Biomarker linked to aggressive breast cancers, poor outcomes in African-Americans

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Among African-American women with breast cancer, increased levels of the protein HSET were associated with worse breast cancer outcomes, according to results presented here at the Sixth AACR Conference on the Science of Cancer Health Disparities in Racial/Ethnic Minorities and the Medically Underserved, held Dec. 6-9.

"Our data indicate that HSET represents a potential new biomarker for poor breast cancer outcome among African-American women with the disease," said Ritu Aneja, Ph.D., associate professor in the Department of Biology at Georgia State University in Atlanta. "Using this biomarker effectively could give oncologists critical new information and potentially save lives by allowing earlier recognition of more aggressive breast cancers in African-American women, with the subsequent use of more customized treatment regimens to better manage disease."

African-American women are often diagnosed with breast cancer at a younger age than non-Hispanic white women and are more likely to have cancers that spread, recur, or result in death. Identification of biomarkers that can help clinicians predict if African-American women will have aggressive cancer is a high priority, according to Aneja.

Prior research has linked HSET overexpression to lung cancer metastasis to the brain, and has shown that HSET is upregulated in a particularly aggressive form of breast cancer that most commonly occurs in African-American women, triple-negative breast cancer.

To evaluate whether HSET could be a clinical breast cancer biomarker in ethnically distinct populations, Aneja and colleagues analyzed breast tumor samples from 149 African-American women and 44 non-Hispanic white women, looking for levels of HSET.

Breast tumor samples from African-American women were three times more likely to show high levels of HSET in a region of cells called the nucleus when compared with breast tumor samples from non-Hispanic white women. In addition, higher levels of nuclear HSET were linked to poorer outcomes among African-American women, but not non-Hispanic white women. African-American women with the highest levels of HSET were three to four times more likely to have shorter overall survival, progression-free survival, and metastasis-free survival when compared with African-American women with the lowest levels of HSET.

"We were surprised to find that HSET levels appeared to be a better predictor of cancer outcome than other routinely used breast cancer predictors, such as assigning triple negative status," said Aneja. "We are working around the clock to define ways in which this new biomarker can be used most effectively and as soon as possible in the clinical setting."

More information: Abstract Number: PR12

Presenter: Ritu Aneja, Ph.D.

Title: Nuclear HSET, a predictor for metastasis, disease relapse and poor survival, is a racial disparity biomarker in triple negative breast cancer patients

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Introduction: Human spleen, embryo, and testes protein (HSET, also known as KifC1) is a minus end-directed kinesin that has recently been

implicated in carcinogenesis. HSET overexpression predicts lung cancer metastasis to the brain, and HSET is upregulated in triple-negative (TN) breast cancer that most commonly occurs in African American (AA) patients. While mounting evidence links HSET to tumorigenesis, especially in the breast, HSET is yet to be evaluated as a clinical biomarker in breast cancer. Here, we investigated the association of HSET with demographic and clinicopathological factors and disease progression in breast tumors among ethnically-distinct populations.
Methods: HSET expression was analyzed by immunohistochemistry of formalin-fixed, paraffin-embedded breast carcinoma core biopsies from 149 African American (AA) and 44 Caucasian (CA) totaling 193 patients. Immunostaining was assessed semi-quantitatively for the nucleus and cytoplasm separately. Weighted indices were correlated with tumor and patient characteristics (including ethnicity) along with clinical outcomes.
Results: We found that nuclear HSET expression was highly associated with race, with AA women being thrice as likely to present with nuclear localization compared to CA regardless of TN status. Nuclear HSET expression was also significantly associated with the proliferation marker Ki67 and clinicopathological factors like tumor grade, stage, and size; Nottingham prognostic index (NPI); and TN status. High HSET expression was exclusively associated with poorer outcomes in AA patients and not in CA patients. Within the AA population subset, patients with the highest tertile of HSET expression demonstrated the poorest overall survival (HR = 4.1, p = 0.007), progression-free survival (HR = 3.0, p = 0.014), and metastasis-free survival (HR = 3.5, p = 0.01). These associations were also significant using HSET as a continuous variable in multivariate analysis when potentially confounding factors like age, TN status, and tumor stage were matched. Interestingly, overall, progression-free, and metastasis-free survival were significantly associated with nuclear but not cytoplasmic HSET.
Conclusions: Expression of nuclear HSET is a valuable prognostic biomarker in AA but not in CA breast cancer patients, underscoring its role in the aggressiveness of this disease in the AA population. HSET overexpression appears to be correlated with poorer prognosis in AA breast cancer patients even after adjusting for age, TN status and other tumor characteristics. In summary, our study is the first to identify and report HSET as a novel clinical biomarker of worse prognosis in AA women with breast cancer.

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