BLADDER CANCER

Urinary EGFR and EpCAM predict cancer-specific survival

The results of a proteomic study of urinary bladder cancer (UBC) biomarkers reveal that urinary epidermal growth factor receptor (EGFR) and epithelial cell adhesion molecule (EpCAM) might be effective prognostic biomarkers in patients with urothelial bladder cancer. “There is an urgent need for accurate urinary biomarkers for the noninvasive detection of UBC,” explain lead authors Doug Ward and Richard Bryan. “Such biomarkers have yet to demonstrate the necessary accuracy to rival cystoscopic inspection of the bladder.”

“...this biomarker combination was highly prognostic for death from UBC...”

In a translational approach, proteomic techniques were used to catalogue the proteins released from eight different UBC cell lines *in vitro*. From an initial 2,078 proteins, candidate biomarkers were identified using comparisons with

the ‘normal’ urothelial cell secretome and data from the Human Protein Atlas. These comparisons revealed five candidate biomarkers, of which EGFR appeared the most promising candidate, owing to its detection in conditioned media from seven out of eight cell lines and its known association with cancer. Subsequent investigations confirmed that the majority of the detected EGFR was the soluble extracellular domain of this protein.

Following identification as a potential biomarker, EGFR concentrations were measured in the urine of 436 patients with UBC. Urinary EGFR alone was found to be an indicator of inferior cancer-specific survival (HR 2.89; 95% CI 1.81–4.62); however, only a subset of patients had elevated urinary EGFR. When urinary EGFR measurements were combined with those of the extracellular domain of EpCAM, this biomarker combination was highly prognostic for death from UBC: compared with being ‘double negative’ for both markers, patients with high EGFR and low EpCAM had a 6.7-fold increase

in risk of mortality; those with high EpCAM and low EGFR had a twofold increase; and those with high levels of EpCAM and EGFR had a 2.6-fold increase.

In conclusion, these findings indicate that measurements of EpCAM and EGFR, combined into a multivariate analysis, might be a better prognostic indicator in patients with UBC than standard clinical observations alone. When asked about the clinical importance of these findings, the authors declared: “These measurements might underlie a simple clinical test to rapidly identify the most aggressive tumours and help clinicians to select the most appropriate treatments.” They also highlighted the need to validate this prognostic tool in an independent set of patients.

Peter Sidaway

Original article Bryan, R. T. et al. Protein shedding in urothelial bladder cancer: prognostic implications of soluble urinary EGFR and EpCAM. *Br. J. Cancer* doi:10.1038/bjc.2015.21