

CRUK/Wellcome Trust Clinical Research Fellow PhD expressions of interest

Project title

Deciphering cancer evolution through representative sequencing

Primary supervisor: Dr Samra Turajlic (ICR/Crick)

Associate supervisor: Dr Kevin Litchfield (Crick)

Associate supervisor: Prof James Larkin (ICR)

Associate supervisor: Dr Nelson Alexander (Roche)

Clinical specialities that will be considered: oncology, pathology, surgery; candidates that have not entered specialist training are welcome to apply.

Project summary

While 100s-1000s of solid tumours have been profiled to date, a fundamental under-sampling bias is inherent in current methodologies. Existing clinical and research protocols respectively sample ~0.0005% and ~2.0% of the total tumour mass, creating a sampling bias which impacts both fundamental insights into clonal dynamics and tissue-based biomarkers. Working with an industry partner we have developed a novel tumour sampling methodology that would address both these issues. Representative Sequencing (Rep-Seq) protocol comprises homogenisation of all residual tumour material not taken for pathology (material which is otherwise treated as waste and destroyed) into a well-mixed solution, coupled with next generation sequencing. In a pilot exercise this approach accurately captures clonal dynamics as shown in our recent publication ([https://www.cell.com/cell-reports/pdf/S2211-1247\(20\)30460-5.pdf](https://www.cell.com/cell-reports/pdf/S2211-1247(20)30460-5.pdf)). We have set up a prospective study (HoLST-F), (<https://clinicaltrials.gov/ct2/show/NCT03832062>), which will recruit 500 tumours across breast, colorectal, gastric, pancreatic, ovarian and renal cancers, as well as sarcomas and melanomas to explore clonal dynamics and tumour microenvironment, as the driving source of selection. The recruitment is already underway.

The candidate will be based in a multi-disciplinary team of cancer evolutionary biologists and translational research clinicians concerned with both basic evolutionary principles and application of evolutionary rules in the clinic. There will be an opportunity to train in both dry and wet lab aspects. We collaborate nationally and internationally and there will be ample opportunities for training at the ICR, Crick and with our pharma partner Roche.