Development of Urinary RNA Biomarkers for Renal Cell Carcinoma Prognosis

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Background. Renal Cell Carcinoma (RCC) is diagnosed in approximately 65,000 people annually in the United States, accounting for ~3% of all human cancers. The death rate for patients diagnosed with RCC is about 22%. Additionally, recurrence-free survival of patients deemed high-risk using conventional tumor stage and grade criteria is only 44%, and the molecular components that drive high grade, metastatic disease, remain largely unknown. Since tumor histology has limited value in determining patient outcome, there is a clear need for better predictive tools to guide treatment strategies. The ability to predict the risk of tumor recurrence at the time of diagnosis could modulate RCC treatment strategies to include more aggressive approaches for patients deemed high risk. This personalized approach would help to further stratify patients where traditional histological diagnoses fall short. Urine provides an easily obtainable liquid biopsy that is suitable RNA purification and NextGen sequencing, and can be used to identify biomarkers at the transcript level capable of distinguishing between metastatic and non-metastatic patients.
Methods. Urine was collected at the time of diagnosis from 24 patients whose tumors did not recur (>5 years follow-up) and 28 patients who experienced metastatic disease. The samples were centrifuged, cellular debris discarded, and RNA was purified from the resulting supernatant. RNA sequencing was carried out on the Illumina HiSeq 2500 platform. ROC, MDS and random forest approaches were used to investigate the predictive accuracy of the 20 urinary transcript molecular signature. ATCG, Protein Atlas, and GEO datasets were queried to investigate the normal/tumor tissue specificity of the signature.
Results. 20 transcripts were identified that reliably classified non-metastatic and metastatic patients using dimensionality reduction. Additionally, a previously unobserved isoform was discovered for one of the gene transcripts. Furthermore, the biomarker panel has promising classification power in publicly available data.
Conclusions. The results of these studies show that urine is a suitable biospecimen for biomarker discovery. The validation of such a panel of biomarkers could have significant clinical utility in understanding the prognosis of a patent at a critical early junction when treatment plans are established. Additionally this study could provide a roadmap for the development of additional prognostic and diagnostic tests.