Mini Review

Pharmaceutical BIOPROCESSING

Stem Cell Bioprocessing

Abstract

In order to advance the goal of employing stem cells for cell treatment, the Stem Cell Bioprocessing Group is concentrated on creating scalable cell growth technologies using a micro-carrier platform. Commercial cell production cannot be scaled up using conventional techniques for flask- and tray-based generation of anchorage-dependent stem cells.

The potential of stem cell research for tissue engineering-based therapeutics and clinical applications in regenerative medicine has been thoroughly recognised in recent years. Chung developed the first complete organ transplant in 2006 utilising adult stem cells and a clinical evaluation scaffold. Seven patients with myelomeningocele who received bladder transplants made possible by stem cell therapy saw significant improvements in their quality of life, marking a new milestone. Although the bladder is a fairly straightforward organ, the discovery shows the amazing advantages of the multidisciplinary approach of tissue engineering and regenerative medicine (TERM), which includes stem cell study and stem cell bioprocessing. Undoubtedly, the application of engineering principles and practises is required in the development of bioprocess technologies for the transfer of the current laboratory-based practise of stem cell tissue culture to the clinic as therapeutics in order to achieve control, reproducibility, automation, validation, and safety of the process and the product. Fundamental research (from embryonic biology to the 'omics' technologies and developments in immunology) and current industry experience (biologics), particularly on automation, quality assurance, and regulation, will need to contribute to the effective translation. It will be crucial to design, integrate, and implement various components on time; mistakes made in the past with regard to marketing, pricing, production, and advertising (such as when skin analogues were commercialised) shouldn't be repeated.

Keywords: Stem Cell • Bioprocessing • Tissue engineering

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Introduction

Human pluripotent stem cells (hPSCs), which have the unique capacity to self-renew and develop into almost all cell types, offer an alternate cell source for a number of somatic tissues. In various phase I clinical trials, hPSC derivatives were examined for their potential as therapeutic products as well as for drug development and disease modelling. Prior to enhanced differentiation techniques that enable the manufacture of lineage-specific cells at high efficiency and purity, the development and manufacturing of hPSC-derived cells first concentrated on the improvement of differentiation efficiency, i.e. the upstream bioprocessing. Examples include the generation of 30–90% pure cardiomyocytes using either growth factor or small molecule guided protocols, and the generation of 70–90% pure oligodendrocyte progenitor cells (OPCs) and neural progenitor cells (NPCs) from hPSCs using either an embryoid body (EB)-based protocol or the monolayer protocol via dual inhibition of SMAD (Small Mothers Against Decapentaplegic) signalling. The creation of such effective differentiation techniques is a sign of significant advancements in the upstream bioprocessing for the generation of hPSC-derived cells. However, additional research is needed to understand downstream bioprocessing (i.e. cell separation), a crucial step and the bottleneck to completing the hPSC-derived products [1-4].

Reliable and repeatable culture conditions and procedures are essential for the success of stem cell bioprocessing. For stem cell bioprocessing, this entails scaling up stem cells to an end product that has undergone differentiation and is of adequate quality and quantity for use in clinical and commercial settings. This alternative is not only unpleasant but also economically unviable

due to the high cost of labour, consumables, and time, as well as the inherent variability in manual procedures. Successful clinical product development requires automation and the application of an effective bioprocess paradigm.

After effective hPSC differentiation is accomplished, downstream bioprocessing has emerged as the bottleneck in the generation of hPSC-derived cells for therapies. To create a safe cell therapy, it is essential to identify particular markers for targeted lineages and develop a plan to exclude undifferentiated cells. With high cell purity, the strain on subsequent bioprocessing should be lessened by the elimination of undesirable cell types. To assure consistent products after cell separation, a strict quality control system and very sensitive assays must be developed. To minimise the number of preclinical studies, it is desirable to have in vitro tests that can forecast the in vivo effect.

Regenerative medicines utilising human cells and tissues will be used in the upcoming healthcare revolution. The goal of regenerative medicine is to develop biological remedies or in vitro replacements for tissues that have lost their ability to function in vivo owing to failure or illness. Despite the fact that science has revealed this approach's biomedical potential and those early products have shown the efficacy of such therapies, bioprocess technology must still be developed in order to successfully translate stem cell and tissue culture from the laboratory to the clinic for therapeutic purposes. This can be done by using engineering principles and practises. By bringing together contributions from international experts on stem cell science and engineering, bioreactor design and bioprocess development, scale-up, and the manufacturing of stem cell-based therapies, this Special Issue of Bioengineering on "Stem Cell Bioprocessing and Manufacturing" addresses the central role in defining the engineering sciences of cell-based therapies [5-8].

Human pluripotent stem cell (hPSC) derivatives have gained significant attention in recent years as promising allogeneic cell therapy products with the potential to treat a wide range of illnesses and a sizable population of patients worldwide. The development of scalable bioreactor technology for the large-scale production of high-quality medicinal PSC derivatives is one of the difficulties that Brian Lee and co-authors addressed in their study of the manufacturing of PSCs in big quantities for commercialization.

Discussion

In order for stem cell bioprocessing to be successful, it is essential to have reliable and repeatable culture conditions and procedures. In the context of stem cell bioprocessing, this entails scaling up stem cells to an end product that is differentiated and has a sufficient quality and quantity for clinical and commercial objectives. This alternative is not only unpleasant but also economically unviable because to the high cost of goods, labour, and time, as well as the inherent variability in manual procedures. Successful clinical products must be produced with automation and a productive bioprocess paradigm.

Stem cell bioprocessing can be divided into three groups: (i) process components, (ii) process requirements, and (iii) process function. Since no one technique can meet all needs, a combination of generic, "off-the-shelf," and customised production paradigms must be taken into account. Together with the design and implementation of the scaffold and bioreactor, the process components also include the cell source and type, the identification of the proper signals needed for cellular development, and the cell source and type. Transporting products is just one of the practical aspects of bioprocessing that are addressed by the process requirements, which also satisfy good manufacturing principles (GMPs) like quality assurance, bioprocess monitoring control, and automation. Ultimately, the process components and requirements must guarantee the functioning, integration, and endurance of the final product, to name just a few crucial elements that are part of the process function [9-10].

Conclusions

In regenerative medicine, bioprocessing and commercialization of stem cell/tissue-engineered products can bring discoveries from the lab bench to the patient's bedside. Even if many of these jobs are difficult and may take time to complete, certain of the existing problems must continue to be the core area of our research and development. Any bioprocess start-up operation must focus on process characterization and optimization. For a process to be converted into a manufacturing operation, standardised operating procedures and expertise must be made possible. Nutrients and metabolites should be improved in the present bioreactor process monitoring systems so that these crucial culture

parameters can be tracked constantly and in real time for effective process management. The development of sophisticated monitoring platforms that enable cellular-level monitoring will be one of the next challenges in bioprocessing and manufacturing. It will be necessary to take into account completely integrated, modular, automated, and controlled systems in a fully enclosed bioprocess operation from harvest to delivery. The authors believe that small-scale modular systems operating in a "in-series and in-parallel" manner, where overcapacity is taken into account, can ultimately scale up stem cell/tissue-engineered bioprocesses, the entire process as a supply chain model. Systems with lower infrastructure costs are capable of scaling up, and the integration, modularity, and parallel operation are the solutions to the issue.

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