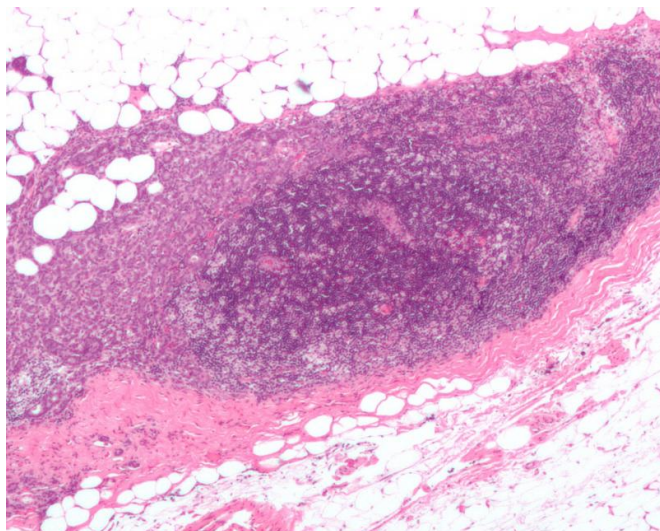


One in five breast cancer patients could benefit from existing treatment, genetic study reveals

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Micrograph showing a lymph node invaded by ductal breast carcinoma, with extension of the tumour beyond the lymph node. Credit: Nephron/Wikipedia

Researchers from the Wellcome Trust Sanger Institute and their collaborators have discovered that a greater number of breast cancers are genetically similar to rarer cases with faulty BRCA1 or BRCA2 genes. The results published today (13 March) in *Nature Medicine* open up the possibility of up to 20 per cent of women being treated with PARP inhibitors, a class of drug previously only thought to be effective for women with an inherited BRCA1 or BRCA2 mutation.

Breast cancer is the most common cancer in the UK, affecting nearly 55,000 women a year. Globally it accounts for nearly 1.7 million cancer cases. Between 1 and 5 per cent of breast cancer cases are due to inherited mutations in BRCA1 or BRCA2 [genes](#).

Inherited mutations in BRCA1 and BRCA2 genes mean that some of the machinery required to fix DNA is faulty. People with these faults have higher risks of developing certain cancers, like breast and ovarian cancer.

Drugs called PARP inhibitors have been designed to specifically treat tumours with faulty BRCA1 and BRCA2 genes in breast and ovarian cancers, and their use against prostate cancer is currently being investigated.

In the study, researchers analysed the breast cancer genomes of 560 patients and looked for every single type of mutation possible. The team developed a new computer-based tool called HRDetect to identify patterns of mutations - mutational signatures - in the tumours, which were similar to people who have mutations in the BRCA1 and BRCA2 genes.

Scientists discovered that many [breast cancer patients](#) had mutational signatures that were identical to people with faulty BRCA1 and BRCA2 genes, even though they had not inherited the mutations.

The results suggest that roughly 1 in 5 breast cancer patients could benefit from existing PARP inhibitor treatments. This would need to be tested through a clinical trial, with participants being selected based on the mutational signatures of their tumour.

Dr Serena Nik-Zainal, lead author from the Wellcome Trust Sanger Institute, said: "In the past, [clinical trials](#) for PARP inhibitors have focused mainly on the 1-5 per cent of women with [breast cancer](#). However, our study shows that there are many more people who have cancers that look like they have the same signatures and same

weakness as patients with faulty BRCA1 and BRCA2 genes. We should explore if they could also benefit from PARP inhibitors. The results suggest that clinical trials now need to look at [cancer patients](#) who share the same genetic signature in their cancer. This could change how clinical trials are designed in the future."

Until now, most clinical trials of PARP inhibitors have focused on patients with inherited mutations in the BRCA1 and BRCA2 genes. This research suggests that systematic clinical trials on a wider set of patients will be required to see if they might also be responsive to the drugs.

Dr Helen Davies, joint first author from the Wellcome Trust Sanger Institute, said: "From the mutational signatures we were able to spot many more tumours with defects in their DNA repair machinery that we couldn't see before. This was only possible by sequencing the entire genome of these cancers. Further work needs to be done as there could be tumours with the same mutational signature elsewhere in the body that may respond to these drugs."

Professor Sir Mike Stratton, Director of the Sanger Institute, said: "This work uses mutational signatures to identify the complete set of cancers that will respond to certain drugs that are already known to be effective in a subset. To translate these results into treatments, further sequencing of cancer genomes and more clinical trials are urgently needed, but this is a most promising start."

More information: Helen Davies et al. (2017) HRDetect is a predictor of BRCA1 and BRCA2 deficiency based on mutational signatures. *Nature Medicine*. DOI: [10.1038/nm.4292](https://doi.org/10.1038/nm.4292)

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