MedicalXpress

The making and unmaking of stem-like, aggressive breast cancer cells

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Breast cancers that depend on the hormones estrogen and progesterone are susceptible to treatments targeting these hormones. Take away this dependence and you lose a valuable treatment option.

A University of Colorado Cancer Center study published as a featured article in the journal *Oncogene* shows how progesterone does just this – by suppressing a key microRNA, progestins return breast cancer cells to a stem-cell-like state in which they haven't yet differentiated, and are thus more resistant to chemotherapies and more likely to carry a poor prognosis.

"The reason we were looking into the possible role of microRNAs in the dedifferentiation of breast cancer cells into this aggressive, chemo-resistant phenotype is that microRNAs tend to be good, druggable targets. Because one microRNA may regulate many genes involved in a cancerous signaling pathway, we hoped to find one target with many beneficial effects," says Diana Cittelly, PhD, postdoctoral fellow at the CU Cancer Center and the paper's first author. The study was a collaboration between the CU Cancer Center labs of Jennifer Richer, PhD, and Carol Sartorius, PhD.

Specifically, the study shows that progestins regulate miRNA-29 – a molecule that helps to decide which of a cell's genes are and are not turned into proteins. This regulation of miRNA-29 creates a cascade that stimulates breast cancer cells to revert back to a stem-like state, marked by proteins CD44 and CK5. In animal models, these stem-like cells

helped breast cancer evolve around the blockages of current treatments..

"We can manipulate this miRNA-29 in cell lines," Cittelly says, "and we hope technology isn't too far in the future that will allow us to deliver miRNA-29 in human cancers as well."

Turn off the role of miRNA-29 and the hope is that breast cancers won't be able to gain stem cell-like traits and lose their hormone dependence.

Provided by University of Colorado Denver