Clinical utility of Pseudouridine as a diagnostic Biomarker to detect Prostate Cancer

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BACKGROUND: Genomic data suggests an upregulation of snoRNAs in aggressive prostate cancer. Pseudouridine (ψ), an isomer of uridine (U), is the most common post-transcriptional modification of RNA brought about by snoRNAs. Given the present controversy surrounding PSA testing there have been renewed efforts to identify novel blood, urine, and genetic biomarkers for PCa. We investigated whether ψ can serve as a bio-marker for prostate cancer using cell lines and TMAs.

METHODS: Anti-ψ mAb was purchased from MBL. A 25-base 28S rRNA sequence that was shown to undergo pseudouridinylation was used as a template and regular and ψ versions were custom synthesized from IDT. For the dot blot assays various amounts of RNA were spotted and UV cross-linked to a nylon membrane and then probed with anti-ψ. IHC studies were carried out using TMAs purchased from US BioMax. We developed an in-house RNA based ELISA assay to detect RNA.

RESULTS: Anti-ψ antibody differentiated between two 28S rRNA sequences differing only at the U or ψ position. RNA from androgen insensitive cells appeared to have more ψ than AR sensitive cells. Indirect immunofluorescence studies also showed similar trends, with ψ to be nuclear excluded and spatially localized to a diffused and homogeneous cytoplasmic distribution with intense signals from the peri-nuclear space. IHC results show staining to be primarily localized to the cytoplasm of glandular cells, with negligible staining of gland cells of normal cells adjacent to the tumor (NATs). H-score analysis shows significant difference between adenocarcinoma cores and NATs.

CONCLUSIONS: Our results establish a clear relationship between Ψ expression and clinical advancement of disease. Since ψ cannot be salvaged, going into circulation and finally excreted in the urine, it could serve as a biomarker for prostate cancer.

Conflict of Interest: none

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