Project Title: "Reconstruction of Tumour Evolution and Metastatic Spread in Kidney Cancer"

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Research Group: Cancer Dynamics

TRACERx Renal 300 (Tx300) and PEACE (Posthumous Evaluation of Advanced Cancer Environment) Renal programme together span the full arc of clear cell renal cell carcinoma (ccRCC) disease, from surgical resection of primary tumours through to the metastatic landscape captured postmortem. Tx300 is the largest multi-region sequenced ccRCC cohort assembled to date, comprising 314 primary tumours and 2,865 tumour regions with matched genomic, transcriptomic, epigenetic and histological (H&E) data. PEACE contributes around 26 postmortem ccRCC cases with multi-organ, multi-site sampling spanning all major metastatic sites. Together, these datasets offer a rare opportunity to study kidney cancer evolution at unprecedented depth and scale and aims to reconstruct how this disease evolves over time.

This PhD project is computational and will use these datasets to investigate fundamental questions in cancer biology and cancer evolution, for example:

1. How do specific somatic alterations shape the tumour transcriptome, histology and immune microenvironment?
2. Do somatic alterations in epigenetic regulators (like *PBRM1*, *SETD2* and *BAP1*) drive the epigenetic reprogramming during tumour progression?

In Tx300, this will build on an existing detailed picture of driver selection, clonal architecture and disease progression and by integrating transcriptomic and histological data to explore the phenotypic consequences of somatic events. In PEACE, the focus will be on characterising the metastatic architecture of ccRCC and patterns of metastatic seeding.

The successful student will design and apply computational analyses integrating genomic, transcriptomic and imaging data, developing reproducible workflows for large-scale multi-modal datasets. Findings will be integrated with external resources (e.g. TCGA, Genomics England) to validate discoveries and contextualise them within the broader ccRCC landscape, and biological hypotheses generated computationally can be tested experimentally using banked tissue in collaboration with wet-lab colleagues. We welcome applicants from quantitative backgrounds (e.g. mathematics, physics, computer science, bioinformatics, data science & AI or a related field).

References

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