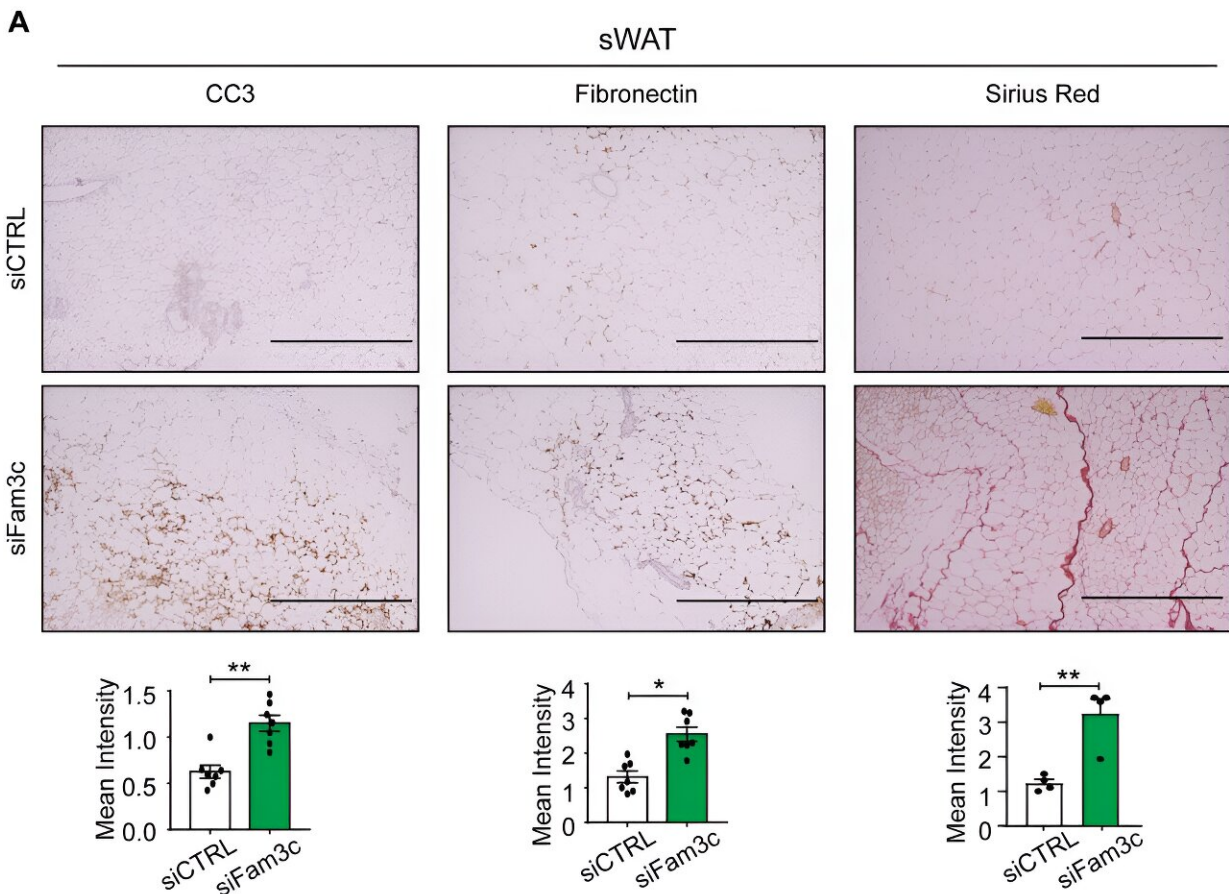# Study reveals critical role of FAM3C in breast cancer progression

January 8 2024, by JooHyeon Heo

Fam3c knockdown in sWAT of MMTV-PyMT mice increases cell death and fibrosis of CAAs, ultimately inhibiting the growth and metastasis of primary tumors. (left and center) Immunohistochemistry staining images and quantification of CC3 and fibronectin in sWAT from 8-week-old mice. (right) Sirius Red staining images and quantification of sWAT from eight-week-old mice. Credit: *Cancer Research* (2023). DOI: 10.1158/0008-5472.CAN-23-1641

A study conducted by Professor Jiyoung Park and her research team in the Department of Biological Sciences at UNIST has identified FAM3C, a metabolism-regulating signaling molecule produced by cancer-associated adipocytes (CAAs), as a key regulator of breast cancer progression within the tumor microenvironment (TME).

