CNOT9/DBN1 Actin Dysregulation in QNBC Metastasis & Heterogeneity

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Metastatic triple negative breast cancer (TNBC) is the most aggressive form of breast cancer, with a 5-year survival rate of 12%. Mesenchymal quadruple negative breast cancer (QNBC) is a molecular subtype of TNBC, lacking expression of the androgen receptor and commonly associated with poorer prognosis, distant metastasis, and heightened aggressiveness. Currently, there is a significant gap in both generalized and personalized treatments for TNBC & QNBC cases, due to the lack of expression of key druggable receptors for immunotherapy and increased tumor microenvironment (TME) heterogeneity, in comparison to other cancers. In this study, 6 QNBC patient tumors' RNAseq data was analyzed in R Studio to visualize transcriptional variation and tumor cell distribution, prompting analysis of DBN1 and actin-binding genes' upregulation. Additionally, MDA-MB-231 cells were cultured to model QNBC in-vitro. After reaching ~85% confluency, cells were passaged and split into four groups: CNOT9, DBN1, Non-Targeting, and Control. The CNOT9 and DBN1 groups were knocked down with respective siRNA, while the Non-Targeting group underwent transfection with an siRNA control, and the Control group underwent no treatment. Post knockdown, groups underwent analysis with a metastatic potential assay and quantification through hemocytometer counting. This study's results found that knocking down CNOT9 and DBN1 significantly decreased the metastatic potential of QNBC, revealing potential immunotherapeutics and combination therapies, while also highlighting novel migratory pathways. This study also found that DBN1 contributes to a highly heterogeneous tumor microenvironment through regulating EMT states, underscoring its potential for making QNBC tumors more responsive to treatment.

Awards Won:
Fourth Award of $600