It's a match - circulating tumor DNA in urine and plasma reveal complementary information in prostate cancer.

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Background & objectives

Liquid biopsy using plasma and urine has proven useful in detecting, diagnosing, and monitoring many cancers. In urological cancers, urinary circulating tumor DNA (uctDNA) might improve the sensitivity of liquid biopsy-based approaches by proximal sampling, i.e., analysis of biofluids collected proximal to the tumor site. While evidence suggests that ctDNA in urine can be informative in renal and bladder cancer, less is known about the presence and applicability of uctDNA in prostate cancer patients. Here, we aimed to determine the presence, levels, and potential clinical applications of ctDNA in plasma and urine of metastasized prostate cancer patients (mPCa, n=77).

Methods

We analyzed matching urine and plasma samples using a shallow whole-genome sequencing approach. The tumor fraction and somatic copy number alterations (SCNA) were assessed using the ichorCNA algorithm.

Results

Our data shows that even though the tumor fractions do not significantly differ in plasma and urine, there is a great variability at the patient level. SCNAs were detected with a high concordance in plasma and urine in 21% of patients, while in 26% and 17% of patients, SCNAs were detected in plasma or urine only. Surprisingly, ctDNA discovery in plasma and urine was not affected by whether their primary tumor was still present. In addition, longitudinal sampling was performed for monitoring purposes in a subset of patients (n=26). ctDNA detection was slightly more likely in patients who coincided with clinical progression. We invariably detected similar ctDNA patterns in almost all patients' plasma and urine. In patients who responded to therapy, ctDNA declined. In contrast, at progression, the ctDNA levels increased or remained elevated. While uctDNA usually correlated closely with ctDNA in plasma, in some cases, both fluids yielded complementary information that might have been missed if only one sample had been collected.

Conclusion

Our data indicate that the presence of ctDNA in urine provides complementary information about a patient's tumor that the sole analysis of plasma may miss. Since urine represents a desirable proposition given the quantities that can be collected at great ease, uctDNA holds promise in the clinical management of prostate cancer.