Mini Review

Pharmaceutical BIOPROCESSING

Membrane Utilizes through Allogeneic Stem Cell Transplantation

Nina Watson*

Oxford Suzhou Centre for Advanced Research (OSCAR), University of Oxford, Suzhou 215123, China

*Author for correspondence:

Ninawatson56@edu.in

Received: 01-Nov- 2022, Manuscript No. FMPB-22-81349; **Editor assigned:** 03-Nov-2022, PreQC No. FMPB-22-81349 (PQ); **Reviewed:** 17-Nov-2022, QC No. FMPB-22-81349; **Revised:** 22-Nov-2022, Manuscript No. FMPB-22-81349 (R); **Published:** 30-Nov-2022, DOI: 10.37532/2048-9145.2022.10(6).116-119

Abstract

The use of stem cells and cell therapies, especially autologous cell therapies, is becoming more and more common. However, inventive engineering must be used to reduce the prohibitively high cost of these therapies in order for these technologies to be put into widespread clinical use. Membranes have the potential to revolutionize the bioprocessing and production of cellular products as well as significantly lower the price of autologous cell therapies. The expansion of CAR-T cells, the production of various human stem cells, and the production of extracellular vesicles (EVs) through the use of hollow fibre membrane bioreactors are examples of successful membrane applications.

Keywords: Cell culture • Autologous cell therapy • Bioreactor • Hollow fibre membrane bioreactor

Introduction

Autologous cell therapies are now used to treat diseases and degenerative conditions that would otherwise be incurable by manipulating, expanding, processing, and then re-implantation of a patient's own cells. Immune rejection-related complications may be avoided because the cells used in these treatments come from the patient themselves [1]. As a result, autologous therapies are regarded as being more feasible than other regenerative medicine technologies. Autologous cell therapies that have been effective in clinical practice thus far include:

Burns can be treated with autologous cell therapy, multiple myeloma and multiple scoliosis can be treated with autologous stem cell transplantation, and blood cancers can be treated with CAR-T therapy [2, 3].

The block flow diagram in demonstrates that autologous cell therapies, such as chondrocyte implantation therapy, are multi-step processes. Cells from the patient are first obtained during this procedure, either through a blood sample or a biopsy. As a result, in contrast to conventional treatments, each one is tailored to the particular patient. As a result, processes developed for the production of autologous therapies are not based on "scale up," but rather on parallel "scale out" using disposable platforms that can only be used once.

Membranes, with the exception of liquid membranes, provide a physical barrier with distinct surface properties and selective transport properties. Membranes have the desirable properties, and they can be cleverly used to solve some important problems in the bioprocessing and production of autologous cellular products. CAR-T therapy, the cultivation of adherent cell types, stem cell expansion, and the isolation of extracellular vesicles (EVs) are just a few examples of how membrane technologies have been put to use.

To fulfil this crucial function, novel membranes with specialized functions and surface properties, as well as novel membrane modules that can adapt to changing requirements for surface area and transport properties, are being developed [4, 5].

Discussion

The high cost of autologous cell therapies is a major obstacle. For instance, the CAR-T treatments tisagenlecleucel and Kymriah, which have been approved for use by the NHS in the United Kingdom, cost a hefty GBP 282,000 per treatment. Studies have shown that the actual cost is even higher when post-treatment care is taken into account. A significant portion of the cost of goods is borne by the bioprocessing and production of cellular products. As depicted in the process flow diagram, current processing technologies are largely based on replicating cell culture and manipulation in laboratories with varying degrees of automation. For the "open operation," in which the product or component is exposed to the operational environment, it is necessary to invest in infrastructure to create ultraclean environments (good manufacture practice, or GMP).To perform all processing steps in hospitals without the need for dedicated GMP facilities, novel bioprocessing technologies, new equipment, and new devices are urgently required to form a fully enclosed, fully automatic, and single-use system. Along these lines, films can assume a significant part.

It has long been known that the immune system plays a crucial role in the growth and development of cancer, with the immune system constantly "immunosurveilling" potential cancer cells. Further research demonstrated that the killing of precancerous and cancerous cells by specific T lymphocyte populations known as killer T cells is an important part of this natural cancer prevention. T Cell Receptors (TCRs) are these T cells' innate "guidance system" that they use to identify cancerous and precancerous cells. These TCRs can distinguish single amino acid changes in antigenic peptide sequences with enough sensitivity .However, it is estimated that over 90% of all immature T cells and all T cells with self-reacting TCRs are destroyed before maturation to prevent autoimmunity. As a result, the majority of T cells in the blood are either inactive or only marginally reactive against tumor-associated mutated self-antigens. To use T cells effectively as a cancer treatment, this issue must be circumvented.

Tumour-Infiltrating Lymphocytes (TILs), which can be found inside of tumor tissues, were utilized in the initial form of T cell therapy [6]. This was done because T cells in tumours will be more likely to react with mutated self-antigens on tumors.Be that as it may, notwithstanding this until treatment has appreciated just restricted achievement [7].

Combining monoclonal antibody (mAb) therapy, which has high reactivity but low cytotoxicity on its own, with low-reactivity, high-cytotoxicity T cell therapy resulted in a breakthrough in this treatment's efficacy. By genetically altering T cells, researchers were able to attach high-affinity cancer-specific antibodies known as chimeric antigen receptors (CAR) to the surface of highly cytotoxic T cells in order to create the first CAR-T cells [8].Through various clinical preliminaries; it was shown that these recently made Vehicle Lymphocytes were incredibly great at treating particular kinds of disease [9].

