High sensitive rapid detection of urinary EVs with up converting nanoparticle based lateral flow immunoassay

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MOLECULAR BIOTECHNOLOGY AND DIAGNOSTICS

Introduction

Bladder cancer (BlCa) poses a substantial health burden globally, demanding advancements in diagnostic methodologies. Presently existing approaches, while effective, are invasive and cost-intensive. Therefore, this study has aimed to develop a rapid, cheap, and non-invasive diagnostic tool utilizing an upconverting nanoparticle (UCNP) based-lateral flow immunoassay (LFIA) to directly detect extracellular vesicles (EVs) from cancer cell line and urine samples.

Materials and Methods

Urinary extracellular Vesicles (uEVs) from individual patients of bladder cancer (BlCa) (n=20), benign prostate hyperplasia (BPH) (n=20), and healthy (n=30) samples were captured using anti-CD63 antibody. Subsequently, the same CD63 antibody as a tracer labeled with UCNPs were used to detect these uEVs within microtitration wells. Following absorption from the mixture of sample and reporter solution onto the lateral flow strip, the strips were read with an Upcon reader device, resulting in up-converted luminescent signals after 1.2 hours (Fig. 1).

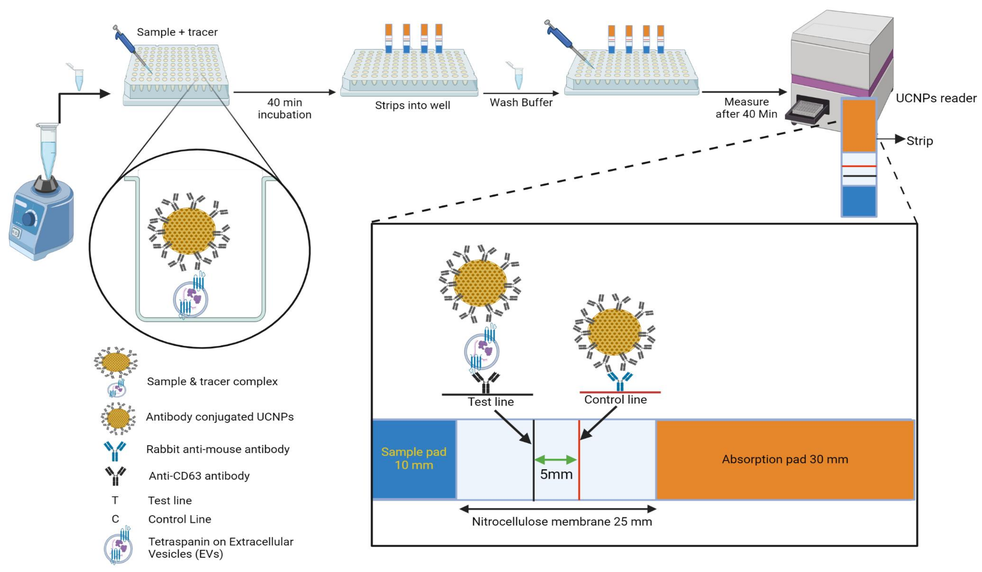

Figure 1. Illustration of CD63-CD63-UCNP Lateral flow immunoassay for urinary EVs detection.

Results

So far, The results from this study demonstrates its high sensitivity in detecting EVs derived from cancer sources, with a detection limit of 1.9×10^5/µL. Specifically, CD63-CD63-UCNP assay was able to distinguish significantly between BlCa patients and individuals with benign conditions (p=0.003), as well as healthy individuals (p= 0.0001). However, more samples are required to further validate this study.

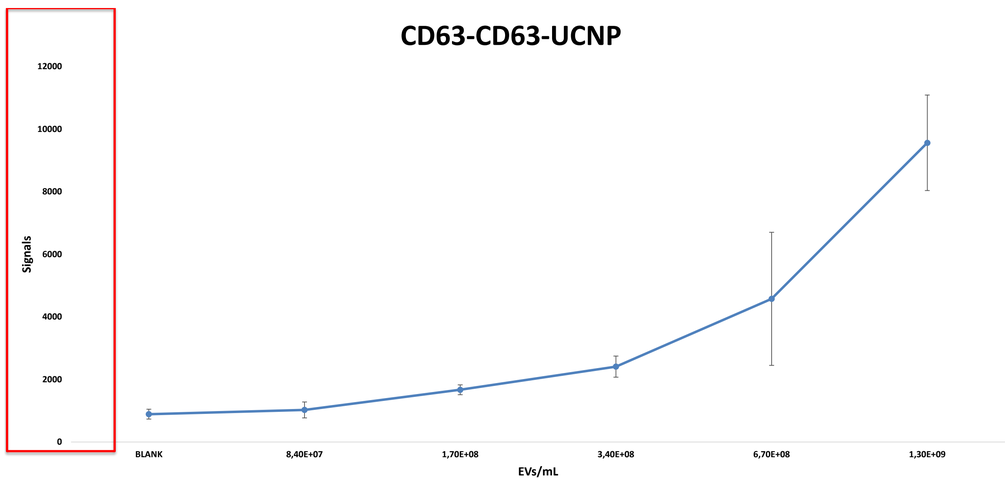

Figure 2. Standard curve of CD63-CD63-UCNPs assay.

