ML 04-19 (29/01/2019)

J Orthop Surg Res. 2019 Jan 25;14(1):34. doi: 10.1186/s13018-019-1070-8.

Efficacy and safety of culture-expanded, mesenchymal stem/stromal cells for the treatment of knee osteoarthritis: a systematic review protocol.

Harrison-Brown M[1], Scholes C[2], Hafsi K[3], Marenah M[3], Li J[3], Hassan F[4], Maffulli N[5,6], Murrell WD[3,7,8].
Author information

Abstract

BACKGROUND:

Osteoarthritis is a progressive multifactorial condition of the musculoskeletal system with major symptoms including pain, loss of function, damage of articular cartilage and other tissues in the affected area. Knee osteoarthritis imposes major individual and social burden, especially with the cost and complexity of surgical interventions. Mesenchymal stem/stromal cells have been indicated as a treatment for degenerative musculoskeletal conditions given their capacity to differentiate into tissues of the musculoskeletal system.

METHODS:

A systematic search will be conducted in Medline, Embase, Cochrane Library, Scopus and relevant trial databases of English, Japanese, Korean, German, French, Italian, Spanish and Portuguese language papers published or in press to June 2018, with no restrictions on publication year applied. References will be screened and assessed for eligibility by two independent reviewers as per PRISMA guidelines. Cohort, cross-sectional or case controlled studies will be included for the analysis. Data extraction will be conducted using a predefined template and quality of evidence assessed. Statistical summaries and meta-analyses will be performed as necessary.

DISCUSSION:

Results will be published in relevant peer-reviewed scientific journals and presented at national or international conferences by the investigators.

TRIAL REGISTRATION:

The protocol was registered on the PROSPERO international prospective register of systematic reviews prior to commencement, CRD42018091763 .

J Nanobiotechnology. 2019 Jan 25;17(1):16. doi: 10.1186/s12951-018-0437-z.

Exosome origin determines cell targeting and the transfer of therapeutic nanoparticles towards target cells.

Sancho-Albero M[1,2], Navascués N[1,2], Mendoza G[1], Sebastián V[1,2], Arruebo M[3,4], Martín-Duque P[5,6], Santamaría J[1,2].
Author information

Abstract

BACKGROUND:

Exosomes are considered key elements for communication between cells, but very little is known about the mechanisms and selectivity of the transference processes involving exosomes released from different cells.

RESULTS:

In this study we have investigated the transfer of hollow gold nanoparticles (HGNs) between different cells when these HGNs were loaded within exosomes secreted by human placental mesenchymal stem cells (MSCs). These HGNs were successfully incorporated in the MSCs exosome biogenesis pathway and released as HGNs-loaded exosomes. Time-lapse microscopy and atomic emission spectroscopy allowed us to demonstrate the selective transfer of the secreted exosomes only to the cell type of origin when studying different cell types including cancer, metastatic, stem or immunological cells.

CONCLUSIONS:

In this study we demonstrate the selectivity of in vitro exosomal transfer between certain cell types and how this phenomenon can be exploited to develop new specific vectors for advanced therapies. Specifically, we show how this preferential uptake can be leveraged to selectively induce cell death by light-induced hyperthermia only in cells of the same type as those producing the corresponding loaded exosomes. We describe how the exosomes are preferentially transferred to some cell types but not to others, thus providing a better understanding to design selective therapies for different diseases.

Biotechnol Lett. 2019 Jan 24. doi: 10.1007/s10529-019-02649-7. [Epub ahead of print]

Mesenchymal stem cell sheets: a new cell-based strategy for bone repair and regeneration.

Chen M[1], Xu Y[1], Zhang T[1], Ma Y[2], Liu J[3], Yuan B[3], Chen X[1], Zhou P[1], Zhao X[1], Pang F[1], Liang W[4].
Author information

Abstract

Mesenchymal stem cells (MSCs), a class of adult stem cells, are considered a promising source for bone regeneration. Although combining MSCs with biomaterial scaffolds offers an interesting clinical strategy for bone tissue engineering, the presence of the scaffolds could induce an undesirable effect on cell-cell interactions. Moreover, before the application of scaffold materials in bone tissue reconstruction, cells must be manipulated with proteolytic enzymes, such as trypsin or dispase that degrade extracellular matrix (ECM) molecules and cell surface proteins, which can result in the cell damage and loss of cellular activity. Therefore, the development of alternative strategies for bone regeneration is required to solve these problems. Recently, a novel tissue engineering technology named 'cell sheet' has been efficaciously utilized in the regeneration of bone, corneal, cardiac, tracheal and periodontal ligament-like tissues. The cell sheet is a layer of cells, which contains intact ECM and cell surface proteins such as growth factor receptors, ion channels and cell-to-cell junction proteins. MSC sheets can be easily fabricated by layering the recovered cell sheets without any scaffolds or complicated manipulation. This review summarizes the current state of the literature regarding the use of MSCs to produce cell sheets and assesses their applicability in bone tissue regeneration and repair.

Bioeng Transl Med. 2018 Sep 20;4(1):51-60. doi: 10.1002/btm2.10104. eCollection 2019 Jan.

