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EDITORIAL

Liquid Biopsy: Domain of Biochemists

A **liquid biopsy,** also called **fluid biopsy,** is the sampling of non-solid biological tissue samples, mainly blood but also include samples like urine, saliva, amniotic fluid, cerebrospinal fluid, etc. along with their genomic and/or proteomic assessment. This approach provides noninvasive access to genetic information like mutation analysis and even epigenetic changes with the use of circulating biomarkers. It is a novel revolutionary technique that is opening doors to previously unexpected perspectives.

Recent developments include various types of liquid biopsy depending on the disease that is being studied. For example, in oncology, it is used to detect various cancer-derived materials in blood like intact circulating tumor cells (CTCs), cell-free circulating tumor DNA (cfDNA); also called circulating tumor DNA (ctDNA), circulating small RNA, extracellular microvesicles (including exosomes) containing small-RNA, mRNA and DNA. As tumor volume increases, the phagocytic capacity of macrophages to clear apoptotic and necrotic fragments exceeds, resulting in passive release of cfDNA into circulation. This DNA in blood sample drawn from the patient can be purified and subjected to detailed molecular analysis by the biochemists using novel techniques like next generation sequencing or PCR-based techniques. These findings could hold a promising future for early detection, diagnostic and monitoring tool for malignancies including validation of treatment efficiency and monitoring of relapse cases. The "circulating transcriptomes" which include miRNAs, mRNAs, lncRNAs, could provide additional information in analyzing tumor-specific changes. In simple words, it could be a game changer in the field of oncology diagnostics which will undergo a paradigm shift. Although a liquid biopsy of circulating tumor cells has been approved by the FDA as a useful prognostic method for various cancers, its clinical implementation is not yet well known.

Similarly, **various other biomarkers can be used to study other diseases** like circulating endothelial cells are being sampled for myocardial infarction diagnosis; cell free fetal DNA extracted from maternal blood for antenatal diagnosis and isolation of protoporphyrin IX from blood for atherosclerosis. In antenatal diagnosis, the detection of fetal DNA in maternal blood has yielded a simpler, noninvasive source of fetal genetic material for analysis. Plasma DNA technology has also found recent applications in the fields of organ transplantation, posttrauma monitoring, and infectious agent detection.

Future clinical applications of this novel techniques include screening for presence of diseases, patient stratification and therapy selection, monitoring treatment response and drug resistance; detection of minimal residual disease after surgery, recurrence or relapse cases. Initially used for prognosis alone, liquid biopsy data are now being extended to cancer diagnosis. In particular, the identification of specific mutations in target genes can also aid in therapeutic decisions, both in the response to the given treatment and in the detection of resistant cases. Based on genetic data it can provide for targeted therapy, personalized or precision medicine.

Main **advantages of this technique** lies in it being a simple, quick and noninvasive alternative to surgical biopsies. It is also more acceptable and convenient from patient's perspective and can be easily repeatable for monitoring the progression of various diseases over a period of time. It is a better option for certain cancer patients which are not good candidates for tissue biopsy which is an invasive procedure that carries risk.

However, certain **challenges** are yet to be overcome before implementation of liquid biopsy in real practice, such as scarcity of sample obtained, high technical expertise, lack of standardization, high cost factor, etc. In fact, due to the low concentration of CTCs, ctDNA, and exosomes currently recoverable from the patient's blood sample, the analytical results encounter the hurdle of unsatisfactory specificity and sensitivity.

The **question remains unanswered** as to whether tissue biopsy will remain the gold standard or can liquid biopsy take its place in near future. As of now, liquid biopsy will complement the tissue biopsy in its ease of sampling thus allowing larger sector of patients to be tested. For example, while liquid biopsy informs treatment decisions in lung cancer with an epidermal growth factor receptor (EGFR) mutation, targeted therapies do not exist for all cancers. More results of clinical studies and comparisons are needed to further explore the actual potential of liquid sample based testing. So, we are not quite there yet but it still is an exciting opportunity to work upon in future.

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