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Molecules can block breast cancer's ability to spread

Researchers have identified a specific group of microRNA molecules that are responsible for controlling genes that cause breast cancer metastasis. The study, led by scientists at Memorial Sloan-Kettering Cancer Center (MSKCC), appears in the January 10, 2008, issue of *Nature*.

MicroRNAs are known to inhibit the activity of entire sets of genes associated with cancer metastasis—a process that leads to the majority of cancer-related deaths. The new work explains how the loss of certain microRNAs allows cancer cells to migrate through organ tissue and to grow more rapidly.

The researchers examined human breast cancer cells with strong metastatic ability and found that the cells had lost large numbers of three different microRNA molecules. Conversely, when researchers put those molecules back into human breast cancer tumors in mice, the tumors lost their ability to spread.

In addition, the researchers looked at breast cancer patients and discovered that those with tumors that had lost these molecules were much more likely to suffer from cancer metastasis to the lung and bone.

The identification of molecules that inhibit a cell's metastatic potential may help guide clinical decision-making in the future by enabling oncologists to more accurately identify patients at highest risk for metastatic relapse, said the study's lead author Sohail Tavazoie, MD, PhD, a postdoctoral fellow in the Oncology-Hematology Fellowship program at MSKCC.

In further analyzing one of these microRNAs, called miR-335, investigators found that miR-335 works by suppressing certain genes that are associated with human metastasis, particularly SOX4, which acts as a transcription factor (meaning that it regulates a group of genes responsible for cell development and migration), and tenascin-C, which functions outside the cell in what is called the extracellular matrix and is implicated in cell migration.

We now have a better understanding of the role this molecular pathway plays as a suppressor of breast cancer's ability to spread to the lung and bone, and we have identified the genes involved in that process. These findings may enhance our ability to come up with more effective drugs to prevent or treat cancer metastasis," said Joan Massagué PhD, Chair of the Cancer Biology and Genetics Program at MSKCC, a Howard Hughes Medical Institute Investigator, and the study's senior author.

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The study was co-authored by William L. Gerald, MD, PhD, a surgical pathologist and member of the Human Oncology and Pathogenesis Program at MSKCC, and by members of Dr. Massagué's laboratory, including Claudio Alarcón, graduate student; Thordur Oskarsson, PhD, research fellow; David Padua, graduate student; Qionqing Wang, PhD, research fellow; and Paula D. Bos, graduate student.

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