

## DIAGNOSIS

# Combined urine assays improve detection of urothelial cancer

Detection of urothelial carcinomas of the bladder or upper urinary tract has traditionally been achieved with the use of imaging and urine cytology. Cystoscopy and flexible ureteroscopy, despite their high sensitivity and specificity, are invasive and expensive, and can miss small or flat lesions. Urine cytology, on the other hand, is highly specific (>90%) for the detection of urothelial cancer, but is somewhat limited by a low sensitivity (<50%), particularly for low-grade tumors. Two recently published studies assessed the diagnostic value of combining cytology with other urine assays in an attempt to improve the sensitivity of urothelial carcinoma detection.

For the first study, Xu and colleagues used a combination of urine cytology findings and the results of a specialized fluorescence *in situ* hybridization (FISH) kit to determine the presence of upper tract urothelial carcinoma (UTUC). Although the FISH kit included probes that were specific for bladder cancer, it had previously shown considerably higher sensitivity than urine cytology for detecting UTUC. The combined cytology and FISH system—dubbed ‘Cyto-FISH’ by

the authors—yielded an overall sensitivity of 85.9%, which was significantly greater than that of cytology alone (45.1%,  $P < 0.001$ ) and higher (but not significantly so) than that of FISH alone (78.9%,  $P = 0.378$ ). The overall specificities of Cyto-FISH, cytology alone and FISH alone were similar (97.8%, 100.0% and 97.8%, respectively). Cyto-FISH also performed better than each singular modality for detecting low-grade and low-stage tumors.

For the second study, Bravaccini *et al.* tested the diagnostic performance of a three-way combination of urine cytology, FISH and TRAP (telomeric repeat amplification protocol) to detect urothelial carcinoma of the bladder. The TRAP assay, which measures telomerase activity, has previously been shown to have a higher sensitivity but lower specificity compared with cytology for detecting bladder cancer. The three-way combination (cytology performed in parallel to the in-series combination of TRAP and FISH) yielded the best trade-off in sensitivity and specificity (78% and 78%, respectively).

The results of these studies suggest that the low sensitivity of urine cytology



© Les Cunliffe | Dreamstime.com

for detecting urothelial carcinoma can be bolstered by combining it with other noninvasive urine assays.

*Nick Warde*

**Original articles** Xu, C. *et al.* Utility of a modality combining FISH and cytology in upper tract urothelial carcinoma detection in voided urine samples of Chinese patients. *Urology* 77, 636–641 (2011) | Bravaccini, S. *et al.* Combining cytology, TRAP assay, and FISH analysis for the detection of bladder cancer in symptomatic patients. *Ann. Oncol.* doi:10.1093/annonc/mdq740