Identifying tumour characteristics as predictors of immunotherapy response in aggressive breast cancers

Tumour characteristics could be used to predict whether patients with an aggressive subtype of breast cancer are able to respond to immunotherapy, according to new research from the Cancer Research UK Cambridge Institute and Fondazione Michelangelo published today, Date, in Nature.

Breast cancer is the leading cause of death in woman, in most of the countries around the word. However, the clinical behaviour is extremely heterogeneous. The triple-negative subgroup despite only accounting for 15% of all breast cancer cases, is particularly aggressive and contribute proportionally more to the overall deaths from breast.

Triple negative breast cancers are cancers whose cells don't have receptors for the hormones oestrogen and progesterone, or a protein called Human Epidermal Growth Factor Receptor 2 (HER2).

Because they lack these three molecular markers, there are significantly fewer treatment options for patients beyond chemotherapy. Fewer treatment options result in a worse prognosis for patients, and so finding novel therapies for this subtype is crucial.

Immunotherapy has transformed the treatment of many solid tumours, however, it's best use in breast cancer is still unclear. Clinical trials have shown that a type of immunotherapy called Immune Checkpoint Blockade (ICB) can benefit some patients with TNBC, but we lack reliable methods of predicting which patients may respond to the treatment.

As ICB targets cell to cell interactions, the effectiveness of ICB as a treatment for breast cancer depends both on the cells within the tumour and how those cells are arranged spatially within the tumour.

New research from the Ali Group, in collaboration with Fondazione Michelangelo and San Raffaele Hospital in Milan, used 660 tumour biopsy samples from patients before their treatment, during treatment and after treatment to map tissue structure and identify unique predictors of whether a patient would respond to treatment.

They looked within the samples for the presence of 43 key proteins, indicative of the characteristics and behaviour of different cells. Using a technique called imaging mass cytometry, they produced detailed images, which revealed precisely how each of the 43 proteins were distributed across the tumour. With statistical modelling, the researchers were able to identify unique features that differed between a patient who was able to respond to ICB and one that wasn't.

The team found that they were best able to predict which patients would be able to benefit from ICB treatment by combining information about the tissue features from before and during treatment. This suggests that early biopsies would be a useful addition to clinical practice to help guide personalised treatment plans and improve patient outcomes.

Dr ***Raza Ali***, co-Senior Author and Group Leader at the Cancer Research UK Cambridge Institute, said: "Immunotherapy harnesses the body's own defences to fight cancer. To be effective, we found that immunotherapy requires certain immune cell types to be in the right spatial context. We are now taking this research further by investigating whether a simple test could be used to identify which tumours are likely to respond to immunotherapy, so that it could be used in a routine clinical setting."

Ciccy Wang, first author, said: "Using a cutting-edge multiplexed imaging technology, we characterised the multicellular architecture of breast tumours and, for the first time, showed how it is remodelled by immunotherapy, revealing insights into how the different arrangements of cells in different patients results in different treatment outcomes. What we found suggests that similar approaches could be useful in other tumour types to understand why patients respond differently to immunotherapy."

Dr ***Giampaolo Bianchini***, co-Senior Author and Head of Breast Cancer Group at the San Raffaele Hospital and Scientific Coordinator of Translational Researches at Fondazione Michelangelo, said "Our work represents a significant contribution toward precision immunology. We are now working to integrate this information with data derived by RNA and DNA-sequencing to unveil a comprehensive view on the landscape of the TNBC ecosystem".

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Cancer Research UK Cambridge Institute (www.cruk.cam.ac.uk)
The Cancer Research UK Cambridge Institute combines basic and clinical research with innovative technologies to address key questions in the diagnosis and treatment of cancer. As one of the largest cancer research facilities in Europe, we provide an unrivalled biomedical research environment, bringing together the world-class science of the University of Cambridge with clinical and industrial partners at the Cambridge Biomedical Campus. Our research focuses on tumour ecology and evolution, ranging from basic experimental and computational biology through translational cancer research to clinical application.

Fondazione Michelangelo Onlus (www.fondazionemichelangelo.org)
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