Liquid Biopsies in Genitourinary Malignancies

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Measurement of extracellular circulating tumor DNA (ctDNA) in various body fluids and secretions represents a non-invasive method to capture a molecular snapshot of the systemic tumor burden in patients with various stages of cancer. At the same time, deep insights regarding the cancer's molecular characteristics may be gleaned from comprehensive ctDNA profiling to understand the mechanisms driving cancer progression and response to treatment, amongst other important clinical questions that may alter management strategies. Given these advantages, it is easy to see why these novel diagnostic tests have engendered such great excitement in oncology practices. In the management of genitourinary tumors, the use of ctDNA is further boosted by its accessibility: these tumors are in close proximity to the urinary tract, and it is postulated that higher levels of tumor-associated cfDNA can be isolated directly from genitourinary secretions enabling more accurate detection and tracking of the disease.

Notwithstanding, there are many challenges present in the detection and interpretation of the results gathered in the context of genitourinary cancers. First, there is a wide array of techniques for identifying and measuring cfDNA from malignancies, some involving tumor-informed methods, others relying on panel-testing of commonly occurring genomic alterations detected in cancer. Optimization and customization of these methods are necessary for each of the genitourinary malignancies. Additionally, specific challenges abound for various tumor types. Kidney cancer is notorious for shedding low levels of ctDNA, making systemic detection difficult. For prostate and germ cell tumors, the diagnostic accuracy of ctDNA-based liquid biopsies needs to exceed the accuracy of established, time-tested, non-invasive biomarkers widely available today. In urothelial carcinoma, although the detection of urine-based ctDNA holds promise, technical challenges, such as distinguishing false positives from pre-existing mutations within normal urothelium, need to be resolved to arrive at a reliable testing modality.

With the burgeoning genomic sequencing technology platforms enabling ever more affordable testing, data points are increasingly being gathered to address many of the outstanding issues hindering wide implementation of this technology. In this issue of the *SIUJ*, we summarize the most up-to-date knowledge regarding the use of ctDNA in the management of prostate, urothelial, renal cell, and germ cell tumors[1–4]. We also explore whether urine or plasma is the ideal fluid for liquid biopsies to reflect the systemic tumor burden and molecular characteristics[5,6]. In addition, this issue features results of an original study using urinary ctDNA to stage patients with muscle invasive bladder cancer at the time of radical cystectomy[7]. These reports will introduce this important novel platform and its capabilities, point out several unmet challenges, and help readers imagine a new era of precision medicine powered by molecular diagnostics.

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