Project Title: "**Establishing the impact of cellular and tissue context on malignant transformation**"
Group Leader: Samra Turajlić
Research Group: Cancer Dynamics

Our lab programme spans basic, translational and clinical science and we study both tumour initiation and progression in the context of renal cell cancer and melanoma. We combine deep phenotyping of patient samples, mathematical simulations, per-clinical modelling (including IPSC, organoids and genome engineering, as well as patient-derived tissue fragments).

Research Area of Interests:
Germline variants in the von Hippel–Lindau (VHL) gene lead to a multiorgan tumour predisposition syndrome known as VHL disease. Distinct classes of VHL germline variants are associated with characteristic, tissue-specific patterns of tumour formation. Understanding the mechanisms of this genotype-phenotype correlation can provide valuable insights would begin to answer long-standing questions in cancer biology regarding tissue and cell specificity of oncogenes and tumour suppressor genes and could guide development of targeted therapeutic interventions.

Proposed Research Question:
Patient-derived induced pluripotent stem cells (iPSCs) fully retain the patient's genotype and can differentiate into multiple tissue lineages. Using these iPSCs, we aim to model tumour initiation in vitro across relevant lineages for individual VHL patients. Through these models, we seek to elucidate the mechanisms by which specific classes of germline VHL variants determine the tissue specificity of tumour development. The project will involve emerging methods in iPSC differentiation and genome engineering. These methods could then be applied in other cancer predisposition settings.

The PhD will be based at the CRUK Manchester Institute, with access to world-class facilities and close links to The Christie Hospital and The University of Manchester and will benefit from the collaborative Manchester ecosystem.