Microfluidic devices for the interrogation of single circulating tumor cells

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Abstract 367
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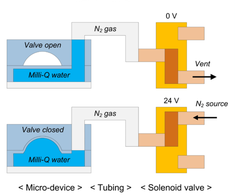
Introduction

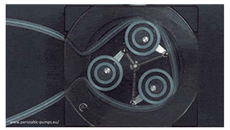
Genetic and phenotypic characterization of Circulating Tumor Cells (CTC) offer the opportunity for a "real time liquid biopsy". Heterogeneity and rarity of CTCs command the need for individual cell characterization. Following an enrichment procedure of CTC from blood, the identification, isolation and manipulation of single cells for further analysis without cell loss remains challenging. Here, we present microfluidic devices for parallel single cell whole genome amplification (psc WGA) and parallel probing of drug response of single cancer cells (psc probing).

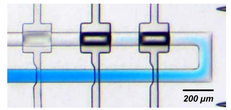
Microfluidics

Valve

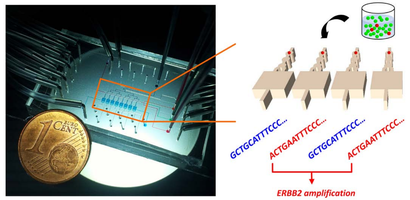


Peristasltic pump



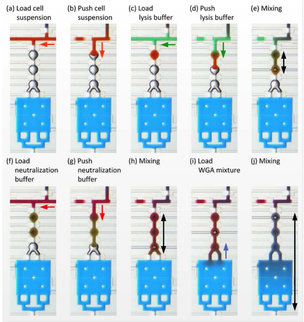


Parallel Single Cancer Cell Whole Genome Amplification

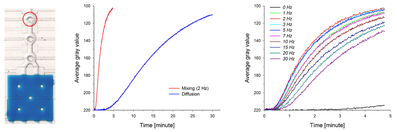


Single cancer cells were addressed in 8 individual reaction chambers, subsequently lyzed, and their DNA amplified on-chip. Button-valve assisted mixing performed WGA in 23 nl.

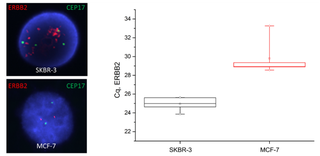
Experimental scheme



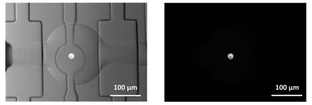
Button valve assisted mixing efficiency test

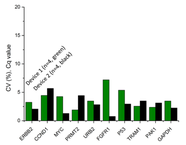


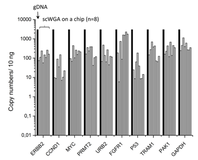
On-chip single cell whole genome amplification



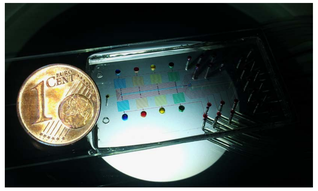
Single cell in a chamber





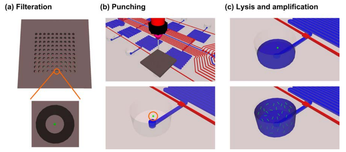


Whole Genome Amplification Using Self-seeding Micro-wells

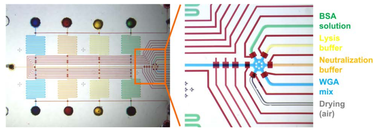


For WGA of CTC present in a large number of other cells, we developed a scWGA platform by combining a self-seeding microwell plate and a microfluidic device. We demonstrated that deposition of 1 ml of leukocyte depleted-whole blood on the micro-well plate, isolation of individual tumor cell, lysis and DNA amplification in a microfluidic chamber.

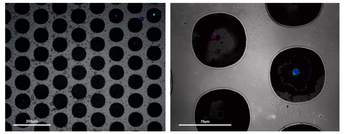
Experimental scheme



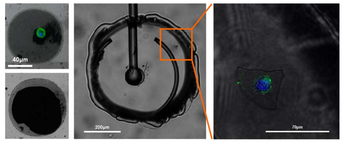
Device design



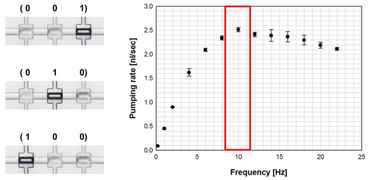
Cells in micro-wells



Single cell isolation

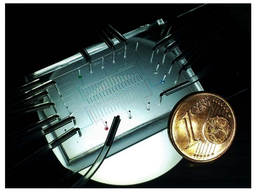


Peristaltic pump



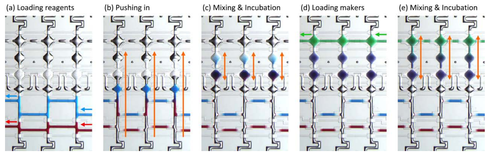
Pumping rate: 2.5 nl/sec at 10 Hz

Drug Dose Response on Single Cancer Cells

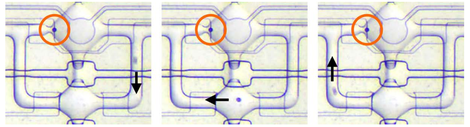


The microfluidic device is designed and developed for capturing single cells, dosing various concentrations of drugs and exposing the cells to the drugs.

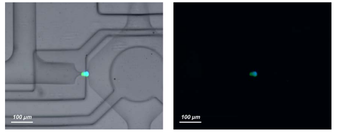
Experimental Scheme



Micro-particle capturing



Single cell capturing



Conclusion and Outlook

We successfully developed microfluidic devices for individual CTC characterization. For genetic make-up, whole genome amplification of single cells either in suspension or in a self-sorting microwell plate was demonstrated. On-chip cell lysis and DNA amplification were performed and validated by qPCR targeting specific genes. In addition microfluidic devices were designed and tested to investigate single cell response to cancer drugs.

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