High-Throughput Microfluidic Gene-Editing via Cell Deformability within Microchannels

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OTHER INFORMATION

KEYWORDS

biotechnology, gene therapy, microfluidic, gene editing, soft lithography, intracellular delivery, SLIPS functionalization, immunotherapy, gene modification, gene editing, microchannels, nanomaterials, microchannels, anti-fouling, gene delivery

CATEGORIZED AS

- **Biotechnology**
  - Genomics
- **Engineering**
  - Engineering
- **Materials & Chemicals**
  - Nanomaterials
- **Medical**
  - Disease: Genetic Diseases and Dysmorphic Syndromes
  - Gene Therapy
  - Therapeutics
- **Nanotechnology**
  - Materials
  - NanoBio
  - Tools and Devices
- **Research Tools**
  - Cell Lines

SUMMARY

UCLA researchers in the Departments of Pediatrics and Chemistry & Biochemistry have developed a microfluidic device for delivery of biomolecules into living cells using mechanical deformation, without the fouling issues in current systems.

▶ Nucleic Acids/DNA/RNA

RELATED CASES

2017-109-0

BACKGROUND

Gene therapy and gene modification technologies are increasingly being studied and developed for clinical applications. One of the main limitations towards realization of these types of technologies is an efficient, cost-effective means for insertion of genetic material into the cell, or transfection. Current gene delivery systems, such as viral vectors or electroporation, are limited by cost, difficult scale-up and time-intensive processing. Intracellular delivery of biomolecules by cell membrane deformation within microfluidic devices has been demonstrated previously, where target cells are temporarily deformed as they pass through channels. In the deformed state, gene-editing biomolecules (e.g., CRISPR-CAS9 constructs, RNA/DNA, enzymes) are able to pass through the cell membrane. However, this technology is largely limited by the accumulation of biomatter on channel surfaces, known as fouling, resulting in clogged devices.

INNOVATION

The inventors have designed a microfluidic device for cell transfections that is able to circumvent the issues of fouling and clogging. The inner surfaces are covered by an omniphobic slippery liquid layer coating and also contain anti-fouling nanofeatures. This strategy estimates a transfection rate of 50,000 cells/sec, which is significantly faster than the current gold standards of viral vectors and electroporation.

APPLICATIONS

- Use in gene therapy to deliver gene editing-related biomolecules to cells (CRISPR/Cas9)
- Live-cell protein labeling and imaging
- Immune cell activation for cancer immunotherapy
- Delivery of small-molecule drug candidates

ADVANTAGES

- No fouling or clogging of channels
- Scalable and compatible using current manufacturing processes
- Faster and less toxic than current methods of cellular transfection
- Could prepare all the cells necessary for a 12-kg child’s gene-modified bone marrow transplant in one hour, instead of many hours and additional processing steps

RELATED MATERIALS

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- D’Onofrio, T. “G., et al. “Controlling and measuring local composition and properties in lipid bilayer membranes.” J. Bio. Phys. 28, 605-617 (2002).
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PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	11,999,931	06/04/2024	2017-109
Germany	Issued Patent	60 2017 062 465.9	10/05/2022	2017-109
European Patent Office	Issued Patent	3500662	10/05/2022	2017-109
France	Issued Patent	3500662	10/05/2022	2017-109
United Kingdom	Issued Patent	3500662	10/05/2022	2017-109

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- Determining Oil Well Connectivity Using Nanoparticles

- Multiple-Patterning Nanosphere Lithography
- High-Throughput Intracellular Delivery of Biomolecular Cargos via Vibrational Cell Deformability within Microchannels
- Scalable Lipid Bilayer Microfluidics for High-Throughput Gene Editing
- Guided Magnetic Nanospears For Targeted And High-Throughput Intracellular Delivery

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