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Title: Association of Social Adversity and Allostatic Load with Breast Cancer Clinicopathology and Survival among Black Women

Black women(BW) have higher mortality and experience more stressors than White women (WW) in the US. Chronic exposure to stress can lead to the dysregulation of major physiologic systems. Allostatic load (AL), capturing the cumulative physiological effects across major regulatory systems, is an effective measure of physiologic dysregulation secondary to stress, and inversely associated with socioeconomic status (SES) and positively associated with BC risk among BW, but not among WW. This racial disparity may be attributed to the environment and its effects on the body's response to chronic stress. We previously found that higher AL was associated with more aggressive breast tumor phenotypes among BW, and mortality was higher among women residing in low income neighborhoods, suggesting that social and biological factors may contribute to BC heterogeneity and survival. In this study, we will investigate the causal impacts of social adversity on BC clinicopathology and survival outcomes, incorporating AL as a key mediator, and attempt to establish a framework using social determinants and AL to explain why BW experience increased risk for aggressive breast tumor clinicopathology and shorter survival. Our long-term goal is to understand and address the sociobiological predictors of survival among BW with BC. We hypothesize that social adversity contributes to chronic physiologic stress, measurable as AL, resulting in more aggressive BC clinicopathology and shorter survival. We will use epidemiologic and clinical data from the parental BC study including social/environmental measures and AL. Our aims are: Aim 1. Investigate the association of social adversity with aggressive breast tumor clinicopathology. We hypothesize that social adversity is associated with aggressive breast tumor clinicopathology among BW with BC. Aim 2. Investigate the association of social adversity with overall survival and BC-specific survival. We hypothesize that greater social adversity is associated with shorter survival among BW with BC. We also hypothesize that relationships in Aims1 and 2 are mediated by AL. Aim 3. Determine the associations of AL with aggressive breast tumor clinicopathology and with survival. We hypothesize that higher AL is predictive of more aggressive tumor clinicopathology, shorter survival among BW with BC. Our study may indicate AL is a prognostic marker and target for novel interventions and therapeutics, improve BC survivor among BW, and contribute to greater health equity. We will propose to validate our results in larger cohort of BW with BC in our full research proposal planning to submit to NIH/NCI, DOD or ACS.