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Editorial

Liquid Biopsy: A New Emerging Technique

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Liquid biopsy contrary to tissue biopsy utilizes samples of blood, urine, or other body fluid to look for cancer cells from a tumor or small pieces of DNA, RNA, or other molecules released by tumor cells into a person's body fluids. Liquid biopsy is a new test with several potential advanced uses in cancer treatment, with a few U.S. Food and Drug Administration (FDA)-approved uses. Research into its benefits is continuing [1]. Prostate cancer (PCa) is common in men and can be localized or aggressive. Biomarkers such as PSA has limited specificity and sensitivity. There is an urgent need for better biomarkers that can differentiate benign from malignant prostate conditions, localized from metastatic as well as aggressive from slow disease.

Despite good initial response to Androgen Deprivation Therapy (ADT), tumors eventually progress to metastatic castration resistant PCa (mCRPC). Liquid biopsy assays, analyzing circulating free tumor DNA (ctDNA) or circulating tumor cells (CTCs) in plasma or other body fluids have proven as a useful source for biomarkers and have already entered the clinics [1] as to this date, mCRPC remains an incurable disease [1] CDK12(Cyclin-Dependent Kinase)-mutated prostate cancer patients are likely to benefit from platinum-based chemotherapy, especially with the help of dynamic ctDNA-based liquid biopsies to monitor their CDK12 mutation status [2]. Liquid biopsy is a powerful tool for isolating genetic material, proteins, and whole tumor cells from the blood. This technology has rapidly advanced, allowing for better insights into the pathogenesis and treatment response in different stages of prostate cancer [3].

Prostate Cancer (PCa) is the second leading cause of cancer mortality amid men in the US. Presently, PCa diagnosis and screening is performed by combining Prostate Specific Antigen (PSA), digital rectal examinations (DRE), and 12-core needle biopsy. Increased circulating PSA levels (≥4 ng/mL) and abnormalities observed during DRE may predict PCa, which is further confirmed by histopathological analysis of biopsies. Nevertheless, the low specificity of these screening tests contributes to over diagnosis and, consequently, overtreatment. Thus, there is a need for additional accurate non-invasive biomarkers technologies to improve the diagnostic accuracy and complete management [4]. A major limitation of testing markers in advanced disease remains the invasiveness of biopsies of metastases. This can be overcome by liquid biopsies, particularly blood which contains Extracellular Vesicles (EVs), Circulating Tumor Cells (CTCs), and cell-free nucleic acids [5].

All deaths in PC occur at the metastatic castration-resistant (mCRPC) stage. Tumor cells surviving Androgen-Deprivation Therapy (ADT) continue to grow despite inhibition of steroid synthesis and Androgen Receptor (AR) signaling. Resistance may involve the emergence of active AR variants (AR-Vs) and/or cell plasticity, a concept based on the relationship among reserve stem, neuroendocrine, and luminal cells in glandular acini, which remain relevant in cancer [5]. Studies support the evidence that prostate cell subtype genes are traceable in the blood of patients with advanced disease. Data from over 1000 patients confirmed that overexpression patterns in the blood of 35 of 40 patients are best represented in metastases [5].

Whole blood RNA has been used as an alternative to define gene expression profiles related to progression for diverse cancers, including PCa. This minimally invasive approach may predict treatment resistance and outcome and improves therapeutic options. [5] Studies support the idea that prostate cell subtype genes are traceable in the blood of patients with advanced disease.

Liquid biopsies were developed as an alternative to conventional tissue biopsies since they can be obtained in a non-invasive or minimally invasive way, thus avoiding the risks related to the collection of tissue biopsies and allowing serial sampling during the course of disease. In PCa, they have a value for diagnosis, differentiating between aggressive and indolent PCa, active surveillance, post-operative monitoring, early detection of recurrence and tracking tumor evolution. The most common parts in liquid biopsies are circulating tumor cells and circulating cell-free DNA or RNA . More recently, Extracellular Vesicles (EVs) have been proposed as an alternative source of biomarkers in liquid biopsies [6]. Data suggest that the fraction of PC-derived EVs in urine is sufficiently large to allow the detection and tracking of

PCa derived RNAs. Hence, urine appears to be a superior source of EV-RNAs for the diagnosis and active surveillance of PC, however, it is unlikely to be suitable for post-operative monitoring of PCa progression.

