Efficient, Reagent-Free Cell Separation Using Optical-Sensor–Guided Centrifugation

with Ben Josey

Ben Josey, PhD (field application scientist at Corning Life Sciences), joined BPI on 3 December 2020 to deliver an "Ask the Expert" presentation about using optical-sensor–guided centrifugation for cell therapy development. Cell-separation techniques fall into four basic categories: filtration, centrifugation, affinity purification, and emerging methods such as microfluidics and acoustofluidics. Selecting the technology best suited to an application requires careful balancing of method precision and process efficiency, the latter of which includes factors such as batch size, time, labor, and cost. Josey described how the Corning X-Series cell-separation platform helps to strike such a balance by adding intelligent sensor control to centrifugation.

Josey's Presentation

Josey noted that centrifugation is a conventional approach to processing blood products for cell therapy production. Centrifugation accelerates stratification of different cell types into distinct density layers. Traditionally, scientists have used density-gradient media to increase separation precision. For instance, mononuclear cells (MNCs) have been isolated by layering samples on top of media such that target cells fall below or remain above it during processing. However, that can be a tedious manual step that leaves room for sample variation and operator error, both of which can reduce target-cell yield and viability.

The X-Series platform addresses such concerns in a convenient, closed-system format that is compatible with swing-bucket centrifuge rotors. In a typical workflow, samples are loaded into the main chamber of a single-use cartridge through a spike port or welded sterile tubing. The cartridge is attached to the system's control module and placed in a programmable centrifuge, where the module executes a preprogrammed protocol. During processing, infrared optical sensors and an accelerometer embedded within the controller monitor cell stratification and *g* force, respectively. Based on the resulting data, the module opens and closes valves in the cartridge to move cell fractions into discrete chambers. When processing has finished, separated fractions can be withdrawn from the cartridge using the sample-access tubing. Onboard memory continuously records system inputs and process data, which are passed back to a docking station for report building.

Josey highlighted the versatility of his company's platform. Although it enables process automation, the system can be programmed to incorporate manual media exchanges and resuspensions. Processing time can be shortened or extended based on process needs, and X-Series cartridges come in two designs to accommodate diverse operations. Tripartite X-Lab cartridges are ideal for separation of cell populations. With two chambers and tubing configurations optimized for multiple media or buffer exchanges, X-Wash cartridges are designed for cryoprotectant removal, cell washing, and volume reduction.

Users report consistently high cell recoveries and viabilities across several applications. Josey shared a case study in which a team used the X-Lab system for isolation of peripheral blood mononuclear cells (PBMCs). The team recorded 92.8% target-cell recovery and significant reduction of platelets, granulocytes, and red blood cells (RBCs). Josey highlighted that X-Series processing consistently depletes >99% of RBCs without need for a lysis step. That capability represents a significant advantage for processes in which RBC contamination is problematic. In a second case study, a team evaluated X-Wash removal of dimethyl sulfoxide (DMSO) from cryopreserved leukopaks obtained from three donors. DMSO concentrations diminished by >95% after an initial wash, and >99% of DMSO had been removed after a second wash step, with negligible losses in cell recovery and viability. Other successful applications of the X-Series platform included concentration of cell products from 240 mL to 3 mL and effective cell-washing workflows.

In addition to optimized, reagent-free centrifugation, the X-Lab and X-Wash systems are registered with the US Food and Drug Administration (FDA) as class 1 medical devices and enable full compliance with regulations for batch documentation. X-Series software also provides tiered report access to help ensure data integrity.

Questions and Answers

What sample sizes can the X-Series platform handle? It can process samples of 40–240 mL. For best results, small samples should be diluted with buffer, media, or serum to 60 mL.

How easily can the platform accommodate different processes? The system can be adapted to meet diverse processing needs. The optical sensors and accelerometer in the control module enable precise movement of cells into the collection chamber. Thus, scientists can consider different *g*-force speeds in the centrifuge and gain settings in the sensors to optimize their processes. However, users should note that control modules are designed to be "plug and play" upon programming. That feature helps to ensure regulatory compliance.

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