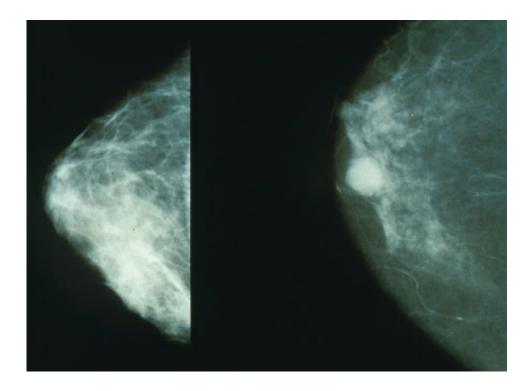


## Scientists make promising discovery in fight against breast cancer

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

Researchers from the University of Liverpool have created a biomedical compound that has the potential to stop the spread of breast cancer. The paper, "Targeted Destruction of S100A4 Inhibits Metastasis of Triple Negative Breast Cancer Cells," is published in *Biomolecules*.

Scientists from the Chemistry and Biochemistry Departments at the



University of Liverpool and Nanjing Medical School in China have discovered a possible way to block proteins produced in the body when a patient has cancer and which causes its spread to other parts of the body. This process, called metastasis, is largely responsible for patient deaths.

The major problem hindering the successful treatment of commonly occurring cancers is not the primary tumor which can usually be removed by surgery, but its spread to other organs of the body.

Prof Philip Rudland, Emeritus Professor in the University of Liverpool's Department of Biochemistry, said, "As a general rule, cancer that has spread is treated with chemotherapy, but this treatment can rarely be given without severely harming or becoming toxic to the patient. The importance of our work was to identify a specific and important target to attack, without toxic side effects."

The research team have in the past discovered that specific proteins are involved in the metastatic process; these proteins are different from those involved in the production of the primary tumor. One such example is a protein called "S100A4," and is the protein chosen by the research team to target for the identification of chemical inhibitors of metastasis, using model systems of cells from the highly metastatic and incurable hormone receptor-free breast <u>cancer</u>.

Using these model systems, researchers discovered a novel compound that can specifically block the interaction of this metastasis-inducing protein S100A4 with its target inside the cell. Researchers in the Department of Chemistry then synthesized a simpler chemical and connected it to a warhead which stimulates the normal protein degrading machinery of a cell.

This compound now works at very low doses to inhibit properties associated with metastasis, an improvement of over 20,000-fold on the



original unarmed inhibitor, with virtually no toxic side effects. Moreover, in collaboration with Chinese researchers at Nanjing Medical School, they have shown that this compound inhibits metastasis in similar metastatic tumors in mice, suggesting a potential therapeutic role.

Dr. Gemma Nixon, Senior Lecturer in Medicinal Chemistry at the University of Liverpool said, "This is an exciting breakthrough in our research. We now hope to take the next steps, and repeat this study in a large group of animals with similar metastatic cancers so that the efficacy and stability of the compounds can be thoroughly investigated and if necessary improved by further design and syntheses, prior to any clinical trials."

"Significantly, this particular protein we're investigating occurs in many different cancers, which could mean this approach may be valid for many other commonly occurring human cancers."

**More information:** Thamir M. Ismail et al, Targeted Destruction of S100A4 Inhibits Metastasis of Triple Negative Breast Cancer Cells, *Biomolecules* (2023). DOI: 10.3390/biom13071099

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