High-volume microfluidics for cell-based diagnostics and therapeutics

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Advances of microfluidics technology now enables extremely high flow processing rate, leading the novel diagnostic and therapeutic applications. In this talk, I will introduce several unique diagnostic and therapeutic applications of high throughput microfluidic cell separation systems.

Microfluidic cell separation technologies have been used for various diagnostic applications, but its limited flow throughput has always been limiting its value. Low volume throughput of traditional microfluidic systems is especially detrimental for detection and recovery of low-abundance targets, such as circulating tumor cells (CTCs) and blood-borne pathogens. Often, low abundance of these targets requires the processing of at least 1mL~10mL of raw blood or other complicated biofluids, just to collect enough targets (often at the abundance level less than 1~100/mL) for downstream analysis. Recent advances in inertial microfluidics and other types of high-throughput cell sorting systems are used to enable various diagnostics. It is expected that the flow volume throughput can be further enhanced to enable extracorporeal blood circuit type therapeutic interventions (e.g. ECMO) in the future.

A. High throughput CTC (circulating tumor cell sorting from blood using inertial microfluidics

Using the novel technique of Dean Flow Fractionation (DFF)[1], low-abundance CTCs from metastatic cancer patients were collected without relying on antibody or capture agents, therefore allowing downstream cell analysis and culture. Because of the high volume throughput of the inertial microfluidic systems, one can process 7.5mL of raw blood within 10 mins[2].

B. Therapeutic Intervention to mitigate sepsis using microfluidic extracorporeal blood circuit

A biomimetic blood separation technique called cell margination has been used to continuously separated activated immune cells (neutrophils) and bacteria directly from the raw blood, for mitigation of sepsis in animal model (mouse with cecal ligation and puncture). A modest dose intervention was shown to exhibit significant reduction in inflammation and number of circulating activated neutrophils in the long term (day 5 from the intervention)

C. Bloodborne pathogen detection and drug-resistance profiling directly from the blood

The ability of DFF technology to collect and enrich rare cells directly from the blood can also be used for collecting bloodborne pathogens directly from the blood and analyze their identity (at ~100 CFU/mL) and drug resistance profiles (10^5 CFU/mL) much faster (~10hrs), without blood culture and nucleotide amplification. Further improvement of sensitivity is expected by optimizing cell separation and analysis protocols.

ACKNOWLEDGEMENT

This work was supported by SMART center (Singapore-MIT Alliance for Research and Technology Centre – BioSyM IRG), DARPA DLT (Dialysis-Like Therapeutics) program, and NIH.

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