C ● N T R A

Computational Oncology Training Alliance

ESR 1 - Comparing tumour phylogenies from single cell data versus bulk sequencing data

Research project	Recent advances in sequencing technologies allow profiling the genetic heterogeneity of tumours on a single cell resolution and several new computational methods take advantage of this high-resolution data (e.g. Jahn, Kuipers, Beerenwinkel Genome Bio 2016 and Ross & Markowetz, Genome Bio 2016). At the same time, for clinical applications bulk sequencing of a very small number of biopsies (often just a single one) will remain the gold standard. This poses the question how well the evolutionary principles visible in single cell data can be recovered from bulk sequencing data and in general how evolutionary approaches based on single-cell data compare to those from bulk sequencing data. In this project we will make use of several data sets for which both single cell and bulk sequenced data are available for the same tumours (e.g. Gawad et al, PNAS 2014; McPherson et al, Nature Genetics 2016). We will compare clonal phylogenies computed from both data types and assess the impact of different noise levels in the data, sequencing depth and other biases like allele dropout. As a result, we will understand better how principles of tumour evolution can be applied in clinical practice.
Supervisor	name Florian Markowetz e-mail Florian.Markowetz@cruk.cam.ac.uk website www.markowetzlab.org
Host institution	University of Cambridge, United Kingdom Cancer Research UK Cambridge Institute (CRUK-CI)
PhD program	https://www.graduate.study.cam.ac.uk/courses/directory/cvcrpdmsc
Expected results	1) Method comparison and benchmarking 2) Characterisation of the limitations of evolutionary inference from clinically relevant samples.
Planned secondments	1) ETHZ/Beerenwinkel for advanced statistical methodology (3 months) 2) SEVENBRIDGES to learn how academic approaches are used in applied clinical settings (3 months).
Required profile	The successful candidate will have a degree in a quantitative discipline (computer science, statistics, mathematics, physics, ..) as well as data analysis and programming experience (ideally in R and Python). CRUK-CI is a very interdisciplinary place and excellent communication skills are important. Close engagement with cancer biology and experimental research is expected.