

Tumor microenvironment of TNBC varies between African-American and European-American women

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The presence of tumor-infiltrating lymphocytes (TILs) varied significantly in the tumors of African-American and European-American women with triple negative breast cancer (TNBC), suggesting that TILs may be a useful prognostic biomarker, according to the results of a study presented at the Tenth AACR Conference on The Science of Cancer Health Disparities in Racial/Ethnic Minorities and the Medically Underserved, held here Sept. 25-28.

TNBC is a highly aggressive breast cancer subtype that afflicts African-American women at a higher rate than white women, and often involves a worse prognosis, said the study's lead author, Nikita Wright, BS, a PhD candidate at Georgia State University in Atlanta. TNBC does not express three of the proteins that cause other types of breast tumors to grow—estrogen receptor, progesterone receptor, or Her2/neu. Therefore, there are no targeted therapies currently available for TNBC.

Previous research has shown that African-American women tend to develop more aggressive subtypes of TNBC than European-American women, exacerbating the disparity in survival, Wright said.

"Thus, there is an urgent need to investigate robust, clinically applicable biomarkers that can help clinicians discern which patients are likely to have a more aggressive disease course and guide the personalized treatment of TNBC," she added.



TILs are immune cells that kill tumor cells and are associated with tumors of higher grade and stage, TNBC status, and lymph node metastasis. Previous research has also shown that higher counts of TILs are associated with better survival in TNBC patients. Wright said further research would be required to explain the mechanisms, but one theory is that more aggressive tumors elicit stronger infiltration of lymphocytes into the tumor.

To compare the presence of TILs in African-American and European-American patients with TNBC, Wright and colleagues tested resection samples from 142 TNBC patients at Emory Hospital in Atlanta, and compared overall (stromal) TILs between patients of African-American and European-American descent. None of the patients had undergone neoadjuvant chemotherapy.

The results showed that African-American patients harbored significantly more overall TILs than European-American patients. Significant differences were also observed among early-stage TNBC patients, but not among late-stage patients.

The study also showed that high peripheral TILs were associated with better 10-year survival among early stage African-American TNBC patients, after adjusting for age, Nottingham grade, and stage.

A greater presence of overall and peripheral TILs were also associated with a lack of androgen receptor (AR) expression among early stage AA TNBC patients. The lack of AR reception classifies some TNBC cases as quadruple negative, and this subtype is more prevalent among African-American compared to European-American TNBC patients, Wright said.

Among African-American patients with early-stage TNBC, high TIL counts were also associated with younger age at diagnosis, increased



intramammary lymph node involvement and increased BRCA1-associated protein and programmed cell death protein 1 expression, Wright said. Considering the range of characteristics that were associated with higher TIL counts, Wright said testing for TILs could potentially provide clinicians with useful information for TNBC patient prognosis.

"These findings uncover a previously unrecognized disparity in the tumor microenvironment between African-American and European-American TNBC patients," Wright said. "If confirmed, these findings suggest TILs can be used to predict patient prognosis in the early stages of disease for African American TNBC patients. This insight is clinically actionable and of great potential value for guiding treatment of these patients so that their survival may be improved."

Wright said the study's main limitation is that it only included patients who did not receive neoadjuvant chemotherapy. She said retrospective studies that examine racial disparities in TILs among <u>patients</u> who did receive <u>neoadjuvant chemotherapy</u> could help confirm the role of TILs in TNBC.

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