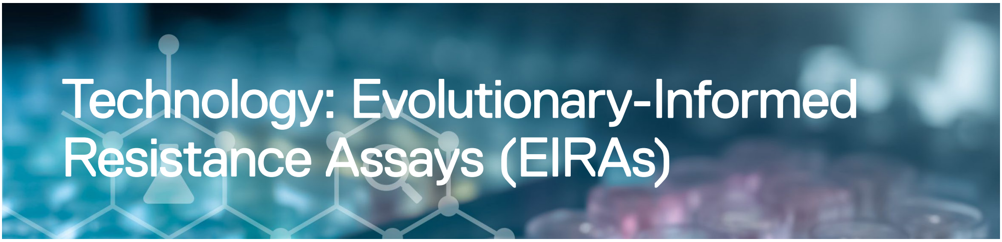
ICR The Institute of
Cancer Research



Technology: Evolutionary-Informed Resistance Assays (EIRAs)

The Institute of Cancer Research, London, is seeking collaborators from biotech and pharma who wish to tackle drug resistance upfront in their drug development projects.

The technology combines in vitro evolution with new computational methods to quantify drug resistance. The Institute of Cancer Research (ICR) would process collaborators' compounds through EIRAs. Readouts of the platform can help guide drug development.

Key points

- The new technology – Evolutionary-Informed Resistance Assays (EIRAs) – is positioned to help collaborators understand how resistance may evolve to their proprietary drug(s).
- The assay uses pre-clinical cell models and bespoke computational methods to measure the propensity for resistance to evolve to a drug, which may be a proxy for the time to treatment failure (TTTF) in clinical practice.
- The readout of the technology can help guide drug development in the following areas:
  - Positioning new drugs against existing treatments with a 'resistance propensity' score
  - Informing biomarker strategy for patient stratification in clinical trials by guiding the functional characterisation of resistance
  - Identifying rational drug combinations by choosing those with the lowest levels of cross resistance
- The technology has been developed by a team from the ICR's Centre for Evolution and Cancer, including Centre Director Professor Trevor Graham and postdoctoral research Dr Freddie Whiting. The Centre has pioneered new understandings of cancer evolution and drug resistance, and is allied to one of the world's most successful academic centres for cancer drug discovery and development.

Technology Intellectual Property

- A patent (GB 2501439.0) covering EIRAs' computational framework to infer drug resistance dynamics using lineage tracing and population size data has been filed.
- Development of the technology took place using a standard-of-care chemotherapy in pre-clinical cell models of colorectal cancer.

Ongoing Development

The team has begun exploring the use of EIRAs in colon, ovarian and breast cancer using therapies including CDK4/6 inhibitors, EGFR and MEK inhibitors, PARP and POLθ inhibitors.

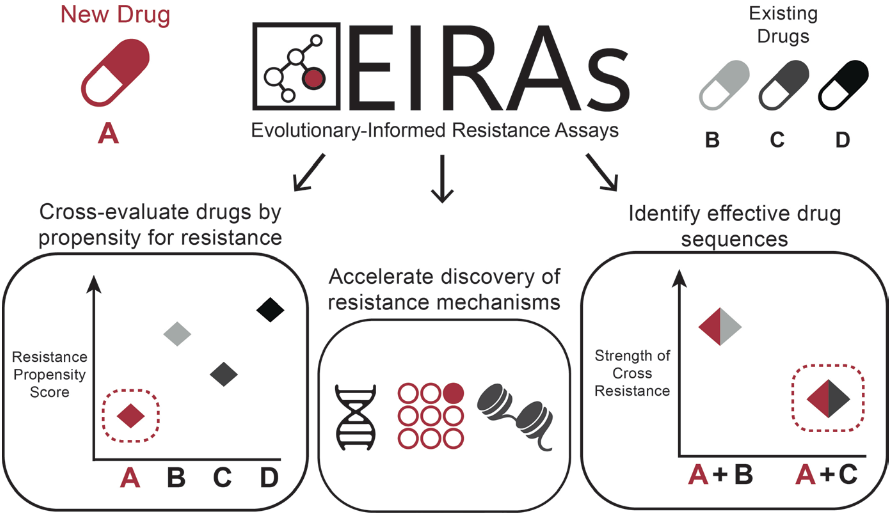


Fig 1. Schematic illustrating the outputs of the EIRAs platform

Technical limitations of existing technologies

Current pre-clinical assays focus on the short-term response of cancer cells to treatment. Drug developers lack technologies that enable resistance to be quantified in a standardised way. The long-term response to a drug is dictated by the presence and/or the rate of emergence of resistance. Quantifying resistance has proven difficult because it requires statistical models that capture a wide range of unpredictable evolutionary dynamics.

Our platform

The EIRAs platform combines lineage tracing of cancer cell in vitro models with computational models that adopt theories from evolutionary biology. These measurements are used to generate predictions for the propensity and mechanisms of resistance to the given treatment.

Direct comparisons can be made between different candidate drugs. These comparisons can be extended across relevant in vitro disease models, and the method is agnostic to the modality of the drug.

Drugs that have been independently run through EIRAs can identify shared mechanisms of resistance, identifying pairs with low levels of cross resistance.

Lineage tracing is used to read out changes in cancer clone sizes during treatment. These clone sizes are inputted into a Bayesian Inference framework which predicts the mechanism of drug resistance (clonal selection, phenotypic plasticity or more complex mechanisms). The output provides a rationale and prioritisation for subsequent functional characterisation(s).

The team

Dr Freddie Whiting is a Postdoctoral Researcher at the ICR. Trevor Graham is Professor of Genomics and Evolution and Director of the Centre for Evolution and Cancer at the ICR.

Key publication

Whiting et al, 2025. Quantitative measurement of phenotype dynamics during cancer drug resistance evolution using genetic barcoding. *Nature Comms*, **16**, 5282. *doi.org/10.1038/s41467-025-59479-7.*

Contact

Joo-Hee Sir PhD
Business Development Manager
Email: joohee.sir@icr.ac.uk
Tel+44 20 3437 6099