That is why blood assays are needed. However, PCa-derived EV fraction in blood plasma at least in patients with localized PC is too low to enable tracking of PCa-derived RNAs. Moreover, the composition of plasma EVs is much more complex than urinary EVs as EVs are sampled from many more different cell types, hence EV isolation methods that would allow enrichment with cancer-derived EVs are required for the development of EV-based blood tests for the detection and monitoring of PCa [6]. The difficulty of obtaining suitable tumor material for molecular testing is one of the reasons impeding clinical implementation of genomic profiling. Biopsies of osteoblastic metastatic lesions, are technically challenging and distressing for the patient. A single tumor biopsy, from either primary or metastatic lesions, is limited in its ability to capture spatial heterogeneity. Indeed, primary PCa is among the most spatially heterogeneous and clonally complex cancer types. Liquid biopsies have emerged as an attractive way to study tumor molecular landscapes in a minimally invasive manner, allowing for pictures of the overall tumor burden. Additionally, liquid biopsy–based biomarkers could serve as early endpoints in clinical trials to accelerate drug development [7].

The field of liquid biopsies in PC has advanced over the last decade, developing prognostic and predictive biomarkers, and holding promise for a minimally invasive means of monitoring tumor evolution. Liquid biopsies could guide therapeutic decisions and accelerate the development of accuracy medicine in PCa. However, issues relating to standardization of assay sensitivity and specificity, prospective clinical qualification of different assays, as well as cost and accessibility need to be addressed to endorse their implementation in routine clinical practice. [7] Plasma tumor DNA (ptDNA) is a potential early noninvasive biomarker of treatment outcome in metastatic castration-resistant prostate cancer (mCRPC) [8]. The inclusion of biomarkers with risk assessment models tumor such as hormone-naive, high-risk localized cancer. These findings underline the feasibility of combining molecular and functional imaging ad require a validation in larger prospective studies leading to future possible standardization and cost-effectiveness in clinical routine application.

Liquid biopsy has been recognized as a minimally invasive means to detect aberrations across numerous cancer types. With the development of DNA repair targeted therapies, this is appealing. There is an urgent need to develop better biomarkers to help guide oncologists' decisions in different settings. However, there are still challenges to overcome prior to implementing liquid biopsies in routine clinical practice such as preanalytical considerations including blood collection and storage [9]. In summary, Liquid Biopsy (LB), including the analysis of circulating tumor material in the blood or urine, has emerged as a powerful tool in the management of prostate cancer. In localized tumors, LB can distinguish between low- and high-grade cancers and can guide the decision to proceed with or postpone tissue biopsy. In advanced disease, LB has proven prognostic ability and has been used in clinical trials to assess response. Finally, for a minority of patients, LB can identify genomic alterations with significant therapeutic implications. Technological advances and creative uses of LB promise to improve the management of prostate cancer patients soon [10].

References

1. Dillinger T, Sheibani-Tezerji R, Pulverer W, Stelzer I (2022) Identifcation of tumor tissue–derived DNA methylation biomarkers for the detection and therapy response evaluation of metastatic castration resistant prostate cancer in liquid biopsies. Molecular Cancer 21: 7
2. Zhu S , Bao Y, Zheng L, Zhao J(2022) Chronological Liquid Biopsy Reveals the Impact of Platinum–Based Chemotherapy on a Prostate Cancer Patient's CDK12 Mutation: A Case Report . OncoTargets and Therapy 15: 947–952.
3. Jang A, Rauterkus GP, Vaishampayan UN, Barata PC (2022) Overcoming Obstacles in Liquid Biopsy Developments for Prostate Cancer. OncoTargets and Therapy 15: 897–912.
4. Kshirsagar P, Seshacharyulu P, Muniyan S, Rachagani S (2022) NA–gold nanoprobe–based integrated biosensing technology for noninvasive liquid biopsy of serum miRNA: A new frontier in prostate cancer diagnosis. Nanomedicine: Nanotechnology, Biology, and Medicine 43: 102566
5. Derderian S, Vesval S, Wissing MD, Hamel L(2022) Liquid biopsy–based targeted gene screening highlights tumor cell subtypes in patients with advanced prostate cancer. Clin Transl Sci 15: 2597-2612
6. Bajo-Santos C , Brokāne A, Zayakin P, Soboļevska K (2023) Plasma and urinary extracellular vesicles as a source of RNA biomarkers for prostate cancer in liquid biopsies.
7. Casanova–Salas I, Athie A, Boutros PC , Re M (2020) Quantitative and Qualitative Analysis of Blood-based Liquid Biopsies to Inform Clinical Decision–making in Prostate Cancer.
8. Conteduca V, Scarpi E, Caroli P, Lolli C (2022) Combining liquid biopsy and functional imaging analysis in metastatic castration-resistant prostate cancer helps predict treatment outcome. Molecular Oncology 16: 538–548.
9. Trujillo B, Wu A, Wetterskog D, Attard G (2022) Blood–based liquid biopsies for prostate cancer: clinical opportunities and challenges. British Journal of Cancer 127: 1394-1402.
10. Ionescu F , Zhang J, Wang L (2022) Review Clinical Applications of Liquid Biopsy in Prostate Cancer: From Screening to Predictive Biomarker. Cancers 14: 1728