Poster Number: 9

MetroHealth Medical Center

RESEARCH DAY 2023
Abstract Submission Form

Poster Title: **The Oncogenic activity of YB1 Contributes to Health Disparities in Triple Negative Breast Cancer**

Authors: **Lamyae El Khalki [1,2,3], Wei Wang [1,2], Akram Alkrekshi [1,2], Vesna Markovic [2], Amer Khiyami [2], Ricky Chan [3], Adam Perzynski [1,2], Natalie Joseph [1,2] and Khalid Sossey-Alaoui [1,2,3],**

Presenter's Name: **Lamyae El Khalki**

Location of Laboratory: **Rammelkamp building R455**

Category: **Cancer Biology**

Triple negative breast cancer (TNBC) is the most aggressive form of breast cancer (BC) because of the absence of cell surface receptors ER, PR and Her2 which can be specifically targeted with hormonal and antibody treatments. Cytotoxic chemotherapy remains the major course of treatment with dismal response in TNBC patients. TNBC tumors represent most of BC related deaths, due to the rapid recurrence, metastasize, and chemo-resistance. AA women with TNBC have worse clinical outcomes compared with Caucasian American (CA) women who have the same disease, tend to develop this disease at younger age, and are less responsive to standard of care treatments, compared to CA women. Tumor intrinsic biological mechanisms contribute to unequal TNBC disease burdens. Here, we show that YB1, a multifunction gene, plays a major role in the observed TNBC disparities between AA and CA women. We show that YB1 is significantly highly expressed in AA TNBC tumors compared to CAs, and increased levels of YB1 also correlate with poor survival in AA patients with TNBC. We confirmed these findings in independent TNBC tumors cohorts, including a cohort from MetroHealth, a SafetyNet hospital that serves the most vulnerable patient population in North-East Ohio. We also used a combination of genetic and pharmacologic manipulations of YB1, both in vitro and in animal models of TNBC to show that YB1 oncogenic activity is more enhanced in TNBC cell lines of AA origin, by increasing the tumorigenicity and aggressivity of AA TNBC cell lines. In addition, our RNA-Seq analyses of human TNBC specimens identified novel genes and pathways that are differentially activated in tumors of AA origin as compared to their CA counterparts. PI3K-AKT, transcriptional regulation, metabolic regulation and Wnt signaling were among the top pathways that we found to be differentially regulated between AA and CA tumors. Investigation of these pathways may lead to a better understanding of the genetic and biological differences between AA and CA TNBC and may open new opportunities for the development of novel therapeutic strategies that are specifically tailored to AA TNBC patients and, in the long run, reduce disparities in this vulnerable population.