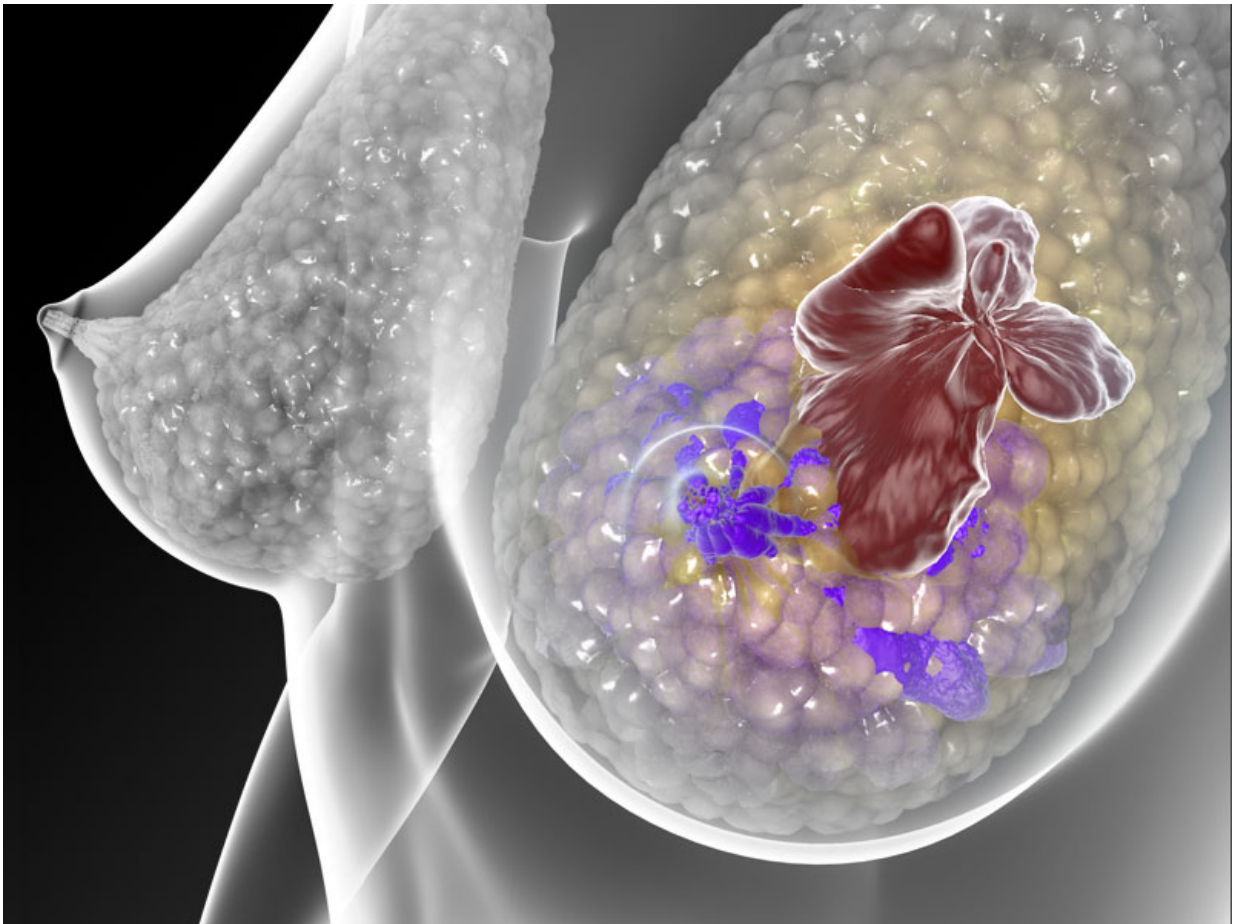


# Blood test detects when hormone treatment for breast cancer stops working

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Breast cancer patients with mutations in the estrogen receptor gene ESR1 are known to develop resistance to hormone therapy. A new study finds that resistance to hormone therapy usually evolves in the advanced stage of disease, suggesting that earlier treatment may help some patients avoid drug resistance. Credit: C. Bickel / Science Translational Medicine

Scientists have developed a highly sensitive blood test that can spot when breast cancers become resistant to standard hormone treatment, and have demonstrated that this test could guide further treatment.

