Similarities between embryos and breast tumors identified

June 30 2015

It may seem incredulous, but breast tumors may have something in common with embryos ... at least in mice, say researchers at The University of Texas MD Anderson Cancer Center.

A study led by Sendurai Mani, Ph.D., associate professor of Translational Molecular Pathology and Jeffrey Chang, Ph.D., assistant professor of Integrative Biology at The University of Texas Health Science Center at Houston, found that tumors that resemble six-day-old mouse embryos are more prone to metastasize than those that look like tissues from adult mice. Specifically, they noticed that the same genes that are turned on in developing mice are also present in metastatic tumors.

Although every cell contains the same set of genes, which ones are activated are unique across tissues and medical conditions. This pattern of activation, also called a gene expression signature, may indicate different subtypes of a disease, including those that predict disease survival or prognosis. Gene expression signatures are thought to be useful for identifying effective treatments for select groups of patients.

"Looking at the embryo to learn more about cancer is a novel and important finding for researchers," said Mani. "It is difficult to predict metastasis by merely analyzing the primary tumor and often, no mutations can be found. Clinicians still need to know whether a tumor is going to metastasize."

The researchers aimed to isolate a marker from the gene expression signature and identified one marker based on the biology of a developing embryo.

One process that is activated in early embryonic development is called the epithelial-mesenchymal transition (EMT). Tumors that form in the linings of organs known as the epithelium, which account for over 85 percent of solid tumors, can activate this complex biochemical program which leads to metastasis in the lab. They found that the EMT gene expression signature did not predict metastasis in human tumors.

A key insight to this problem is that for cancer cells to metastasize, they must change their characteristics. In the primary tumor, cancer cells must grow quickly before they stop growing and enter a "migratory state" where they disseminate to the metastatic site. To establish tumor spread, they need to switch back to a fast-growing cell. Scientists call this ability to change characteristics "plasticity."

"Recent findings have shown that carcinomas have to shed off their EMT features and activate the reverse process, MET, in order to promote metastasis and create heterogeneous tumors at distant sites," said Mani.

Mani's team wondered if tumors likely to spread would behave like embryos, in particular, early stage embryos.

"During early stages of embryo development, this phenomenon of plasticity is more prevalent compared to that in embryos at later stages or even in adult tissues, and our findings clearly demonstrate that metastatic tumors bear remarkable similarities in gene expression profiles to that of mouse embryos at day 6.5 of early gestation," said Mani.

"Our findings clearly demonstrated that metastatic tumors are more like

the embryo," he said. "We found that tumors having gene expression signatures similar to mouse embryonic development day 6.5 were more prone to develop metastasis compared to tumors with more adult-differentiated signatures."

This first-of-its-kind signature stands out in its ability to predict metastatic propensity in cancer patients by analyzing the bulk of the primary tumor rather than residual issues or scarce circulating tumor cells. More importantly, the signature is applicable to a wide class of breast tumor subtypes.

Study results were published in the June 30 issue of Nature *Scientific Reports*.

Provided by University of Texas M. D. Anderson Cancer Center