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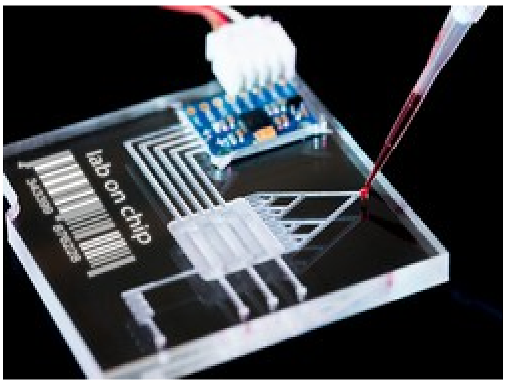
Integrated Microfluidic System for Long-Term Cell Cultivation, Monitoring and Analysis

Results in Brief

A new era for single-cell analysis using microfluidic systems

Droplet microfluidics technology has emerged as a powerful tool for biomedical and biological research. A study, supported by FP7 program, expanded its applications by offering a precise control over the cultivation and analysis of single cells at unprecedented resolution and throughput.

HEALTH



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Droplet microfluidics promises to bring an unparalleled level of cellular microenvironment control using only minute amounts of samples. However, the vast majority of cell-based microfluidic devices available today are still in the proof-of-concept state. In addition, there is no system that supports long-term cell growth in well-controlled conditions and allows reproducible and sequential operations in an automated fashion.

Dr. Linas Mazutis, supported by the EU-funded BIOCELLCHIP (Integrated microfluidic system for long-term cell cultivation, monitoring and analysis) project set out to develop a high-throughput microfluidic system for single-cell isolation and analysis. Among different microfluidic systems developed during this project, two of them have brought particularly high impact.

The first BIOCELLCHIP microfluidic system provides spatiotemporal control over the biochemical and physical environment of the isolated cells. The microfluidic bioreactor was used to reproduce the bone marrow niche ex vivo and study megakaryocyte adaptation, offering a unique opportunity to recreate complex physiological organs on a chip. Using this system, researchers optimised platelet production from megakaryocytes derived from induced pluripotent stem cells. The system was patented and delivered to the market through a spinoff biomedical company. Considering the particularly high demand for donor independent platelets in hospitals, the developed bioreactor will likely find immediate applications in the future.

The second BIOCELLCHIP microfluidic system provides an innovative approach for simultaneous barcoding and sequencing of tens of thousands of single-cells. The concept is based on massively parallel single-cell isolation into microscopic aqueous compartments (nanoliter droplets) together with barcoded oligonucleotide primers and other biochemical reagents. Once cells are encapsulated they get lysed and their mRNA molecules are tagged (barcoded) during reverse transcription reaction, followed by next-generation sequencing and computational analysis. Researchers utilised the system to sequence over 10 000 individual embryonic stem cells at an extremely low cost. Their results helped them identify the presence of rare sub-populations expressing markers of distinct lineages. Moreover, they observed that certain transcription factors fluctuated across the entire cell population, and could be associated with distinct cellular states. The developed system was eventually patented and commercialized through a second spinoff company.

Overall, both microfluidic systems are expected to revolutionise biomedical research in different areas, providing a high-throughput approaches for studying key cellular processes and cell heterogeneity with high precision and reduced cost.

Keywords

Droplet microfluidics technology | single-cell sequencing | RNA-Seq | barcoding | induced pluripotent stem cells | platelet

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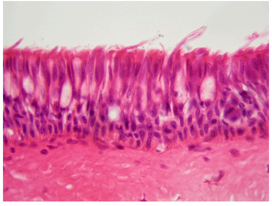

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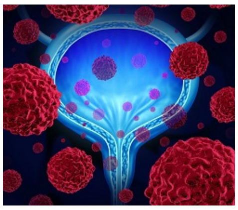

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