Cranfield Health

Cranfield UNIVERSITY

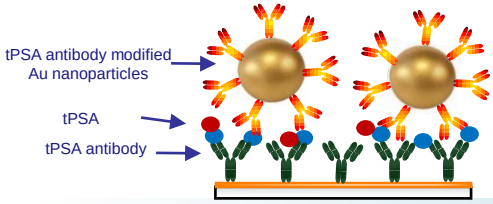
POINT-OF-CARE TESTING FOR PROSTATE CANCER DIAGNOSIS

Y. Uludag, IE. Tothill*
Cranfield Health, Cranfield University, Cranfield, Bedfordshire, MK43 0AL, UK

Introduction

Prostate carcinoma is a fatal malignancy and is a major cause of death in men in the population aged 55 and over. Prostate cancer is the commonest form of cancer in men in Europe with 301,500 incident cases a year that corresponds to 24.1% of all cancer cases[1]. Early and accurate detection of prostate cancer is very important, since there is no cure if the cancer spreads out to the other organs of the body. The increase in prostate specific antigen (PSA) levels in serum above the normal limits (4 ng ml^{-1}) is the primary indication of prostate malignancy; therefore PSA is used as a biomarker for the diagnosis and prognosis of the prostate cancer[2,3]. ELISA type PSA tests are usually performed at centralised laboratories using expensive automated analyzers and time consuming procedures[4]. This process requires sample transportation, increased waiting time and high medical costs. Therefore there is a need to develop a detection system that is cost effective, quick to process, uses low sample and reagent volume and easily operated. Biosensor technology has the potential to use validated biomarkers for the development of point-of-care devices[4]. In this study the suitability of a QCM and an SPR biosensor were investigated for tPSA test.

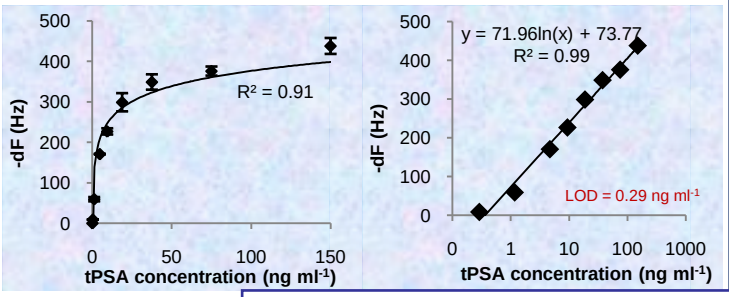
Methodology



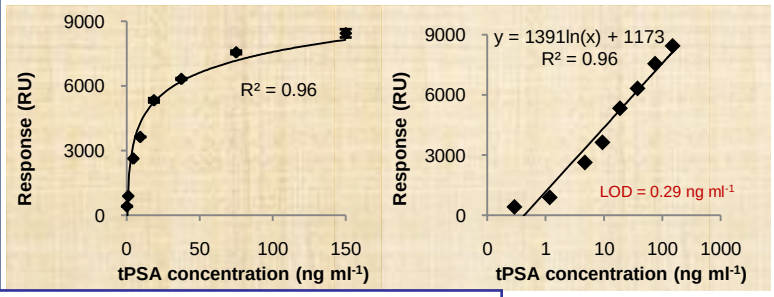
A QCM biosensor (QCMA-1; Sierra Sensors GmbH, www.sierrasensors.com) and an SPR biosensor (Biacore 3000, GE Healthcare) were used for tPSA (total PSA) detection. Initially a matrix elimination buffer containing additives was formulated. This buffer was designed to reduce the non-specific binding of sera proteins to the sensor surface by 98%[5]. Concentrations of tPSA were prepared as 50% PSA-ACT(complexed PSA) and 50% PSA (free PSA). A sandwich assay was performed using tPSA detection antibody modified Au nanoparticles for signal amplification. After the bindings 100 mM HCl (+20mM NaOH for high concentrations of PSA) were used to regenerate the sensors.

Results

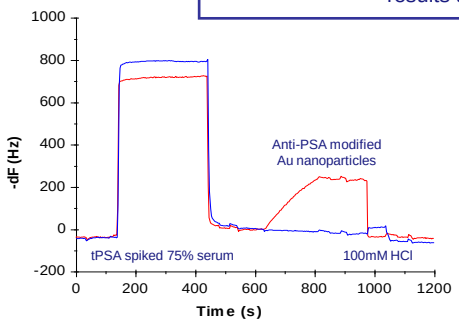
QCMA-1 assay

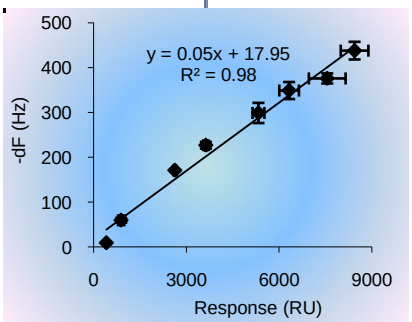


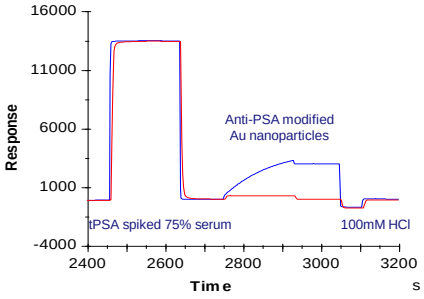
Biacore 3000 assay



Calibration curves for the detection of tPSA that is spiked in 75% human serum. Sandwich assay results using tPSA detection antibody modified Au nanoparticles.







The comparison of QCMA-1 and Biacore 3000 results for tPSA sandwich assay in 75% human serum.

Discussion & Conclusion

Free PSA (direct) binding to the anti-PSA capture antibody data fitted to 1:1 Langmuir binding model and K_D calculated as 9.46 × 10^{-10} M using Biacore 3000 and 5.56 × 10^{-10} M using QCMA-1 instruments[5]. tPSA detection assay in human serum resulted in detection of tPSA concentrations down to 0.29 ng ml^{-1} in 75% serum with a linear detection range of 0.29 -150 ng ml^{-1} using both instruments when 40 nm Au nanoparticles were employed to enhance the sensitivity. The tPSA concentration of male human serum (from Sigma) used in this study was calculated as 0.41 ng ml^{-1} using QCMA-1 and 0.56 ng ml^{-1} using Biacore 3000 instruments. These results indicate that data obtained from both QCMA-1 and Biacore 3000 instruments are compatible with each other and additionally both instruments can be used for the fast and easy detection of tPSA in patient samples.

References

1.J. Ferlay, P. Autier, M. Boniol, M. Heanue, M. Colombet, P. Boyle, Annals of Oncology, 18 (2007) 581.
2.E.P. Diamandis, Trends in Endocrinology and Metabolism, 9 (1998) 310.
3.M.K. Brawer, P.H. Lange, World Journal of Urology, 7 (1989) 7.
4.I.E. Tothill, Seminars in Cell & Developmental Biology, In Press, available online.
5.Uludag Y, Tothill IE. Real-time detection of prostate specific antigen (PSA) in human serum using a fully automated QCM biosensor. Submitted for publication.

i.tothill@cranfield.ac.uk
y.uludag.s06@cranfield.ac.uk

www.cranfield.ac.uk/health