Diagnostic validation of urinary Tyr-phosphorylated proteins as bladder cancer marker

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Scopo del lavoro:
Different urinary markers of transitional cell carcinoma (TCC) have been proposed in the years. None of them, however, is approved by the international guidelines or used with scientific safety by urologists in their clinical practises. Cystoscopy continues to represent the gold standard method of diagnosis, and is highly accurate, sensitive and specific. The urine cytology is instead non-invasive but has a high rate of false negative, especially in low-grade TCC.

We try to give a significant answer of these open questions using a proteomic approach, that is widely used in molecular oncology. Using proteomic approaches, we previously demonstrated¹ that the levels of Tyr-phosphorylated proteins (TPPs) are highly increased in bladder cancer tissues and that soluble TPPs can be also detected in patient urine samples. Now, we have evaluated their diagnostic performances measuring urinary TPP levels in 230 urine samples from bladder cancer patients and healthy subjects.

Materials & Methods:
Patients with suspected bladder cancer were enrolled in this study before undergoing transurethral resection of the bladder or radical cystectomy. Patients with a histological diagnosis different from bladder cancer or with a previous bladder cancer history were subsequently excluded. Urines for the control group were collected from healthy blood donors, after an interview, to exclude urological problems. Only volunteers more than 50 years old were enrolled. The urinary levels of TPPs were analyzed using an experimental diagnostic test (pYtest, provided by Nurex srl). The area under the ROC curve (AUC), sensitivity, specificity, positive and negative predictive values (PPV and PNV) were calculated using Bayes' theorem (MedCalc 11.3.3).

Results:
Urinary TPP levels from 87 bladder cancer patients (7 Tx, 47 Ta, 17 T1, 12 T2/3, 4 CIS) and from 143 healthy subjects were measured. The AUC was 0.875 with a 95% confidence interval of 0.826-0.915. For the best cut-off value (261.26 standard units), a sensitivity of 80.46% and a specificity of 79.72% were obtained. PPV and PNV were 70.1% and 87.7%, respectively.

Discussion
The proteomic approach is finding its excellent status in uro-oncology too, not only to understand the molecular pathways of carcinogenesis, but also to detect possible markers in the urine samples. Preliminary evaluation confirms the excellent diagnostic performances of TPPs as bladder cancer marker.

Conclusioni
We need to increase the enrolled patients with a multicenter study to confirm and validate the proteomic approach through the individualisation of TPPs with the pYtest. Next aim is to recruit more patients to confirm the statistic results obtained and validate definitely the pYtest like a bladder cancer marker.