Keywords: IDO, process development, MSCs

Background & Aim: AD-MSCs have been extensively used for a variety of human ailments in the past decades, but their full potential is yet to be fully exploited. Although a multitude of clinical trials have been performed, showing promising results of injecting AD-MSCs in joints suffering from osteoarthritis (OA), there is still no approved product in the market for this specific indication, and the only approved MSC products are allogeneic and mainly for graft-vs-host disease. For OA, non-ATMP solutions like direct SVF injections are already at commercialization phase. In the past few years at Theracell in Greece, we have been developing an autologous MSC product, characterized by a rich variety of assays (matrix approach), aiming to launch a clinical trial soon.
Methods, Results & Conclusion: From 1 gr of adipose tissue obtained by a lipoectomy without hospitalization, we can manufacture more than 50 million MSCs in 2 weeks using GMP-grade materials, achieving cell duplication times of less than 24h and applying a matrix of assays for characterization and quality control. We monitor more than 25 parameters of identity, safety and performance to ensure high quality of final product. Surface markers that are monitored are apart from the classical (and obsolete) CD73/CD90/CD 105, the IFNγ-inducible markers HLA-DR and CD40. Potency assays include PBMC-proliferation inhibition and expression of IDO after IFNγ stimulation (licensed MSCs). Under hospital exemption rule, (named-patient-basis), our autologous MSC product was initially administered in ~80 consenting patients by intra-articular injection of 20 million MSCs in 2ml, with a 12-month follow up and retrospective analysis of the data. There were no serious adverse events, lending support to the notion that the therapy is safe and we gathered first promising results that hint at efficacy in what concerns pain reduction (VAS score) and amelioration of quality of life (WOMAC and KOOS scores). There are still great challenges to face, like the cost, especially taking into consideration that relatively cheaper options for OA already exist, and the regulatory hurdles for ATMPs in order to produce a batch that is not for a life-threatening disease. But the process development we achieved can also be exploited for acellular therapies, like exosomes/secretome from AD-MSCs for an off-the-shelf therapy, cheaper and effective, hoping to contribute to a brighter future for MSCs.

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Mesenchymal Stem/Stromal Cells

DISRUPTING CELL THERAPY STORAGE AND DISTRIBUTION WITH HYPOTHERMIC PRESERVATION OF ADIPOSE-DERIVED MESENCHYMAL STROMAL CELLS

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Keywords: Mesenchymal Stromal Cells, Cell Encapsulation, Hypothermic Storage.

Background & Aim: Cell and gene therapies (CGT) have reached new therapeutic targets but have noticeably high prices. Solutions to reduce production costs might be found in CGT storage and transportation since they typically involve cryopreservation, which is a heavily burdened process. Encapsulation at hypothermic temperatures (e.g., 2–8°C) could be a feasible alternative. In this study, we aim to determine the ability of alginate encapsulation to maintain cell viability, identity, and function in the context of MSC-based therapy manufacturing.
Methods, Results & Conclusion: Adipose tissue-derived mesenchymal stromal cells (MSC(AT)) expanded using fetal bovine serum (FBS)- (MSC-FBS) or human platelet lysate (HPL)-supplemented mediums (MSC-HPL) were encapsulated in alginate beads (BeadReady™ kits kindly provided by Atelerix) for 30 min, 5 days, and 12 days. After bead release, cell recovery and viability were determined to assess encapsulation performance. MSC identity and functional immunophenotype, MSC tri-lineage differentiation potential, metabolic activity, and hematopoietic support capacity were determined and compared between timepoints. MSC(AT) were able to survive encapsulated for a standard transportation period of 5 days, with recovery values of 56 ± 5% for MSC-FBS and 77 ± 6% for MSC-HPL (which is a negligible drop compared to earlier timepoints). Importantly, MSC function did not suffer from encapsulation, with recovered cells showing robust differentiation potential, expression of immunomodulatory molecules, and hematopoietic support capacity. MSC(AT) encapsulation was proven possible for a remarkable 12 day period. There is currently no solution to completely replace cryopreservation in CGT logistics and supply chain, although encapsulation has shown potential to act as a serious competitor.

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Mesenchymal Stem/Stromal Cells

IMPROVED EFFICACY OF MESENCHYMAL STROMAL CELLS STABLY EXPRESSING CXCR4 AND IL-10 IN A XENOGENEIC GRAFT VERSUS HOST DISEASE MOUSE MODEL

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Keywords: MSCs, GvHD, CXCR4 IL10.

Background & Aim: Mesenchymal stromal cells (MSCs) currently constitute one of the cell types more frequently used in advanced therapies due to their safety profile together with immunomodulatory and regenerative properties. Previous clinical trials have shown that MSCs can modulate graft versus host disease (GvHD) after allogeneic hematopoietic transplantation, although only moderate therapeutic effects have been observed in clinical trials. The aim of this study was to increase the anti-GvHD effect of MSCs by means of the lentiviral-mediated expression of CXCR4 and IL10.
Methods, Results & Conclusion: Adipose tissue derived human MSCs (Ad-MSCs) were transduced with a bicistronic lentiviral vector carrying the cDNAs of CXCR4, a molecule involved in cell migration to inflamed sites, and IL10, a cytokine with potent anti-inflammatory properties. Genetically modified MSCs (CXCR4-IL10-MSCs) showed the characteristic phenotype of MSCs, including morphology, *in vitro* differentiation capacity and immunophenotype. Additionally, no changes in the characteristic cytokine secretion profile were observed in genetically modified MSCs, except in IL10 secretion. *In vitro* experiments showed that the stable expression of these molecules in Ad-MSCs efficiently enhanced their migration towards SDF-1α and improved their immunomodulatory properties compared to unmodified