

Sample Collection Impacts the Performance of Urinary Matrix Metalloproteinases (MMPs) as Diagnostic BioMarkers for Bladder Cancer Recurrence

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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 assay utilizing urinary MMPs, such as MMP-2 and MMP-9, as monitors of disease-free status and cancer recurrence in bladder cancer. In the process of developing the assay, we established the background frequency and levels of both MMP-2 and MMP-9 in the urine of normal controls. Background levels of MMPs were found in the urine of approximately 10% of disease-free males and approximately 30% of disease-free females, with MMP-9 being the most commonly detected endogenous MMP. Little or no MMP-2 was detected in disease-free individuals. We investigated whether addition of a “clean-catch” sample collection procedure would decrease the endogenous background levels of MMPs found in a disease-free population. We found that the addition of “clean-catch” to our standard operating procedure for sample collection reduced both the frequency and levels of MMPs.

In addition, we tested the potential impact of the “clean-catch” sample collection methodology on clinical sensitivity and specificity by performing a small pilot study using urinary levels of MMP-2 and MMP-9 to discriminate disease-free patients from those with bladder cancer. At a fixed protein level resulting in 90% (9/10) sensitivity, addition of “clean-catch” procedure to the urine sample collection protocol increased MMP-9 marker specificity from approximately 74% (11/42) to approximately 91% (5/54). Further validation of these results and full development of a clinical test to monitor for bladder cancer recurrence are currently underway.