

ENABLING NEXT-GENERATION CELL LINE DEVELOPMENT USING CONTINUOUS PERFUSION AND NANOFUIDIC TECHNOLOGIES

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The manufacturing process for a biologic begins with establishing a clonally derived, stable production cell line. Generating a highly productive cell line is time and resource intensive and involves screening of a large number of candidates. While miniaturization and automation strategies can reduce resources and increase throughput, they have matured and recent advances have been incremental. With increasing pressure on time to commercialization and the increasing diversity and complexity of therapies in discovery research, there is a need to transform cell line development to accelerate patient access to novel therapies and nanofluidic technology are on potential solution. In this study, we present cell line development data on the Berkeley Lights integrated platform. Cells are manipulated at a single cell level through use of OptoElectronic Positioning (OEP) technology which utilizes projected light patterns to activate photoconductors that gently moves cells. Common cell culture tasks can be programmed through software allowing thousands of cell lines to be cultured simultaneously. Cultures can be interrogated for productivity and growth characteristics while on the chip at ~100-fold miniaturization and continuous perfusion of cell culture medium enables effective and robust cell growth and product concentration despite starting from a single cell. Concepts from perfusion culture are also applied to measure productivity and product quality. We demonstrate that commercial production CHO cell lines can be cultured in this nanofluidic environment and show that sub clone isolation, recovery, and selection are achieved with high efficiency. Overall, this technology has the potential to transform cell line development workflows through the replacement of laborious manual processes with nanofluidics and automation, and can ultimately enable the rapid selection of high performing cell lines.