Collaboration Yields New Potential Options for Attacking Stem Cells in Triple-Negative Breast Cancer

(subhead) Study sheds light on link between cancer stem cells and inflammation

New research from the University of Michigan Comprehensive Cancer Center and Georgia Regents University finds that a protein that fuels an inflammatory pathway does not turn off in breast cancer, resulting in an increase in cancer stem cells. This provides a potential target for treating triple negative breast cancer, the most aggressive form of the disease.

The researchers identified a protein, SOCS3, that is highly expressed in normal cells but undetectable in triple-negative breast cancer. They showed that this protein is degraded in cancers, blocking the cellular off-switch of a feedback loop involving the inflammatory protein interleukin 6, IL6. When the switch does not get turned off, it enables cancer stem cells to grow.

“We have known for a long time that there are important links between inflammation and cancer, including similar pathways that regulate normal and cancer stem cells,” says study author Max S. Wicha, M.D., distinguished professor of oncology and director of the U-M Comprehensive Cancer Center.

“This work helps explain why these pathways shut off in normal tissues after injury but remain active in cancers, resulting in an increase in cancer stem cells. Furthermore, they suggest that

blocking these inflammatory loops may be a means of targeting cancer stem cells, improving patient outcome," he says.

The study appears in the Nature Publishing Group journal *Oncogene*.

Currently, there are no molecularly targeted therapies aimed at triple-negative breast cancer, which is a type of cancer negative for estrogen receptor, progesterone receptor and the HER2 protein – all key targets for current therapies. Patients with this form of disease tend to have worse outcomes.

The researchers tested a drug, bortezomib, in mouse models of triple-negative breast cancer and found that it stops the protein degradation, resulting in the inflammatory loop shutting off, which reduces the cancer stem cells, thereby blocking metastasis. Bortezomib is currently approved for treatment of the blood cancer multiple myeloma.

This team previously showed the IL6 can stimulate breast cancer stem cells in HER2-positive breast cancers; they are designing a clinical trial which uses an IL6 blocker. The new research suggests that adding bortezomib to the IL6 inhibitor may be a way to target stem cells in triple-negative breast cancer.

More laboratory testing is needed before a clinical trial can begin. The researchers suspect that this pathway may apply to other cancers as well and are investigating that further.