

**Supervisor:** Dr Alan McIntyre

**Project title:** Functional investigation of metabolism genes in kidney cancer

**Description:**

Altered metabolism is a hallmark of cancer. Tumour metabolic requirements shift based on phenotypic changes, including increased proliferation and survival in the low oxygen (hypoxic) and nutrient-depleted tumour microenvironment. To identify novel metabolic oncogenes, we investigated metabolism genes across 10 cancer types (>6000 patient samples) to identify those that had correlated increases in DNA copy number and RNA expression. Furthermore those metabolism genes for which high RNA expression was associated with worse patient survival were also identified. A number of genes fulfilled these criteria in kidney cancer. Kidney cancer is the 8<sup>th</sup> most common cancer in the UK with >10,000 new cases annually. Nearly 30% of patients will die of the disease within 5 years. A major type of kidney cancer is clear cell renal cell carcinoma (ccRCC) and >90% of ccRCC have a mutation in the von Hippel–Lindau protein which result in stabilisation of the hypoxia inducible factors (HIF1 $\alpha$  and HIF2 $\alpha$ ) in normoxic conditions. Regions of low oxygen (hypoxia) are frequently found in solid tumours and arise from the combination of high metabolic and proliferative rate and aberrant tumour vascularisation. Hypoxia is associated with therapy resistance, metastasis and worse patient outcome. HIF1 $\alpha$  and HIF2 $\alpha$  are transcription factors and their stabilisation in hypoxia leads to a changes in key genes which trigger more aggressive growth and survival, and contribute to the major hallmarks of cancer. In particular the HIF proteins change the expression of many metabolic genes. This project aims to investigate the hypoxic expression and role of the identified metabolism genes in kidney cancer using a combination of molecular and cell biology approaches including 3-dimension cell culture.

**Theme(s):** Functional studies of metabolism genes associated with worse kidney cancer patient survival.

**Keywords:** Metabolism, kidney cancer, hypoxia, functional analyses, 3D culture.

**Fee band:** High cost laboratory-based research

Available to Home & EU students/International Students

Please email a CV with a covering letter to Dr Alan McIntyre ([alan.mcintyre@nottingham.ac.uk](mailto:alan.mcintyre@nottingham.ac.uk)), who can also supply more information to interested parties.

<http://www.nottingham.ac.uk/medicine/people/alan.mcintyre>