Study finds promising therapeutic target for aggressive type of breast cancer

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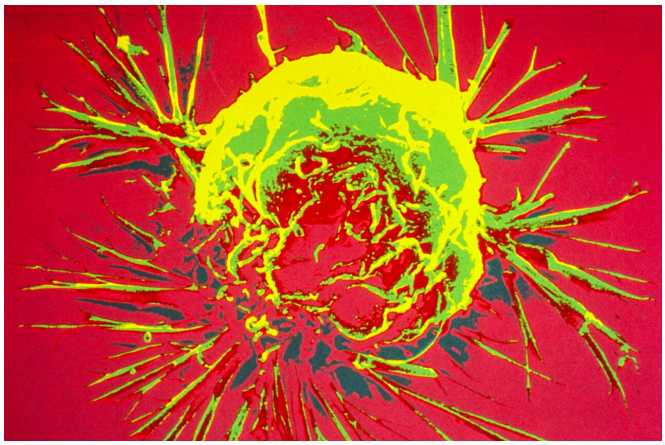

A breast cancer cell, photographed by a scanning electron microscope. Credit: Bruce Wetzel and Harry Schaefer, National Cancer Institute, National Institutes of Health

A new *Nature Communications* study led by University of Kentucky Markey Cancer Center researchers suggests that an enzyme known as Prolyl 4-hydroxylase subunit alpha-1 (P4HA1) is a potential therapeutic target for triple negative breast cancer.

Collagen prolyl 4-hydroxylase (P4H) expression and collagen hydroxylation in cancer cells are necessary for breast cancer progression. Performed in the lab of UK College of Medicine associate professor Ren Xu, the study found that P4HA1 expression was induced in triple-negative breast cancer, and P4HA1 expression enhanced hypoxia-inducible factor (HIF) 1? stability, thereby increasing cancer stem cell population. When P4HA1 was inhibited in patient-derived xenograft models, the triple-negative breast cancer became more sensitive to chemotherapeutic agents docetaxel and doxorubicin.

Triple-negative breast cancer is a moniker given to a particularly aggressive group of breast cancers that often affect younger women. Unlike the receptor-positive types of breast cancer, which have biomarkers that tell oncologists which treatment the patient should respond to, triple negative breast cancers have no definitive biomarkers yet. If the patient does not respond well to the current standard of care, it's up to the oncologist to make an educated guess about which chemotherapy will be effective.

Unfortunately, these conjectures mean that more than 50 percent of patients are likely to experience cancer recurrence in the first three to five years after treatment.

"Approximately 15 percent of all breast cancer cases are triple-negative breast cancers, and these patients frequently have metastases and a high rate of relapse after initial treatment," said GaoFeng Xiong, first author on the study. "Being able to identify a novel target like P4HA1 to suppress triple-negative breast cancer progression and chemoresistance is crucial for treatment."

More information: Gaofeng Xiong et al. Collagen prolyl 4-hydroxylase 1 is essential for HIF-1? stabilization and TNBC chemoresistance, *Nature Communications* (2018). DOI: 10.1038/s41467-018-06893-9

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