Establishing a Biomarker Discovery Platform to Progression to Treatment Resistant Neuroendocrine Prostate Cancer

Samavia Ahmad[1], Jeffery Martin[1], Bre-Anne Fifield[1], Elizabeth Fidalgo da Silva[1], Lisa A. Porter[1], Sindu Kanjeekal[2]
[1]Department of Biomedical Sciences, University of Windsor, [2]Department of Oncology, Windsor Regional Hospital

Prostate Cancer (PC) Is the Most Common Cancer Among North American Men

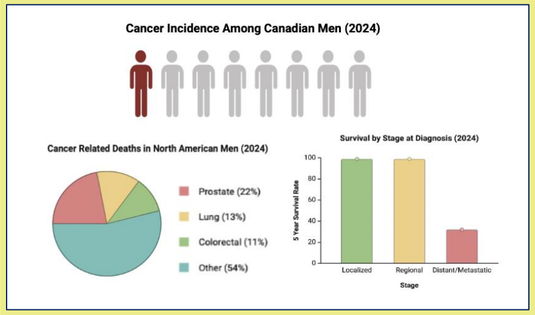

Figure 1. Prostate cancer (PC) is the most commonly diagnosed cancer in North American men, affecting 1 in 8 over their lifetime. Despite early treatability, it remains a leading cause of cancer-related deaths, contributing to 22% of male cancer mortality. >99% of cases diagnosed before the metastatic stage show at least a 5 year survival. These statistics emphasize the urgent need for improved detection strategies for aggressive disease subtypes like NEPC.

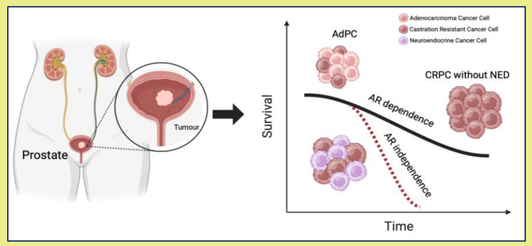

Figure 2. PC typically begins as androgen receptor (AR)-positive adenocarcinoma (AdPC), which responds to hormone-based therapies. Over time, tumours can lose AR expression or undergo neuroendocrine differentiation, transitioning to neuroendocrine prostate cancer (NEPC), a more aggressive and treatment-resistant form.

Prostate Cancer Disease Progression and Current Therapeutical Limitations

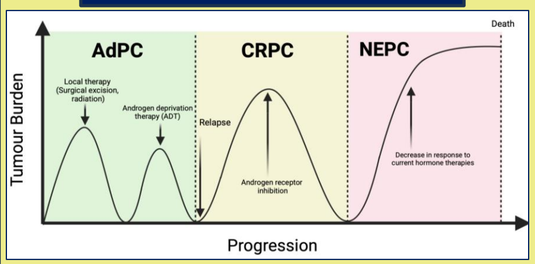

Figure 3. NEPC lacks effective treatment options and continues to grow despite intervention, while AdPC and castration-resistant prostate cancer (CRPC) are responsive to standard therapies. Once a tumour transitions to NEPC, patient outcomes decline significantly.

Validating the Need for New Biomarkers for Prostate Cancer

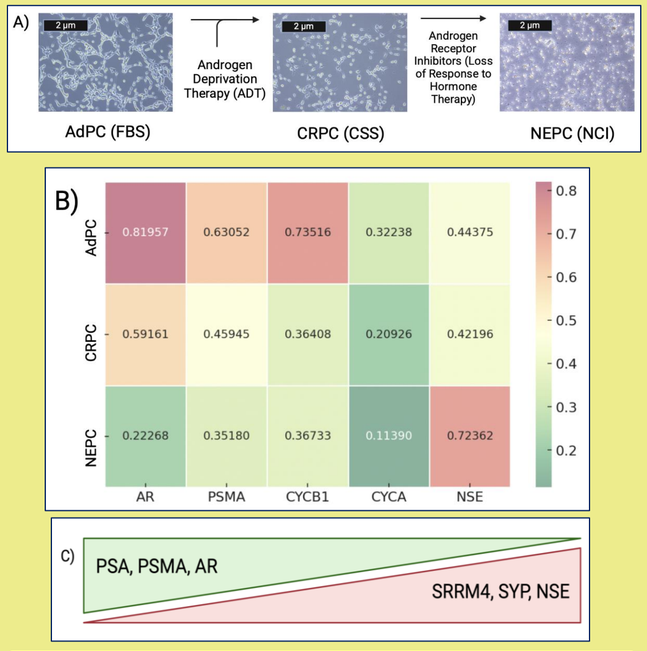

Figure 4. Rationale for exploring novel biomarkers using existing cell line models. Transcriptomic analysis of these models reveals distinct gene expression changes, particularly in cell cycle regulators. These patterns form the basis of our biomarker discovery platform, which we are now applying to human samples.

