Category: Cancer Genomics

Identification of the bimodal transcriptional regulation of SP1 transcription factor in sub-sets of gastric cancer

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Abstract

Stomach cancer is the second leading cause of cancer death and fourth most common cancer in the world. Deregulated transcription programs and signaling pathways are the major driving forces involved in the initiation and progression of cancer. Identification of the dysregulated transcription programs and genes from the transcriptome of gastric tumors would pave the way for i) the identification of major dysregulations involved in gastric cancer, ii) stratification of tumors, and iii) development of targeted therapies. Specificity protein (SP1) is a transcription factor and aberrant expression of SP1 is known to confer proliferative and metastatic advantage to tumor cells. The role of SP1 mediated expression in gastric cancer was investigated in the genome-wide mRNA profile of gastric cancer cell line upon SP1 silencing. Gene-set based cumulative expression analysis of the available SP1 regulated gene-sets revealed the involvement of certain SP1 target genes in a sub-set of gastric tumors while the another group of genes in another sub-set. This shows the bi-modal involvement of different SP1 regulated genes in different sub-types of gastric tumors. The expression of a set of SP1 genes were found positively correlated with the oncogenic signatures of MYC, E2F and mTOR signaling with their elevated expression in intestinal type tumors. Another category of SP1 genes, which are up-regulated upon SP1 silencing were found expressed in diffuse type tumors along with the activated VEGFA, OCT4, and TGF-β signaling. These results reveal that SP1 transcriptionally activates the genes involved in intestinal type and represses the genes involved in diffuse type gastric tumors. This shows the dual role of SP1 regulated transcription in sub-sets of gastric tumors and warrant further investigation in diagnostic and therapeutic contexts.