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Possible treatment for breast cancer patients could roll out to clinical trial immediately

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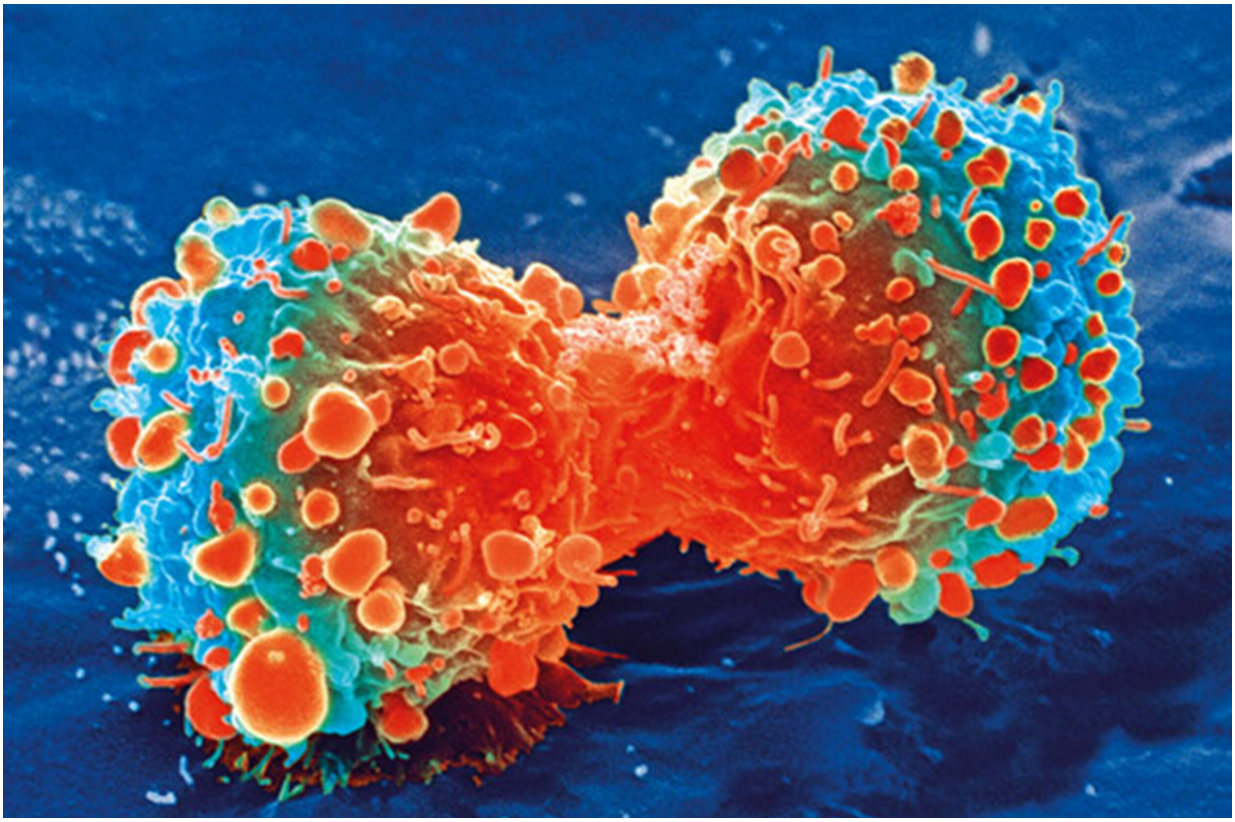

Cancer cell during cell division. Credit: National Institutes of Health

A worldwide collaborative study led by scientists at the University of Sussex has proposed a new treatment strategy for patients with a rare but aggressive subtype of cancer known as triple negative breast cancer.

The treatment targets healthy cells using drugs that are already available and currently in use for patients with leukaemia and lymphoma.

Around 15% of breast cancer cases are diagnosed as triple negative breast cancer—a form of solid cancer where cells don't have receptors for the oestrogen (ERα) and progesterone hormones (PR), or a protein known as HER2. Current treatments involve surgery or chemotherapy, however prognosis still remains poor.

A new study led by Georgios Giamas, Professor of Cancer Cell Signalling at the University of Sussex, has provided strong evidence for the development of a new type of treatment to halt progression of the disease by using existing drugs to target the surrounding healthy tissues of cancerous cells, known as fibroblasts.

Prof Giamas said: "Cancer is a systemic disease so instead of only focusing on cancer cells to find a cure, sometimes we need to step back and look at the bigger picture known as the tumour microenvironment'. This means looking at the surrounding cell types—the 'normal cells' - that can actually contribute either positively or negatively to the progression of the disease."

Using samples from triple negative breast cancer patients, researchers found that overall survival was markedly worse when levels of the protein PIK3Cδ were high in surrounding healthy tissue. Interestingly, this was not the case for the other two subtypes of breast cancer(ERα+ and HER2+).

PIK3Cδ inhibitors were tested in two different breast cancer mouse models with results showing a reduction in tumour growth. As PIK3Cδ is mainly expressed in white blood cells, scientists believe that these drugs acted predominantly on the immune system. The findings suggest that if treatments could control levels of PIK3Cδ in the surrounding

normal cells, then survival outcomes for patients would improve.

Prof Giamas said: "The lack of effective therapies for triple negative breast cancer is well-established, despite the emergence of approaches like immunotherapy.

"Our results suggest that repurposing already available drugs which act as inhibitors for PIK3Cδ could stop the progression of the disease. As the drugs are already available and FDA approved, clinical trials could begin immediately to further investigate the use of these inhibitors for triple negative breast cancer treatment."

Dr. Teresa Gagliano, first author of the study and currently Senior Scientist at the University of Zurich, said: "If we had focused only on the cancer cells, we would have never identified PIK3Cδ, and the possibility of an alternative therapy. Sometimes it's fundamental to think outside the box."

The study, funded by Action Against Cancer, involved scientists from across three continents and six different countries and was published in the *Journal of Clinical Investigation*.

The findings will be of interest to oncologists who may decide to take this forward to clinical trial, if the Medicines and Healthcare products Regulatory Agency (MHRA) review and authorise the drug.

More information: PIK3Cδ expression by fibroblasts promotes triple-negative breast cancer progression, *Journal of Clinical Investigation* (2020). DOI: 10.1172/JCI128313

Provided by University of Sussex