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**"Assessing the Tumor Suppressive Impact and Regulatory Mechanisms of SPDEF Expression in Breast Cancer"**

**Background:** Prostate-Derived Ets Factor/Sam Pointed Domain Ets Factor (SPDEF) is a transcription factor of the Ets family encoded by the gene SPDEF and associated with organs containing lumens such as the prostate, salivary gland, breast, colon, and uterus. SPDEF expression has been implicated with carcinogenesis in numerous tissue lineages with opposing associations; for instance, tumor suppressive effects have been reported in head/neck squamous cell carcinoma and prostate cancer while oncogenic effects have been reported in pancreatic adenocarcinoma and ovarian carcinoma. The role of SPDEF expression in breast cancer has been less studied; thus, the objective of this project is to evaluate patterns between gene expression and breast cancer prognosis and survival. In addition, due to the heterogenous nature of breast cancer, a thorough genomic analysis was conducted to investigate a variety of potential gene regulatory mechanisms and demographic associations.

**Methods:** Tumor genome and patient demographic data were extracted from The Cancer Genome Atlas (TCGA) registry and retrospectively analyzed with statistical software on GraphPad Prism. The following gene regulatory mechanisms were examined as potential sources of altered expression levels: mutations, copy number alterations, co-expression, and promoter methylation.

**Results:** SPDEF was identified as a breast cancer tumor suppressor gene, with low expression significantly associated with poorer survival and increased rates of distant metastasis and relapse. Various demographic variables were also analyzed to evaluate expression patterns, and we noted decreased SPDEF levels linked to a younger age at initial pathologic diagnosis, the Basal PAM-50 tumor subtype, as well as Black or African American race. Furthermore, investigation of regulatory mechanisms of expression led to a significant relationship involving 2 CpG islands and 3 DNA methyltransferase genes.

**Conclusions:** The expression of identified promoter methylation components aligned with previously determined demographic patterns of SPDEF expression, thereby reinforcing the presence of their regulatory role and subsequent impact on breast cancer prognosis. Ultimately, this enriched understanding of SPDEF's tumorigenesis role, its predisposition for particular patient and tumor subsets, and its regulatory mechanisms can contribute to the quest for more targeted breast cancer therapies. By not only identifying SPDEF as a tumor suppressor gene with clinical implications but also pinpointing the influential intracellular processes, these results can be utilized to devise temporally and locationally specific treatment strategies.