

Liquid biopsy: future in diagnostic medicine

Editorial

Tumour derived circulating cells and nucleic acids offer tremendous potential to diagnose cancer. The present diagnostics rely on biopsy as a primary tool for surgical intervention of tumour. The various types of biopsies range from fine needle biopsy to surgical biopsy. The disadvantages with the method include surgical invasive techniques which are not patient friendly. Also important is the risk associated with the procedures which may result in cancer spreading or metastasis. Liquid biopsy is a powerful technique based on non-invasive technique which is available to detect cancer early from clinical samples without the need for surgical biopsy.

Each tumour cell is bathed in tissue fluid which gets drained into lymphatic system. It is supplied by rich arterial supply and also has venous drainage. However the tumour cells are not tightly packed and have low adhesion tendency. When a biopsy procedure is carried out either using needle or scalpel the tumour cells may get dislodged. Metastasis may occur through the blood supply or through the surrounding fluid. Liquid biopsy is a newer line of approach where the early markers of cell necrosis can be detected.

Cancer is preceded by a long periods of necrosis of tumour tissue in small amounts. It is also associated with inflammatory mediators characterised by mutations and epigenetic regulation of genes followed by cell proliferation. There are several rounds of cell proliferation and cell death at the site. The micro necrosis releases cells into circulation including minor amounts of DNA and RNA. The non-coding RNA has been implicated in controlling micro RNA functions. Tumour-derived exosomes are small vesicles which may carry the tumour products to the exterior by fusion with cell membrane. They reach either neighbouring cells or are carried by transport to distant locations in the body and bring about metastasis. Thus cell to cell communication by exosomes may be important in cancer progression. Exosome also have markers which are specific to the tissue. This helps in localisation of cancer to the organ or tissue. Exosomes have become important tumour markers and can be used as diagnostics in cancer. Liquid biopsy is the term used to detect these exosomes, DNA and RNA from tumour derived circulating cells.

Blood samples can readily be used to conduct PCR based detection. PCR amplification and deep sequencing of universally tagged DNA molecules are the key features. Ultrasensitive sequencing for the detection of low abundant mutant DNA is challenging. The prospects of digital PCR involves sample partitioning into many individual PCR reactions which can be run parallelly. It allows researchers to even quantify tumour DNA at specific stretches with sensitivity as low as 0.1% of the total DNA of blood. The target molecules are contained

Volume 1 Issue 1 - 2016

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Received: September 24, 2016 | **Published:** October 28, 2016

in these reactions. Tagged-Amplicon Sequencing (Tam-Seq) involves de-novo identification of rare cancer mutations. Emulsion digital PCR and flow cytometry are used together in a technique known as BEA Ming. It uses beads, emulsification process, amplification, and then magnetics to achieve the necessary level of sensitivity.

Cell free tumour DNA was successful in detecting 82% of patients with brain tumours. Ovarian cancers, gastrophageal and colorectal cancers have been detected in 75% of patients. Cancers of kidney, pancreas and breast have been detected in less than 50% of patients. There is a lot of excitement around liquid biopsies since they offer a cost effective method and its usefulness in cancer treatment and prognosis is also undisputable. It is not yet available commercially and is restricted to clinical research setting. It would be benefiting to the entire population if such screening methods are available for fast and easy detection of cancers and is going to transform future of medicine.¹⁻⁵

The author is actively involved in research and teaching at the Division of Bioinformatics and Computational Genomics, Nitte University Centre for Science Education and Research (NUCSE), Nitte University, Paneer Campus, Mangalore, India. The author is involved in teaching Biomedical Science and Food Safety and Biotechnology at the post-graduate level. The field of interdisciplinary science is the future of medicine and the journal proudly promises major strides in the area of Biosensors.

Acknowledgements

None.

Conflict of interest

The author declares no conflict of interest.