Effect of Smoking on TGF-beta Signaling in Breast Cancer Patients

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Breast cancer is the most common form of cancer in women, and tobacco smoke has been classified as a carcinogen by the International Agency for Research on Cancer. While nicotine is known to cause abnormalities in cell signaling, biomolecular links between smoking and breast cancer development are still incomplete. In this project, datasets from The Cancer Genome Atlas (TCGA) and Gene Expression Omnibus (GEO) were evaluated to assess alterations in pathways involving TGF-beta (transforming growth factor-beta), a multifunctional cytokine that can promote tumorigenesis, by comparing nicotine-treated versus untreated cells (controls). Data analysis performed on clinical breast cancer samples from TCGA indicated that 81% of 207 breast cancer patients had altered gene expression in TGF-beta pathway-related genes. Demographic analysis of clinical samples also showed differences in alterations of genes from the TGF-beta pathway across different ethnicities. Gene expression analysis of breast cancer cell lines (MCF7) treated with nicotine (chRNA5) and tobacco (tobacco smoke) showed alteration in signaling pathways known to be implicated in tumorigenesis. The top altered genes and multiple top pathways identified were related to TGF-beta pathways, validating nicotine-associated alterations. Additional gene alterations and implicated pathways suggest nicotine's influence on cancer metabolism may extend beyond currently identified mechanisms. These findings also suggest that different forms of nicotine exposure, such as vaping and smoking, may all cause altered gene expression, with some overlap and some differences in implicated biological pathways. The results from this study suggest that smoking may promote breast cancer by modulating the TGF-beta pathway.

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