CRUK Cambridge Centre Clinical PhD project

PhD Project Title	Genetic basis of inherited kidney and related tumours
Head of Laboratory (PI) Name	Eamonn R Maher
Second supervisor if applicable	
Programme	Urology
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Laboratory Location	Academic Laboratory of Medical Genetics

Project Outline	**Aims and objectives** Investigation of familial forms of kidney cancer enables early detection of cancer and provides insights into molecular mechanisms (as exemplified by VHL disease). The principal aim of this project is to increase understanding of the molecular basis of renal cell carcinoma (RCC). Specific objectives are: (i) to identify novel causes inherited RCC, (ii) to determine the genetic basis of young onset and multicentric RCC, (iii) to elucidate the mechanisms of tumourigenesis and role in sporadic cancers of novel inherited RCC genes.
Experimental plan	1. Whole exome and whole genome sequencing of cohorts of familial, young-onset and multicentric RCC 2. Identification of likely pathogenic variants in candidate tumour suppressor genes and proto-oncogenes and confirmation in additional patient cohorts. 3. Functional studies to identify mechanism of cancer predisposition and approaches for targeted therapies for novel inherited RCC genes
Main Techniques	Whole exome and whole genome next generation sequencing, bioinformatics analysis of large data sets, variant interpretation, epigenomic analysis, *in vitro* tumour suppressor assays, clinical cancer genetics.
Key References	Qin Y et al. The tumor susceptibility gene TMEM127 is mutated in renal cell carcinomas and modulates endolysosomal function. Hum Mol Genet 2014;23:2428-39 Clark GR et al. Germline FH mutations presenting with pheochromocytoma. J Clin Endocrinol Metab. 2014;99):E2046-50 Gossage L et al. VHL, the story of a tumour suppressor gene (Review). Nat Rev Cancer. 2015;15:55-64 Jafri M et al. Germline Mutations in the CDKN2B Tumor Suppressor Gene Predispose to Renal Cell Carcinoma. Cancer Discov. 2015l;5:723-9 Maher ER. Hereditary renal cell carcinoma syndromes: diagnosis, surveillance and management (Review). World J Urol. 2018 Apr 21 Whitworth J et al. Comprehensive cancer predisposition gene testing in an adult multiple primary tumor series, Am J Hum Gent (2018 (in press)