

Development of a Diagnostic Test for Monitoring Bladder Cancer Recurrence Using Urinary Matrix Metalloproteinases (MMPs) as Clinical Biomarkers

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With increasing cancer therapeutic efficacies and the development of better methodologies for early detection, the cancer survivor population has been growing steadily over the years. Currently 3.5% of the US population is made up of cancer survivors. In addition to the risk of having a recurrence of their primary cancer, these patients also have an increased risk of developing a secondary cancer. To date, due to the increased risk of this patient population, and the need for monitoring methodologies with high performance characteristics, more costly and complex diagnostic procedures generally reserved for diagnosing symptomatic patients have been used for recurrence monitor. However, as this patient population grows, there is a clear need for the development of more cost effective clinical algorithms and assays that would result in more efficient management of cancer survivors.

Matrix metalloproteinases are a family of zinc-dependent endopeptidases that have been shown to be key regulators of tumor growth and metastasis formation. Detection of matrix metalloproteinases (MMPs) in the urine of cancer patients has been shown to correlate with disease status in a variety of cancers, including bladder cancer. Numerous studies have now shown that, in particular, biologically active MMP-2 and MMP-9 are found at higher frequency in the urine of cancer patients than in the urine of normal, age-match, sex-matched controls.

Our group is developing a non-invasive diagnostic test utilizing urinary MMPs, such as MMP-2 and MMP-9, as monitors of disease-free status and cancer recurrence in bladder cancer. Initial studies using urinary levels of MMP-2 and MMP-9 to discriminate disease-free patients from those with bladder cancer resulted in approximately 86% (24/28) sensitivity and 84% (169/202) specificity at a fixed protein level. Further validation of these results and full development of a clinical test to monitor for bladder cancer recurrence are currently underway. In addition, we have incorporated a novel analytical algorithm called Clinical Intervention Determining Diagnostic (CIDD), which results in extremely high (~100%) Negative or Positive Predictive Value, allowing the physician to better manage this patient population.