NEDD9 protein supports growth of aggressive breast cancer

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Researchers at Fox Chase Cancer Center have demonstrated that a protein called NEDD9 may be required for some of the most aggressive forms of breast cancer to grow. Their findings, based on the study of a mouse model of breast cancer, are presented in a recent issue of *Cancer Research*, available on-line now.

"For the first time, we have been able to present evidence that directly demonstrates reduced levels of NEDD9 in a living animal that limit the appearance of aggressive metastatic breast cancer," says co-author Erica A. Golemis, PhD, Fox Chase professor and co-leader of the Molecular Translational Medicine Program.

According to Golemis, the protein could serve as a biomarker, a molecule that could be detected to indicate the diagnoses of aggressive forms of breast cancer in the clinic. NEDD9 may also provide a target for some future therapeutic against metastatic cancer, Golemis says.

In 1996, the Golemis laboratory first identified NEDD9, a so-called scaffolding protein that forms part of a complex of molecules just inside the cell membrane. NEDD9 and related proteins collectively act as transmitters, relaying signals from the cell surface to the cell interior to control cancer cell growth and movement. Over the past three years, scientists from laboratories around the world have contributed to a body of evidence showing how excess amounts of the NEDD9 contribute to metastasis in a number of cancers, including melanoma, lung cancer, and glioblastoma.

"One thought is that producing excess NEDD9 gives tumors a selective advantage over other cells," Golemis says, "so we are trying to determine how NEDD9 might provide that advantage."

To better understand the role of NEDD9 in breast cancer, the Fox Chase researchers studied a variety of mice, bred by colleagues at the University of Tokyo to lack the NEDD9 gene. These NEDD9 "knockout" mice were then made to turn on an oncogene that induces breast cancer in mice, and compared to normal mice given the same treatment. While the NEDD9 knockout mice developed breast cancers, they did so more slowly and less efficiently than normal mice, and without the activation of the central protein pathways most responsible for cancer growth and metastasis. In fact, mammary tumor growth in the knockout mice showed marked genetic differences from the very moment premalignant lesions were detected, as compared to the normal mice.

"This was the first study able to address the question of what happens in breast cancer if this gene isn't around," Golemis says. "And the answer is that we see a more moderate cancer development, which alone speaks volumes on the role of the protein in aggressive breast tumors."

According to Golemis, the emerging body of research on NEDD9 shows that the protein forms an important node in the complex, interwoven pathways that dictate the fate of individual cells. These pathways regulate the entirety of a cell's life, from how select genes are transcribed to form new proteins to how a cell divides or even dies.

"By their nature, cancer cells are evolutionary machines, constantly looking for ways to exploit these vast networks of protein signaling pathways that are an inherent part of cell function," Golemis says. "The more we understand these pathways, the better we will understand the ways cancer cells evolve to use those pathways, and how to stop them."

Source: Fox Chase Cancer Center (news : web)