Liquid biopsy-based detection of bladder cancer using soluble immune checkpoints

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Abstract

Background: Urinary bladder cancer (BC) is one of the most common malignancies of the urinary tract, requiring timely detection and monitoring to improve patient outcomes. Currently, BC diagnosis and surveillance of non-muscle invasive BC rely on cystoscopy, an invasive, costly, and often uncomfortable procedure for patients. Given these limitations, there is an urgent need for non-invasive biomarkers that can reduce healthcare costs and improve patient care.

Soluble immune checkpoints (sICs) are regulatory molecules that modulate immune responses and circulate in bodily fluids, making them promising candidates for cancer detection. Liquid biopsies enable the measurement of these markers in blood or urine, offering a less invasive alternative to cystoscopy. By assessing sIC levels, liquids biopsies could facilitate early BC detection, potentially improving diagnostic efficiency and patient management.

Objective: This study aimed to evaluate the potential of 14 sICs as non-invasive biomarkers for BC detection.

Methods: Patients were recruited from the BLAdder cancer Blood and Urine Study (BLABUS), a prospective cohort including individuals with suspected BC. The study included 187 BC cases and 54 controls presenting with macroscopic hematuria but with normal cystoscopy and urography findings. Plasma levels of 14 sICs (CD28, GITR, CD27, TIM-3, CD137, CD152, HVEM, IDO, LAG-3, BTLA, CD80, PD-1, PD-L1, and PD-L2) were measured using the ProcartaPlex Human Immuno-Oncology Checkpoint Panel 1. T-tests with Benjamini-Hochberg correction were applied to identify differences between cases and controls. A logistic regression-based classification model was developed to predict malignancy.

Results: Ten sICs (TIM-3, CD28, CD137, CD152, HVEM, IDO, LAG-3, BTLA, GITR, CD80, PD-1, PD-L1, and PD-L2) showed significantly different levels between cases and controls ($p<0.05$). A classification model incorporating TIM-3, CD152, HVEM, IDO, LAG-3, BTLA, GITR, PD-1, PD-L1, and PD-L2 demonstrated a strong performance, achieving an overall accuracy of 83.8% (95% CI: 78.6 – 88.2). The model exhibited high sensitivity (98.7%) but moderate specificity (42.6%) with a positive predictive value 85.2% and a negative predictive value of 74.2%.

Conclusion: These findings suggest that sIC levels may serve as potential diagnostic biomarkers for BC. However, further validation is necessary to assess the clinical utility and robustness of the proposed classification model.

Do you have any conflicts of interest?

No, I do not have a conflict of interest.