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Scientists identify gene in breast cancer pathway

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Scientists at Albert Einstein College of Medicine of Yeshiva University have discovered how a gene crucial in triggering the spread of breast cancer is turned on and off. The findings could help predict whether breast tumors will metastasize and also reveal potential drug targets for preventing metastasis. The study will appear in the May 20th online edition of the *Journal of Cell Science*.

A few years ago, Einstein scientists discovered a gene called ZBP1 (zipcode binding protein 1), which helps cells to move, grow and organize spatially. "ZBP1 is very active in the developing embryo but largely silent in adult tissues," says Robert H. Singer, Ph.D., professor and co-chair of anatomy and structural biology and co-director of the Gruss-Lipper Biophotonics Center at Einstein. He is one of ZBP1's discoverers and leader of the current study.

Researchers have subsequently found that ZBP1 is reactivated in several types of cancer, including breast, colorectal, and non-small cell lung cancers; but the gene is silenced in metastasizing cancer cells, as was shown by Dr. Singer and another Einstein scientist, John Condeelis, Ph.D., who also is co-chair of anatomy and structural biology and co-director of the Gruss-Lipper Biophotonics Center at Einstein. The purpose of the current study was to find how the ZBP1 gene is activated and silenced and how it influences the spread of breast cancer.

After examining mouse, rat, and human breast cancer cells, Dr. Singer and his team found that ZBP1 silencing occurs when a methyl group

(CH3) attaches to ZBP1's promoter region (the segment of a gene where gene expression is initiated). The attachment of CH3 prevents the promoter from binding to a protein called beta-catenin. And without beta-catenin, the ZBP1 gene is effectively silenced.

The study also showed that the silencing of ZBP1 increases cancer cells' ability to migrate and promotes the proliferation of metastatic cells.

The findings have important implications for forecasting breast cancer outcomes. According to the researchers, signs of ZBP1 silencing in breast cancer cells would indicate that a breast tumor is likely to spread—information that would help in choosing a treatment strategy.

The study also points to potential targets for drug treatment. "If you could turn on this protein in cancer cells, or prevent it from being turned off, you could seriously reduce the ability of the cells to metastasize," says Dr. Singer.

The research team is investigating whether the ZBP1 gene in cancer cells could be reactivated—and the cells prevented from metastasizing—by selectively removing CH3 from the ZBP1 promoter.

More information: The paper, "Increased proliferation and migration of breast metastatic cells results from ZBP1 repression by blocking beta-catenin promoter binding," is published in the May 20, 2009, online edition of the *Journal of Cell Science*. Wei Gu, M.D., Ph.D., instructor in anatomy and structural biology at Einstein, is the lead author. Feng Pan, Ph.D., now at NYU School of Medicine, is a co-author.
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Source: Albert Einstein College of Medicine (news : web)