

Hedgehog signaling pathway for breast cancer identified

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Molecules called long non-coding RNAs (lncRNAs) have been implicated in breast cancer but exactly why they cause metastasis and tumor growth has been little understood...until now.

Scientists at The University of Texas MD Anderson Cancer Center report that hedgehog, a unique cell signaling pathway known to contribute to many types of cancer, may be behind breast cancer metastasis. This molecular message service works with the lncRNA known as BCAR4 giving the genetic green light for tumor growth.

"Our study of BCAR4 and the hedgehog signaling pathway has provided evidence for lncRNAs' regulator roles in aggressive breast cancers progression," said Liuqing Yang, Ph.D., assistant professor of molecular and cellular oncology, whose findings are published in this month's issue of *Cell*. "Emerging evidence has revealed lncRNAs as a new class of players in the development and progression of cancer."

When the hedgehog signaling pathway is activated abnormally by proteins known as chemokines, it allows increased expression of genes controlled by a transcription factor called GLI2. Transcription factors are proteins that activate other genes. Yang's team found that BCAR4 is required for GLI2-controlled gene activation. This molecular "liaison" of BCAR4 via the hedgehog signaling pathway and GLI2 is the first understanding of the tie between hedgehog and BCAR4 in breast cancer.

This new information led Yang to explore the potential for an emerging



therapy known as locked nucleic acids (LNA) for breast cancer. His findings are published in this month's issue of *Cell*.

"Therapeutic targeting of lncRNAs has not been well documented for breast cancer," said Yang. "In our study, we aimed to determine their potential through use of an LNA-based therapy."

Yang found that there was indeed a good outcome for LNAs in treating breast tumor spread when studied in mice, and human tissue and cell lines.

"Therapeutic delivery of LNAs targeting BCAR4 strongly suppresses breast cancer metastasis," he said. "We confirmed the link between BCAR4 and the hedgehog signaling pathway as a viable avenue for a new approach to treating aggressive breast cancers."

Provided by University of Texas M. D. Anderson Cancer Center

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