Optofluidics aids cell line development for antibody-based therapies

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June 15, 2020 -- Implementation of optofluidics in cell line development can help advance multiple lead candidate molecules with increased screening capacity. A researcher from GlaxoSmithKline (GSK) discussed how her team uses an optofluidic system in a June 15 presentation at the BioProcess International Spring Digital Week's 2020 virtual meeting.

In the talk, speakers from pharmaceutical giant GSK and optofluidics developer Berkeley Lights discussed how GSK is using the Beacon optofluidic system from Berkeley Lights to advance its drug development activities, in particular cell line development.

Beacon has not only helped GSK meet all of its product development milestones, but has also shaved three months off critical path timelines.

Putting light to work

Berkeley Lights was co-founded in 2011 by University of California, Berkeley, electrical engineer Ming C. Wu, PhD, based on the development of optofluidics technology that uses light to gently move cells around on nanofluidic chips. Now, the company's Beacon optofluidic system can be used to efficiently identify cell lines secreting both traditional and nontraditional antibody-based molecules in under one week.

Using the Beacon technology for cell line development can reduce workflow timelines from eight to 12 weeks for well-plate-based workflows to five days for Beacon Opto cell line development, according to the company. Cells are grown on nanofluidic chips with small volumes within NanoPen chambers (100,000 times smaller than microwells). The properties of the chambers allow media and reagents to freely flow in and out while cells stay in place. On-chip enrichment allows for the production of various desired phenotypes which can be sorted by cell markers such as size or viability. Clones can be grown on each chip in just a number of days and cells are recovered via manipulation of light.

Monoclonal antibodies act as specific protein targets for diseases such as autoimmune diseases, infectious diseases, and cancer. Traditionally, monoclonal antibodies are produced from fusions of antibody B cell lymphocytes with myeloma cells and a single epitope.

Recently, nontraditional complex antibodies including antibody fragments, multitarget antibodies, and bispecific antibodies are being developed for use in antibody-based therapies. These molecules are notoriously difficult to clone. Despite the barriers to production of the molecules, Berkeley Lights collaborators from the University of Queensland have used the Beacon system to develop a recombinant spike protein for its COVID-19 vaccine, according to product manager Anupam Singhal, PhD.

Regardless of candidate, the Beacon Spotlight assay enables quantitative antibody titer measurements on thousands of clones for selection purposes. When using the Opto cell line development workflow, the company assures 99% monoclonality (genetic identity).

Case study of implementing Beacon in cell line development

The clonality assurance of the Beacon technology was one of the features that was attractive to a group of bioprocess researchers at GSK, led by Robyn Emmins, PhD. In order to provide characterization of cell lines to support molecule candidate selection under ever-decreasing timetables, the team became one of the first commercial companies to implement Beacon technologies into their cell line development workflows in 2017.

Within what Emmins calls "original" cell line development workflow, which was a low-throughput and high-resource system, she identified shake flask evaluations as a main bottleneck for production. To address this concern, GSK invested in a Sartorius Ambr15 cell culture system that allowed for high-throughput automated microbioreactor cultivations. The increased bioprocessing capacity spurred the need for a new cloning system to complement the increased throughput of the cell culture technology.

To begin integrating Beacon technology into GSK cell lines, the team conducted a series of proof-of-concept studies. With these tests, they were able to determine that transfection of their cell lines is very sensitive in the Beacon system and clones must be screened early. They were able to use the Beacon Spotlight assay to determine antibody binding of several GSK modalities. Ultimately, the team determined that if they started with a high-quality cell line, the Beacon technology could assist them with improved cell line generation by improving productivity.

Since implementing the Beacon technology, the team has worked on optimizing the system in their workflow. Beacon is able to deliver 1.2 times greater cloning efficiencies compared to fluorescence-activated cell sorting (FACS)-based processes with lower variability.

Moreover, Beacon isolates more than five times as many clones per project compared to older workflows. Whereas FACS processes supported only a single lead molecule per project with around 300 clones, Beacon on-chip Spotlight assay has doubled to tripled the team's screening capacity with multiple leads (8 leads with screens over 800 clones per lead). In combination with other factors, a 90% success growth post-export has enabled the team to progress candidates more rapidly than ever before.

Another area of optimization that the GSK team is working toward is data management. The Beacon generates around 10 gigabytes of data per chip, which is nearly two terabytes of data per year. GSK is using machine learning to identify artefacts from Spotlight data and subtract them from the data, which aids them in making smarter, data-rich cell line selections.

Overall, Emmins explained that her team has benefited from integrating Beacon into their cell line development process. In the 18 months since Beacon was implemented, the team has not delayed any of its timelines. In fact, the team has shaved three months off their critical path timelines with the assistance of Beacon technology.