

STREAMLINING CELL THERAPY MANUFACTURING: AUTOMATED PRODUCTION AND INTEGRATED DATA MANAGEMENT

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The manufacturing of cell therapy is a complex sequence of different unit operations. The substantial amount of manual and/or (semi-)automated manufacturing steps in a strictly regulated environment raise the need for scalable manufacturing and data management tools. Bioreactors have long been advocated as enabling technology for manufacturing of cell-based products. Automated bioreactors are not only able to substitute manual culture operations, but provide real-time monitoring and control of the culture environment, ultimately leading to improved process robustness. Additionally, they can be more easily integrated in an 'Industry 4.0' framework where data integration is required in real-time for process planning, regulatory compliance, etc.

This work presents the integration of new a new bioreactor and a software platform, allowing more automation and efficient streamlining of the cell therapy manufacturing processes. On one hand, a closed benchtop perfusion bioreactor system with a reduced footprint was developed that is suitable for point-of-care use. Precise monitoring of the culture environment (pH, DO₂ and T°) was achieved thanks to flexible sensor ports. The perfusion circuit was designed as a closed, single-use silicone tubing circuit linking a culture medium reservoir to a perfusion chamber via a peristaltic pump (cfr. Figure 1). A reusable cassette enclosed the disposable circuit and contained all the electronics required for bioreactor operation and environment control. A proof of concept study provided validation of the system on the perfusion culture of skeletal progenitor cells seeded onto 3D scaffolds. Regular sampling of the medium was performed during culture to measure glucose and lactate concentrations. Metabolic profiles, Live/Dead staining and DNA quantification of the constructs indicated similar cell growth kinetics compared to previously validated perfusion cultures of identical constructs.

Additionally, an online platform for centralised management of cell production process data was developed, named MyCellHub. The software enables efficient and regulatory compliant logging and management of all data related to cell manufacturing. Role-specific profiles in the software were made for operators, QA/QC units and process managers allowing to both log, access and visualize data relevant to their role. Every step of the manufacturing processes can be overseen in real-time with the aid of a digital audit trail. Based on this data, process analytics are provided and automated activity logs and batch records can be generated.

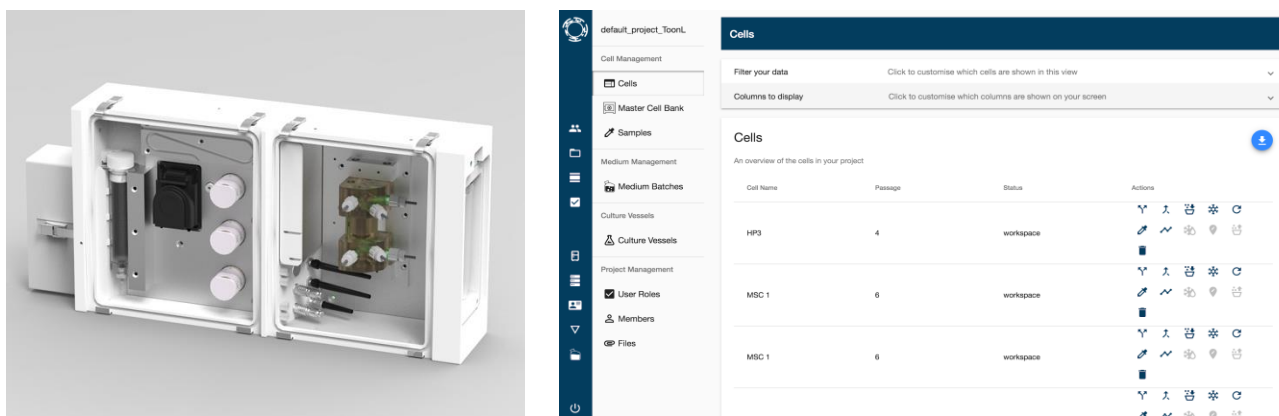


Figure 1: (left) Bioreactor cassette containing the perfusion circuit and all the electronics required for bioreactor operation and environment control. (right) Data management interface on the MyCellHub platform.