Expansion of Human Skin-derived Schwann Cells in Stirred Suspension Bioreactors

A. Pawluk[1], B. Abraham[1,2], E. L. Roberts[1,2], T. Chu[3,4], R. Midha[3,4] and M. S. Kallos[1,2]

[1] Pharmaceutical Production Research Facility, University of Calgary, Calgary, Canada
[2]Department of Biomedical Engineering, University of Calgary, Calgary, Canada
[3]Department of Clinical Neurosciences, Cumming School of Medicine, University of Calgary, Calgary, Canada
[4]Hotchkiss Brain Institute, Cumming School of Medicine, University of Calgary, Calgary, Canada

I. Introduction

Peripheral nerve injuries (PNIs) commonly cause disability and require long-term rehabilitation. Treatment options that address gaps in current care would be beneficial to society. In injuries that resulted in discontinuity, the conventional treatment option is autologous nerve grafting which is invasive and causes damage to donor nerve tissue sites [1]. Alternatively, Schwann cell therapy can be considered, potentially from a less invasive source such as the skin; Schwann cells function to myelinate axons and repair damaged nerves [2]. The bottleneck in Schwann cell therapy is reproducible production of clinically relevant numbers of Schwann cells. Currently, static culture is being used in clinical trials [3], however it is not monitored and is often less efficient when scaling up. Stirred suspension bioreactors provide a well-mixed, automated, and scalable system for producing the required cell densities for therapy. The objective of this research was to optimize a reproducible method to generate enough human skin-derived Schwann cells for clinical need and/or transplantation studies.

II. Methods

Stirred suspension (100 mL) bioreactors were used to expand human skin-derived Schwann cells on Cytodex 3 microcarriers as an attachment surface. An agitation rate of 40 rpm was used with 50% medium changes on Days 3 and 6. Intermittent agitation was used for the first 24 hours of cell growth in the bioreactors, and the cells were grown for 7 days. The impact of cell seeding density on fold increase was studied, as well as the ability to produce clinically relevant numbers of cells via low cell seeding densities thawed directly into bioreactors. Approximately $1x10^6$ cells can be purified from a minimally invasive punch skin biopsy in a clinical setting.

III. Results and conclusions

Comparison between low cell seeding density (approximately 5000 cells/cm^2) and high cell seeding density (approximately 10,000 cells/cm^2) conditions at a microcarrier density of 0.5 g/L is shown in Figure 1. The low- and high-density conditions required approximately 600,000 and 1.3 million cells for inoculation. The low condition provided a more reliable sampling system, required less than the required number of starting cells and provided similar cell proliferation results on Cytodex 3 microcarriers compared to the high condition; the fold increases for the low- and high- density conditions respectively were 5.4 and 5.3. The maximum cell density was 49,000 cells/cm^2 via the high condition and 24,000 cells/cm^2 via the low condition. Both conditions provide an efficient bioprocess for the scale-up of these Schwann cells; if there were a surplus availability of cells for inoculation, the high-density condition would provide a greater number of cells.

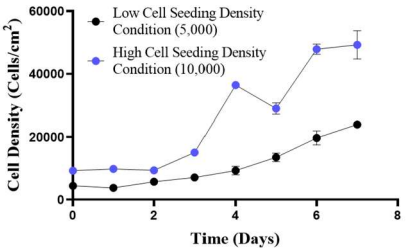

Fig. 1 Growth of human Schwann cells in bioreactors

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References

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