The expression, function and clinical implication of circular RNAs in prostate cancer

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Background: A poorly characterized component of the prostate cancer (PCa) transcriptome are circular transcripts (circRNAs), which have been implicated in many diseases. circRNAs form a covalently closed loop that increases stability and creates biomarker potential, while eluding poly-A capture. As a result, full diversity of the PCa transcriptome and its implication remained hidden. In this study, we delineated the transcriptomic landscape and pinpointed functional circRNAs in PCa.

Methods: We utilize multi-cohort RNA-seq data, coupled with customized loss-of-function screen to delineate the transcriptional and functional landscape of circRNAs in PCa.

Results: Analysis of back-splicing events showed widespread RNA circularization in PCa. The degree of circRNA production was correlated to disease progression in multiple patient cohorts. Loss of function screening identified hundreds of circRNAs essential to PCa cell growth. We identified circRNAs that are functional in neuroendocrine PCa. We also provided evidence that a small proportion of circRNAs translate into protein and circRNAs are abundant in exosomes from PCa patient plasma.

Conclusions: Our study provided the first circRNA landscape in PCa and identified circRNAs associated with PCa development and progression. Our functional genomic screens generate numerous opportunities for furthering mechanistic understanding of PCa pathogenesis and progression. These data advocate for adoption of ultra-deep RNA-Seq without poly-A selection to interrogate cancer transcriptome.

Conflict of Interest: the authors declare no conflict of interest

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