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Examining the Role of Obesity and Leptin Signaling in Triple Negative Breast Cancer

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OBJECTIVES/GOALS: In triple negative breast cancer (TNBC), obesity is associated with poor outcomes. Adipose stem cells (ASCs) from obese patients (obASCs) secrete higher levels of adipokines compared to ASCs from lean individuals. Leptin, one of these adipokines, has been implicated in many cancers. This study seeks to examine the role of leptin signaling in TNBC. METHODS/STUDY POPULATION: Previous work in conjunction with a collaborating lab has shown that leptin signaling promotes metastasis and increased expression of epithelial-mesenchymal transition (EMT) markers in triple negative breast cancer cell lines. This project expands upon this work through using both patient-derived cell lines and and patient-derived xenografts (PDX), and examines the role of leptin signaling both in vitro and in vivo. To determine the effects of obesity upon a PDX model of TNBC, a high fat diet was used to induce obesity in vivo. A pharmacological inhibitor of the leptin receptor was used to test the requirement for leptin signaling both in vivo and in vitro. RESULTS/ANTICIPATED RESULTS: Exposure to conditioned media harvested from obASCs increased the percentage of TNBC cells that expressed cancer stem cell markers, whereas exposure to an inhibitor of the leptin receptor decreased the percentage of cells with cancer stem cell markers. PDX tumors implanted into mice with diet-induced obesity had an increased volume compared to tumors implanted into lean controls. Further analysis will be conducted on metastasis, circulating tumor cells, and survival in both lean and obese mice. DISCUSSION/SIGNIFICANCE: Understanding the complex signaling events in the obese tumor microenvironment is essential, as these molecular differences may contribute to different outcomes for obese and lean individuals with triple negative breast cancer. Therefore, study of the crosstalk between obASCs and TNBC cells is critical.

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"How do you define Resilience?" Examining the Psychological Resilience of Black Adults Living with Sickle Cell Disease (SCD)*

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OBJECTIVES/GOALS: This study examines psychological resilience in adults living with Sickle Cell Disease (SCD) in the U.S. aiming to explore how psychological resilience is defined by this community. METHODS/STUDY POPULATION: Participants were recruited between 2014 – 2018, from across the U.S. as part of an ongoing cross-sectional study: Insights into Microbiome and Environmental Contributions to Sickle Cell Disease and Leg Ulcers Study (INSIGHTS). Inclusion criteria included age of 18 or older, with a clinical history of SCD, and were interviewed if they completed the Brief Resilience Scale (BRS) as part of INSIGHTS. 150 study participants were separated by their BRS scores into "High" and "Low" scoring quartiles. 30 participants were randomly selected, 15 from the lowest quartile and 15 from the highest. All participants completed the Connor Davidson Resilience (CD) measure at the end of their qualitative interview. All identified as Black with an average age of 42.5 (13 F, 17 M). RESULTS/ANTICIPATED RESULTS: Three main concepts emerged within both groups in response to the question "How do you define resilience?" (a) not giving up (b) how one deals with challenges and (c) moving forward. DISCUSSION/SIGNIFICANCE: Our analysis shows that the BRS may not be a precise or accurate indicator of the resilience of adults living with SCD. Therefore, it remains to be seen if these measures are descriptive of these individuals true psychological or physiological state as they have not been used in this community until now.

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The effect of non-invasive transcutaneous auricular vagus nerve stimulation (taVNS) on hypoxic-ischemic injury in newborn rats

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OBJECTIVES/GOALS: Neonatal hypoxic-ischemic encephalopathy (HIE) is an acute neurologic syndrome where decreased blood flow and oxygen to the brain causes acute and chronic brain dysfunction. The only proven neuroprotective intervention for HIE is hypothermia treatment started within 6 hours of birth and 50% of survivors have long-term deficits. METHODS/STUDY POPULATION: Pre-clinical adult stroke studies demonstrated that vagus nerve stimulation (VNS) has anti-inflammatory effects and attenuates brain damage. Transcutaneous auricular VNS (taVNS) is safe and feasible in infants and may improve the motor skill of bottle feeding. We hypothesize that a combined hypothermia-taVNS treatment shortly after HIE birth will have neuroprotective effects, improve motor function, attenuate infarct volume inflammation compared to hypothermia alone. The HIE model includes ligation of the right common carotid artery in postnatal day 7 (P7) rats followed by 90min hypoxia (8% oxygen) and 2hr hypothermia. taVNS or sham taVNS was administered using a bipolar electrode placed on the auricular concha region for 30min, [30sec trains, 0.5msec duration, 20Hz frequency, followed by 4.5min breaks] RESULTS/ANTICIPATED RESULTS: Experimental groups include +HIE/+taVNS, +HIE/-taVNS, and -HIE/-taVNS. To assess motor function, grasping reflex and forelimb grip strength tasks were assessed prior to surgery through P10. Infarct volume was assessed at 72h after injury by staining coronal sections with cresyl-violet. Thirty-four rat pups underwent surgery with an 8.82% mortality rate. taVNS was well tolerated by the P7 rats when delivered below perceptual threshold (0.4-1.1mA). There was no difference in elementary motor function or infarct volume between any group. DISCUSSION/SIGNIFICANCE: Future studies will include 2.5hr hypoxia for a more severe brain injury and a -HIE/+taVNS control group. These initial pre-clinical studies in neonates are important in determining whether taVNS may translate as a treatment to improve outcomes after neonatal HIE.

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