ICR The Institute of Cancer Research

Licensing and collaboration opportunity

Monitoring tumour evolution using methylation signatures in circulating tumour DNA

The Institute of Cancer Research, London, is seeking a partner to continue the development into commercial applications of a method of determining and tracking tumour evolution using the methylation signature of ctDNA.

Key Features

- Our data indicate that methylation profiling of ctDNA allows a patient's tumour evolution to be tracked using a liquid biopsy sample instead of repeated invasive tissue biopsies.
- These discoveries provide the foundation for the development of sensitive, reliable and non-invasive tumour monitoring methods enabling rapid, cheap and accurate monitoring of a patient's cancer evolution.
- This approach means treatments could be quickly adapted according to evolutionary changes occurring in the cancer, avoiding unnecessary treatments that are unlikely to work but may cause side effects.
- Further applications include the selection of personalised treatment regimens and the rapid and reliable evaluation of the effects of therapeutic agents in clinical trials.

Intellectual property

The Institute of Cancer Research (ICR) has filed a PCT patent application (PCT/EP2021/050851) covering the methods of determining and tracking tumour evolution using the methylation signature of ctDNA.

Commercial Opportunity

The ICR is seeking commercial partners to develop these discoveries into clinical tests to determine a phylogenetic relationship between different tumours in a patient and evaluate the effectiveness of different treatments.

About the programme

Circulating tumour DNA (ctDNA) allows the tracking of cancer evolution at high resolution, overcoming many of the limitations of invasive tissue biopsies.

But profiling of ctDNA almost always requires prior knowledge of what genomic alterations to track because ctDNA is a complex mix of fragmented pieces, making it difficult to identify the contribution of different cancer cell populations. Due to technical limitations of ctDNA samples, even high depth whole-genome sequencing cannot capture the subclonal composition of cancer cell populations at high resolution.

ICR researchers have discovered that the methylation profile of ctDNA can be used to track evolutionary changes in the cancer cell population

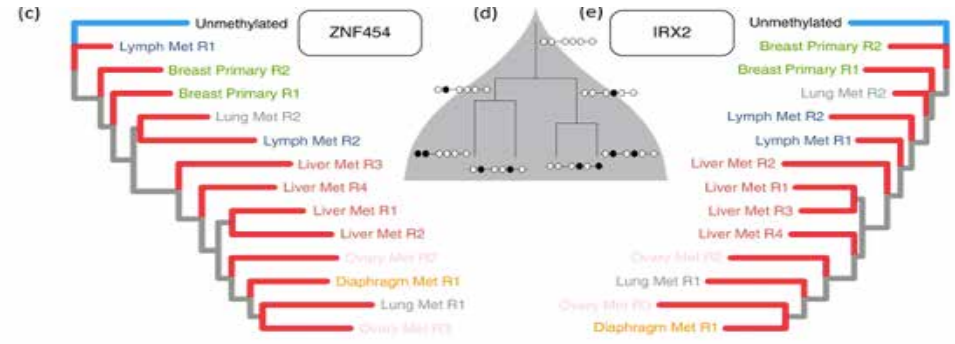

Figure 1: Tumour phylogenetic tree of a patient reconstructed using methylation clock analysis (epimutations instead of nucleotide substitutions) of methylation clock haplotypes for ZNF454 (c), corroborating the overall phylogenetic structure revealed by whole-genome sequencing. (d). The same can be done for IRX2, leading to the construction of a consistent tree (e).

from multiple metastatic sites at single-molecule resolution without prior knowledge. Profiling the methylation signature of ctDNA in the 'CpG island' of the genome provides a 'molecular barcode' corresponding to an identifiable cancer cell lineage. Profiling methylation patterns of polynucleotide sequences in ctDNA samples allows tracking of tumour evolution.

Cancer evolution

Researchers at ICR pioneered the application of evolutionary biology to cancer and established cancer stem cells as the units of natural selection. These discoveries demonstrated the need to understand the complexity of cancer to target treatments at specific mutations and helped to explain why cancers are so prone to evolving resistance to treatment.

The Centre for Evolution and Cancer is answering three big questions: why are humans so vulnerable to cancer; what determines the unpredictable development of cancers in the body over time; and why is drug resistance so common?

A multidisciplinary team is working together to identify the genetic diversity in individual tumours and exploring the use of genetic profiling as fingerprints that could predict the progression of the disease, metastases or drug resistance.

Key publication

Cresswell, GD et al, *Mapping the breast cancer metastatic cascade onto ctDNA using genetic and epigenetic clonal tracking.* Nat Commun 2020 (11):1446. https://doi.org/10.1038/s41467-020-15047-9

Lead scientist

Professor Andrea Sottoriva leads the Evolutionary Genomics and Modelling Team and is Director of the ICR's Centre for Evolution and Cancer.

Business & Innovation Office

The ICR's interactions with industry partners are led by our Business and Innovation Office, which oversees a large portfolio of partnership and licensing opportunities across a range of oncology research.

Contact the Business and Innovation Office for more information on our licensing and partnering opportunities.

Read more about our commercialisation work and sign up for our industry email newsletter at icr.ac.uk/partnerships

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