Developing Potential Phosphoprotein Biomarkers for Kidney Cancer From Urinary Extracellular Vesicles

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Extracellular vesicles (EVs), lipid bilayer-surrounded spheres of cytosol, hold a crucial role in exchanging cellular information. They transport numerous proteins, nucleic acids, and lipids between cells and participate in several signaling pathways. Due to their unique contents, EVs show great promise as sources of disease biomarkers. This project aimed to establish potential phosphoprotein biomarkers for low-grade and high-grade renal cell carcinoma (RCC) by identifying the significantly upregulated proteins in urinary EVs. Forty-five urine samples obtained from the Indiana University Biobank, consisting of 15 high-grade RCC, 15 low-grade RCC, and 15 healthy control, were processed through a combination of EV isolation, protein extraction, and protein digestion before an LC/MS and proteomics software analysis. After normalization, unpaired t-tests, and passing a strict statistical threshold, 67 and 97 potential phosphoprotein biomarkers were ultimately identified for low-grade and high-grade kidney cancer, respectively. Pathway analyses on these biomarker candidates revealed that both subtypes of kidney cancer had elevated levels of phosphoproteins that take part in the Rho GTPase cycle and Rho family signaling pathways. Additionally, upregulation of phosphoproteins in the IL-12 and IL-37 signaling pathways was found in high-grade RCC and low-grade RCC, respectively. The results of the pathway analyses are validated by numerous publications confirming the pathways' significance in cancer growth and progression. By examining these pathways affected by the disease and their correlation with the potential disease biomarkers, both early detection and targeted treatment of kidney cancer could be achieved with only a few samples of the patient's urine.

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