Novel platform for monitoring bladder cancer recurrence using expression analysis of small non-coding RNAs.

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Abstract Disclosures

Background:
Bladder cancer patients are routinely monitored after treatment by cystoscopy due to a high rate of recurrence. In the absence of an accurate non-invasive screening test to monitor recurrence, bladder cancer will remain the most expensive malignancy to manage. We have developed a non-invasive test that interrogates small non-coding RNAs (sncRNAs) present in urinary exosomes. Analyzing the urine exosome data with a novel statistical classification algorithm provides a platform that unequivocally differentiates between patients with no evidence of disease and those with recurrence.

Methods:
Urine samples were collected from patients previously treated for bladder cancer (n = 82) who are currently under routine surveillance cystoscopy. Patients without bladder cancer or without evidence of recurrent disease served as the control cohort. A Sentinel sncRNA signature specific for bladder cancer was generated by interrogation of urine exosomal RNAs on Affymetrix 4.0 arrays that probes for > 6600 sncRNAs. A customized platform to interrogate the most informative (~120) Sentinel sncRNAs, was then used to screen urine exosomal RNA derived from patients at risk for recurrent disease. Data were then analyzed using a statistical classification algorithm that provides the miR-BCPx (bladder cancer progression score). This novel analytical approach requires no *a priori* knowledge of the sncRNA function to generate an unbiased classification into those with stable disease versus those with recurrent tumor.

Results:

Bladder cancer patients have significantly elevated levels of exosomal RNA relative to control cohort. In a small blinded testing male cohort, comparison of the miR-BCPx score generated to the disease status demonstrates that the miR-BCPx identifies patients with recurrent tumor with 100% sensitivity (59/59) and 96% specificity (22/23).

Conclusions:

Implementation of the miR-BCPx as a surveillance screen for bladder cancer patients provides an affordable, non-invasive alternative to cystoscopy for monitoring disease stability, and can readily be deployed in the clinic to reduce the number of screening cystoscopies needed.