Detection of Prostate Cancer-Associated Transcripts in Urinary Extracellular Vesicles

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BACKGROUND

There is an opportunity to improve the diagnosis and classification of prostate cancers. Extracellular vesicles (EVs) containing RNA and proteins from their cell of origin are released and can be detected in biofluids such as urine, making them a rational target for biomarker discovery and detection.

METHODS

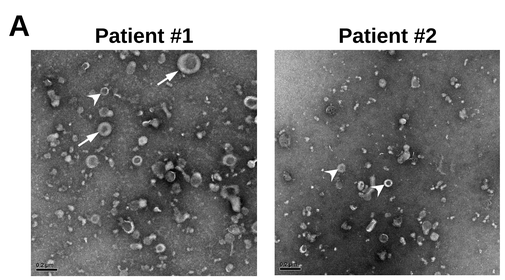
30 mL of first-catch urine is collected following DRE → EVs are isolated from the urine supernatant by ultrafiltration → Gene expression is analyzed by targeted RNA sequencing

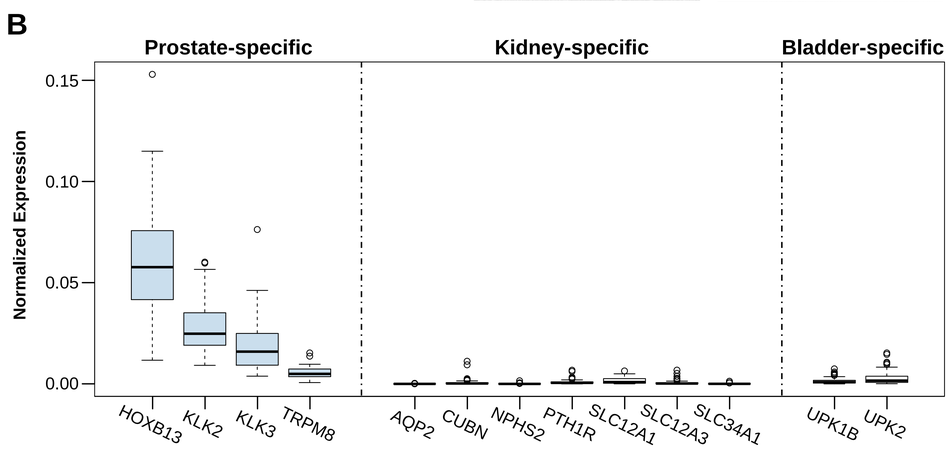
Samples collected as part of the Emory EDRN Prostate Biomarker Clinical Validation Cohort

PROSTATE-SPECIFIC RNAs ARE ENRICHED IN URINARY EVs

(A) TEM analysis of the EV fraction of post-DRE urine indicates the presence of larger microvesicles (~200 nm, arrows) and smaller vesicles likely to be exosomes (10-100 µm, arrowheads).

(B) Prostate-specific genes were detected at higher levels than kidney- or bladder-specific genes in post-DRE urine EVs (n = 60).



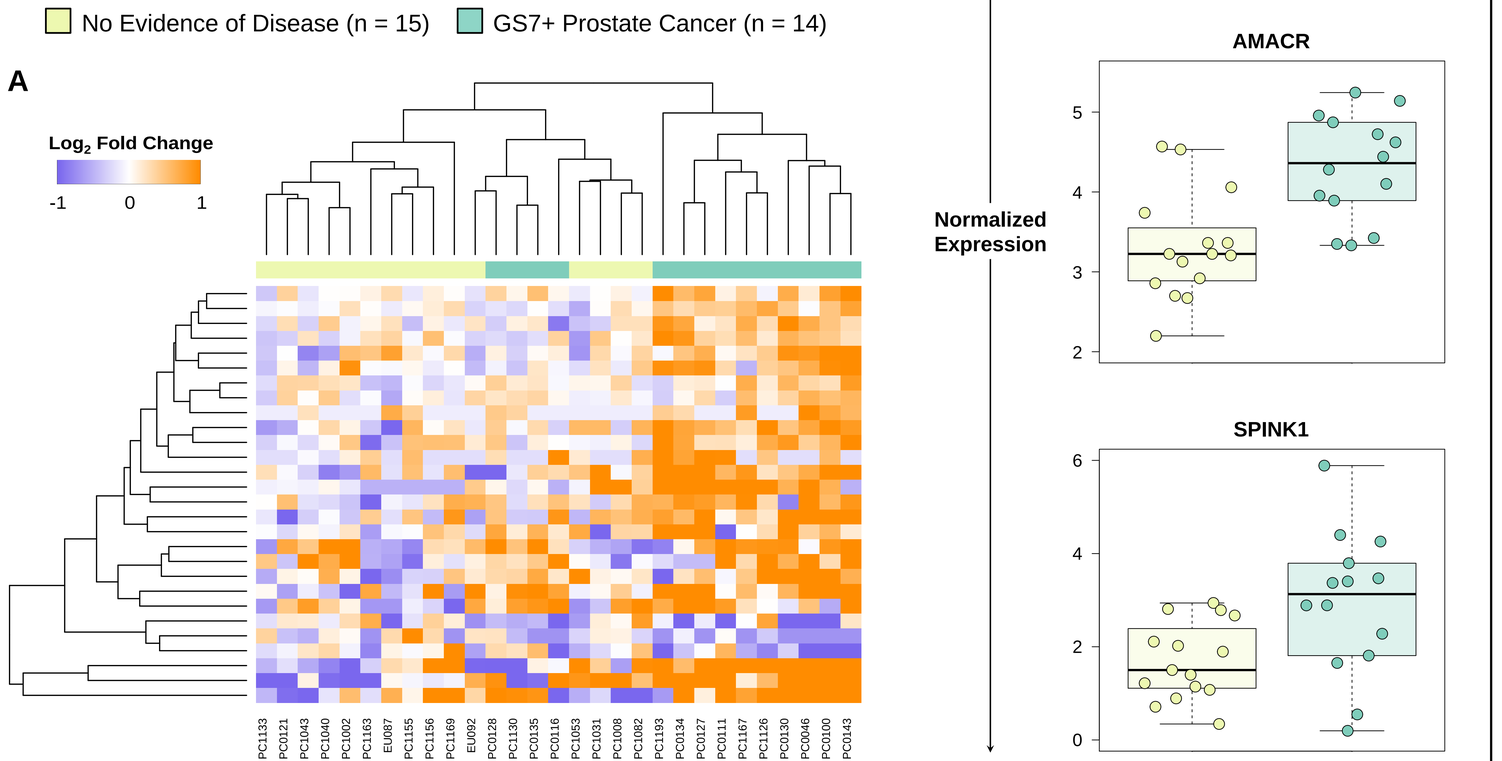


DISTINCT URINARY EV GENE EXPRESSION PROFILES ARE OBSERVED FOR PATIENTS WITH GS7+ PROSTATE CANCER

(A) 28 genes had significantly different expression in patients with GS7+ prostate cancer

- Hierarchical clustering indicated distinct urinary gene expression profiles of patients with GS7+ prostate cancer as compared to patients with no evidence of disease

(B) Known prostate cancer-associated genes were significantly higher in the urinary EVs of GS7+ prostate cancer patients



CONCLUSIONS

- Differential gene expression can be detected in the urinary vesicles of patients with aggressive prostate cancer and there is the potential to stratify patients based on their urinary EV gene expression profile
- This approach could offer an alternative method for the identification of aggressive prostate cancer prior to prostate biopsy or during active surveillance

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