Development of liquid biopsy for detection of presymptomatic diseases

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Early detection is crucial for its ultimate control and the prevention of malignant progression of cancer. Here in Japan, a nationwide 5-year project was conducted between 2014 and 2019 to develop a novel tool for early detection of cancer using serum circulating microRNAs (miRNAs). miRNAs are small non-coding RNA made up of 18-24 base pairs with single chain molecules and modulate gene expression by decreasing target mRNA stability or repressing translational efficiency. They can stably exist in severe conditions, including urine, because some of the miRNA are at least partly packaged into extracellular vesicles (EVs) or included by an RNA-induced simple complex (RISC) with the Agonature2protein to protect against the elimination of RNase. Therefore, circulating miRNA, so-called extracellular miRNA, has garnered a great deal of attention as a novel target of liquid biopsy. Based on the samples of the National Cancer Center Biobank, we collected more than 50,000 serum samples from patients with malignant diseases as 13 types of cancer, including rare cancers such as ovarian cancer, gliomas, and sarcomas. Subsequently, comprehensive miRNA microarray analyses were performed for all samples. This serum miRNA database provides insights regarding miRNA biomarker candidates for each cancer type. Although circulating miRNAs packaged in EVs are thought to be a cell-to-cell communication tool, the functional characteristics of the miRNAs listed in the project are still unknown. We explores the potential contribution of liquid biopsy using EVs and extracellular miRNA to diagnosis and monitor cancer, including an assessment of prognosis and early detection of disease recurrence in patients with cancer.

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