XENO-FREE EXPANSION OF LATE-ADHERENT HUMAN OLFACTORY MUCOSA CELLS: TOWARDS AN ALLOGENEIC THERAPY FOR NEURAL REGENERATION

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Human olfactory mucosa cells (hOMCs) are anchorage dependent cells that have potential for treatment of spinal cord injury. However, current hOMC therapies relied on autologous transplantation and it is not feasible to prepare and characterize sufficient quantities of cells (in the order of 10^7 - 10^8 cells) within a timeframe to treat acute injury. Thus an allogeneic (universal) "off-the-shelf" approach would offer an alternative for this case.

We incorporated the regulator-approved c-MycER^{TAM} gene (ReNeuron) into primary late-adherent hOMCs to extend their *ex vivo* proliferation in the presence of the synthetic drug 4-hydroxytamoxifen (4-OHT). Polyclonal populations of hOMCs were generated and characterized, with an ultimate goal of developing a potential cell therapy product for application in spinal cord injury. Due to the lack of scalability, the availability of labour intensive manual processes and fetal bovine serum (FBS) supplementation, we aimed to develop a xeno-free process for the expansion of a these cells.

An initial issue for the manufacture of hOMCs is that key bioprocess parameters have not been established. In this work, we performed cell growth characterization to provide information about their growth i.e. effect of initial cell seeding density, long-term culture, and metabolite profiles to ultimately define the expansion process window.

Although widely used, FBS is a finite resource that raises concerns about the presence of adventitious agents. Alternative human-derived (xeno-free) or chemically-defined (serum-free) supplements were assessed for their ability to sustain cell growth. From these studies, human platelet lysate supplementation at 2-5% (% v/v) was found to be a viable xeno-free option to sustain growth of hOMCs with no adverse effects on their phenotype.

Finally, we sought to replace the current manually intensive monolayer expansion process with a more flexible and scalable platform such as suspension culture on animal-free microcarriers. Successful expansion of c-MycER^{TAM}-derived late-adherent hOMCs on plastic microcarriers at 80-mL scale was achieved to establish a suspension culture expansion platform for the translation of a potential candidate cell therapy for neural regeneration.

In summary, we show a systematic approach to address main hOMC bioprocessing challenges for an allogeneic therapy to treat patients suffering from spinal cord injury.