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RENAL PATHOLOGY. EXPERIMENTAL AND CLINICAL

SP051 EXOSOMAL SHUTTLE RNA IN URINARY EXTRACELLULAR VESICLES AS BIOMARKER OF CLEAR CELL RENAL CELL CARCINOMA

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Introduction and Aims: Clear cell renal cell carcinoma (ccRCC) is the most lethal urologic malignancy, and a steady increase has occurred in its incidence, yet there is no effective clinical screening test for ccRCC. The causes of ccRCC are poorly understood, but the expressions of specific mRNA patterns have now been linked to the diagnosis and prognosis of many human cancers. In recent years interest in tumor markers for diagnostic purposes is growing. Extracellular vesicles (EVs) have been isolated in various body fluids, including urine. The cargo of urinary EVs is composed of proteins and nucleic acids reflecting the physiological and possibly pathophysiological state of cells lining the kidney. Because urine is a noninvasive and readily available biofluid, the discovery of urinary EVs has opened a new field of biomarker research.
The purpose of the present study was to examine the global content of exosomal shuttle RNA (esRNA) in urinary EVs of patients with ccRCC and to study whether some RNAs have different expression values in patients with ccRCC respect to healthy subjects. Thus, we hypothesized that detecting ccRCC-associated RNA in urinary EVs would help to diagnose and to predict the onset of ccRCC.
Methods: Twelve patients with diagnosed ccRCC who received unilateral nephrectomy were enrolled. We collected pre-surgery urine. A group of healthy volunteers (n = 11) with negative urinalysis was enrolled as controls. The second morning urine specimen was collected from patients and healthy volunteers. EVs were isolated from the urine samples using differential centrifugation. Following EV isolation and lysis, esRNA was extracted, quantitated and quality assessed. The esRNA extracted was labeled and hybridized to the Illumina microarray able to interrogate over 29,000 transcripts. Next, we evaluated whether the functions of the disrupted genes in patients might be related to ccRCC by pathways analysis. The dysregulated genes, were then validated by qRT-PCR in an independent set of 12 patients and 10 controls.
Results: The qRT-PCR identified a number of potential diagnostic biomarkers which might be applied to distinguish ccRCC patients from healthy individuals at early stage. While some potential biomarkers were already present in pathways involved in the pathogenesis of cancer as glutathione-mediated detoxification pathway, glucocorticoid receptor and growth hormone signaling, other biomarkers were new.
Conclusions: Using this approach, we identified a cluster of nine urinary esRNA that taken together could be used as noninvasive signature biomarkers for ccRCC.