# New microfluidics platform separates cell types for RNA profiling

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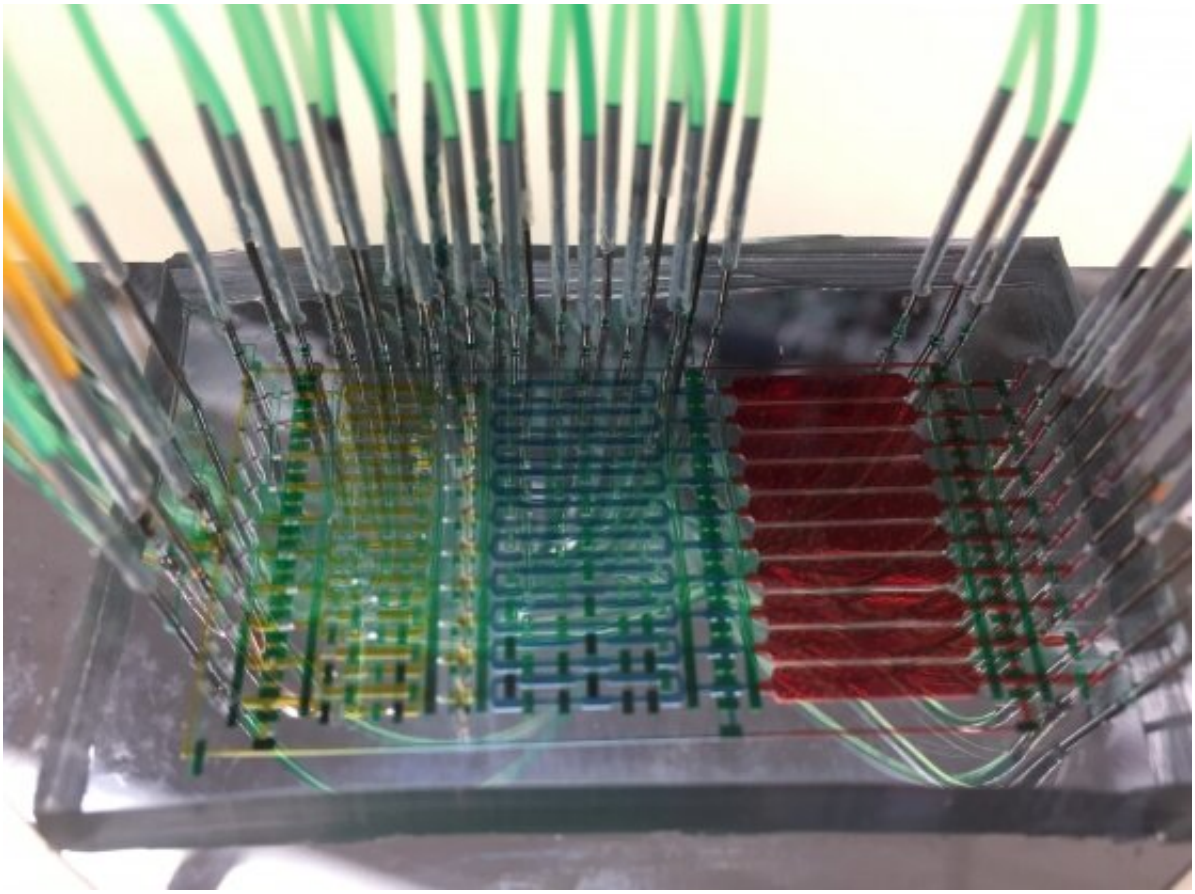

Credit: Miguel Reyes

A team led by scientists at the Broad Institute, MIT, and Massachusetts General Hospital has developed a prototype device that uses microfluidics to sort cell types extracted from clinical samples for RNA

sequencing.

"This platform allows us to isolate specific cell subsets in a sample, so we can perform RNA sequencing and address biological questions in different cell types," explained first author Miguel Reyes, a graduate student researcher at the Broad Institute and PhD candidate at MIT. "We've condensed this complicated pipeline into a single, more accessible device, with the potential to scale up for studies that require large cohorts—an aspect that many analysis tools have struggled with."

The work appears in *Science Advances*, led by Reyes and senior authors Paul Blainey, core member at the Broad Institute and associate professor in the Department of Biological Engineering at MIT, and Nir Hacohen, institute member at Broad, director of the Center for Cancer Immunotherapy at Massachusetts General Hospital, and associate professor at Harvard Medical School.

The team developed their platform to help researchers analyze cells at greater resolution. For blood and other types of clinical samples, bulk RNA sequencing—in which all cells from a single sample are analyzed together—is a standard analysis. However, using this method on mixtures of diverse cells provides limited information on specific cell types.

This new platform can potentially fill the gap between bulk RNA sequencing of blood samples and high-resolution, single-cell RNA sequencing—a process that is still difficult to scale up for large numbers of samples.

By integrating the cell-sorting process into a single device, the platform removes the need to acquire, program, and monitor complex liquid-handling robots, or integrate multiple instruments into the workflow, according to the researchers. The team benchmarked their system

against standard approaches, usually implemented manually, for cell subset purification and RNA-seq library construction, and found that it performed equally well or better while being more resource-efficient.

As a pilot analysis, the researchers also sorted and sequenced immune cells from five patients with systemic lupus erythematosus and five healthy control individuals at Brigham and Women's Hospital. They used the platform to isolate CD4+ T cells, CD8+ T cells, B cells, and CD14+ cells, and determined that a classic lupus gene expression signature is expressed primarily in B cells.

"There are literally millions of blood samples that have been profiled solely in the form of whole blood, without any cell separation—and it's difficult to ask questions about the different cell types with only that kind of data," said Hacohen. "The field needs a cost-effective way to turn the whole-blood samples into subsets of cells that can be analyzed on their own."

The team envisions a pipeline in which single-cell analysis could be used first on an initial batch of samples as an unbiased discovery tool. "A team could then use a platform like this to isolate the types they want to study—on a scalable level, potentially in large cohorts where single-cell isn't yet feasible," said Blainey. "We've shown that the miniaturization and process integration for this type of work is possible."

**More information:** Miguel Reyes et al. Multiplexed enrichment and genomic profiling of peripheral blood cells reveal subset-specific immune signatures, *Science Advances* (2019). DOI: 10.1126/sciadv.aau9223

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