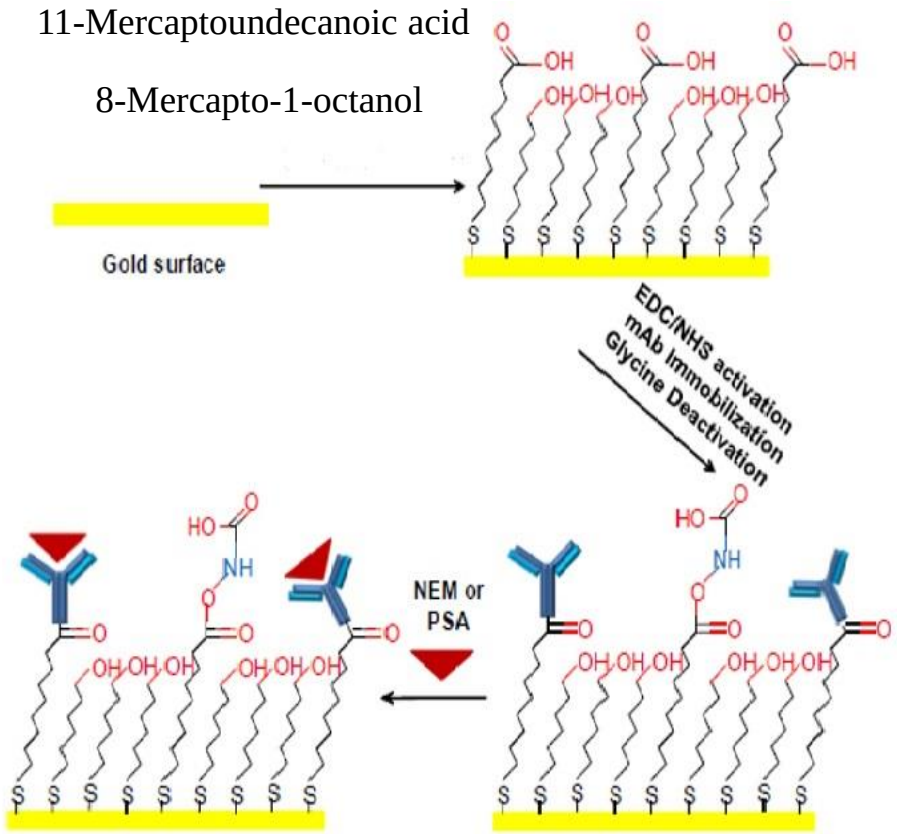
INTRODUCTION

- Prostate cancer (PC) is the most common cancer affecting men and its prognosis is dependent on early detection.
- Serum PSA screening has improved the early detection of PC but the test is not reliable.
- Both, positive and negative PSA tests need confirmation with costly, repetitive and invasive TRUS-guided biopsy.
- Combining PSA test with a cancer- specific biomarker(s) can potentially improve PC detection specificity.
- We have discovered a novel prostate tumor-specific protein (neuroendocrine marker/NEM). NEM expression and secretion in the prostate seems to be cancer-specific with manifold increase in serum levels.
- We have also developed a new NEM-PSA combination test that employs an inexpensive, disposable nanosensor chip that can detect sub-picomolar levels of antigens.

