

# Results of innovative triple negative breast cancer project paves the way for new six-year study to improve response to immunotherapy

Submitted by: Against Breast Cancer

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Promising results of his team's research into the extracellular matrix of triple negative breast cancer has led Dr Oliver Pearce to being awarded a CRUK Career Establishment Award of over £800,000 to continue and develop his work for a further six years.

Dr Pearce was the first recipient of a seed grant following our call for proposals in 2017. These grants were designed to promote innovative research that had the potential to impact the way metastatic breast cancer is diagnosed, treated or even prevented.

Up to £50,000 in value for projects with a maximum term of 1 year. Dr Pearce used his grant for the gathering of preliminary data necessary to support a larger grant application which he has now successfully done.

Dr Pearce, the Group Leader in the Centre for tumour microenvironment at Bart's Cancer Institute in London, initially applied for funding towards a project aiming to identify how breast cancer tumours remodel their surroundings to protect them from attack by the bodies' own immune system.

Known as the Glycan Shield Project, it would be the first detailed study of the components that make up the extracellular matrix (ECM) of triple negative breast cancer, including both the protein and sugar structures which it is believed may deactivate immune cells, stopping them from destroying the tumour.

Dr. Pearce hypothesized that abnormal glycans in the ECM, (which describes the molecules that make up a tissue in which cells function) deactivate immune cells, turning off their cell-killing function. Through molecular analysis and assessment of the ECM, he hopes to decode how immune cells are deactivated.

"The seed grant from Against Breast Cancer allowed us to take an idea and accelerate it forward effectively finishing a project that would otherwise have taken several years." Dr Oliver Pearce  
Group Leader in the Centre for tumour microenvironment  
Bart's Cancer Institute, London

In less than 2 years the data his team has captured using the funds of the seed grant allowed the forms the foundation for the hypothesis being investigated with Cancer Research UK, making Against Breast Cancer's support extremely important.

This information provided the first high detailed study of the ECM of TNBC at both the translational and post-translational level. Unique matrix protein structures identified may have the potential for further development as prognostic biomarkers, or targeting molecules for the delivery of anticancer agents, or the target of therapeutic antibodies for matrix focused cancer therapies.

This work will be done in collaboration with Dr. Alexandra Naba (University of Illinois, Chicago), Dr. Pedro Cutillas (QMUL), and Dr. Stuart Haslam (Imperial College, London).

The focus of his research on understanding how the tumour ECM forms a barrier to immunotherapy response could be particularly important for patients with TNBC who have limited treatment options but could also be good candidates for immunotherapy.

Results of the research funded by Against Breast Cancer grant found a composition of ECM proteins which associate with poor prognosis across many cancers tested. Dr Pearce's team started to explore how these proteins may be involved in immunotherapy failure. In addition, they characterized these same extracellular matrix proteins and found they have altered structure, which makes them vulnerable to targeting.

With the Career Establishment Grant provided by Cancer Research UK the goal is to target these ECM proteins and in doing so improve response to immunotherapy. To achieve this the objectives are to identify which ECM proteins are involved, characterise their structure to identify targets, then test their functional role using engineered tumour microenvironments. Finally testing their inhibition as a route to restoring immunotherapy response.

Using a combination of biochemistry, molecular biology, and genetic engineering. The special approaches that his lab uses are unique characterization methods and 3D engineered tumour models.

Richard Bahu, Chair of Trustees at Against Breast Cancer said "This is fantastic news for Dr Pearce and his team, together they demonstrated the major impact Against Breast Cancer's seed grant made to their research. Our supporters will be thrilled to learn it was their fundraising, supporting this world class research that was core to enabling the deserved recognition and major investment this innovative research programme requires."

How will the work help patients with breast cancer?

Dr Pearce hopes the information generated by this work to design targeted therapeutics could be used in combination with current immunotherapies to improve patient response rates. This is important because immunotherapy offers prolonged or perhaps progression free survival, however it only works in around 10-15% of patients with solid tumours like TNBC. His target is to make immunotherapy work for those 80-90% of patients as well.

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Against Breast Cancer is a charity dedicated to funding ground-breaking research to increase survival after a breast cancer diagnosis by focusing on secondary spread, the main cause of breast-cancer related deaths. We fund research that addresses critical gaps in scientific resources and knowledge to help doctors diagnose and treat secondary breast cancer faster and more effectively, and to understand factors that may increase or reduce the risk of secondary spread so that people can make informed diet and lifestyle choices.

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