

Microfluidics for Cancer Diagnosis and Precision Therapy

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There are approximately 5 billion cells in one milliliter of blood with red blood cells (RBCs) accounting for >99% of all cellular components. Besides blood constituents, pathogenic microorganisms or diseased cells can also be present in peripheral blood. In fact, this is of clinical significance as their presence in blood can present possible routes for disease detection, diagnosis and even therapy. However, the presence of the large number of RBCs complicates disease diagnosis such as in the detection of rare circulating tumor cells (CTCs) in blood of cancer patients. Here, we address these issues and demonstrate that physical biomarkers such as cell size and deformability can be effectively used for cancer cell detection for diagnosis as well as for precision therapy from peripheral blood. Here, we made use of microfluidics due to its many inherent advantages such as high sensitivity and spatial resolution, short processing time and low device cost. We developed a suite of microfluidic biochips that exploit the principles of size/deformability based separation as well as inertial focusing to allow for high throughput continual detection and separation of CTCs. We will showcase examples of diagnosis of cancer via the detection and retrieval of CTCs from peripheral blood of patients via a routine blood draw (aka liquid biopsy) as well as enabling precision therapy through microfluidic culture and drug evaluation of patient derived CTCs. These simple, efficient and cost effective microfluidic platforms will be imperative in effective and specific enrichment of clinical samples for subsequent downstream molecular analyses, expansion and culture. Some of these devices have since been commercialized.

References

1. Lim, SB, NV Menon, CT Lim, Microfluidic Diagnostics: Tiny Device, Big Applications, 21:e49749 EMBO Reports, 21, e49749, 2020.
2. Lim, SB, WD Lee, J Vasudevan, WT Lim, CT Lim, Liquid biopsy: one cell at a time, npj Precision Oncology, 3, 23, 2019.
3. Lim, SB, T Yeo, WD Lee, AA Bhagat, SJ Tan, DSW Tan, WT Lim, CT Lim, Addressing Cellular Heterogeneity in Tumor and Circulation for Refined Prognostication, PNAS, 116, 36, 17957-17962, 2019.
4. Ramanathan, V, RH Soon, P Zhang, K Jiang, CT Lim, Cancer diagnosis: From tumor to liquid biopsy and beyond. Lab on Chip, 19, 11-34, 2019.
5. Khoo, BL, G Greci, YB Lim, SC Lee, JY Han, CT Lim, Expansion of patient-derived circulating tumor cells from liquid biopsies using a CTC microfluidic culture device. Nature Protocols, 3, 34-58, 2018.
6. Lim, SB, SJ Tan, WT Lim, CT Lim, Integrative genomic approach identifies a 29-gene extracellular matrix-related prognostic and predictive indicator (EPPI) for early-stage non-small cell lung cancer, Nature Communications, 8, 1734, 2017.
7. Wang, X, F Kong, JC Yeo, L Yu, S Sonam, M Dao, X Gong, CT Lim, Soft tubular microfluidics for 2D and 3D applications. PNAS, 114, 10590-10595, 2017.
8. Warkiani, ME, BL Khoo, L Wu, AKP Tay, AAS Bhagat, J Han, CT Lim, Ultra-fast, label-free isolation of circulating tumor cells from blood using spiral microfluidics. Nature Protocols, 11, 134-148, 2016.
9. Yeo, T, SJ Tan, CL Chew, DPX Lau, YW Chua, SK Sai, I Gopal, GS Tan, TKH Lim, DSW Tan, WT Lim, CT Lim, Microfluidic enrichment for the single cell analysis of circulating tumor cells. Scientific Reports, 6, 22076, 2016.
10. Hou, HW, ME Warkiani, BL Khoo, ZR Li, RA Soo, DSW Tan, WT Lim, JY Han, AAS Bhagat, CT Lim, Isolation and retrieval of circulating tumor cells using centrifugal forces. Scientific Reports 3, 1259, 2013.