ICR The Institute of Cancer Research

A predictive test for personalising breast cancer treatment

The Institute of Cancer Research, London, is seeking partners to continue the development a gene expression signature into a predictive biomarker for predicting prognosis and treatment response for patients with early-stage ER+/HER2+ breast cancer.

A patent application has been filed (GB2116745.7) covering a gene expression profiling method that can classify tumours into molecular subtypes for predicting response to specific therapies and the risk of relapse.

About the programme

Breast cancer patients currently have their tumours classified according to the presence of three 'gold standard' biomarkers: the oestrogen and progesterone hormone receptors (ER and PR) and the HER2 receptor. About 15% to 20% of tumours have higher levels of HER2, of which about 50% are either ER or PR positive.

Patients with ER+/HER2+ receive standard hormone treatments such as aromatase inhibitors, which lower oestrogen levels in the body. However, resistance to these treatments is relatively high for patients with ER+/HER2+ tumours, and new biomarkers are urgently needed to help improve treatment for these women – to detect likely treatment resistance and prioritise them for other treatment options while minimising unnecessary side effects.

A research team at the ICR has now identified a set of new biomarkers that predict resistance to aromatase inhibitors in ER+/HER2+ tumours and could enable the identification of patients at a higher risk of relapse.

The findings were made through a study of more than 300 patients from POETIC – a phase III trial of almost 4,486 patients from across the UK, that aims to determine whether a two-week course of aromatase inhibitor treatment before and after surgery improves long-term outcomes compared with post-operative treatment alone.

Key publications

1. Patent reference GB2116745.7 – 'Prognostic and Treatment Response Predictive Method'.

2. Bergamino, Lopez-Knowles et al. *HER2-enriched subtype and novel molecular subgroups drive aromatase inhibitor resistance and an increased risk of relapse in early ER+/HER2+ breast cancer.* **eBioMedicine**. August 16 2022. DOI: 10.1016/j.ebiom.2022.104205.

Key points

Gene expression signatures – derived from an analysis of breast cancer samples collected from the POETIC trial – can stratify ER+/ HER+ tumours into molecular subtypes that can help predict response to aromatase inhibitors and the risk of relapse.

The method has the potential to be developed into a predictive biomarker test to help personalise treatment, including escalation and de-escalation strategies, to improve resistance to treatment in breast cancer.

It could particularly benefit women with early-stage breast cancer who are undergoing or will be treated with hormone therapies.

Lead scientists/inventors

Dr Maggie Cheang is the leader of the integrative genomics analysis team at the ICR. She focuses on identifying and developing multi-parametric molecular classifiers to predict sensitivity of each tumour type to therapeutic agents in phase II and III clinical trials.

Dr Cheang co-invented the 50 genes-based classifier for the intrinsic subtypes of breast cancer, commonly known as PAM50, which is currently licensed by Veracyte as Prosigna and has been implemented into multiple international clinical practice guidelines. She also chairs the UK National Cancer Research Institute (NCRI) Clinical Trial Pathology Advisory Group.

Professor Mitch Dowsett's studies into the role of hormones in breast cancer led to the clinical development of aromatase inhibitors. His interest in the pharmacodynamics of hormone treatment led to the widespread use of the marker Ki67 in pre-surgical studies for evaluating new drugs.

He views the pre-surgical setting as being uniquely informative for the in vivo study of breast cancer biology and new therapeutic strategies. To achieve this, he has been involved as the biological leader of many clinical trials – including POETIC.

The other co-inventors are **Elena Lopez Knowles**, Senior Scientific Officer at the ICR, and **Milana Bergamino**, Medical Oncologist and Clinical Research Fellow at the ICR.

Our 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.

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