TNF Ligand Promotes Angiogenesis in Triple Negative Breast Cancer Through Activation of Inflammatory Regulatory Networks

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Triple negative breast cancer (TNBC) is a highly aggressive form of breast cancer with a lack of effective treatment options and high rates of metastasis. Angiogenesis, the formation of new blood vessels, supplies tumors in TNBC with nutrients and oxygen required for growth. In this study, single cell RNA sequencing was used to create a transcriptomic profile of 75,787 cells and 29,795 genes from 11 healthy breast tissue samples and 10 TNBC tissue samples. Analysis of endothelial cells in the dataset, which line the body's blood vessels and direct angiogenesis, revealed that angiogenic pathways were upregulated in the TNBC tissue. Further exploration of the data demonstrated that the TNF (Tumor Necrosis Factor) ligand, or regulatory molecule, primarily induced the angiogenic phenotype of TNBC endothelial cells through the activation of 4 inflammatory target genes--- SELE, VCAM1, ICAM1, and SELP. Gene regulatory network reconstruction was then utilized to elucidate the molecular signal transduction pathways that contributed to inflammatory angiogenesis. Chronic inflammation has been linked to the stimulation of vessel growth in cancer, but the exact intra- and inter-cellular mechanisms behind this process are not fully understood. This study provides statistically significant evidence supporting the connection between cancer inflammation and angiogenesis, and offers insights into signaling pathways that promote tumor progression. These findings could be crucial for future drug and monoclonal antibody therapies that aim to develop novel treatment methods for TNBC patients.

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