Significant higher DNA levels were found in the serum of metastatic cancer patients (mean of 209 ng/mL) as compared to nonmetastatic patients (mean 100 ng/mL) ($P<0.02$). Healthy controls showed lower levels of free DNA in the serum by using a radioimmunoassay (1). Microsatellite alterations in plasma DNA of small cell lung cancer patients were discovered more than twenty years later ushering in the advent of liquid biopsy in lung cancer (2). Since then, cell-free circulating DNA analysis has been employed for multi-cancer early detection. Machine-learning classifiers have been developed using different circulating free DNA, including methylation patterns (3). Since the seminal Leon *et al.* study in 1977, over forty-five years have passed before the development of a circulating free DNA-based test for early detection of multiple types of cancer (1). The detection of circulating free DNA in plasma or serum could serve as a liquid biopsy. The mechanisms underlying the release of nucleic acids into the blood, which were largely unknown at the time of the initial study by Leon et al., are now believed to be due to apoptosis and necrosis of cancer cells, although fragments of cellular nucleic acids can also be actively released (1). It has been estimated that in a patient with a tumor weighing 100 g, which corresponds to 3×10^{10} tumor cells, up to 3.3% of tumor DNA could enter the bloodstream each day. The size of the circulating tumor DNA fragments can vary, ranging from small fragments of 70 to 200 base pairs to larger fragments of nearly 21 kilobases (4). The prompt applicability of detecting mutations in serum or circulating tumor cells has been observed in EGFR mutant non-small cell lung cancer patients (5,6). Nowadays, circulating tumor DNA analysis is widely implemented and and can be conveniently adapted to adjust adjuvant chemotherapy among circulating tumor-positive patients with stage II colon cancer (7). The successful development of liquid biopsy has taken several decades and involved hundreds of investigators. Notably, the pioneer study in blood platelets from patients with prostate cancer and brain tumors revealed that platelets were carriers of RNA biomarkers, such as EGFRvIII RNA, which were detectable in resected glioma tissue and platelets from the same patient (8) .

A new book published in AME Journals has added to the history of liquid biopsy, providing an overview of the multi-approaches used in clinical research and the applicability of liquid biopsy in lung cancer. AME has gathered significant contributions from numerous investigators covering a broad array of indications for the detection and management of driver alterations, including gene fusions. The book is predominantly centered on the early detection and bona fide of liquid biopsy in early, surgically resected non-small-cell lung cancer. The book produced by the AME publishing team explores all possible aspects in which liquid biopsy could be of great assistance in diagnosis and therapeutic decisions. It is fascinating to learn that targeted next generation sequencing and other complex molecular techniques are now applicable to blood samples.

The book also focuses on multiple aspects of circulating lung tumor cells, a field that is constantly evolving with ebullient research work, such as the *ex-vivo* culture of circulating lung tumor cells. Circulating free DNA is also given a special section, and finally, the section on extracellular vesicles, specifically exosomes, is particularly rewarding to read. The field of exosomes is very promising and still has the potential to provide many innovative ideas for research and clinical applications. The book is not merely a compilation of articles but a successful continuation of old and seminal studies, some of which were mentioned earlier, in a new and innovative way. By challenging the perception that there is nothing new in the field of liquid biopsy, AME has managed to provide new evidence and insights in this meaningful book.

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