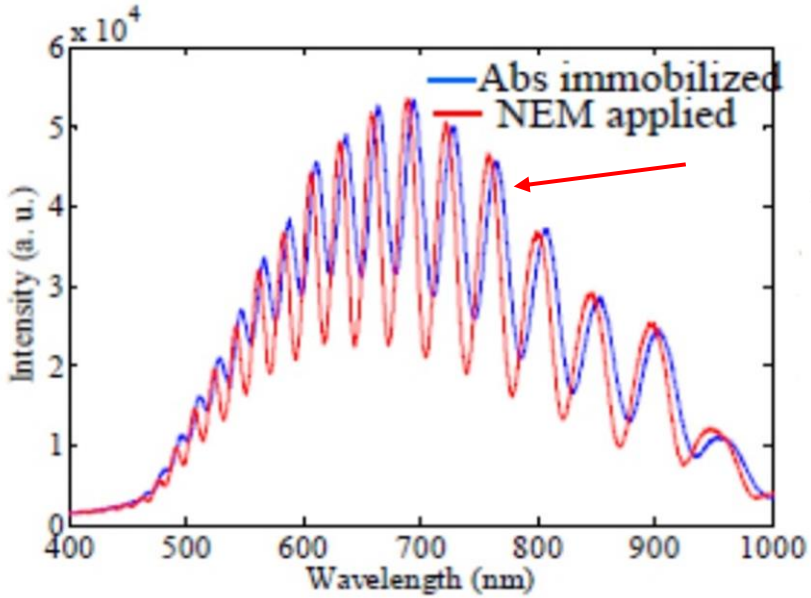
MATERIALS AND METHODS

1. Biochip Surface Preparation

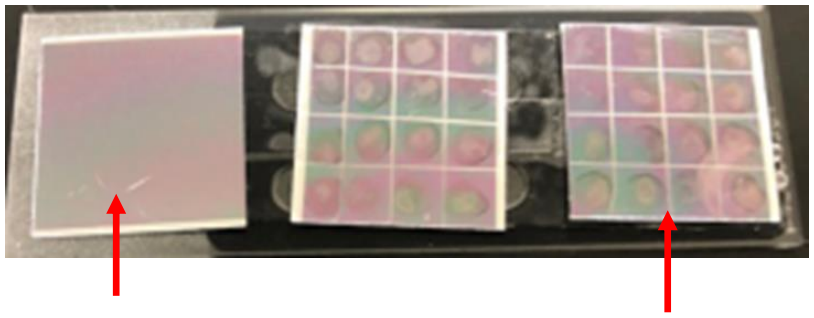


Schematic of surface functionalization procedure of the Au-coated AAO surface

2. Measurement



Clear shift of interference fringes after NEM binding. Due to binding of NEM to its antibody

