Urine as an Alternative to Blood for Cancer Liquid Biopsy and Precision Medicine

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Liquid biopsy is a powerful tool to provide cancer genetics via detection of biomarkers like circulating tumor DNA (ctDNA) in blood to reduce cancer death through precision medicine and has shown potential in the early detection of cancer. However, urine analysis of ctDNA, a completely noninvasive and possibly more practical procedure for cancer screening, has not been thoroughly explored. Using hepatocellular carcinoma (HCC) as a model, we examined if urine can be an alternative to blood for liquid biopsy. Our study indicated that quantification of TP53 and CTNNB1 genes by qPCR assays in matched plasma and urine samples showed that the plasma samples generally had more DNA. However, detection of mutations in these genes as HCC genetic biomarkers in urine achieved higher sensitivity (31%) than in plasma (22%) for HCC patients, suggesting more detectable HCC ctDNA in urine. High molecular weight (HMW) urine DNA showed over 95% genome coverage concordance and insignificant differences in variants compared to peripheral blood mononuclear cell (PBMC) DNA, indicating it can provide a comprehensive germline sequence of individuals for analysis. To integrate more genetic markers and improve urine screening sensitivity, enrichment of targeted genes for duplex sequencing and custom-built software for fast Next Generation Sequencing (NGS) data analysis are in progress. Lastly, efficient urine DNA collection and preservation methods were developed for a practical urine screening kit. In conclusion, our data suggests that urine can replace or complement blood for liver cancer liquid biopsy and precision medicine with potential applications to other cancers as well.

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