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Tech Advances Will Help Cell Therapy Makers Cope with Variable Starting Materials

By **Gareth John Macdonald** - April 5, 2023

Credit: Extreme Media/Getty Images

Autologous cell therapies are made from living cells, harvested from specific people. Every batch of inputs is different which makes predicting how each will perform in manufacturing a major challenge.

Indeed, for Matthieu de Kalbermatten, CEO of France-based cell therapy developer CellProthera, starting material variability is the major issue facing the industry.

"The main challenges in the manufacturing of cell-based therapeutics come from the variability of the starting material, the constraints and limitation of quality-controlled production area, and the high cost of infrastructure maintenance and reagents.

"But really these are all directly linked to the inherent characteristics of the working material, the cell, a delicate living organism which varies from one individual to the other, requires particular care in handling, and multiple tailor-made innovative ingredients to mature into a medicinal product. "

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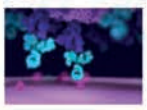

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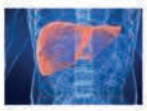

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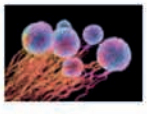

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Variability

Material variability impacts every aspect of manufacturing, from the technology used to the handling and containment infrastructure required, says de Kalbermatten, citing the post-heart attack therapy his firm is developing by way of example.

"Our starting material is a blood bag containing a certain amount of CD34+ stem cells—the cells of interest for us—that has been harvested from a patient after administration of a growth factor.

"In our ongoing trial, we typically see a significant variability in the number and quality of CD34+ collected. This is a real issue as each step in the manufacturing process has been designed to work optimally for a certain level of quality within a range.

"Variability at start reduces the overall yield of the production process and increases the risk of batch failure," he says.

Part of CellProthera's solution has been to build flexibility into its manufacturing processes using disposable bioprocessing systems that can be switched in and out as required.

"Single-use systems fit well with our autologous therapy, which does not require production at large scale. Plastic material such as tubes, bags, and connectors make up most of the disposable kits."

Contamination control

But variability is not the only material-related challenge cell therapy markers face, says de Kalbermatten.

"Cells are very sensitive to contamination and their handling requires the utmost care and the highest level of clean room quality. The productivity of operators is limited by the strict rules and space.

"Indeed, we can't have more than three people at the same time in the clean room. In addition, each time our operators have to shift the cells back and forth between the laminar flow cabinet and the equipment used for centrifugation increases the risk of error and of breach in the sterility of the process."

CellProthera works with cell and gene therapy centers in France and in the U.K. that have the infrastructure and the trained staff in place and can better spread out the maintenance cost of their infrastructure over several projects.

Technology solutions

Looking forward, de Kalbermatten predicts technology will play a greater role in reducing variability in starting materials and minimizing the risk of contamination during production.

"It's really exciting to see new technology flourishing in the field of cell selection for example, where microfluidic systems are progressing because they have minimal impact on cells and can improve the yield. There are also exciting developments under way in terms of automatization and in-process controls.

"The ultimate goal is indeed to have a completely closed system that would reduce risks of contamination and overall production costs, while offering an in-process control loop to enable the steering of the process in real-time and as a function of the specific characteristics of each patient's starting material."