Study Shows How Normal Cells Influence Tumor Growth

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(PhysOrg.com) -- It was once thought that the two communities of cells within a cancerous breast tumor - fast-growing malignant cells and the normal cells that surround them - existed independently, without interaction. Then evidence emerged indicating that the normal-looking cells encouraged cells within the tumor to become malignant, but how the one community influenced the other wasn't known.

A new study led by Ohio State University cancer researchers published in the Oct. 22 issue of *Nature* has begun solving the mystery. It shows for the first time that the loss of a gene called PTEN from one type of those surrounding cells can dramatically alter the tumor environment in ways that foster tumor growth.

"Our findings reveal a new role for this gene in the tumor environment, which could lead to entirely new treatments for breast cancer and perhaps other solid tumors using agents that target cells surrounding the tumor, as well as the cancer cells themselves," says co-principal investigator Gustavo Leone, associate professor of molecular virology, immunology and medical genetics at the Ohio State University Comprehensive Cancer Center-Arthur G. James Cancer Hospital and Richard J. Solove Research Institute.

The findings should also improve the understanding of breast cancer and of other conditions that are influenced by the local tissue environment such as autoimmune disease, lung fibrosis and neurodegenerative diseases.

The PTEN gene produces a protein that is a key regulator of cell metabolism, and it is lost in many human cancers.

This new study shows that when PTEN is lost in fibroblasts, a principle cell component of the tissue that surrounds a tumor, it dramatically alters the structure and biochemical make-up of the tumor environment. For example, levels of the fibrous protein collagen rise, inflammatory cells called macrophages migrate into the tumor and the number of tumor blood vessels increases. These events all favor tumor growth.

"Our study demonstrates that PTEN in surrounding fibroblasts plays an important role in suppressing cancer development," says co-principal investigator Michael Ostrowski, professor and chair of molecular and cellular biochemistry and co-director of the cancer center's Molecular Biology and Cancer Genetics Program.

To show this, Leone, Ostrowski and their colleagues removed PTEN from fibroblasts in the mammary glands of mice. They were surprised to discover that PTEN regulates a second gene, called Ets2, which executes the changes that occur in the tumor environment when PTEN is lost.

"Remarkably, this animal model mimics many of the features observed in human breast cancer, " Leone says, "so it should help us evaluate experimental agents that might be used in combination therapies that target faulty cells in the tumor environment, as well as cancer cells."

Source: Ohio State University Medical Center