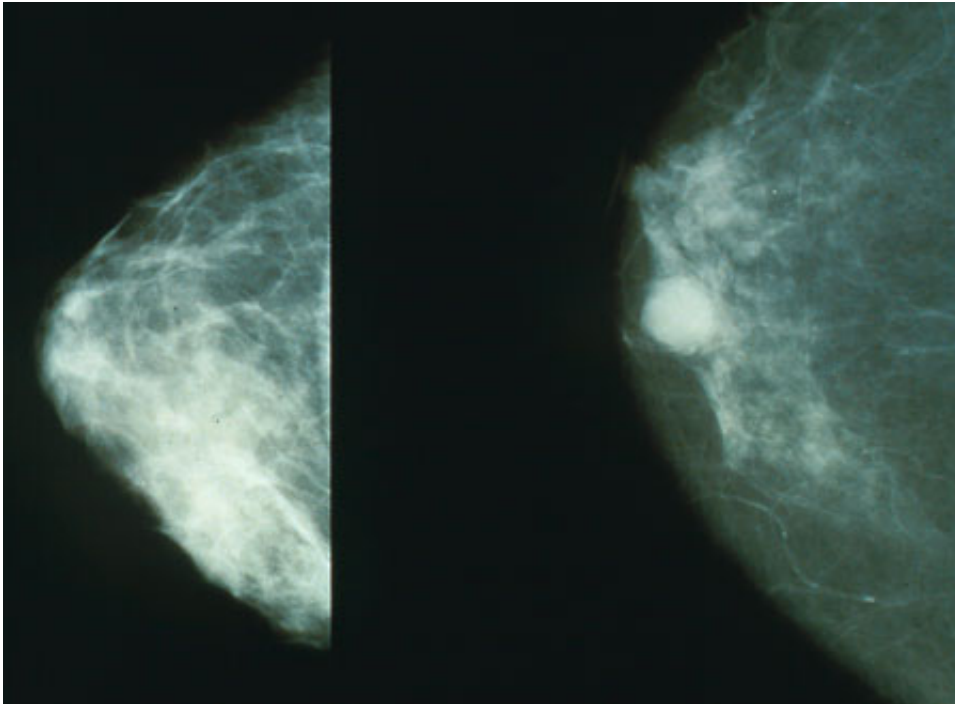


Novel breast cancer gene found

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Mammograms showing a normal breast (left) and a breast with cancer (right).
Credit: Public Domain

A new study identifies a gene that is especially active in aggressive subtypes of breast cancer. The research suggests that an overactive BCL11A gene drives triple-negative breast cancer development and progression.

The research, which was done in human [cells](#) and in mice, provides new routes to explore targeted treatments for this aggressive tumour type.

There are many types of breast cancers that respond differently to treatments and have different prognoses. Approximately one in five patients is affected by triple-negative breast cancer; these cancers lack three receptor proteins that respond to hormone therapies used for other subtypes of breast cancer. In recent years it has become apparent that the majority of triple-negative tumours are of the basal-like subtype.

Although new treatments are being explored, the prognosis for triple-negative cancer is poorer than for other types. To date, only a handful of genomic aberrations in genes have been associated with the development of triple-negative breast cancer.

The team looked at breast cancers from almost 3000 patients. Their search had a particular focus: they examined changes to genes that affect the behaviour of stem cells and developing tissues, because other work they have done suggests that such genes, when mutated, can often drive cancer development. Among these was BCL11A.

"Our understanding of genes that drive stem cell development led us to search for consequences when these [genes](#) go wrong," says Dr Pentao Liu, senior author on the study, from the Wellcome Trust Sanger Institute. "BCL11A activity stood out because it is so active in triple-negative cancers.

"It had all the hallmarks of a novel breast cancer gene."

Higher activity of the BCL11A gene was found in approximately eight out of ten patients with basal-like breast cancer and was associated with a more advanced grade of tumour. In cases where additional copies of the BCL11A gene were created in the cancer, the prospects for survival of the patient were diminished.

"Our gene studies in human cells clearly marked BCL11A as a novel

driver for triple-negative breast cancers," says Dr Walid Khaled, joint first author on the study from the Wellcome Trust Sanger Institute and University of Cambridge. "We also showed that adding an active human BCL11A gene to human or mouse breast cells in the lab drove them to behave as cancer cells.

"As important, when we reduced the activity of BCL11A in three samples of human [triple-negative breast cancer](#) cells, they lost some characteristics of cancer cells and became less tumorigenic when tested in mice. So by increasing BCL11A activity we increase cancer-like behaviour; by reducing it, we reduce cancer-like behaviour."

When BCL11A was inactivated in an experimental system in mice, no mice developed tumours in the mammary gland, whereas all untreated animals developed tumours.

The team also showed that BCL11A is required for normal development of breast stem cells and progenitors, which are thought to be the cells that, when mutated, give rise to basal-like breast cancer.

"This exciting result identifies a novel [breast cancer gene](#) in some of the more difficult-to-treat cases," says Professor Carlos Caldas, Professor of Cancer Medicine and Director of the Cambridge Breast Cancer Research Unit at the University of Cambridge, and Head of Breast Cancer Functional Genomics at Cancer Research UK Cambridge Institute. "It builds on our work to develop a comprehensive molecular understanding of [breast cancer](#) that will inform clinical decisions and treatment choices.

"Finding a novel gene that is active in cancer should also help in the search for new treatments."

The team propose that BCL11A is a strong candidate for development of

a possible targeted treatment.

More information: Khaled, WT, Lee SC et al. (2015) BLC11A is a triple-negative breast cancer gene with critical functions in stem and progenitor cells. *Nature Communications*, published online in advance of print publication [DOI: 10.1038/ncomms6987](https://doi.org/10.1038/ncomms6987)

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