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Functional heterogeneity of mesenchymal stem cells from natural niches to culture conditions: implications for further clinical uses

Luis A Costa[1], Noemi Eiro[1], María Fraile[1], Luis O Gonzalez[1,2], Jorge Saá[1], Pablo Garcia-Portabella[1], Belén Vega[1], José Schneider[3], Francisco J Vizoso[4]
Affiliations expand

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Free PMC article

Abstract

Mesenchymal stem cells (MSC) are present in all organs and tissues. Several studies have shown the therapeutic potential effect of MSC or their derived products. However, the functional heterogeneity of MSC constitutes an important barrier for transferring these capabilities to the clinic. MSC heterogeneity depends on their origin (biological niche) or the conditions of potential donors (age, diseases or unknown factors). It is accepted that many culture conditions of the artificial niche to which they are subjected, such as O_2 tension, substrate and extracellular matrix cues, inflammatory stimuli or genetic manipulations can influence their resulting phenotype. Therefore, to attain a more personalized and precise medicine, a correct selection of MSC is mandatory, based on their functional potential, as well as the need to integrate all the existing information to achieve an optimal improvement of MSC features in the artificial niche.

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Efficacy and Safety of Intra-Articular Cell-Based Therapy for Osteoarthritis: Systematic Review and Network Meta-Analysis

Wei Ding[1], Yong-Qing Xu[2], Ying Zhang[2], An-Xu Li[2], Xiong Qiu[2], Hong-Jie Wen[3], Hong-Bo Tan[2]
Affiliations expand

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Abstract

Objective: Osteoarthritis (OA) is a chronic joint disease characterized by degeneration of articular cartilage and secondary osteogenesis. Cell-based agents, such as mesenchymal stem cells, have turned into the most extensively explored new therapeutic agents for OA. However, evidence-based research is still lacking.

Methods: We searched public databases up to February 2020 and only included randomized controlled trials. The outcomes included the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), the Knee Injury and Osteoarthritis Outcome Score (KOOS), the visual analogue scale (VAS) score, and serious adverse events (SAEs). A network meta-analysis was also performed in this work.

Results: We included 13 studies in the meta-analysis. The effect size showed that cell-based therapy did not significantly reduce the WOMAC score at the 6-month follow-up (standard mean difference [SMD] -3.6; 95% confidence interval [CI] -0.90 to 0.18; P = 0.1928). However, cell-based therapy significantly improved the KOOS at the 12-month follow-up (SMD 0.68; 95% CI 0.07-1.30; P = 0.0288) and relieved pain (SMD -1.05; 95% CI -1.46 to -0.64; P < 0.0001). The findings also indicated that high-dosage adipose-derived mesenchymal stem cells (ADMSCs) may be more advantageous in terms of long-term effects.

Conclusions: Cell-based therapy had a better effect on KOOS improvement and pain relief without safety concerns. However, cell-based therapy did not show a benefit in terms of

the WOMAC. Allogeneic cells might have advantages compared to controls in the WOMAC and KOOS scores. The long-term effect of high-dose ADMSC treatment for OA is worthy of further study.

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Advances in human mesenchymal stromal cell-based therapies - Towards an integrated biological and engineering approach

Tom A Wyrobnik[1], Andrea Ducci[2], Martina Micheletti[3]
Affiliations expand

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Free article

Abstract

Recent advances of stem cell-based therapies in clinical trials have raised the need for large-scale manufacturing platforms that can supply clinically relevant doses to meet an increasing demand. Promising results have been reported using stirred-tank bioreactors, where human Mesenchymal Stromal Cells (hMSCs) were cultured in suspension on microcarriers (MCs), although the formation of microcarrier-cell-aggregates might still limit mass transfer and determine a heterogeneous distribution of hMSCs. A variety of MCs, bioreactor-impeller configurations, and agitation conditions have been established in an attempt to overcome the trade-off of ensuring good suspension while keeping the stresses to a minimum. While understanding and controlling the fluid flow environment of bioreactors has been initially under-appreciated, it has recently gained in popularity in the mission of providing ideal culture environments across different scales. This review article aims to provide a comprehensive overview of how rigorous engineering characterisation studies improved the outcome of biological process development and scale-up efforts. Reconciling these two disciplines is crucial to propose tailored bioprocessing solutions that

can provide improved growth environments across a range of scales for the allogeneic cell therapies of the future.

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Human perivascular stem cells prevent bone graft resorption in osteoporotic contexts by inhibiting osteoclast formation

Stefano Negri[1,2], Yiyun Wang[1], Takashi Sono[1], Seungyong Lee[1], Ginny Ching-Yun Hsu[1], Jiajia Xu[1], Carolyn A Meyers[1], Qizhi Qin[1], Kristen Broderick[3], Kenneth W Witwer[4], Bruno Peault[5,6], Aaron W James[1]
Affiliations expand

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Abstract

The vascular wall stores mesenchymal progenitor cells which are able to induce bone regeneration, via direct and paracrine mechanisms. Although much is known regarding perivascular cell regulation of osteoblasts, their regulation of osteoclasts, and by extension utility in states of high bone resorption, is not known. Here, human perivascular stem cells (PSCs) were used as a means to prevent autograft resorption in a gonadectomy-induced osteoporotic spine fusion model. Furthermore, the paracrine regulation by PSCs of osteoclast formation was evaluated, using coculture, conditioned medium, and purified extracellular vesicles. Results showed that PSCs when mixed with autograft bone induce an increase in osteoblast:osteoclast ratio, promote bone matrix formation, and prevent bone graft resorption. The confluence of these factors resulted in high rates of fusion in an ovariectomized rat lumbar spine fusion model. Application of PSCs was superior across metrics to either the use of unpurified, culture-defined adipose-derived stromal cells or autograft bone alone. Under coculture conditions, PSCs negatively regulated osteoclast formation and did so via secreted, nonvesicular paracrine factors. Total RNA sequencing

identified secreted factors overexpressed by PSCs which may explain their negative regulation of graft resorption. In summary, PSCs reduce osteoclast formation and prevent bone graft resorption in high turnover states such as gonadectomy-induced osteoporosis.