The test gives an early warning of resistance to aromatase inhibitors, which are used to treat women with oestrogen receptor (ER)-positive [breast cancer](#), the most common kind.

A team at The Institute of Cancer Research, London, and The Royal Marsden NHS Foundation Trust found that the test could detect mutations to the oestrogen receptor gene ESR1 - which conveys resistance to hormone [treatment](#) - specifically in women treated with aromatase inhibitors.

Detecting mutations in this gene from [cancer](#) DNA in the bloodstream could allow doctors to rapidly identify which patients are no longer benefiting from treatment and switch them to an alternative drug.

The work is published in the journal *Science Translational Medicine* today (Wednesday), and was funded by several organisations including the NIHR Biomedical Research Centre at The Royal Marsden and The Institute of Cancer Research (ICR), Breast Cancer Now, The Criddle Ross Smith Charitable Trust and Cancer Research UK.

Researchers initially took blood samples from 171 women with ER-positive breast cancer, and then validated their results in three independent groups of patients.

They found that ESR1 mutations could be detected by an ultra-sensitive method known as multiplexed digital PCR analysis, which can read the genetic code of tiny amounts of DNA released by tumours.

This method proved able to detect DNA errors as sensitively as tumour

biopsies, with 97 per cent matching between the two methods, and could in future remove the need for such an invasive procedure.

Researchers at the ICR and The Royal Marsden found that once ESR1 mutations were detected, mutated cancer cells multiplied and became the dominant type in the body - driving the disease to become more aggressive and progress rapidly.

Women who had breast cancers with ESR1 mutations were three times more likely to progress than those without.

The stage at which the cancer was treated had a huge influence over how cancers became resistant to aromatase inhibitors, which are used as standard after surgery in postmenopausal women with ER-positive breast cancer. Mutations in ESR1 only occurred in 6 per cent of patients first treated with [aromatase inhibitors](#) when their cancers had not spread, but in 36 per of patients when the disease had already spread round the body by the time the drugs were administered. The research suggests more advanced cancers evolve drug resistance much more readily, reinforcing the importance of early diagnosis and early treatment for cancer.

Study leader Dr Nicholas Turner, Team Leader in Molecular Oncology at The Institute of Cancer Research, London, and Consultant Medical Oncologist at The Royal Marsden NHS Foundation Trust, said:

"Looking for cancer DNA in the blood allows us to analyse the genetic changes in cancer cells without the need for invasive biopsies. Our study demonstrates how these so-called liquid biopsies can be used to track the progress of treatment in the most common type of breast cancer.

"The test could give doctors an early warning of treatment failure and, as clinical trials of drugs that target ESR1 mutations are developed, help select the most appropriate treatment for women with advanced cancer."

Professor Paul Workman, Chief Executive of The Institute of Cancer Research, London, said: "We are in a new era of personalised cancer medicine, and liquid biopsies offer the hope that treatment can be monitored and adapted according to the evolution of an individual patient's cancer.

"In the space of the last couple of years there has been astonishingly rapid progress in the development of liquid biopsies to detect specific cancer [mutations](#) in the bloodstream. I am excited by the prospects of these new tests and would like to see them assessed in clinical trials as soon as possible, so we can show that their use to adapt treatment can offer real benefits for cancer patients."

**More information:** "Analysis of ESR1 mutation in circulating tumor DNA demonstrates evolution during therapy for metastatic breast cancer," by G. Schiavon et al. [stm.sciencemag.org/lookup/doi/...  
scitranslmed.aac7551](https://stm.sciencemag.org/lookup/doi/10.1126/scitranslmed.aac7551)

Provided by Institute of Cancer Research

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