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Sl No.	Name of Editor	Qualifications	Current Affiliation	Official Address	Official Email Id
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From the desk of Editor-In-Chief

Cell free Nucleic Acid Technologies and Their Recent Status in Health Care System.

Although tissue genotyping is the most specific method for diagnosing different genetic diseases including cancers, it is expensive, time-consuming, needs expertise and manpower and requires sophisticated infrastructure and instruments. In contrast, body fluids, particularly the blood, are easily available and are an extensive source of a large number of biomarkers. Genetic materials from blood are particularly important in the context of a diagnosis of gene-related disorders including cancers. Hence the term liquid biopsy that enables the diagnosis or analysis of tumours using only a blood or fluid sample rather than a solid tissue biopsy. The liquid biopsy has got several advantages over the tissue biopsy which include cheaper cost, rapid result, a good monitoring activity and a more reliable result due to lack of inherent heterogeneity in tissue biopsy[1].

Cell free nucleic acids(cf-NA) are important components of the liquid biopsy that enabled the liquid biopsy a crucially important procedure in the specific and rapid diagnosis of inherent genetic diseases, cancers, neurological diseases, cancer and diabetes mellitus. Cell free nucleic acids are generated from the dead or apoptosized cells or they may be actively transported out of the diseased or healthy cells by exosomes or protein complexes. These molecules may be segments of DNA or non-coding RNAs which are very stable in blood and hence are excellent robust sources of genetic biomarkers from blood [2-5]. First detected in 1948, their potentiality as a biomarker of genetic diseases initially hovered around as non-invasive prenatal genetic markers [6,7]. Their role as cancer biomarkers was initially described by Leon et al as prognostic markers and Sorensen et al as diagnostic markers. With progress in cf-NA research, the detection of oncogenes like ras, trisomies, subchromosomal aberrations and monogenetic disorders were possible from the cf-NA, and the importance of their use as genetic biomarkers increased significantly.

The cf-NA technology has encompassed almost all domains of cancer treatment and diagnostics. Quantification of cf DNA and detection of cf RNA give important cues for cancer screening, detection, diagnosis, staging and prognosis. Investigations related to detection of pattern of fragmentation, nucleosome spacing, and methylatyion of cf DNA have enabled the researchers to localize different cancers. cf DNA mutation analysis and detection of non coding cf RNA help significantly in detection of drug resistance and selection of appropriate therapy.

As far as the recent studies have elucidated, cf NA can be isolated and separated from circulating exosomes (40-100 nm), microvesicles (100-3000 nm) and apoptotic body (800-5000 nm). The first two are generated from budding out or exocytosis of the cell membrane or some internal part of the cell while the later one is the resultant product of programmed cell death or apoptosis.

However, in spite of the emerging importance, successful detection of cf-NA is still very challenging due to their significantly smaller size and ultra-low concentration, which is the major restricting factor for their routine use in clinical field. At present broadly two methods are mainly used: the PCR method and the method of genomic sequencing. PCR methods used for detecting the cf-NA include different types of PCR including the real time PCR, allele specific PCR, droplet digital PCR etc. genomic sequencing methods that have been successfully used to detect the cf-NA till now are next generation sequencing method (NGS) and micro-array methods.

With all these facts, the overall prospective of use of cf-NA is still debatable. Due to lack of proper understanding about the cell free nucleic acid in circulation and prevalence of large amount of other non-informative cell free nucleic acids in the circulation (almost 1000 times)[8], their uses in the clinical field are still now not widely accepted by the oncologists and clinicians. Overcoming most of these barriers, however, depend on the future development of the molecular diagnostics, bio-informatics and advancement in the knowledge of their combinatorial use. We hope that with these advents the liquid biopsy or the cf-NA technology will become one of the major diagnostic, monitoring and predicting tools in human health care system.

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Professor (Dr) Anindya Dasgupta

Editor in Chief,

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