CRUK Cambridge Centre MRes rotation project

Rotation Project Title	**Mapping the origins of tumour development using single-cell technology**
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Programme	Urological Cancer and Early Detection
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Laboratory Location	Hutchison MRC Research Centre (Dept. Oncology)

Project Outline	**Aims and objetcitves** Most common cancers harbour extensive intrapatient genomic heterogeneity, including cases where multifocal tumours appear to have arisen independently (i.e. share no somatic mutations) [1]. This implicates molecular 'driver' events that precede the first tumour-promoting genetic mutations (such as metabolic, signalling or epigenetic changes). We have identified differential epigenetic profiles that are both recurrent and early events in prostate cancer [2, 3]. We are leveraging these epigenetic profiles to develop molecular diagnostic assays and also to provide insights into the processes that shape tumour development and disease evolution. In this project you will gain experience of cancer genomics, epigenome profiling, single-cell technologies and data analysis methods, working closely with postdocs in the group and expert collaborators.
Experimental plan	Surgical samples from prostate cancer patients (V. Gnanapragasam, Addenbrooke's) will be used to generate single-cell preparations (weeks 1-4). Transcriptome and epigenome profiling of these single-cell preparations (weeks 5-12) will be analysed and compared with existing bulk tissue profiles (weeks 13-15). Data analysis will focus on characterising the cell populations present in tumour and adjacent normal tissues and will explore the origins of these early and recurrent epigenetic profiles in tumour development.
Main Techniques	• analysis of single-cell transcriptomes and epigenomes from prostate tissue samples • sample preparation • sequencing • introduction to high-throughput genomics data analysis.
Key References	**Prostate ICGC Group**. *Analysis of the genetic phylogeny of multifocal prostate cancer identifies multiple independent clonal expansions in neoplastic and morphologically normal prostate tissue. Nat Genet. 2015;47(4):367-72.* **Massie CE**, *et al. HES5 silencing is an early and recurrent change in prostate tumourigenesis. Endocr Relat Cancer. 2015;22(2):131-44.* **Massie CE, Mills IG, Lynch AG.** *The importance of DNA methylation in prostate cancer development. J Steroid Biochem Mol Biol. 2017;166:1-15.*