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Metabolomic profiling reveals potential markers and bioprocesses altered in bladder cancer progression

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Although alterations in xenobiotic metabolism are considered causal in the development of bladder cancer, theprecise mechanisms involved are poorly understood. In this study, we used high-throughput mass spectrometryto measure over 2,000 compounds in 58 clinical specimens, identifying 35 metabolites which exhibited significantchanges in bladder cancer. This metabolic signature distinguished both normal and benign bladder from bladdercancer. Exploratory analyses of this metabolomic signature in urine showed promise in distinguishing bladdercancer from controls and also nonmuscle from muscle-invasive bladder cancer. Subsequent enrichment-basedbioprocess mapping revealed alterations in phase I/II metabolism and suggested a possible role for DNAmethylation in perturbing xenobiotic metabolism in bladder cancer. In particular, we validated tumor-associatedhypermethylation in the cytochrome P450 1A1 (CYP1A1) and cytochrome P450 1B1 (CYP1B1) promoters of bladdercancer tissues by bisulfite sequence analysis and methylation-specific PCR and also by in vitro treatment of T-24bladder cancer cell line with the DNA demethylating agent 5-aza-20-deoxycytidine. Furthermore, we showed thatexpression of CYP1A1 and CYP1B1 was reduced significantly in an independent cohort of bladder cancer specimenscompared with matched benign adjacent tissues. In summary, our findings identified candidate diagnostic andprognosticmarkers and highlightedmechanisms associatedwith the silencing of xenobioticmetabolism. Themetabolomicsignature we describe offers potential as a urinary biomarker for early detection and staging of bladdercancer, highlighting the utility of evaluating metabolomic profiles of cancer to gain insights into bioprocessesperturbed during tumor development and progression..

Biography

Nagireddy Putluri is the Director of the Cancer Metabolomics program at Baylor College of Medicine. Asst. Professor Nagireddy Putluri holds a doctorate in Analytical Chemistry (2007) and continued his education as Postdoctoral researcher at Medical College of Georgia (2009-2011) and Louisiana State University (2007-2009) before taking his position at Baylor College of Medicine. As the Director of the Metabolomics Program at the Alkek Center for Molecular Discovery, Baylor College of Medicine, he developed a highly reproducible, robust mass spectrometry platform that could measure more than >1000 metabolites from complex biological specimens. He successfully used this approach to study the metabolomic profiles associated with bladder cancer, a seminal study that was recently published in Cancer Research. Importantly, this paper was selected by the American Association for Cancer Research as a Research Highlight in 2011. His research also focused is in the area of prostate and breast cancer metabolomics. He published over 30 peer reviewed papers in this field and my research on small molecules mass spectrometry, peptides, bladder, prostate and breast cancer research.

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