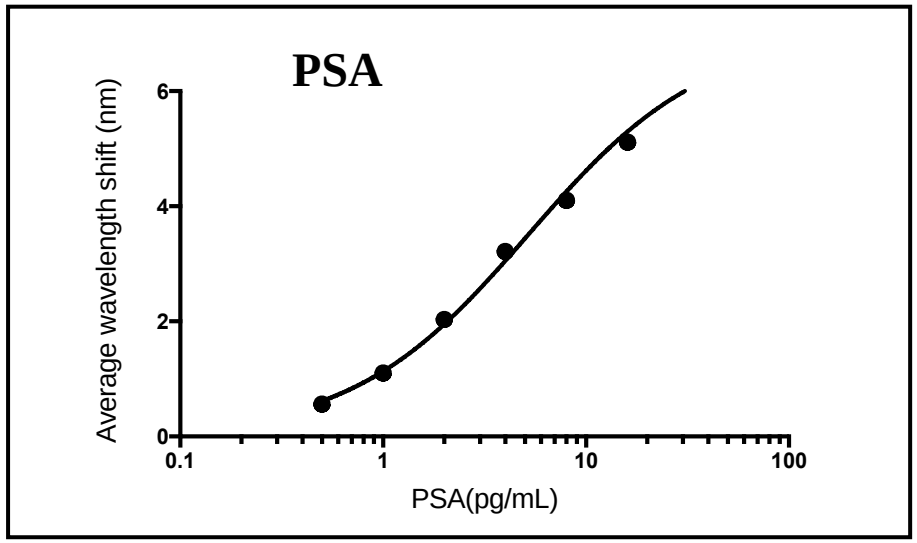


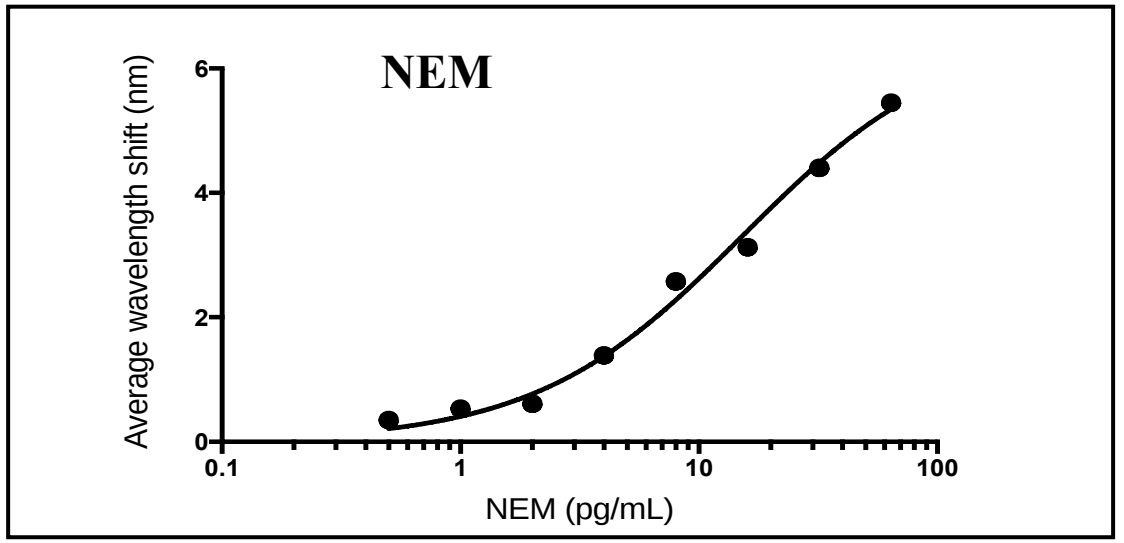
Unfunctionalized Au-coated AAO biochip

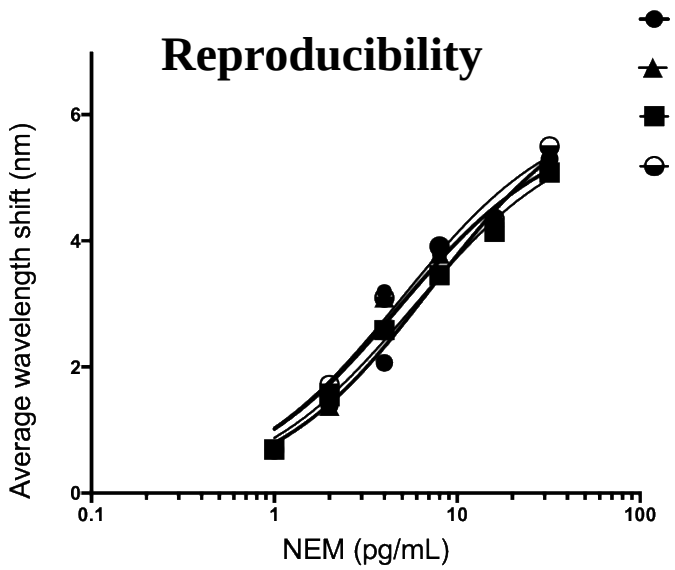
Functionalized Au-coated AAO biochip

RESULTS

Typical calibration curve for PSA and NEM obtained by biochip



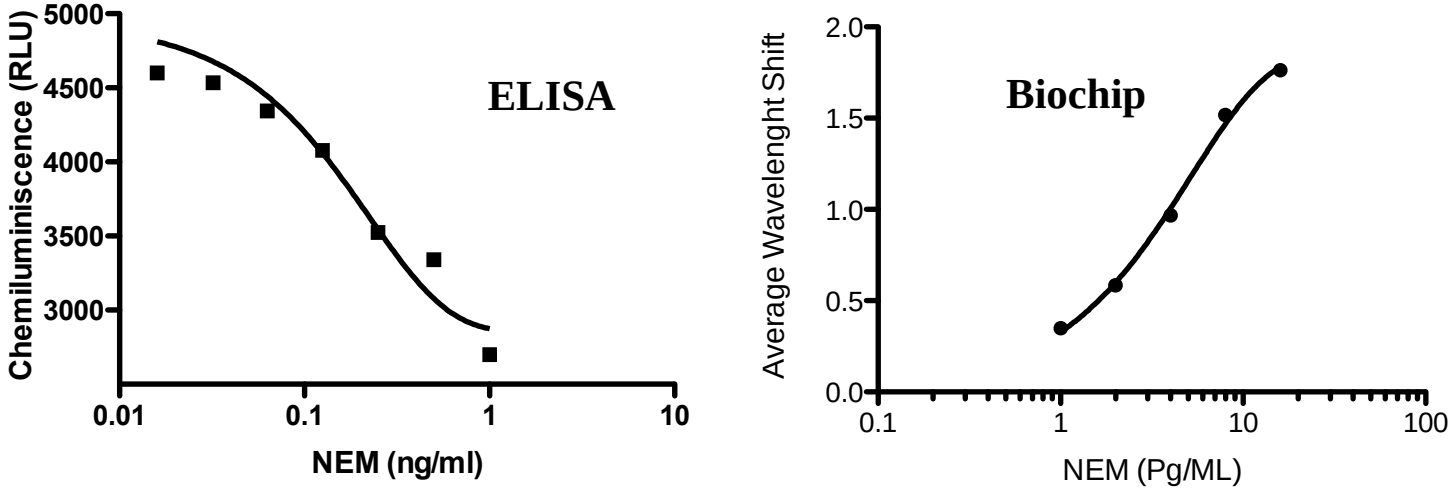




NEM standard curve using 4 separate set of biochips on different days.

