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CASE STUDY No. 006

Controlled Production of Mesenchymal Stromal Cell-Derived Extracellular Vesicles in Stirred-Tank Bioreactors

Researchers' affiliations

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iBET is a private not-for-profit research-intensive institution with over 30 years of experience in developing innovative solutions in Biotechnology and Life Sciences. Key areas of expertise include the bioprocessing and in-depth characterization of Advanced Therapeutic Medicinal Products (ATMPs) such as stem cells for cell therapy.

Challenge

Extracellular vesicles (EV) derived from mesenchymal stromal cells (MSC) are a promising alternative to cell-based therapies. However, **for the clinical use of EVs, scalable and standardized EV manufacturing processes must be developed**. To do so, critical process parameters (CPPs) that impact yield and critical quality attributes of EVs must be identified, therefore contributing to design strategies to more tightly control the production of EVs with therapeutic potential.

Strategy

Developing improved upstream strategies:

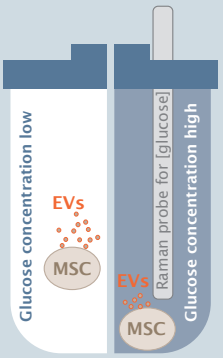
> **Scalability:** MSC-derived EVs were produced in stirred-tank bioreactors, which facilitate easier scale-up than 2D culture systems
> **Reproducibility and yield:** Online process monitoring strategies were integrated towards the implementation of more reproducible workflows. The glucose concentration was investigated as a critical process parameter for EV secretion.

Equipment

> DASbox® Mini Bioreactor System
> BioBLU® 0.3c Single-Use Bioreactor

Results

> EV yields in stirred-tank bioreactors were higher than in a static culture system.
> The number of EVs secreted per MSC was increased at low glucose concentration.



Raman spectroscopy was implemented as a PAT tool to continuously monitor the glucose concentration in the culture medium.

Conclusion

Stirred-tank bioreactors facilitated the scalable production of bioactive MSC-derived EVs. Bioreactors enabled the implementation of Raman spectroscopy to continuously monitor the glucose concentration, which has been identified as CPP for EV secretion. As parameter monitoring is a prerequisite to their control, the implementation of PAT tools could contribute to more reproducible EV production workflows.

In addition, the authors of the study integrated EV production in stirred-tank bioreactors with scalable downstream processing protocols, therefore contributing to address key challenges for large-scale EV production.

Read the full story

Costa et al. *Enhanced bioprocess control to advance the manufacture of mesenchymal stromal cell-derived extracellular vesicles in stirred-tank bioreactors. 2023*

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