



Project Title: “Dissecting Tumour Evolution in Clear Cell Renal Cell Carcinoma”

Group Leader: Samra Turajlić

Research Group: [Cancer Dynamics](#)

Clear cell renal cell carcinoma (ccRCC) is one of the best cancer models for studying tumour evolution. Its progression follows remarkably structured and constrained genomic routes, making it uniquely suited to dissect how recurrent genetic alterations drive tumour initiation, metastasis, and immune evasion.

This PhD project will exploit ccRCC as a model system to investigate fundamental questions in cancer biology, including

1. Why are specific genetic alterations repeatedly selected?
2. How do specific alterations rewire tumour–immune interactions?
3. Can evolutionary trajectories reveal therapeutic vulnerabilities?

One example focuses on recurrent aneuploidy, as ccRCC is almost universally initiated by loss of chromosome 3(p), with subsequent recurrent losses of chromosomes 9(p) and 14(q) strongly associated with metastatic progression. These stereotyped patterns of aneuploidy highlight evolutionary selection pressures on the molecular and functional outcomes of these alterations and provide a tractable framework to understand how chromosomal alterations shape cancer behaviour.

In the lab, we combine deep phenotyping of patient samples, pre-clinical modelling (patient-derived organoids, tissue fragments and iPSCs, combined with genome engineering and functional experiments), multi-omics data analysis and mathematical simulations. We welcome applicants with interests in cancer biology, tumour evolution, immune–microenvironment, and functional genomics. We will fit the exact project to best suit the candidate and their interest and aptitude and both wet lab and dry lab projects are feasible.

Key References

1. Turajlic, S. et al. Tracking Cancer Evolution Reveals Constrained Routes to Metastases: TRACERx Renal. *Cell* 173, 581-594.e512 (2018). <https://doi.org/10.1016/j.cell.2018.03.057>
2. Mitchell, T. J. et al. Timing the Landmark Events in the Evolution of Clear Cell Renal Cell Cancer: TRACERx Renal. *Cell* 173, 611-623.e617 (2018). <https://doi.org/10.1016/j.cell.2018.02.020>
3. Fernández-Sanromán, Á. et al. Tracking Nongenetic Evolution from Primary to Metastatic ccRCC: TRACERx Renal. *Cancer Discov*, Of1-of23 (2025). <https://doi.org/10.1158/2159-8290.Cd-24-0499>
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5. Berg, N. I. v. d. et al. Immunometabolic Gatekeeping: Reconciling Peto's & the T-cell Infiltration Prognostic Paradox. *arXiv preprint arXiv:2511.20883* (2025). <https://doi.org/10.48550/arXiv.2511.20883>