Validation of a new diagnostic platform for prostate cancer using expression profiling of small non-coding RNAs.

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Background:
Confirmation of prostate cancer in men with elevated PSA and suspicious digital rectal exams currently requires a core needle biopsy, which is associated with risks such as infection, among others. The current dilemma associated with prostate cancer diagnosis is the lack of an accurate pre-biopsy screening methodology, resulting in unnecessary biopsies. We describe a non-invasive screening test that interrogates the sncRNAs profiles isolated from urinary exosomes that, in combination with a novel statistical algorithm, accurately classifies patients into those that have prostate cancer versus those that do not.

Methods:
Urine collected from men with biopsy confirmed prostate cancer status (107 with cancer vs 21 controls without cancer) was used to identify informative sncRNAs Profile specific for prostate cancer using Affymetrix 4.0 arrays, which probes for > 6600 sncRNAs. Urine exosomal RNA, purified from a subsequent patient cohort with unknown cancer status, were screened on a customized platform that interrogates the expression of the top ~120 informative sentinel sncRNAs. The expression profile was then analyzed using a statistical classification algorithm to generate miR-PDx score (prostate diagnostic score). Importantly, the algorithm requires no *a priori* knowledge of the biological function of the informative sncRNA entities.

Results:

In a small blinded study of 128 patients designed to mimic prospective prediction of disease status, miR-PDx score generated from the sentinel sncRNAs screening platform correctly identifies patients with prostate cancer with a specificity of 95% (20/21) and a sensitivity of 99% (106/107) in the testing cohort.

Conclusions:

Implementation of the miR-PDx as an initial screen for prostate cancer, utilized in place of PSA screening would have a major impact on the medical economic costs by substantially reducing the number of unnecessary core needle biopsies. This urine test may also provide a powerful method for longitudinal monitoring of disease stability among men who forego core needle biopsy after initial consultation, and enter active surveillance protocols.