OVERVIEW

In the Computational Oncology Group we are tackling some of the deadliest cancers by targeting the causes of chromosomal instability. Pancreatic, oesophageal, lung and ovarian cancers have the lowest survival rates, but they also share a common trait which we can exploit – extreme chromosomal instability (CIN). By therapeutically targeting CIN, we aim to improve outcomes in these tumours.

Our main research areas include:

→ Using tumour organoids to develop therapeutic strategies to target CIN.
→ Developing single cell/nucleus sequencing approaches to detect ongoing CIN.

“Tackling some of the deadliest cancers by targeting the causes of chromosomal instability.”

We are applying these technologies at the earliest stages of tumour development in patients with premalignant lesions, with the goal of preventing aggressive, difficult to treat cancers.

RESEARCH HIGHLIGHTS

Different types of chromosomal instability leave distinct “scars” in the DNA of a tumour which we can detect using whole-genome sequencing. These genetic scars, or “signatures of CIN”, represent a way to detect and quantify different causes of CIN in a tumour.

Using tumour organoids to target CIN

Tumour organoids can be treated in vitro providing a way to link genomic features with drug response. By determining the activity of different types of CIN and linking them to drug response we are building a rational framework for therapy selection in the clinic using CIN as a biomarker.

Predicting therapy response in patients

Our lab is performing a series of retrospective clinical studies looking at predicting response to therapies using signatures of CIN (FIGURE A). The long-term goal is to predict response in prospective clinical trials in order to improve patient stratification and trial success.

Single cell DNA sequencing to detect ongoing CIN

Standard “bulk” whole-genome sequencing does not allow us to separate CIN that is ongoing in a tumour, from CIN that is historical (occurred during the evolutionary history of the tumour). We are using single cell DNA sequencing to interrogate the changes unique to each cell, which enables us to separate ongoing CIN from historical CIN (FIGURE B). Our lab is applying this technology to premalignant lesions allowing us to observe CIN at its earliest stages in tumour development, before it causes aggressive, resistant tumours, with the goal of developing chemo-preventive treatment strategies.

Geoffrey John Macintyre (since December)
Junior Group Leader

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