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Cancer metastasis involves the dissemination of tumor cells into distant organ sites, with the circulatory system playing an important role in the dissemination process.[1] Circulating tumor cells (CTCs), circulating tumor DNA (ctDNA), and exosomes have been found in the blood of cancer patients, making these circulating biomarkers a rich source of diagnostic and prognostic information for personalized cancer management.[2] The development and advancement of microfluidic approaches to isolate and characterize these circulating biomarkers offers tremendous potential for translating these liquid biopsy approaches into the clinic. In the "Microfluidics, Circulating Biomarkers and Cancer" Special Topic of *Biomicrofluidics*, a collection of original contributions and review articles is featured, which highlights the advances being made in this rapidly growing field.

The "Microfluidics, Circulating Biomarkers and Cancer" Special Topic has two review articles of interest. The article by Iliescu *et al.*[3] comprehensively documents the microfluidic advances made in liquid biopsy research. The authors not only discuss on-chip technologies for isolating and characterizing CTCs but also describe methods for the detection of circulating nucleic acids and isolation of exosomes. The coverage of the literature is quite extensive and should be a useful resource for the community. In a second review article by Hao and Zhang,[4] the authors provide an overview of advances in the synthesis, utilization, and clinical potential of magnetic nanoparticles for circulating cancer biomarker screening. The authors also discuss the technological challenges and unmet needs for manufacturing new magnetic nanomaterials with tunable physicochemical properties to achieve improved efficiency, accuracy, and sensitivity for cancer biomarker screening applications.

In the area of ctDNA, the article of Gwak *et al.*[5] is of interest as the authors developed a microfluidic device for the enrichment of circulating DNA in serum samples. They used microvortex principles to mix serum and magnetic particles, and gradient magnetic field to capture the DNA-coated magnetic particles in a single step. Flow conditions and separation protocol was optimized to achieve capture efficiency comparable to a commercial kit. Finally, the device was tested with blood from breast cancer patients, and ctDNA was extracted for downstream processing.

In recent years, exosomes have gained significant interest as important biomarkers for monitoring cancer metastasis because of their ability to carry tumor-derived cargos such as mRNAs and miRNAs.[6] In this regard, the article by Chen *et al.*[7] is an important contribution where the authors demonstrated an integrated microfluidic device for isolation and quantification of exosomes from breast cancer patient samples. Their strategy involved using on-chip valves for fluid control followed by immunomagnetic separation and concentration determination by spectrophotometry. The authors showed that their approach could detect exosomes in the blood of breast cancer patients with high sensitivity and specificity compared to healthy controls.

While increasing evidence from preclinical and clinical studies suggests a correlation between circulating tumor cell (CTC) clusters and worse cancer prognosis,[8,9] there exist few systems capable of purifying CTC clusters with clinically relevant throughput and purity. The article by Kamyabi *et al.*[10] reports an innovative microfluidic system that can process 1 ml of undiluted whole blood within 1 h for isolation and recovery of tumor cell clusters. The system, equipped with 10 000 unique cluster-capturing chambers, was capable of isolating clusters with a consistent capturing and releasing efficiency that were insensitive to the initial cluster concentration. The system's high efficiency in purifying intact and viable clusters highlights its potential for testing it with patient samples.

In addition to the development of new experimental methods for isolating and characterizing circulating tumor biomarkers, theoretical and computational approaches are also valuable to inform

on fundamentals of separation, and the design and optimization of microfluidic devices. The article by Aghilinejad *et al.*[11] describes a fruitful modeling approach to investigate the separation of deformable particles by deterministic lateral displacement (DLD) in the context of CTCs. The authors focus on separation efficacy at high Reynolds number to increase throughput. They provide a useful formula for practitioners to design DLD devices and find that cell deformability and vortices play an important role in defining particle trajectories.

The contributions highlighted in the "Microfluidics, Circulating Biomarkers and Cancer" Special Topic signify the growing interest in developing microfluidic methods for the isolation and characterization of circulating cancer biomarkers. Still, some challenges remain, including improving sensitivity, specificity, throughput, and ease of operation. These challenges will continue to engage the community in developing new microfluidic techniques and pursuing fundamental investigations to translate this knowledge to the clinic.

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