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Urinary Biomarkers Predict Brain Tumor Presence and Response to Therapy

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Introduction: A major difficulty in treating brain tumors is the lack of effective methods for identifying novel or recurrent disease. In this study, we evaluated the efficacy of urinary matrix metalloproteinases (MMPs) as diagnostic biomarkers for brain tumors. **Methods:** Urine, cerebrospinal fluid, and tissue specimens were collected from patients with brain tumors. Zymography, ELISA, and immunohistochemistry were used to characterize the presence of MMP-2, MMP-9, MMP-9/NGAL, vascular endothelial growth factor (VEGF). Results were compared to age- and sex-matched controls and subjected to statistical analysis. **Results:** Evaluation of a specific panel of urinary biomarkers by ELISA demonstrated significant elevations of MMP-2, MMP-9, MMP-9/NGAL, and VEGF (all P less than 0.001) in samples from brain tumor patients compared to controls. Multiplexing MMP-2 and VEGF provided superior accuracy compared to any other combination or individual biomarker. ROC curves for MMP-2 and VEGF showed excellent discrimination. Immunohistochemistry identified these same proteins in the source tumor tissue. A subset of patients with longitudinal follow-up revealed subsequent clearing of biomarkers following tumor resection. **Conclusions:** We report, for the first time, identification of a panel of urinary biomarkers that predicts the presence of brain tumor. These biomarkers correlated with the presence of disease decreases with treatment and can be tracked from source tissue to urine. These data support the hypothesis that urinary MMPs and associated proteins are useful predictors of the presence of brain tumors and may provide a basis for a novel, non-invasive method to identify new brain tumors and monitor known tumors following treatment.

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