Neurotrophin Receptor Isoform Expression Analysis in Breast Invasive Carcinoma: Potential Considerations for Targeted Therapy and Precision Medicine

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Every minute, a woman somewhere in the world will die of breast cancer. Despite significant advances in the field, breast cancer remains the leading cause of cancer death in women globally. Aberrant growth factor (GF) signaling has long been implicated in oncogenesis, and is influenced by complex dynamics including DNA modifications, alternative splicing, receptor heterodimerization, and other protein-protein interactions within a given cellular environment. Neurotrophin receptors are one family of GF receptors that have previously been implicated in cancer proliferation, invasion, and chemoresistance. One such receptor, tropomyosin receptor kinase TrkB, encoded by NTRK2, has been implicated in breast cancer, yet little is known about its isoform-specific expression in patient tissue. This computational analysis sought to investigate expression of various GF and neurotrophin receptor isoforms, and their respective ligands, in human breast invasive carcinoma (BRCA) (n=1105) and normal breast (n=113) tissue samples using RNA-sequencing data from The Cancer Genome Atlas. Analysis involved exon expression visualization, principal component analysis, differential correlation analysis, and machine learning. This work reveals distinct expression patterns of an alternatively spliced TrkB variant in normal vs. tumor tissue. Differential correlation analysis suggests that aberrant protein-protein interactions may exist in tumor tissue. Finally, utilization of machine learning alludes to a possible role for the unique gene-set investigated in differentiating specific BRCA histological subtypes. These results could pave the way toward future research for improving targeted therapies for precision medicine by highlighting isoform-specific expression and potential interactors.

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