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BLADDER CANCER

Noninvasive diagnosis and detection of recurrence

Two new urinary peptide biomarker panels developed in a multicentre study enable the detection of primary and recurrent urothelial bladder cancer (UBC) with high sensitivity and specificity. Pending further validation in a prospective setting, these tests could facilitate noninvasive diagnosis of primary UBC, and detection of recurrent UBC in patients undergoing surveillance, reducing the need for invasive cystoscopy procedures.

In their study, the team analyzed a total of 1.357 urinary samples from patients with UBC, suspected UBC and controls from five clinical centres in Spain, the Netherlands, the USA, Greece and Germany.

"We used CE–MS technology (capillary electrophoresis coupled to mass spectrometry) to discover and validate urinary peptide biomarkers in the form of multimarker panels, which seems advantageous to single biomarkers, considering the complexity of UBC and the high accuracy necessary for the detection and monitoring of this disease," explains Maria Frantzi, lead author of the study published in *Clinical Cancer Research*. "CE–MS provides high-resolution profiling data characterized by high reproducibility; measurement of the proteome combined with online database matching is the key to an all-in-one diagnosis for a wide spectrum of clinical applications."

In the cohort to establish the panel for detection of primary UBC, comprising a total of 721 patients, 212 urinary samples from those with haematuria, acute cystitis or nephrolithiasis served as controls. The cohort of patients undergoing surveillance for UBC recurrence consisted of 636 patients: 164 with confirmed UBC and 472 confirmed negative for recurrence.

The team used two consecutive methods to device a 116-peptide and a 106-peptide biomarker panel with area under the receiver operating characteristic curve values (AUCs) of 0.87 and 0.75 for detection of primary and recurrent UBC, respectively. Cytological data was available for 45% of patients monitored for recurrent UBC included in the study's validation phase. In this cohort, the AUC for recurrence detection of the 106-peptide panel was 0.80 and the AUC for cytology was 0.69; however, combination of both tests increased the performance to an AUC of 0.87.

"Additional prospective investigations, accounting for potential confounding effects, are planned to evaluate the potential of clinical implementation of our biomarker panels," Frantzi concludes.

Clemens Thoma

ORIGINAL ARTICLE Frantzi, M. *et al.* Development and validation of urine-based peptide biomarker panels for detecting bladder cancer in a multi-center study. *Clin. Cancer Res.* http://dx.doi.org/10.1158/1078-0432.CCR-15-2715 (2016)

FURTHER READING Frantzi, M. *et al.* Developing proteomic biomarkers for bladder cancer: towards clinical application. *Nat. Rev. Urol.* **12**, 317–330 (2015)

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