The findings, published in *Cancer Research*, shed light on the potential for targeted therapies in the treatment of breast cancer.

The study demonstrates that overexpression of FAM3C in cultured adipocytes significantly reduces cell death in both adipocytes and co-cultured breast cancer cells, while suppressing markers of fibrosis. Conversely, depletion of FAM3C in CAAs leads to adipocyte-mesenchymal transition (AMT) and increased fibrosis within the TME. The research team also discovered that breast cancer cells stimulate the expression of FAM3C in adipocytes through TGF-β signaling, which can be inhibited by a TGF-β-neutralizing antibody.
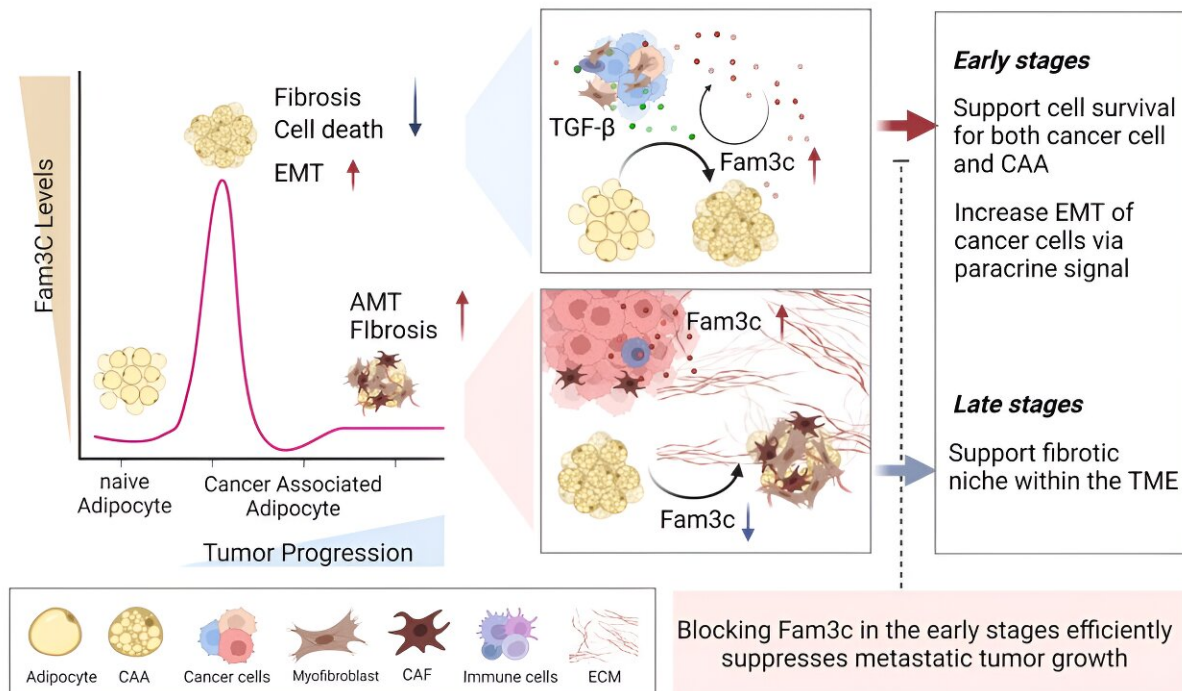
Graphical abstract, showing high FAM3C expression predicts poor prognosis in patients with breast cancer. Credit: *Cancer Research* (2023). DOI: 10.1158/0008-5472.CAN-23-1641

In a genetically engineered mouse model of breast cancer, early knockdown of FAM3C in CAAs significantly inhibited primary and metastatic tumor growth. Furthermore, elevated levels of circulating FAM3C were observed in patients with metastatic breast cancer compared to those with non-metastatic breast cancer.

"These findings suggest that therapeutic inhibition of FAM3C expression in CAAs during early tumor development could hold promise as a novel approach in the treatment of patients with breast cancer," said Professor Jiyoung Park. "Understanding the role of cancer-associated adipocytes and their secretory molecules, such as FAM3C, opens up new

avenues for the development of early diagnosis markers and targeted treatments for breast cancer."

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