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"Investigating the epigenetic role of SPDEF in prostate cancer through identification of proteins involved in SPDEF function"

Prostate cancer (PCa) is the most non-cutaneous cancer diagnosed in men, and results in approximately 30,000 deaths each year in the United States. Therapy resistant PCa, known as castration-resistant prostate cancer (CRPC), does not fully respond to common therapeutics. Most of the deaths from prostate cancer are due to metastatic CRPC indicating the importance of studying PCa to formulate more effective treatments. Previous studies have shown that the SAM pointed domain containing ETS transcription factor (SPDEF) protein plays a key role in the inhibition of prostate cancer metastasis; however, the mechanism for how SPDEF regulates metastasis is still poorly understood. In the present studies, we used a proteomic approach to identify changes in the nuclear proteome in response to SPDEF expression in PC3 cells, a CRPC cell line that normally lacks SPDEF. Mass spectrometry (MS) data of nuclear enriched fractions were used to determine key proteins potentially involved in SPDEF function. The MS data was narrowed down to proteins that showed at least a two-fold increase when SPDEF was overexpressed in PC3 cells. Several databases, including BioGrid, Metascape, and STRING, were used to analyze the MS data and select the target proteins to further analyze. Based on the database outputs as well as the fold enrichment value determined via MS, the following proteins were further studied: cytokeratin 18 (KRT18), grainyhead like transcription factor 2 (GRHL2), epithelial splicing regulatory protein 1 (ESRP1), histone acetyltransferase 1 (HAT1), and minichromosome maintenance complex (MCM) proteins. Quantitative reverse transcriptase polymerase chain reaction (RT-qPCR) or Western blot analyses were used to confirm the effect of SPDEF on the expression of these proteins. For several of the proteins, the RT-qPCR and Western blot data correlate with the MS data to show an increase in expression level when SPDEF is overexpressed. These results suggest a potential role of these proteins in modulating the effects of SPDEF. Further studies, underway, are aimed at understanding the role of these proteins in modulating the anti-metastasis effects of SPDEF in prostate cancer and may help in the design of novel therapies to tame CRPC, for which there is still no cure.