Dr Sharanjot Saini

Exosome microRNAs as liquid biopsies for the monitoring of prostate cancer

Research Objectives
Dr Saini’s lab focuses on harnessing the potential of exosomes as a source of novel cancer biomarkers and for engineering novel therapies against prostate cancer.

Detail

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Bio
Dr Saini is an Associate Professor based at the Medical College of Georgia at Augusta University. Her lab focuses on studying the mechanistic basis of aggressive prostate cancer, with a long-term goal of identifying novel biomarkers and targeted therapies against advanced disease.

Funding
- Department of Defense (W81XWH-1-0303)
- National Institutes of Health (Grant Number RO1CA177984).

Collaborators
- Dr Barbara Bensing
- Dr Ashok Sharma
- Dr Nikhil Patel

References


Personal Response

When do you think your miRNA-based classifier system will be available as a widely available diagnostic tool?

""For the miRNA-based classifier to be available as a diagnostic tool, future validation studies with larger clinical cohorts are warranted. We believe that upon further validation, these markers can be translated to the clinic for diagnosing NED in CRPC patients and predicting response to androgen pathway inhibitors that is currently challenging.""
Exosome microRNAs as liquid biopsies for the monitoring of prostate cancer

**Prostate cancer (PCa)** is the most common malignancy among male cancer patients and one of the leading causes of mortality in men. Since PCa growth is dependent upon androgens – male sex hormones – the goal for first-line therapy of prostate cancer is to block androgen-signalling pathways by inhibiting hormone binding to the androgen receptor (AR). This classic approach initially improves the clinical presentation of the disease by halting the spread, and reducing the size, of the tumour. Unfortunately, for reasons that are not fully understood, cancer cells can adapt to the downregulation of androgen signalling. As a result, in a significant number of cases, PCa progresses to what is known as castration-resistant prostate cancer (CRPC). Treatment options for CRPC include chemotherapies such as Enzalutamide and Abiraterone, which are initially effective at inhibiting the AR-dependent tumour progression. Eventually, however, resistance mechanisms start to emerge, allowing the tumour to evade therapeutic action and resume its uncontrolled spread. One way by which tumour cells bypass the effect of therapy is to differentiate into ‘neuro-endocrine’ tissue, converting to a new variant known as neuroendocrine prostate cancer (NEPC).

Exosomes have recently emerged as a source of non-invasive disease biomarkers that can be detected in blood or urine samples, a feature that makes them suitable for liquid biopsies. Exosomes are vesicles that are derived from the plasma membrane and are involved in the transfer of lipids, proteins, or genetic information between neighbouring cells. The rationale behind analysing exosome samples is that cells use these vesicles to selectively package functional biomolecules, which are often reflective of the physiological and pathological state of the originating cells. The exosomes secreted by cancer cells are often involved in the cell-to-cell communication pathways occurring during malignant growth and can often reveal important information about cancer stage and progression.

**THE DEVELOPMENT OF ‘LIQUID BIOPSY’ TO MONITOR CELL DIFFERENTIATION**

NEPC is highly aggressive and often undiagnosed because of the lack of sufficiently specific markers. Usually, clinicians monitor the levels of a protein called prostate-specific antigen (PSA), which tend to increase when hormonal therapy stops working. NEPC, however, is harder to identify and monitor, as it arises via a cell-reprogramming mechanism of neuroendocrine differentiation (NED). This means that NEPC cells exhibit characteristics of neuroendocrine cells, such as neuronal markers. The cell reprogramming results in extensive soft-tissue metastasis, even when there are low blood levels of PSA. Currently, measurement of high expression levels of neuronal markers such as enolase 2 (EN2), chromogranin A (CHGA) and synaptophysin (SYP) are used to monitor therapy-induced NEPC. These markers, however, lack specificity, prompting clinicians to look for alternatives. Furthermore, NEPC often manifests in patients with multiple metastases, preventing clinicians from performing biopsies that yield conclusive results. For the reasons above, NEPC has very poor prognosis, with a five-year survival rate of less than 20%.

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