HOP: A Novel Tumor Suppressor in Head and Neck Squamous Cell Carcinoma

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Introduction:
Despite recent advances, five-year survival rates for head and neck cancers have not improved significantly over the past 20 years. Therefore, there is a critical need to establish more efficacious diagnostics and therapies. Studies using Gene Chip microarray analysis which identified a list of 2,890 genes differentially expressed between HNSCCA tumors and normal mucosa have been previously reported. Expression of the gene encoding the Homeo-domain-only protein (HOP) was greatly decreased in all tumor samples. Similar to other studies, there was no significant correlation between the level of Hop expression and either the TNM staging or the overall stage of the tumor (see Figure 3). This finding was supported by work from other groups who have suggested that HOP may function as a potent tumor suppressor. Interestingly, HOP has been shown to function as a suppressor of the immediate-early gene transcription factor, SRF, which is important for cellular growth and proliferation in response to mitogenic stimuli. Studies by others have shown HOP functions as a transcriptional repressor by recruiting histone deacetylase to area of active SRF mediated transcription (see Figure 1). In addition, HOP has also been shown to be an important regulator of cardiac and pulmonary organogenesis. Taken together, these results suggest Hop may function as a regulator of cellular proliferation and differentiation. Absence of Hop expression during development leads to abnormal cellular differentiation. Accordingly, loss of Hop in a wide range of tumors correlates with increased proliferation potential suggesting it also functions as a tumor suppressor in a wide range of solid tumors. The following studies were undertaken to further elucidate the function of HOP in HNSCC.

Forced expression of HOP in HNSCC cell lines results in decreased growth and proliferation suggesting Hop functions as a tumor suppressor. Interaction of Hop with SRF is required for tumor suppressor function as mHop has no effect on HNSCC cell line proliferation.

Conclusions:
- Expression of HOP is greatly decreased in HNSCC tumor samples and HNSCC cell lines.
- SRF regulated genes involved in cellular proliferation are upregulated in HNSCC.

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