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Urinary protein changes in subcutaneous walker-256 tumor-bearing rats even before tumor mass palpable

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Early diagnosis of cancer can significantly improve survival rates for cancer patients. Cancer biomarkers are measurable changes associated with the cancer and without homeostatic control; urine reflects early changes in the body with a prospect in cancer early diagnosis. In this study, the Walker 256 tumor rat model was established by subcutaneous injection of Walker 256 tumor cells. To identify urinary proteome changes during the entire development of cancer, urine samples of Walker 256 tumor bearing rats were collected at five time points corresponding to before cancer cell implant, before tumor mass palpable, tumor mass appearance, tumor rapid growth and cachexia respectively. The urinary protein patterns on SDS-PAGE change significantly as tumors progress and urinary proteome was identified using a Fusion-Lumos mass spectrometry by label-free quantitation. Interesting, several differential urine proteins before tumor mass even palpable could be identified with a fold change >2 and p value <0.05, and these early changes in urine could be also identified at tumor mass appearance, tumor rapid growth and cachexia. Twenty-four differential proteins were annotated before as biomarkers of cancer diseases and nine proteins as biomarkers of breast cancer. Additionally, it was found that those differential proteins were involved in several pathways related to cancer, including IL-6 and IL-12 signaling, production of nitric oxide, ROS and apoptosis. Finally, 30 dynamically changed urinary proteins were selected as more reliable cancer biomarkers, and they were validated by targeted proteomics. Our study suggested that urine is a sensitive biomarker source for early detection of cancer and systemic changes reflected in urine proteome during cancer progression can improve the understanding of pathophysiological changes of cancer.

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