SEED • Biosciences

DISPENCELL All-in-One: Industrial Validation for Cell Line Development

In collaboration with Biotech Process Sciences, Merck Biopharma, Corsier-sur-Vevey, Switzerland

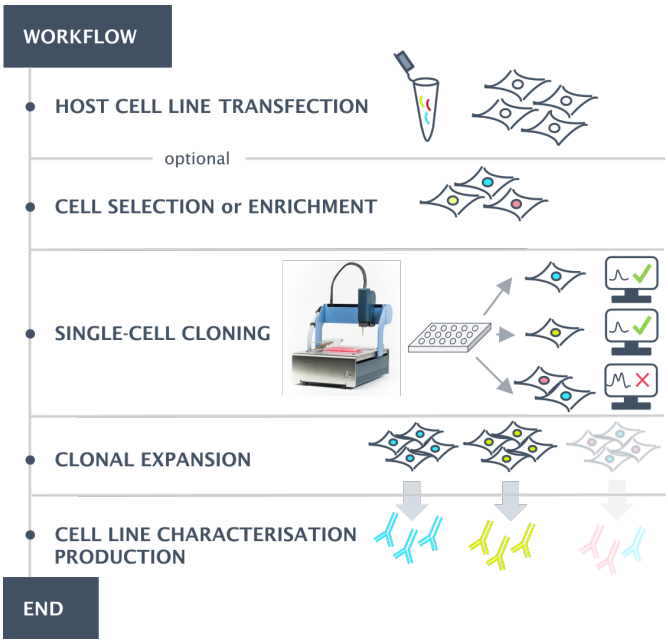

Figure 1: *Workflow for cell line development with DISPENCELL.*

Introduction

- In the development of industrial cell lines, the challenge is to deliver proof of clonality, to ensure a consistent supply and sufficient quality of the protein of interest (Fig.1).

- Limited dilution based on Poisson's equation is time-consuming and inefficient. Recently, single-cell sorters, printers and microfluidic systems have increased throughput and efficiency, but with limited ease of use, rapidity, efficiency and with a negative impact on cell integrity.

DISPENCELL All-in-One is a new solution for gentle and traceable single-cell isolation, consisting of:

- An impedance-based pipetting robot, for automated single-cell dispensing.
- A sensing tip (disposable to prevent contamination).
- Software for post-processing and quality control.

Material and Methods

- Single cells were isolated from a pool of CHO-K1 expressing IgG and dispensed in a 384-well plate using DISPENCELL. Each well then was imaged and cells were counted by two operators (Fig.2).

- The robustness of the peak detection software and the reliability of the impedance-based monoclonality report were assessed through comparison with an imager (Celigo).

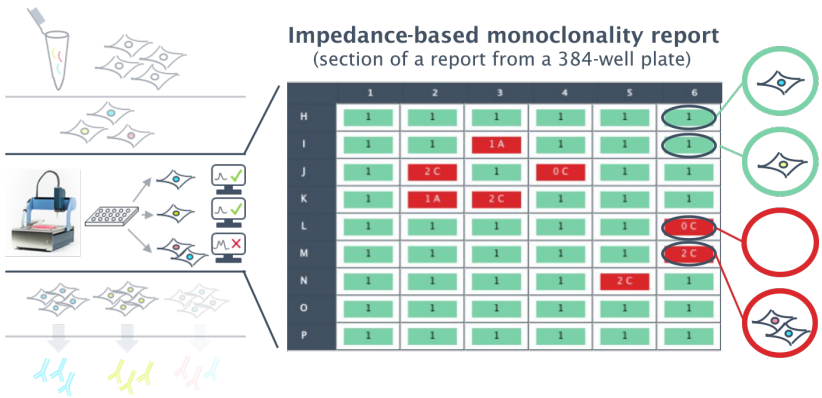

Figure 2: *Example of an impedance-based monoclonality report by DISPENCELL. Green wells contain 1 cell. Red wells contain 0 or >1 cell and should be discarded.*

Results

- When a cell passes through the tip, an impedance signal is recorded (Fig.3). A single cell corresponds to an impedance peak (TOP). For doublets or multiple cells, the impedance signal shows a typical doublet signature (BOTTOM).

