An Integrated Microfluidic Platform For Size-Selective Single-Cell Trapping

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OTHER INFORMATION

KEYWORDS

Microfluidic platform, Cell separation, Single-cell analysis, Hydrodynamic focusing, Microfluidic array

CATEGORIZED AS

- **Biotechnology**
  - Other
- **Medical**
  - Research Tools
- **Research Tools**
  - Other
- **Sensors & Instrumentation**
  - Other

BRIEF DESCRIPTION

Researchers at the University of California, Irvine have developed a fully integrated microfluidic platform that is configured to separate and isolate single cells. The invention uses hydrodynamic filtration to isolate targeted cells of various sizes. Once the single cells are isolated and sorted, they can be studied individually in a purer state free from other contaminating or unwanted cells.

The system does not use biochemical “labels” to identify target cells. It is a label-free separation technique.

FULL DESCRIPTION

Studying single cell populations allows one to better understand the complexity of the cells and to perform scientific experiments to learn how those cells adapt, replicate, respond to stimuli, and function. Isolating cells from unwanted and contaminating cells is therefore desirable in order to obtain cells to perform further research or experiments on in order to learn more about the cells and to find additional applications for them.

There are a variety of cell separation and sorting techniques currently available. Some techniques use an additional biochemical “label” to identify target cells. On the other hand, label-free separation techniques separate cells without using labels and allows the intrinsic physical property of cells to be intact.

There are several label-free cell techniques available which use microfluidic systems including micropore filtration, hydrophoresis, deterministic lateral displacement (DLD), pinched-flow fractionation, and inertial separation under a higher Reynolds number. Microfiltration is currently the simplest and least expensive method for separating cells based on size or deformability. These techniques have a number of applications such as filtering, sorting, and separating tumor cells (CTC), blood cells, and bacterial cells.

Current techniques suffer from numerous disadvantages. They are only capable of separation with a single attenuation diameter. This drawback inhibits efficient separation of specific-sized cells from the cell suspension with heterogeneous size distribution. Another drawback is that most microfiltration devices can only be used for bimodal separation with a single diameter. These disadvantages hinder efficient separation of complex biological samples, which include heterogeneous mixtures of multiple micro particle components.

The invented system is a fully integrated microfluidic platform that is capable of size-selective cell separation based on hydrodynamic filtration and provides for highly effect entrapment of single cells. The invented system can be embodied in a single device.

The system uses different sized microfilters which are used to remove large (25 μm) and small (5μm) particles in sequences, so that continuous separation of a targeted intermediate size (15 μm) population can be achieved. These separated microparticles can then be isolated individually in downstream microfluidic trapping arrays under the application of a reverse flow. This system allows for more efficient separation and recovery of medium sized microparticles and cells, and also facilitates the individual trapping of target cells without moving parts or external forces.

SUGGESTED USES

Separating, isolating, and sorting cells

ADVANTAGES

1) The invention is efficient at cell separation. It can efficiently separate specific-sized cells from cell suspensions with heterogeneous size distributions. The invention’s micopore filters can be altered to handle different diameters.

2) The invention can be easily integrated with downstream dielectrophoresis (DEP) electrodes for cell separation based on their viability and impedance analysis.

3) The invention does not use external forces. The continuous separation of micro particles requires only two inlets for sample delivery which simplifies micro particle introduction without external force associated with electric, magnetic, acoustic or optical sensors.

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	10,526,595	01/07/2020	2015-806
United States Of America	Issued Patent	9,862,941	01/09/2018	2015-806

RELATED CASES

2015-806-0

STATE OF DEVELOPMENT

There are plans for further prototyping and testing.

TESTING

An experiment was performed to isolate mammalian cells from a mixture of HeLa cells, which consisted of 5 and 25 μm diameter microparticles. The particles were filtered and successfully captured.

RELATED MATERIALS

» Melinda G. Simon, Ying Li, Janahan Arulmoli, Lisa P. McDonnell, Adnan Akil, Jamison L. Nourse, Abraham P. Lee, and Lisa A. Flanagan, "Increasing label-free stem cell sorting capacity to reach transplantation-scale throughput", AIP ID: 010406BMF, Biomicrofluidics, November 2014 - 11/20/2014

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