Generally in drug creation cost is decreased through economy of scale during increase. The product's unit cost can be reduced by using larger bioreactors and producing larger batches. However; doses must be made to order rather than made to stock due to the requirement for autologous cells, which ultimately results in a higher unit cost. This not only limits the production scale but also raises the variation in the curative effect from patient to patient.As a result, rather than scaling up, CAR-T manufacturing capacity can only be increased by scaling out and adding more production units that are equivalently functional .As a result, the majority of CAR-T manufacturers continue to use mostly manual culture systems based on flasks or bags. These culture systems can be easily scaled up by adding more flasks or bags. However, in order to maintain a sterile environment, manual flask or bag-based cultures necessitate large, centralized GMP facilities, a significant amount of support equipment, and a significant amount of space, making them extremely space inefficient and, more importantly, costly.

With continuous perfusion, hollow fiber membrane bioreactors (HFBRs) can precisely control the cell culture process and the extracellular environment. By providing a closed system with automated temperature, gas concentration, and inlet media flow rate control, HFBRs have been touted as a solution to many of the issues posed by vessel and wave bag based platforms since their initial development in 1972, HFBRs effectively facilitate the removal of waste products while simultaneously providing fresh nutrients directly to the cells, allowing for the support of much higher cell densities. They typically consist of a controller, positive displacement pump, HFBR cartridge,

waste, media, and buffer reservoirs connected in a continuous loop. Typically, membranes for HFBR cartridges are made by immersion precipitation phase inversion, where a polymer solution is extruded through a spinneret into a precipitation bath where asymmetric hollow fibers with a radial pore density gradient are formed. Polyvinylidene fluoride, polysulfone, and cellulose are examples of polymers that are frequently used in the production of cartridges [10].

Using membranes, EVs can be separated and purified to great potential. The interaction between EVs and membranes with various parameters, such as MWCO, materials, charged or uncharged, and any kind of modifications, is rarely investigated to increase selectivity and reduce losses from EV binding to membranes, despite the widespread use of membrane-based techniques for EV isolation. In order to improve the yield and effectiveness of EV isolation, it is also necessary to investigate and improve the filtration procedure. More research is needed to determine whether membrane separation causes EVs to deform, be disrupted, or lose their properties and functions .In addition, although there are a number of commercial membrane-based separation products on the market, these were initially developed for various processes before being adapted for EV separation. Therefore, EV-membrane interaction research and specialized membranes for EV isolation and purification based on their properties are required. Because the cells can be cultured and retained for a longer period of time while EVs are still produced, integrating stem cell expansion and EV production would greatly increase EV productivity.

Conclusion

Numerous engineering difficulties arise as new technologies become apparent as the age of personalized medicine begins. These obstacles must be overcome before these technologies can be used to their full potential. CAR-T therapies are the best example of this technology. Despite being widely regarded as revolutionary, CAR-T therapies have not yet achieved widespread clinical application, primarily due to the prohibitively high cost of each treatment. Through economies of scale, pharmaceutical prices have remained low to this point. However, this approach is impractical due to the individual nature of personalized medicine. Instead, an alternative business model and cost-effective scale-out strategies are essential for success. Autologous cell therapies require the development of a patient's own cells for reimplantation.Scale-out processes use costly, labor-intensive, and susceptible to contamination flask and wave bag culture methods. An automated, low-cost, closed system alternative may be offered by HFBRs, which were developed for the culture of various cell types in research and commercial settings. However, since there is typically no second chance, rigorous regulatory approval of commercial devices, quality control, and validation methods are necessary for the successful implementation of HFBRs in a clinical setting. In the bioprocessing of autologous cells and cellular products, membrane technologies represent a relatively untapped market. Through the creation of specialized affinity membranes, interesting and challenging issues like cell sorting and EV purification present an exciting research opportunity. Development of new membrane modules, such as those with adjustable membrane areas, would also be interesting.

Acknowledgement

None

Conflict of Interest

Author declares no conflict of Interest.

References

1. Namdaroğlu S, Tekgündüz E, Bozdağ SC *et al.* Microbial Contamination of Hematopoietic Progenitor Cell Products. *Transfus Apher Sci.* 48, 403–406 (2013).
2. Wang S, Sun J, Chen K *et al.* Perspectives of Tumor-Infiltrating Lymphocyte Treatment in Solid Tumors. *BMC Med.*19, 140-146 (2021).
3. Eshhar Z, Waks T, Gross G *et al.* Specific Activation and Targeting of Cytotoxic Lymphocytes through Chimeric Single Chains Consisting of Antibody-Binding Domains and the Gamma or Zeta Subunits of the Immunoglobulin and T-Cell Receptors. *Proc Natl Acad Sci.* 90, 720–724(1993).
4. Harwood CR. Bacillus subtilis and its relatives: Molecular biological and industrial workhorses. *Trends Biotechnol.* 10, 247-252 (1992).
5. Young EJ. Engineering the Bacterial Microcompartment Domain for Molecular Scaffolding Applications. *Front Microbiol.* 8, 1441-1445(2017).
6. Liu Y. Pathway engineering of Bacillus subtilis for microbial production of N-acetylglucosamine. *Metab Eng.* 19, 107–115 (2013).
7. Panahi R. Auto-inducible expression system based

on the SigB-dependent ohrB promoter in Bacillus subtilis. *Mol Biol*.48, 852–857(2014).

8. Feng Y. Enhanced extracellular production of L-asparaginase from Bacillus subtilis 168 by B. subtilis WB600 through a combined strategy. *Appl Microbiol Biotechnol*. 101, 1509–1520 (2017).
9. Schallmey M, Singh A, Ward OP. Developments in the use of Bacillus species for industrial production. *Can J Microbiol*.50, 1–17(2004).
10. Perkins J. Genetic engineering of Bacillus subtilis for the commercial production of riboflavin. *J Ind Microbiol Biotechnol*. 22, 8–18(1999).