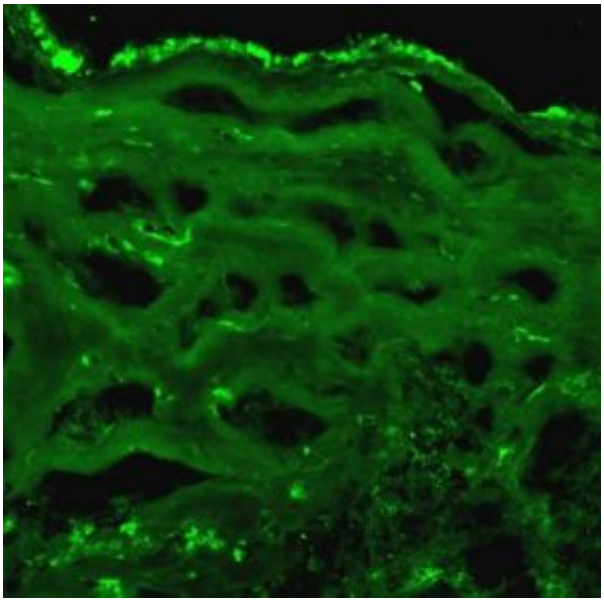
A molecular switch is linked to a common breast cancer

November 8 2007



These photomicrographs from mice show the significant difference in tumor vasculature (blood vessels) as a result of the increased expression of two factors (eIF4G and 4E-BP1) in locally advanced breast cancer. The vessels are stained with a fluorescent dye. The tumor on the right overexpresses the factors. Its vessels are much larger, irregularly shaped, extensive and leaky compared to the vasculature of tumors that do not overexpress the factors (left). The increased vascularization is thought to enable the much larger growth of locally advanced breast cancers. Credit: Robert J. Schneider

Researchers have discovered that a molecular switch in the protein making machinery of cells is linked to one of the most common forms

of lethal breast cancer worldwide. The discovery by researchers at NYU School of Medicine could lead to new therapies for the cancer, called locally advanced breast cancer (LABC).

Although precise data isn't available, LABC may account for 50 percent or more of breast cancers among women in developing countries, and 30 percent of breast cancers among socially disadvantaged and minority women in the United States. This type of cancer is defined by a large tumor that is about 2 inches or larger in diameter, about the size of a plum, when first diagnosed. The cancer may have spread into surrounding lymph nodes or other tissues. However, it hasn't yet spread to more distant areas in the body.

Without treatment, fewer than 20 percent of patients with LABC are living five years after their diagnosis. Unfortunately, even with appropriate treatments, this cancer is deadlier than other types of breast cancer that are detected earlier.

With funding from the Breast Cancer Research Foundation and the Department of Defense, Robert J. Schneider, Ph.D., the Albert B. Sabin Professor of Molecular Pathogenesis, and Silvia C. Formenti, M.D., the Sandra and Edward H. Meyer Professor of Radiation Oncology and Chairwoman of Radiation Oncology, and their colleagues at NYU School of Medicine have made LABC the focus of a coordinated effort to understand the disease.

"This disease has not been sufficiently studied, in part because of the social, psychological, economic, and cultural barriers that may stand in the way of obtaining care," says Dr. Formenti.

"Our study shows that an unusual molecular switch occurs that is essential for the development of these large tumors. We think that this switch could be a target for new therapies," says Dr. Schneider.

The new study is published in the November 9, 2007 issue of the journal *Molecular Cell*.

Drs. Schneider and Formenti led the new study which found that two molecules were unusually abundant or "overexpressed" specifically in locally advanced breast cancers. Further analysis in mice revealed that the molecules orchestrated a switch in the use of messenger RNA, a kind of ferry service that carries information for making proteins. This switch, the researchers found, occurs when tumors become starved for oxygen, a condition known as hypoxia. The switch permits the selective expression of proteins that are required for tumors to carry out angiogenesis, the process of developing a blood supply. It also enables tumors to grow to a large size and to progress.

"The identification of the molecular switch and its importance for development of locally advanced breast cancer reveals realistic targets for the development of new therapeutics to block tumor angiogenesis and progression in breast and possibly other cancers," says Dr. Schneider.

Source: New York University