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Researchers identify mechanism that makes breast cancer invasive

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A new study has identified a key mechanism that causes breast cancer to spread. The research, published by Cell Press on March 30th in the journal *Molecular Cell*, enhances our knowledge about the signals that drive cancer metastasis and identifies new therapeutic targets for a lethal form of invasive breast cancer that is notoriously resistant to treatment.

Amplification of the gene for ErbB2 has been linked with aggressive forms of breast cancer and is associated with a poor outcome. Although ErbB2-positive breast cancers are routinely treated with chemotherapy and the ErbB2-targeted drug trastuzumab (Herceptin), this treatment often fails. "Nearly half of breast cancers with high ErbB2 expression are either initially non-responsive or eventually develop resistance to trastuzumab," explains senior study author, Dr. Tuula Kallunki, from the Danish Cancer Society Research Center. "Therefore, a better understanding of the molecular basis of ErbB2-induced malignancy is critical for further development of targeted treatments."

In the current study, Dr. Kallunki and colleagues discovered that ErbB2 induces expression of proteins called cathepsins. Previous work has linked cathepsins with metastasis of pancreatic cancer, specifically with tumor cell invasion of surrounding tissues and with the establishment of tumor blood supply. Using a three-dimensional model system to study ErbB2-induced cellular invasion, the researchers demonstrated that inhibition of cathepsins prevented ErbB2-driven breast cancer invasion. They went on to identify components of the complex signaling network linking ErbB2 and cathepsin expression with cancer invasiveness.

Taken together, the results demonstrate that the invasive behavior of ErbB2-positive cancer cells is dependent on cathepsin activity and uncover a molecular link between ErbB2 and breast cancer invasion. "Our work has introduced a cellular model system to study ErbB2-induced invasion and identified an invasion-promoting signaling network," concludes Dr. Kallunki. "In addition, our findings provide several potential therapeutic targets against ErbB2-driven invasive cancers."

Provided by Cell Press