Diagnostic Applications and Methods to Isolate Circulating Tumor Cells (CTCs) from Blood
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Each year a million new cancer cases are diagnosed in the United States. Ninety percent of the deaths will be the result of metastasis, not from the primary tumor. Tissue biopsy is a universally accepted tool for cancer diagnosis and determination of treatment. The procedure varies, but is invasive, costly, and can be fatal, and for these reasons is seldom repeated after initial diagnosis. Monitoring of treatment response and for possible relapse is usually done by CT or MRI scan, both of which are expensive and require the tumor to change size perceptibly. Further, cancer can mutate or develop resistance to therapeutics and require modification of the treatment regimen. The initial tissue biopsy often cannot reflect the disease as it progresses, requiring new biopsy samples to determine a change of treatment. All carcinomas, about 80% of all cancer, shed tumor cells into the circulation, most often at the later stages when treatment is more critical. These circulating tumor cells (CTCs) are the cause of metastasis, and can be isolated from patient blood to serve as “liquid biopsy”. These CTCs contain a valuable trove of information that help both patient and clinician understand disease status. In addition to counting the number of CTCs (known to be a prognostic indicator of survival), CTCs can provide biomarker information such as protein expressions and gene mutations, amplifications, and translocations. This information can be used to determine treatment. During treatment, the number of intact and apoptotic CTCs can be measured on a repeated basis to measure the patient’s response to treatment and disease progression. Following treatment, liquid biopsy can be repeated at regular intervals to watch for relapse. Methods to isolate CTCs can be grouped into three categories: i) immunocapture based on surface markers of CTCs, ii) size exclusion based on CTC size, typically larger than blood cells, and iii) negative selection utilizing red blood cell lysis, white blood cell depletion or FICOLL. Various implementations of the CTC isolation methods will be presented.