1 α (an alarmin or DAMP) that is recognised by IL-1R1 on the fibroblasts, promoting a phenotypic switch in the fibroblasts. Here we present detailed transcriptomic and proteomic profiling of fibroblast phenotypes alongside mechanistic analysis of the pathways regulating fibroblast polarisation.

Chair: Rachel Botting
Dental Lecture Theatre D
1pm - 2pm