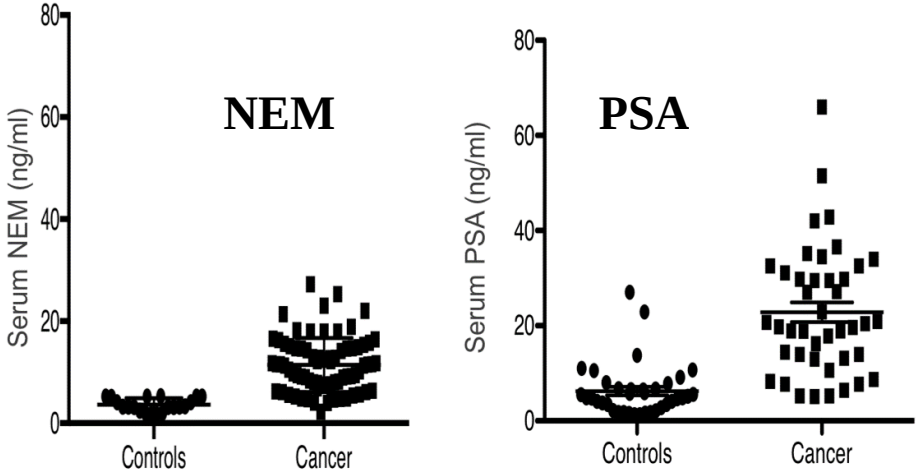
RESULTS

Comparison of NEM biochip assay with NEM ELISA



Biochip was 50x more sensitive as compared to ELISA

Human serum levels of NEM and PSA

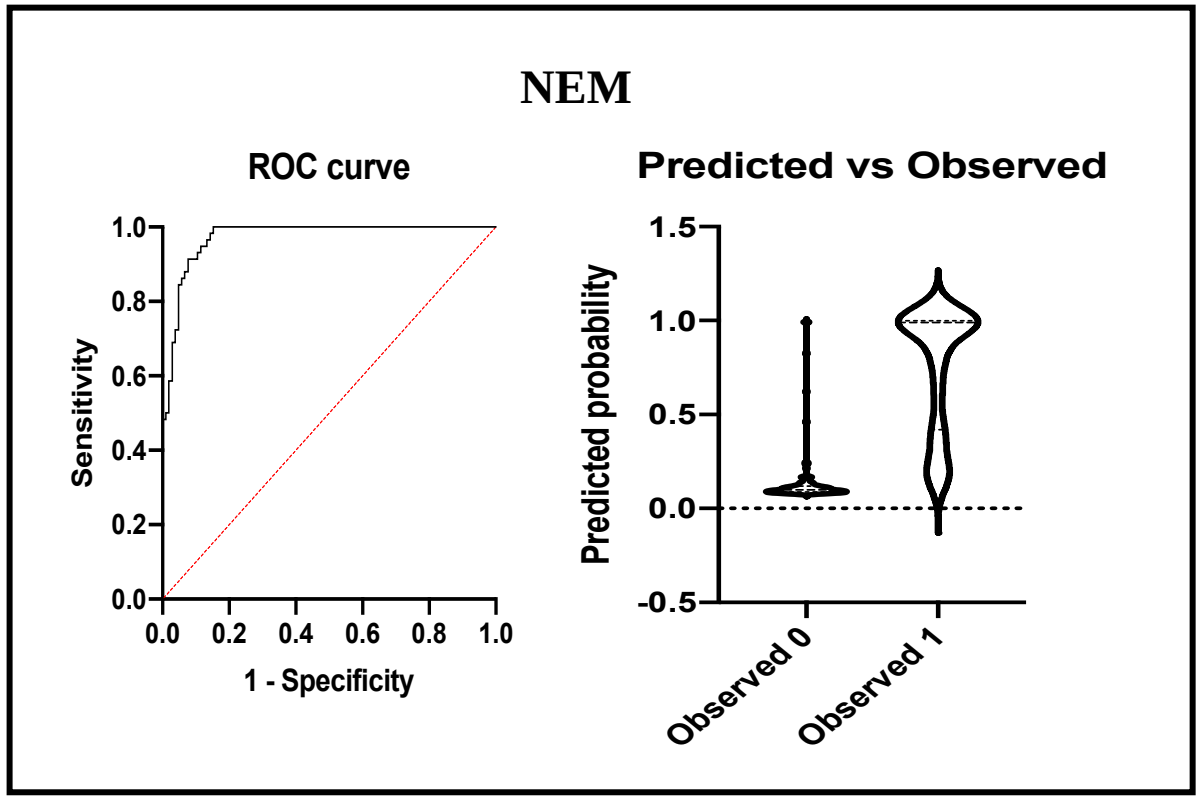


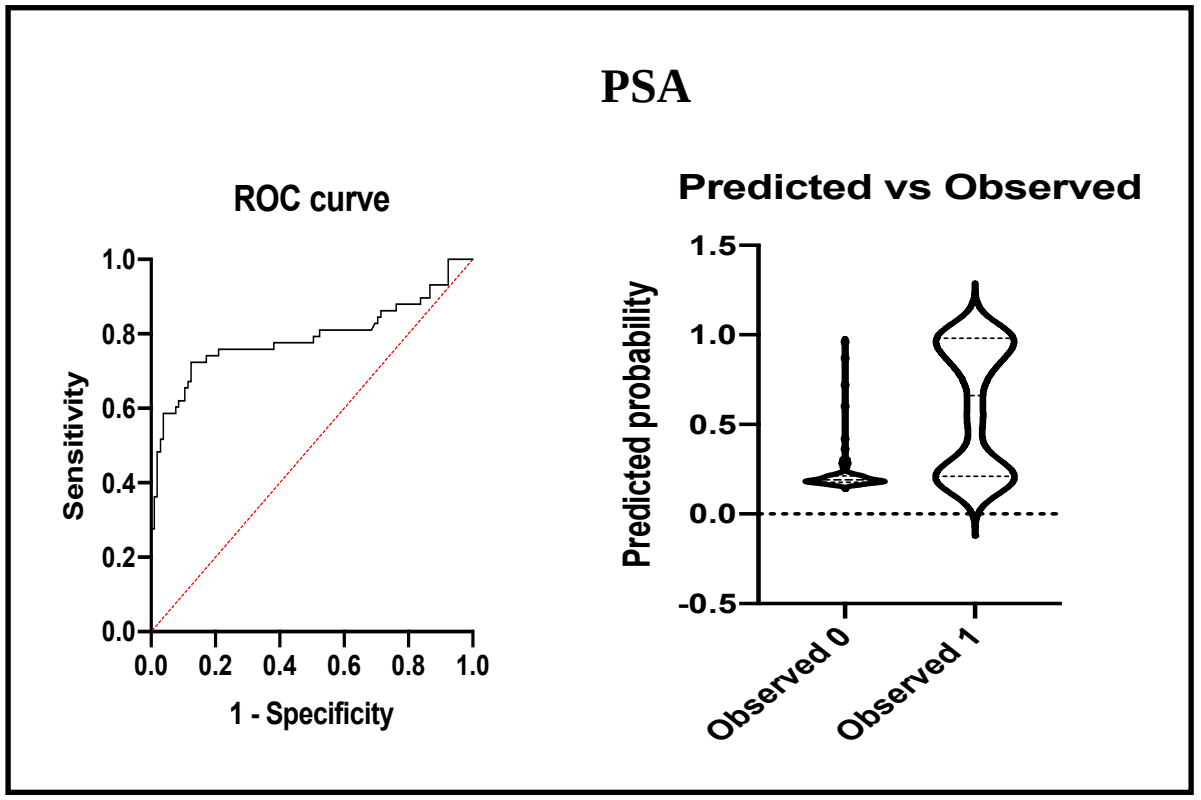
Human serum NEM and PSA levels in controls, and prostate cancer individuals

PCA samples with PSA serum levels <4 ng/mL are considered non-cancer whereas PSA serum levels >4 ng/mL are potential cancer. NEM range: >3.5 ng/mL considered cancer.

