# Novel study into breast cancer origins paves way for personalized treatment

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Breast cancers can look and behave very differently. Understanding why and how they do so is key to designing more tailored therapies for patients and sparing them unnecessary treatments.

In a new study published by the *Journal of Pathology*, Dr Matt Smalley from Cardiff University treads new ground in exploring what drives breast cancers to look and behave so differently from one another.

"The ultimate aim of this research is to be able to take a more personalised approach to medicine," said Dr Smalley from Cardiff University's European Cancer Stem Cell Research Institute. "We hope that in doing so, patients get the therapy best suited to their variety of breast cancer and avoid unnecessary treatment.

"To understand what might be influencing the differences between individual breast cancers, we have used two different genetically modified mouse models in which breast cancers originate in different cell types in each model, by means of a genetic 'trick'," he explained.

"In one part of the study, we created the same cancer-predisposing genetic errors in each of the two cell types. In another part, we created different genetic errors in the same cell type. We then asked whether the tumour types which occurred varied more strongly in their appearance depending on the cells in which they developed, or the genetic errors that caused the cancers, or both."

Dr Smalley continued: "We found that for cells originating in one of the cell types, so-called 'basal' cells, the cancers appeared the same no matter the genetic error, suggesting that in this case the cell of origin was dominant in determining how the cancer formed. However, the cancers that appeared from this cell type resembled a very rare form of human breast cancer, so these cells are probably not relevant to the majority of human cases.

"In contrast, for tumours originating in so-called 'estrogen receptor negative luminal cells', the appearance of the cancers varied depending on the genetic errors used to generate them.

"Remarkably, some of the cancers that formed resembled common human breast cancer types including both estrogen receptor negative and positive disease. We had previously shown this cell type to be the likely origin of Brca1-associated and other aggressive estrogen receptor negative breast cancers.

"Our findings now suggest the same cells are also the origin of aggressive estrogen receptor positive cancers as well. These results add to our understanding of the origins of breast cancer diversity and emphasise the importance of understanding the biology of this cell type to better understand how breast cancer develops."

The research, spearheaded by Dr Smalley from the European Cancer Stem Cell Research Institute at Cardiff University and conducted in collaboration with colleagues from Spain, Brazil and the UK, was funded by Breakthrough Breast Cancer and Cancer Research UK.

Richard Francis, Senior Manager Research Insight at Breakthrough Breast Cancer, said: "Understanding the biology of breast cancer is essential for the future development of new ways to treat and prevent this disease.

"We know that breast cancer is a mixture of many different subtypes and this work goes towards explaining how these arise. Ultimately this information will help the development of precision medicine, where each patient receives the treatment that will benefit them."

Nell Barrie, Senior Science Information Manager at Cancer Research UK, said: "Our scientists have already helped re-define how we view cancer – showing that breast cancer is at least 10 different diseases, each with its own molecular fingerprint and weak spots. This research takes us one step closer to understanding why we see so much diversity in breast cancer, and will help expose each cancer's weakness so we can develop more effective and kinder treatments."

"The hope is that this paper will become a standard work of reference for mouse breast cancer research as there is currently no other benchmark for this type of work," concluded Dr Smalley. "It shows the quality of output from the European Cancer Stem Cell Research Institute as world leaders in analysis of mouse tumour models."

Provided by Cardiff University

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