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Prognostic role found for miR-21 expression in triple-negative breast cancer

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"Triple-negative" breast cancer (TNBC) occurs in patients whose cells do not express receptors for estrogen, progesterone, and/or human epidermal growth factor receptor 2 (ER-/PR-/HER2-). Because of the absence of these predictive biomarkers, treatment assignment can be difficult. Now, researchers report that high levels of the microRNA miR-21 in the tumor microenvironment, but not in the tumor epithelia (cancer cells), are associated with worse clinical outcomes for patients with TNBC, thus identifying a possible TNBC prognostic biomarker, according to a study in The *American Journal of Pathology*.

TNBC accounts for 15% to 20% of breast cancer cases, and patients have shorter recurrence-free survival (RFS) and breast cancer-specific survival (CSS) relative to other major subgroups. It is likely that different subtypes of TNBCs exist, and the heterogeneity may be responsible for a wide variation in response to treatment. "Predictive biomarkers for therapeutic response prediction and novel therapeutic targets that address distinct biological features of TNBC subgroups are needed for these patients," says Lorenzo F. Sempere, PhD, head of the Laboratory of microRNA Diagnostics and Therapeutics at Van Andel Research Institute in Grand Rapids, MI. "These findings add support to the growing importance of miRNA-based diagnostics."

miRNAs are short, noncoding, regulatory RNAs that modulate gene expression in critical developmental, physiological, and pathological processes. In previous work by these authors and others, miR-21 was associated with poorer disease outcomes in cancers of the colon,

pancreas, and breast. The goal of this study was to explore in greater detail the influence of miR-21 on TNBC outcomes, looking both at the amount and the location of miR-21 expression. The authors had reason to believe that changes in the tumor's surrounding microenvironment (a complex of stromal cells, immune cells, extracellular matrix, and cytokines/chemokines) could be even more important than changes within the cancer cells.

Tissue samples from 901 female patients diagnosed with non-metastatic invasive breast cancer were analyzed using a fully automated, tissue slide-based in situ hybridization/immunohistochemical (ISH/IHC) assay. The tissue was acquired from the National Cancer Institute Cancer Diagnosis Program.

miR-21 expression was found in 42.8% (386) of the 901 cases. Using fluorescence microscopy, the cases were divided according to their miR-21 signal intensity, with 694 cases determined to be in the non- or low-expressing group and 207, in the high-expressing group. The authors found that the high-expressing miR-21 group exhibited significantly shorter RFS (hazard ratio (HR), 1.71; P