Study identifies gene important to breast development and breast cancer

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A new study in *Cell Reports* identifies a gene important to breast development and breast cancer, providing a potential new target for drug therapies to treat aggressive types of breast cancer.

Understanding more about how the different types of cells in breast tissue develop improves our knowledge of breast cancer. TAZ represents a potential new target for drug therapies to treat aggressive types of breast cancer.

Background: In cancer, normal cells can become unpredictable or aggressive and thus difficult to treat with anti-cancer drugs. This is especially true in breast cancer. By identifying the genes responsible for this change in cells from breast tissue, researchers hope to identify a way to stop or reverse it.

In breast tissue, there are two main types of cells: luminal cells and basal cells. Normally luminal cells are "programmed" by a particular class of proteins (transcription factors), which prevent them from becoming basal cells, and vice-versa.

Previous work led by Charlotte Kuperwasser, principal investigator, determined that some common forms of breast cancer originate from luminal cells while some rarer forms of breast cancer originate from basal cells.

The research team identified a gene, TAZ, which controls whether breast

cells behave more like basal cells or more like luminal cells, information that might be important in understanding and potentially treating certain difficult-to-treat forms of breast cancer. TAZ helps to regulate how different genes operate in different cell types.

How the Study Was Conducted: The research team identified TAZ by testing the function of more than 1,000 genes to determine which were involved in "reprogramming" luminal and basal cells, therefore reversing lineage commitment.

To further identify the role of TAZ, the research team studied breast tissue at different stages of development using two groups of mice: a control group with the TAZ gene and an experimental group of knock-out mice with the TAZ gene deleted. (Cells in breast tissue are renewed/developed during puberty, pregnancy, and nursing.)

The team also looked at the levels of the TAZ gene in tumors from women with either luminal or basal tumors.

The research team found that the experimental group had an imbalance of cell populations in breast tissue: too many luminal and too few basal. The control group had a normal ratio of luminal to basal cells. In breast tissue from women with cancer, they found high levels of TAZ in basal but not luminal tumors.

First author Adam Skibinski, M.D./Ph.D. student at Tufts University School of Medicine and the Sackler School of Graduate Biomedical Sciences at Tufts University: "We've known for a long time that breast cells can lose their normal identity when they become cancerous, but we are now realizing that normal cells can change their characteristics as well in response to transcription factors like TAZ. This might be a factor in the development of breast cancer."

More information: Skibinski et al., The Hippo Transducer TAZ Interacts with the SWI/SNF Complex to Regulate Breast Epithelial Lineage Commitment, *Cell Reports* (2014), www.cell.com/cell-reports/full … 2211-1247(14)00152-1