Characterization of prostate cancer-associated transcript 47 as a novel prostate cancer oncogene and therapeutic target

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Background

Long non-coding RNAs (lncRNAs) outnumber protein-coding genes, and are emerging as important players in many diseases, including prostate cancer (PCa). Our group recently cataloged the human lncRNA transcriptome by applying *ab initio* bioinformatic analysis to 7,256 RNA seq libraries derived from normal and tumor tissue. This effort identified over 58,000 lncRNA species, comprising 68% of coding elements in the human genome. Non-parametric analysis of transcripts differentially expressed between samples allowed detection of disease-specific lncRNAs. While this method positively identified known PCa-associated lncRNAs PCA3 and SChLAP1, the species most strongly correlated with PCa was a novel lncRNA now termed prostate cancer-associated transcript 47 (PRCAT47). PRCAT47 levels are several-fold higher in PCa primary tumors and metastases vs normal prostate tissue. In turn, immunohistochemistry demonstrates robust PRCAT47 staining in patient PCa samples, with near absence in benign prostate tissue. Given these data, we hypothesized PRCAT47 is a novel PCa oncogene critical for tumorigenesis and disease progression.

Methods and Results

To test the hypothesis, we conducted loss-of-function experiments *in vitro* and *in vivo* to ascertain the relevance of PRCAT47 for PCa cell proliferation and tumor growth. We found that PRCAT47 knockdown in LNCaP and MDA_PCa_2b cell lines significantly inhibited *in vitro* proliferation. Furthermore, MDA_PCa_2b cells subjected to PRCAT47 shRNA gave rise to smaller tumors vs control-treated cells in a mouse xenograft system. In order to determine the relevance of PRCAT47 as a PCa drug target, we collaborated with Ionis Pharmaceuticals, the maker of antisense oligonucleotides (ASOs) engineered for *in vivo* delivery. We found that ASOs directed against PRCAT47 impaired *in vitro* proliferation of MDA_PCa_2b cells. We are currently evaluating the ability of the same ASOs to impair growth of MDA_PCa_2b -derived tumors in mice.

Conclusion

PRCAT47 expression is strongly associated with aggressive and metastatic prostate cancer and critical for PCa cell proliferation and tumorigenesis. It is promising therapeutic target; and we are currently investigating its inhibition in pre-clinical *in vivo* models.

Conflict of Interest Statement

No potential conflicts of interest were closed

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