- DISPENCELL software provides **well mapping**:
  - Monoclonal (1 cell; GREEN).
  - To be discarded (0 cells or >1 cell; RED).

Among 96 wells, 95% had 1 cell, 1% had >1 cell, 4% were empty (Fig.4), **with a 98.7% probability of monoclonality** (number of wells with 1 cell / number of wells with ≥1 cell).

- The software reports the time per plate (42 min) and the plate-filling rate (82%, N=2 plates).

- Compared to the manual analysis, the automated peak analyser resulted in 93% of reliability demonstrating the **robustness of the automated analyser**.

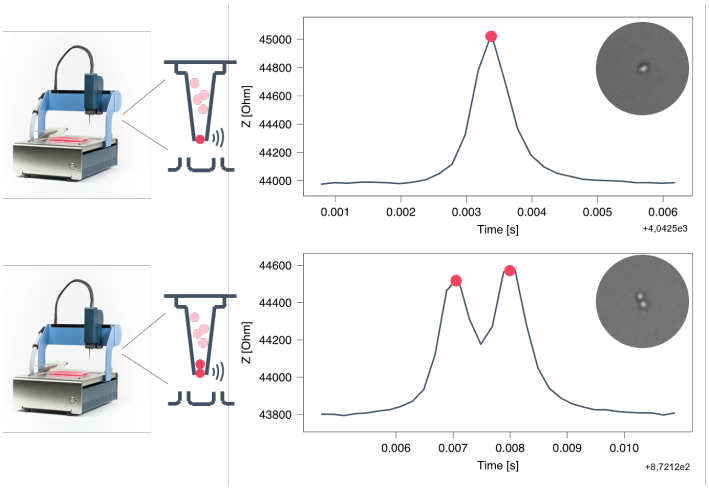

Figure 3: *TOP: Single-cell signature and picture (Well K7). BOTTOM: Doublet signature and picture (Well G21).*

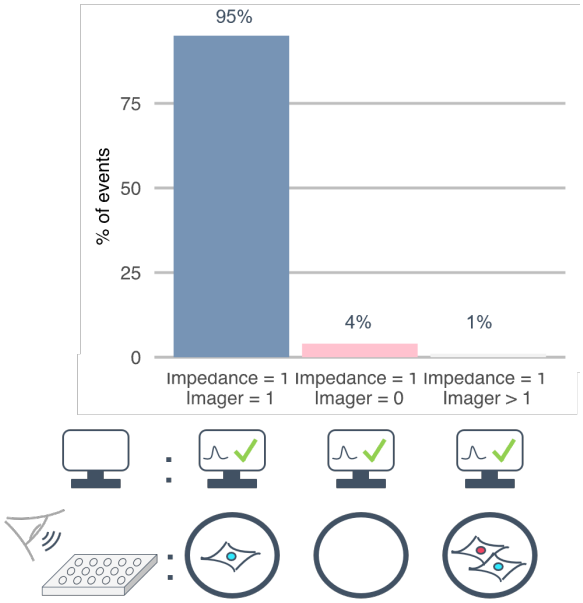

Figure 4: *Correlation between the number of cells per well assessed by impedance (DISPENCELL) vs imager (Celigo) after a dispensing experiment (N= 2 plates).*

References

- *Bonzon, D. et al. (2020) 'Impedance-Based Single-Cell Pipetting', SLAS TECHNOLOGY, 25(3), pp. 222–233.*
- *Muller, G. et al. (2020) 'Traceable Impedance-Based Dispensing and Cloning of Living Single Cells', SLAS TECHNOLOGY, 25(3), pp. 215–221.*
- *Hannart, H. et al. (2021) 'Traceable Impedance-based single cell pipetting: from a research set-up to a robust and fast automated robot', SLAS TECHNOLOGY. In Press.*

DISPENCELL is a convenient, easy-to-use and cost-effective single-cell dispensing alternative to limiting dilution. The practicality of the system and the robustness of the impedance profile are adapted for stringent quality control, as required for industrial cell line development.

For early selection of good producer cells, DISPENCELL could be combined with a FACS or fluidic pre-enrichment step. For monoclonality assessment, DISPENCELL combined with imaging would provide **two independent proofs of single-cell presence**.

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