Characterizing Convergent Transcriptomic Impacts of Norepinephrine Across Breast Cancer Grades via Element AVITI-24

Agrawal, Anchita (School: Jericho High School)

1 in 8 women are diagnosed with breast cancer (BC) in the US, and peripheral nerves are present in upwards of 85% of BC cases. Adrenergic signaling, regulated by stress neurotransmitters like norepinephrine (NE), has been implicated in cancer progression. Yet, recent studies report conflicting roles of NE in cancer and lack multimodal characterization of this tumor-nerve interaction across BC grades. To map RNA, protein, and cellular changes caused by NE, a novel multiomics platform, Element AVITI-24, was used on high-grade triple-negative BC (TNBC) MDA-MB-231 cells and low-grade ER-positive MCF-7 cells cultured with NE. NE treatment significantly downregulated multiple genes associated with proliferation, invasion, and survival in MDA-MB-231s, suggesting NE’s anti-tumor effects. However, NE also significantly downregulated GADD45G, implicated in decreasing cell proliferation, suggesting pro-tumor effects. Differential gene expression analysis of MCF-7 cells also displayed similar converging effects, where NE downregulated both pro-tumor and anti-tumor genes, although fewer in comparison to the high-grade BC cell line. This is the first study to characterize NE's nuanced effects on transcriptomic expression in BC grades and subtypes, displaying that NE plays a larger role in high-grade TNBC lines and exerts both pro-tumor and anti-tumor effects in both low- and high-grade BC. These results provide valuable insights into NE's downstream effects on adrenergic and cancer signaling, as well as subtype-specific responses. Furthermore, the study establishes a novel framework for investigating adrenergic signaling in cancers using an integrated multiomics platform. This guides future targeted exploration of adrenergic agonists and antagonists in subtype-specific BC treatment.

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