University of Tsukuba-led researchers identified a novel molecular mechanism involved in progression and metastasis in TNBC. Musculoaponeurotic fibrosarcoma (MAF) oncogene family protein K (MAFK) is a protein involved in switching on specific target genes. The team previously identified MAFK as a gene that is itself switched on by a protein called TGF-?, which is known to be involved in TNBC development. The researchers confirmed MAFK as a functional link between TGF-? and TNBC. The findings were published in Science Signaling.

"The TGF-? signaling pathway is involved in TNBC progression and metastasis," corresponding author Mitsuyasu Kato says. "However, it's also involved in beneficial processes in healthy cells, and actually helps to suppress the early stages of tumor development. Identifying molecular processes downstream of the TGF-? pathway could offer specific targets for TNBC therapy to combat progression and metastasis without interfering with the beneficial effects of TGF-? signaling."

The team found higher levels of MAFK in TNBC cells than in other breast cancer cell types. A survey of patient data revealed that patients with higher MAFK gene activity had poorer prognosis. Moreover, when the team interfered with the production of MAFK in breast cancer cells, the tumors the cells formed were smaller and metastasized to a lesser degree. Conversely, genetically engineering non-cancerous breast cells to make them produce MAFK caused them to behave like cancer cells.

There was already some evidence of MAFK promoting tumor development in other cancer types, but the underlying mechanism remained a mystery. By screening DNA, the team identified a
gene, GPNMB, which is switched on by MAFK.

"We found that induction by MAFK of cancer-like behaviors in breast cells is dependent on GPNMB," lead author Yukari Okita says. "GPNMB is already known to be present at high levels in the most aggressive and lethal TNBC and to contribute to cancer development; our study identifies induction by MAFK as a missing link between the TGF-β pathway and GPNMB." Shedding light on this pathway therefore offers potential new therapeutic targets for patients with TNBC.


Provided by University of Tsukuba


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