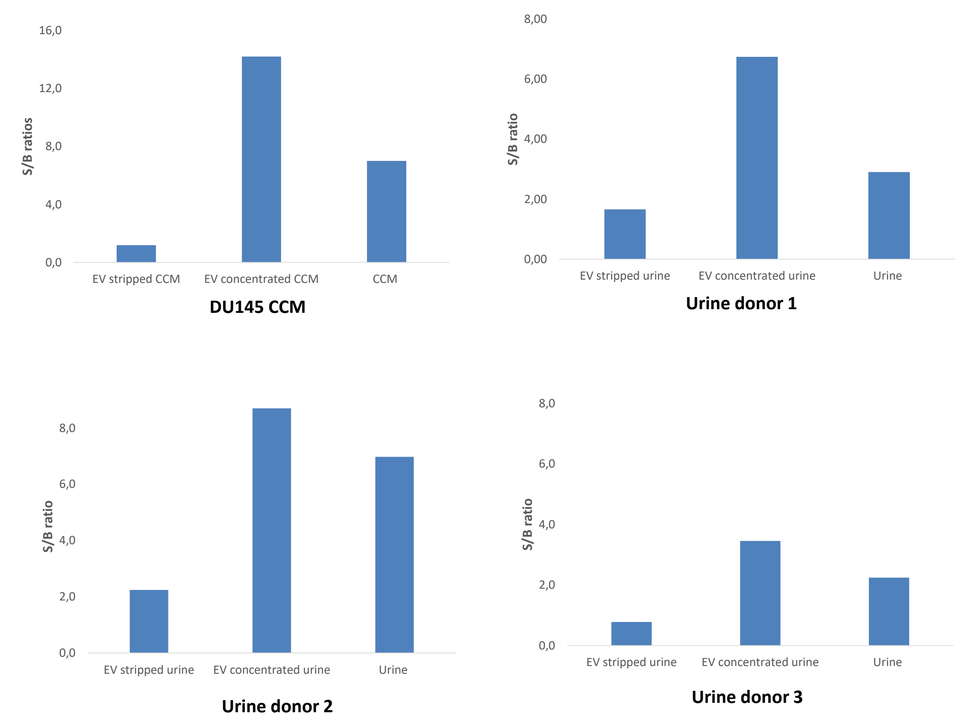

Figure 3. Capture and tracer specificity using EV from cancer cell line and urine. Here, EVs from a) DU145 CCM, b) urine donor 1, c) urine donor 2, d) urine donor 3.

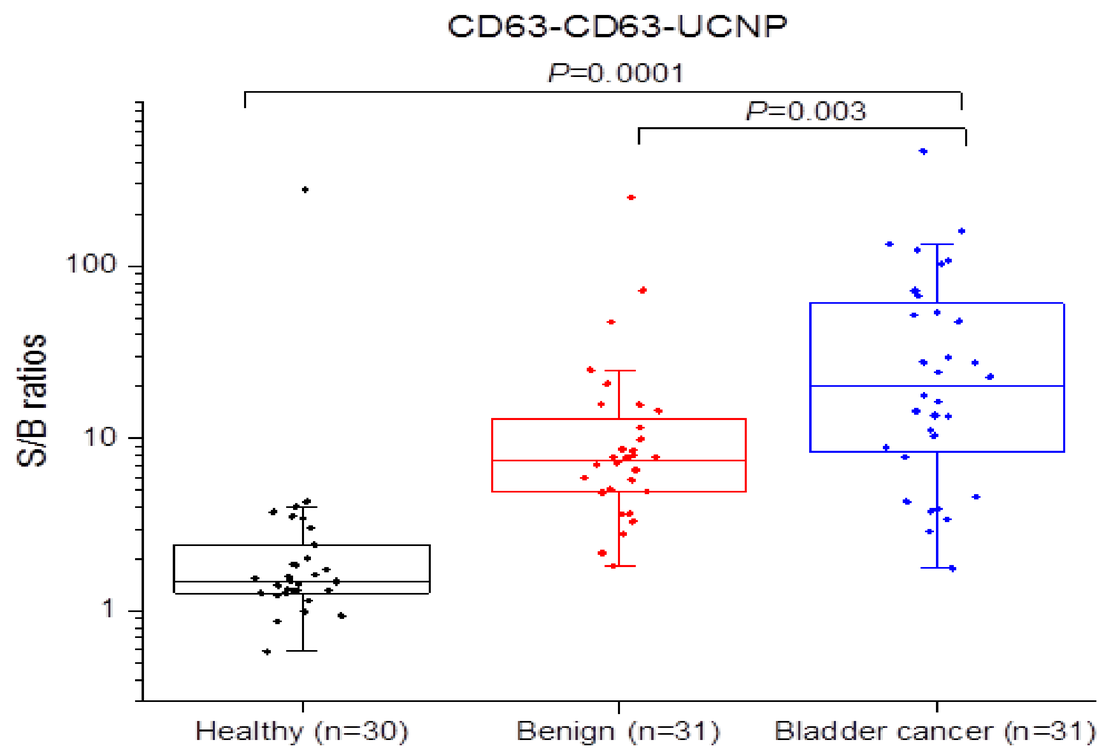

Figure 4. Signal to background (Sg/Bg) ratio of urinary EVs with CD63-CD63-UCNPs assay, differentiating bladder cancer from benign conditions and healthy individuals.

Conclusion

The UCNP- LFIA technology holds promise for use in straightforward, fast and cost effective point of care applications, requiring only a minimal time of 1.2 hours. In future, based on our developed UCNP-LFIA, cancer associated biomarkers in combination with glycan specific antibody will be evaluated to detect bladder cancer more specifically.