Sphere Fluidics Ltd.
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Accelerating biologic drug discovery with picodroplet technology

By improving single-cell analysis, Sphere Fluidics' microfluidics technology is providing new options for antibody discovery and cell-line development.

Picodroplet technology can be used to find rare and valuable variants within heterogeneous cell samples, which makes it well suited for disease research and the discovery of novel biotherapeutics. With intense competition and unmet medical needs pushing researchers to work faster and more efficiently, the streamlining effect of picodroplet technology on antibody discovery and cell-line development is invaluable. Use of the method accelerates drug discovery by increasing throughput, miniaturization, and improving single-cell analysis.

The approach uses novel microfluidics to produce millions of picoliter-volume droplets (called picodroplets) in oil at rates of more than 100,000 per minute. Each picodroplet serves as a miniature test tube housing single cells that, once stabilized using surfactants, remain viable, metabolize, and divide. These picodroplets can be manipulated in a variety of ways, including through picodroplet incubation, sorting, dispensing, splitting, and fusion.

Researchers currently use this approach to measure secreted proteins, perform single-cell analysis, isolate rare cells, and improve yields of therapeutic antibodies. Picodroplet manipulation could also facilitate the rapid and controlled generation of precision-engineered cell libraries via the addition of a gene-editing complex to each individual cell.

These processes are vital components of research in therapeutic discovery and development, and R&D pipeline trends suggest that they will be increasingly important in years to come.

Six of the world's 'top 10' drugs are biopharmaceuticals. Engineered cell therapies are currently being tested in many clinical trials, and gene-edited cells are being used throughout the pharma industry to aid in the discovery and development of new drugs. Researchers in these fields used to have to make do with technologies such as clone pickers, fluorescence-activated cell sorting (FACS), and the traditional limiting dilution approach, but they now have access to a picodroplet method that addresses the shortcomings of these legacy approaches.

Advantages of picodroplets

The legacy approaches have some shared shortcomings. Methods involving limiting dilutions and clone pickers are time consuming, with the former being particularly slow and laborious. At 3–4 weeks per run, clone pickers are faster than limiting dilutions, but they are still relatively slow, and they cannot be used for B cell work. Similarly, FACS requires trained staff, does not allow cell secretion assays, and, owing to the high shear stresses involved, can yield inferior cell outgrowth.

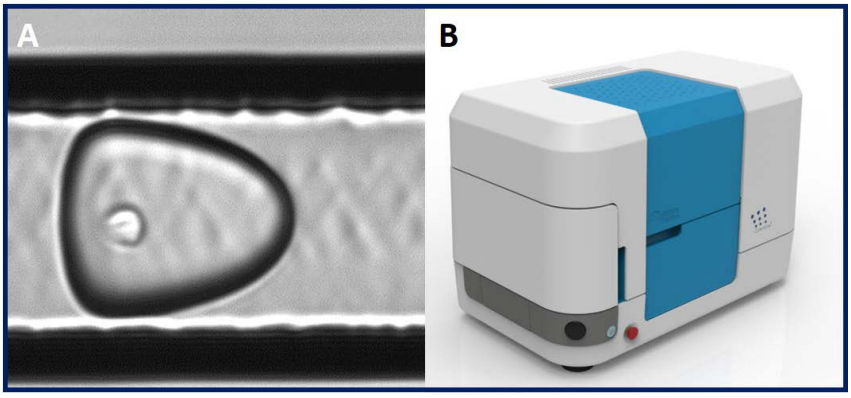

Figure 1: Cyto-Mine is the first integrated device to rapidly and automatically measure secreted protein from individual cells to identify rare and valuable variants. (a) A picodroplet containing a single cell prior to being dispensed into a single well of a microtiter plate. (b) The Cyto-Mine Single Cell Analysis and Monoclonality Assurance System.

Sphere Fluidics' picodroplet technology is the next stage in single-cell analysis. The approach can significantly reduce or even eliminate all of the legacy drawbacks in terms of cost, monoclonality efficiency, ease of use, integration, and ability to perform cell secretion assays. A run takes about half of a working day and screens more than 1 million cells. Clone pickers, in contrast, can take several weeks to perform 10,000-cell runs. The monoclonal efficiency of picodroplet technology is targeting 99.99%, which represents a significant enhancement over all other techniques.

Importantly, picodroplet technology achieves these improvements while minimizing the shear forces applied to cells. This results in a higher proportion of viable cells during single-cell sorting than is possible with FACS. The viability of cells remains constant throughout their encapsulation and their distribution in picodroplets.

Once single cells are encapsulated, scientists can use the technology to obtain accurate measurements of secreted molecules. A fluorescence-based optical detection methodology, followed by sorting, enables the rapid identification and isolation of cells that produce high levels of antibodies or that have a specific antibody profile, giving researchers a way to home in on those most likely to deliver the desired end result.

Researchers can also use picodroplet technology to precisely manipulate and combine single cells with other reagents, including other cells, viruses, or gene-editing tools such as CRISPR–Cas9.

The Cyto-Mine platform

Many biopharmaceutical companies have deployed a range of single-cell analysis platforms, but their utility has been constrained by the cost and unwieldy nature of the current technology.

Current platforms consist of multiple pieces of large, non-integrated equipment. The installation of such a system costs at least $750,000, and consumables and labor add significant additional costs. Once the system is installed, it can take up to four months to deliver a lead drug.

Sphere Fluidics is on the cusp of rendering such non-integrated systems obsolete. In the first half of 2017, the company will introduce Cyto-Mine, an integrated platform for the discovery and development of monoclonal antibodies and other biologics. The small-footprint platform carries a capital expenditure cost of around $450,000.

Cyto-Mine also cuts the time to the delivery of lead drugs to 1–2 months, works with all cell types (e.g., B cells, hybridomas, and Chinese hamster ovary cells) and dramatically reduces the cost of consumables by 14-fold. These time and cost savings will allow researchers to get antibodies and other drugs into the clinic and approved for patient use sooner.

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