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Researchers discover protein that contributes to cancer spread

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In an important finding published online in *Developmental Cell*, researchers at Albert Einstein College of Medicine of Yeshiva University, along with collaborators at Massachusetts Institute of Technology, have identified a protein likely responsible for causing breast cancer to spread.

Metastatic cancer occurs when cancer cells from the original tumor travel to distant sites via the blood system. Most cancer deaths are due to cancer that has spread to other organs. Trying to stop cancer before it metastasizes is the main goal of cancer treatments. Upon diagnosis, 6 out of 10 breast cancer patients have cancer that is still in its primary location making the potential discovery of a marker for invasive cancer of tremendous value that could better inform treatment options.

Until now, early markers of metastatic breast cancer have been hard to find. However, in the Einstein-led study, researchers have identified a protein that is a promising candidate for a metastatic breast cancer marker.

The protein, called Menainv is present in invasive cells within a breast tumor. These cells move into surrounding tissue and eventually to blood vessels. Menainv is not on breast tumor cells that stay put (resident cells). This is the first time that a protein has been shown to contribute to the invasive and metastatic ability of tumor cells, rather than just being an 'innocent bystander' that shows up when cells are invading, strengthening the potential use of this protein as a marker.

The research was conducted under the direction of and in the laboratories of John S. Condeelis, Ph.D., Einstein professor and co-chair of anatomy and structural biology and co-director of Gruss Lipper Biophotonics Center and Frank B. Gertler, Ph.D., Ross Scholar Professor of Biology at MIT.

The latest research was aided considerably by the work of Jeffrey B. Wyckoff, principal associate, department of anatomy and structural biology at Einstein who, with Dr. Condeelis, developed the in vivo invasion assay used to isolate metastatic tumor cells from breast tumors thereby implicating Mena as an important gene for metastasis.

Evanthia T. Roussos, an M.D.-Ph.D. student in Dr. Condeelis' lab and primary co-author of the study, explains, "We have micro-needles filled with growth factors and tissue that we insert into a tumor on an anesthetized mouse. If a cell is invasive, within four hours, it will crawl into the needles. We found that mouse breast tumor cells that we engineered to contain Menainv were invasive whereas cells that did not have Menainv were not."

Another finding from the study that has important implications for patient treatment is that tumor cells harboring Menainv are less likely to be responsive to newer breast cancer treatments that inhibit epidermal growth factor receptors (EGFR). Epidermal growth factor (EGF) has been shown to increase a breast cancer cell's invasive potential. The study investigators propose that drugs which inhibit EGF may lack effectiveness on tumor cells that express Menainv. That's because Menainvcells are so sensitive to EGF that even the small amount of EGF signal that the drugs fail to block may be enough to stimulate EGF receptor and promote tumor cell migration and metastasis.

If Menainv behaves similarly in humans as it does in mice, it would be an especially attractive marker for metastatic breast cancer because the

structure of Menainv would enable an antibody or a PCR assay to be developed to identify it. Such an antibody or PCR assay could be used to diagnose the presence of Menainv in biopsies and blood samples allowing doctors to identify breast cancer patients who are more likely to have progressive disease and recommend the appropriate treatment.

The current study builds on previous research by Dr. Condeelis' group which identified Menainv as the isoform of Mena that is over expressed in the invasive and metastatic subpopulation of tumor cells in breast tumors. The current study shows that Menainv forces tumor cells in mammary tumors of mice to become invasive and eventually metastasize to the lung.

Source: Albert Einstein College of Medicine

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