

CDRI research a ray of hope for triple negative breast cancer patients

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Lucknow: In a ray of hope for patients of triple negative breast cancer (TNBC), the scientists have found that administration of a drug on a specific enzyme found in the human body

can help treat this most aggressive subtype of breast cancer.

"A protein (enzyme) called acyl-CoA synthetase 4 (ACSL4) in human body can be targeted by the medical/scientific fraternity for the treatment of TNBC, which is associated with a high mortality rate," says a study by CSIR-Central Drug Research Institute (CDRI) researchers.

The study is crucial since TNBC has limited treatment options, and researchers have long felt an urgent need for novel therapeutic strategies to improve clinical outcomes of the disease.

"TNBC poses a particularly significant global challenge due to its lack of hormone receptor expression, as a result commonly used targeted anti-hormone therapies like Tamoxifen, Herceptin do not work for this particular breast cancer subtype. Sadly, India bears the highest incidence of TNBC globally," said senior scientist Dipak Datta, who led the research.

He said that this research focuses on an enzyme called acyl-CoA synthetase 4 (ACSL4) and its role in promoting the spread of TNBC.

The study investigates how ACSL4 influences cancer cell behaviour, in terms of its migration from the primary site of tumour to distant secondary organs in the body. The study also explores the possibility of inhibiting this enzyme to develop new treatments for TNBC.

The five-year long study has been published in an internationally acclaimed peer reviewed journal, Proceedings of the National Academy of Sciences (PNAS).

Talking about the methodology, Prof Datta explained that in collaboration with King George's Medical University, Lucknow and Prof Siddhesh S Kamat's group at IISER, Pune, the team conducted a series of experiments on TNBC cell lines, mouse models and human tissue samples.

"Our team employed mouse models of TNBC that closely mimic human pathogenesis of the disease to show that ACSL4 plays a very important role in the spread of this cancer type. It could serve as a promising therapeutic approach for treating this type of cancer," said Datta.

"By targeting this enzyme, it may be possible to disrupt the metabolic and epigenetic changes (the two biological processes that often occur together during cancer development) and leads to treatments of spread of cancer cells in patients suffering from this aggressive cancer subtype" said Abhipsa Sinha, the first author of the study.

"Over 90% TNBC deaths are due to the secondary colonisation of these tumour cells in different distant body organs (metastasis). During the process of metastasis, cancer cells demand high energy and ACSL4 mediated fatty acid metabolism fulfils this requirement. The study suggests developing inhibitors of ACSL4, which means a drug molecule against this enzyme can prevent the spread of cancer. Current therapies are often ineffective, and the lack of targeted treatments makes managing this cancer very challenging," said Prof Datta.

He said that understanding the mechanisms that drive TNBC's aggressiveness and metastasis is crucial for developing new therapeutic strategies.

"This study identifies ACSL4 as a key player in TNBC metastasis, highlighting its potential as a target for future treatments. Given that India is the world's TNBC capital with highest cases, these findings would pave ways for better management of this disease," he added.

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