Elevated Spy1 Corresponds to Decreased Survival and NEPC

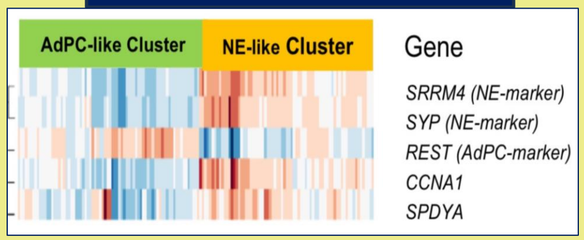

Figure 5. Spy1 (SPDYA) and Cyclin A1 (CCNA1) expression levels are elevated in NEPC-like profiles and correlate with poor prognosis. Their upregulation represents a potential early indicator of neuroendocrine transformation in PC (Bakht, unpublished).

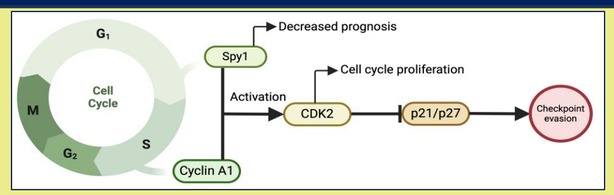

Figure 6. Spy1 activates CDK2, which suppresses tumour suppressors p21 and p27, enabling unchecked cell cycle progression. This mechanism drives DNA damage accumulation and accelerates tumour proliferation, contributing to more aggressive disease and reduced survival (Bakht, unpublished).

Targeting ctRNA Derived from PC Patients to Isolate Tumour Material

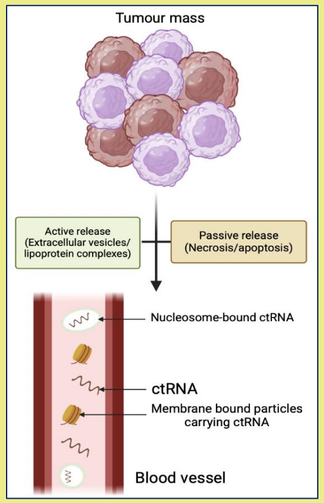

Figure 7. Tumour cells release ctRNA into the bloodstream. This tumour-derived RNA can be isolated from biofluids and sequenced to identify gene expression patterns reflective of PC biology.

Liquid Biopsies Provide a Less Invasive Approach for Prostate Cancer Diagnosis

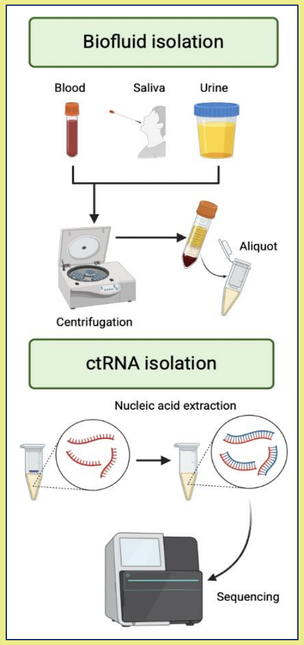

Figure 8. Liquid biopsy workflow using blood, urine, and saliva. These biofluids are centrifuged and processed to isolate ctRNA which can be sequenced to provide data for biomarker analysis.

A Pipeline to Establish a Database and Analyze Gene Markers of NEPC

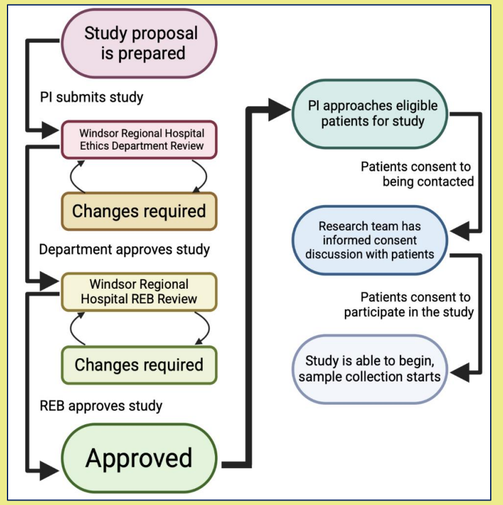

Figure 9. Ethical research begins with protocol approval through a Research Ethics Board (REB), followed by patient recruitment and informed consent. This process ensures participant safety and integrity of sample collection in human studies.

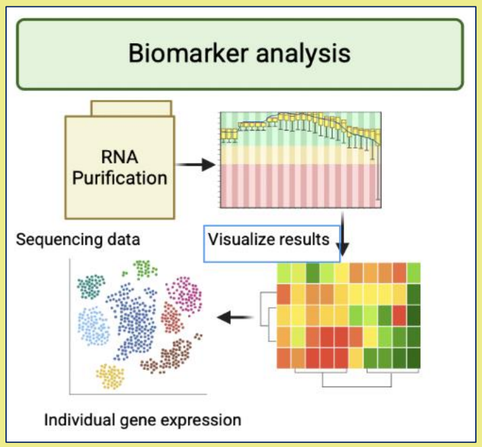

Figure 10. Following ctRNA sequencing, transcriptomic data is analyzed to identify NEPC-related gene expression signatures. This platform supports non-invasive diagnosis and personalized treatment strategies by matching patient profiles with known biomarkers.

Acknowledgements

PORTER LAB
we spark HEALTH INSTITUTE
WINDSOR REGIONAL HOSPITAL
OUTSTANDING CARE—NO EXCEPTIONS!
Cancer Research Society
RIDE FOR DAD
University of Windsor