RESULTS

ROC Analysis of NEM vs PSA



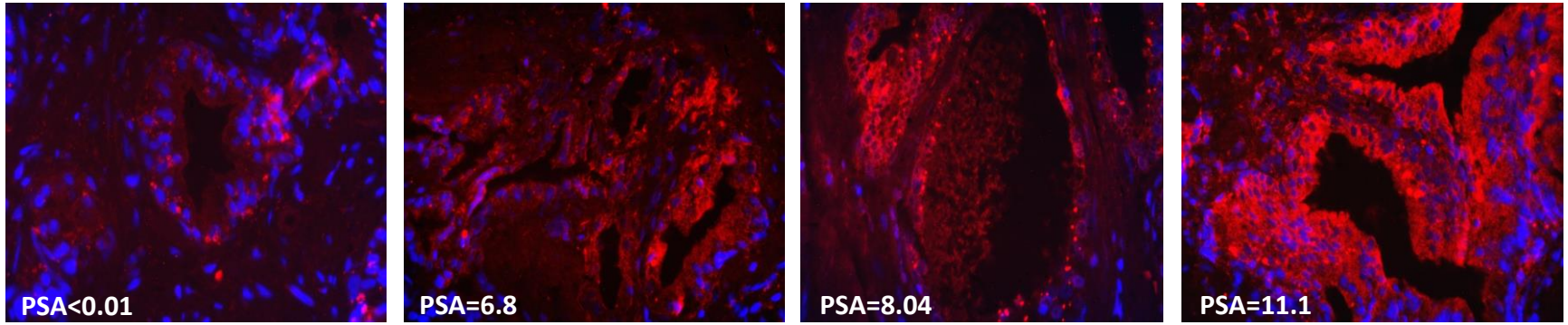


ROC curves for NEM and PSA

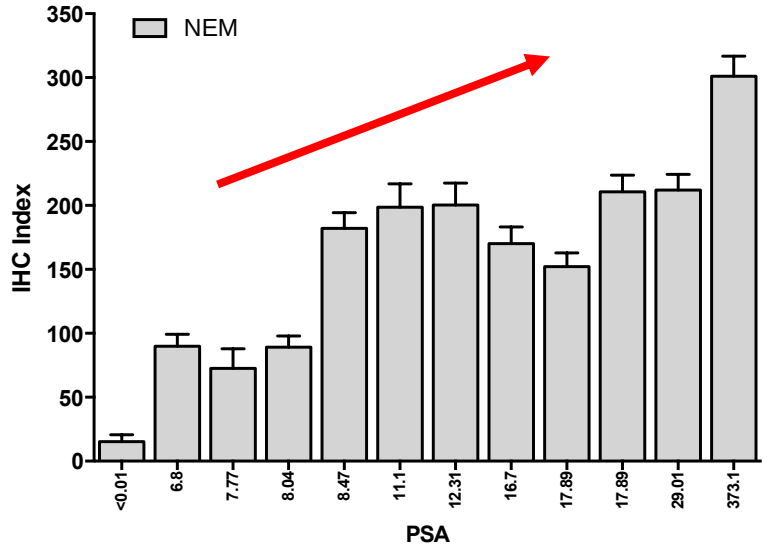
NEM is a better predictor as indicated by: Steeper ROC curve
Area Under the Curve (AUC) for NEM = **0.9978**
AUC for PSA=**0.7961**
AUC_{NEM} is closer to perfect value of 1.0 than AUC_{PSA}

RESULTS

NEM Immunohistochemistry In Prostate Biopsy



Expression of NEM marker in prostate biopsy from some clinical patients. As expected, we observed a positive correlation between serum NEM levels and tissue NEM content.



CONCLUSION

- A novel, low-cost immunosensor device, has been optimized for the detection of two biomarker proteins for prostate cancer.

- To our knowledge, this is the first demonstration of a flat surface nanochip capable of detecting multiple protein biomarkers with ultra sensitivity. Linear over the range of 1-64 pg with a sensitivity of 1 pg/50 µl.

- Low cost of the device, suitability of mass production, and long shelf life offers significant advantages over current devices. Moreover, the ease of fabrication, utilization of commonly available commercial components, and the simplicity and sensitivity of the method makes this system accessible to virtually any biomedical laboratory at a small cost.

- Preliminary results raise a strong possibility that the NEM-PSA combination test that employs an inexpensive, disposable nanosensor chip is a viable prototype for the measurement of biomarkers for prostate cancer and could in future be translated to the device for point-of-care in prostate cancer diagnostics and therapeutics.

- The study presents the preliminary proof of principle for the reliable platform for developing clinically useful biomarker detection devices.

- These results support a possibility that our “NeoPro” test may improve the specificity of PC diagnosis, specifically in “grey zone” PSA patients, and help reduce the number of diagnostic biopsies.

FUTURE WORK

- Additional studies are planned to investigate correlation of NEM with tumor progression/aggressiveness
- Usefulness of serum NEM as a monitoring parameter for the treatment of prostate cancer
- Expression of NEM in other cancers

AKNOWLEGEMENTS

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Medical College of Wisconsin

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