

The Long Noncoding RNA SCHLAP1-AS is Associated with Prostate Cancer Progression

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Background: Long noncoding RNAs (lncRNAs) have recently been shown to serve as drivers of malignancy and represent novel therapeutic targets. We have recently identified over 46,000 novel lncRNAs through *in silico* analyses of nearly 8,000 tumor or normal tissue specimens. In this study, we utilize this compendium of lncRNAs to identify those associated with metastatic progression of prostate cancer (PCa), and functionally investigate our top nominated candidate, SCHLAP1-AS (a lncRNA on the antisense strand of SCHLAP1), in preclinical models of disease.

Methods: Transcriptional profiling of a cohort of prostatectomy patients was used to identify new PCa-associated lncRNAs. The gene most strongly associated with subsequent metastatic progression, SCHLAP1-AS, was further analyzed. Rapid Amplification of cDNA Ends (RACE) was used to define its gene structure, and Fluorescence In-Situ Hybridization (FISH) was used to localize SCHLAP1-AS transcripts. Knockdown and over-expression studies were performed *in vitro* and *in vivo* to elucidate the functions of SCHLAP1-AS. Finally, transcriptional analysis was performed to identify gene sets associated with this candidate.

Results: Of all the assessed protein-coding and non-coding genes, SCHLAP1-AS was the top gene that associated with metastatic progression of PCa, via Area Under the Curve (AUC) assessment on a Receiver Operating Characteristic (ROC) analysis. For multivariable analyses, SCHLAP1-AS remained prognostic while accounting for standard clinicopathologic variables. Additionally, SCHLAP1-AS expression is relatively specific for PCa. Knockdown of SCHLAP1-AS significantly impaired proliferation and invasion of PCa cells *in vitro*, and tumor growth and metastasis *in vivo*. Conversely, SCHLAP1-AS over-expression increases the invasion potential of the prostate epithelial cell line 22Rv1.

Conclusions: We have identified a novel, prostate-specific lncRNA (SCHLAP1-AS) that promotes PCa proliferation and metastasis, and is associated with poor clinical prognosis. Future investigations regarding its mechanisms of action are warranted to further elucidate its role in PCa progression.

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