DIAGNOSTIC CLASSIFIERS FOR STRATIFYING PATIENTS AT RISK OF PROSTATE CANCER

DIAGNOSTIC CLASSIFIERS FOR STRATIFYING PATIENTS AT RISK OF PROSTATE CANCER

CJ McNally[1, 2], MW Ruddock[1], DJ McKenna[2], T Moore[2]
[1]Clinical Studies , Randox Laboratories, Crumlin
[2]Genomic Medicine Research Group, Ulster University, Coleraine

Background: Over 45,000 men are diagnosed with prostate cancer (PCa) each year. Diagnosis typically includes serum prostate-specific antigen (PSA) and a digital rectal examination (DRE). However, these tests can result in high levels of false positives, leading to over-diagnosis and unnecessary, costly, and invasive biopsies. As such, there is a clinical need for diagnostic tests that can differentiate between benign conditions e.g. benign prostatic hyperplasia (BPH), and malignant disease, at an early stage. The aim of the project is to identify biomarker-combinations (classifiers) that will stratify risk of serious disease and allow doctors to manage patients in primary care.

Materials & Methods: Urine and serum samples, collected from *n*=250 patients (normal controls, BPH and pathologically-proven PCa), were analysed using Proteome Profilers, SDS-PAGE, Western Blot, ELISAs, and Randox Biochip Technology. Clinical, demographic, socioeconomic, and biomarker data, was collected from each patient and stored on a database to determine clinical risk score (CRS).

Results: Using proteome profilers, 84 oncology-related proteins were analysed simultaneously using pooled serum samples (control, BPH and PCa). As a result, 6/84 (7.1%) of the analytes were statistically significant ($p < 0.05$). From these analytes, the 4 most significant were then performed on ELISA using *n*=80 serum samples. Tests resulted in 1 analyte achieving differentiation between age-matched BPH (*n*=30) and PCa (*n*=30) serum samples ($p < 0.000$). Statistical modelling and bioinformatic analyses (SPSS and R) has been performed to explore potential clinical utility and pathobiology of potential analytes. In attempts to stratify BPH and PCa patients, current models achieve an area under the curve (AUC) of 0.882 when combined with PSA. Further validations are on-going with a view to develop a multiplex protein assay for clinical use.

Conclusions: Multivariate classifiers have a significant role to play in the diagnosis of PCa. A proteomic test based on multiplex assays would allow patients ‘at risk’ of serious disease to be stratified in primary care.