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Circulating cell-free DNA (ccf-DNA) in cancer patients: From DNA integrity index to liquid biopsy

Cell-free indicates DNA that is found freely in the blood without a nucleus. Circulating cell-free DNA (ccf-DNAs) were first identified by Mandel and Metais in 1948 but their association with disease was not confirmed till 1977 when their increased level in the plasma/serum of cancer patients was proved. In healthy individuals, the main source of ccf-DNA is apoptotic cells which release uniform DNA fragments 185 to 200 base by a programmed enzymatic cleavage; the level is extremely variable but is usually low to negligible. Cancer cells release different and longer DNA fragments resulting from necrosis, autophagy, or mitotic catastrophe; the chance of an active release from cells was also reported and the levels are much higher than in healthy individuals. However, increased levels of ccf-DNA were observed in many diseases including leukemia, solid tumors, pulmonary embolism, myocardial infarction, tissue trauma, and chronic inflammatory diseases. This broad prevalence of diseases with potentially elevated ccf-DNA levels limits the diagnostic specificity and no cutoff value of plasma DNA concentration produced performance characteristics that would make it a good screening tool for neoplastic diseases. Thus a more refined approach was applied by calculating the ratio between cancer cell-derived ccf-DNA and normal cell-derived ccf-DNA in what is called DNA integrity index. More recently detection of tumor-specific molecular aberrations in the ccf-DNA is performed, what is called liquid biopsy. Many studies reported increased serum concentration and DNA integrity index in various solid tumors including breast, gynecological malignancy, HCC and acute myeloid leukemia. The analysis of the length of circulating DNA in plasma was reported as a sensitive marker for solid tumor detection and it was claimed to discriminate between benign and malignant lesions. The rationale of liquid biopsy is that mutations detected in ccf-DNA are highly specific of cancer and can clearly identify circulating tumor DNA (ct-DNA). Ct-DNA was explored as a prognostic or predictive marker for cancer detection; the studies suggested potential clinical applications. The analysis of ct-DNA ranges in scale from single mutations to whole-genome analyses. Liquid biopsy has many advantages compared to conventional sampling methods. The latter is subject to procedural complications, difficulty in obtaining sufficient material of adequate quality for genomic profiling and sampling biases that arise from genetic heterogeneity. A liquid biopsy is also superior to the conventional monitoring methods namely tumor markers that often lack specificity and imaging which exposes patients to ionizing radiation and has limited resolution. Promising as it is ccf-DNA and ct-DNA assays need scrupulous standardization to overlap discrepancies in sensitivities across various studies. However, sample collection is convenient, minimally invasive, and it avoids the need for tumor tissue biopsies. Analyzes of ccf-DNA and ct-DNA may have the potential to complement or replace existing cancer tissue and blood biomarkers in the future.

Biography

Azza Mahmoud Kamel is currently working as Emirate Professor of Clinical Pathology at National Cancer Institute, Cairo University, Egypt since 2007. Previously she worked as Professor of Clinical Pathology (1986- 2007) at National Cancer Institute, Cairo University, Egypt, Founder and Head of BMT Lab. Unit (1993-2007) and Head of Clinical Pathology Department (2005-2007). She pursued her Medical Degree (MB, BCh), Faculty of Medicine, Cairo University (June 1968), Master Degree (MSc) in Clinical Pathology, Faculty of Medicine, Cairo University (October 1972) and Doctorate Degree (MD) in Clinical Pathology(Immunology/Hematology), Faculty of Medicine, Cairo University (July 1976). She has 165 publications in many reputed journals. She conducted many workshops and completed many research projects. She received many awards like State Award in Medicine (1989), Medal of Excellence from the Egyptian Government (1994). She is an active member of Egyptian Society of Cancer, International Society of Hematology, European and African division (ISH), European Association of Hematology (EHA), American Association of Cancer Research (AACR), International Society of Thrombosis and Hemostasis (ISTH).

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