Rescuing mesenchymal stem cell regenerative properties on hydrogel substrates post serial expansion.

Rao VV[1,2], Vu MK[1,2], Ma H[1,2], Killaars AR[2,3], Anseth KS[1,2].
Author information

Abstract

The use of human mesenchymal stem/stromal cells (hMSCs) in most clinical trials requires millions of cells/kg, necessitating *ex vivo*expansion typically on stiff substrates (tissue culture polystyrene [TCPS]), which induces osteogenesis and replicative senescence. Here, we quantified how serial expansion on TCPS influences proliferation, expression of hMSC-specific surface markers, mechanosensing, and secretome. Results show decreased proliferation and surface marker expression after five passages (P5) and decreased mechanosensing ability and cytokine production at later passages (P11-P12). Next, we investigated the capacity of poly(ethylene glycol) hydrogel matrices (E ~ 1 kPa) to rescue hMSC regenerative properties. Hydrogels reversed the reduction in cell surface marker expression observed at P5 on TCPS and increased secretion of cytokines for P11 hMSCs. Collectively, these results show that TCPS expansion significantly changes functional properties of hMSCs. However, some changes can be rescued by using hydrogels, suggesting that tailoring material properties could improve *in vitro* expansion methods.

Mater Sci Eng C Mater Biol Appl. 2019 Apr;97:12-22. doi: 10.1016/j.msec.2018.12.012. Epub 2018 Dec 7.

Synergistic effect of bimodal pore distribution and artificial extracellular matrices in polymeric scaffolds on osteogenic differentiation of human mesenchymal stem cells.

Wojak-Ćwik IM[1], Rumian Ł[2], Krok-Borkowicz M[2], Hess R[3], Bernhardt R[3], Dobrzyński P[4], Möller S[5], Schnabelrauch M[5], Hintze V[3], Scharnweber D[3], Pamuła E[6].
Author information

Abstract

The main objective of this study was to enhance the biological performance of resorbable polymeric scaffolds for bone tissue engineering. Specifically, we focused on both microstructure and surface modification of the scaffolds to augment adhesion, proliferation and osteogenic differentiation of human mesenchymal stem cells (hMSC). Moreover, a new cell seeding method assuring 90% seeding efficiency on the scaffolds was developed. Poly(l-lactide-co-glycolide) (PLGA) scaffolds with monomodal and bimodal pore distribution were produced by solvent casting/phase separation followed by porogen leaching and modified with artificial extracellular matrices (aECM) consisting of collagen type I and high sulphated hyaluronan (sHya). The application of two porogens resulted in bimodal pore distribution within the PLGA scaffolds as shown by scanning electron microscopy and microcomputer tomography. Two types of pores with diameters 400-600 µm and 2-20 µm were obtained. The scaffolds were successfully coated with a homogenous layer of aECM as shown by Sirius red and toluidine blue staining. In vitro study showed that presence of bimodal pore distribution in combination with collagen/sHya did not significantly influence hMSC proliferation and early osteogenic differentiation

compared to scaffolds with monomodal pore distribution. However, it enhanced mineralization as well as the expression of Runt-related transcription factor 2, osteopontin and bone sialoprotein II. As a result PLGA scaffolds with bimodal pore distribution modified with collagen/sHya can be considered as prospective material promoting bone regeneration.

Stem Cells Transl Med. 2019 Feb;8(2):194-204. doi: 10.1002/sctm.18-0147.

Challenges Toward the Identification of Predictive Markers for Human Mesenchymal Stromal Cells Chondrogenic Potential.

Stüdle C[1], Occhetta P[1], Geier F[1], Mehrkens A[1], Barbero A[1], Martin I[1].
Author information

Abstract

Human bone marrow derived mesenchymal stromal cells (BMSCs) represent a putative cell source candidate for tissue engineering-based strategies to repair cartilage and bone. However, traditional isolation of BMSCs by adhesion to plastic leads to very heterogeneous cell populations, accounting for high variability of chondrogenic differentiation outcome, both across donors and across clonally derived strains. Identification of putative surface markers able to select BMSC subpopulations with higher chondrogenic capacity (CC) and reduced variance in chondrogenic differentiation could aid the development of BMSC-based cartilage and bone regeneration approaches. With the goal to identify predictive markers for chondrogenic BMSC populations, we assessed the gene expression profile of single cell-derived clones with high and low CC. While a clustering between high and low CC clones was observed for one donor, donor-to-donor variability hampered the possibility to achieve conclusive results when different donors were considered. Nevertheless, increased NCAM1/CD56 expression correlated in clones derived from one donor with higher CC, the same trend was observed for three additional donors (even if no significance was achieved). Enriching multiclonal BMSCs for $CD56^+$ expression led to an increase in CC, though still highly affected by donor-to-donor variability. Our study finally suggests that definition of predictive marker(s) for BMSCs chondrogenesis is challenged by the large donor heterogeneity of these cells, and by the high complexity and plasticity of the BMSCs system. Multiple pathways and external parameters may be indeed involved in determining the chondrogenic potential of BMSCs, making the identification of putative markers still an open issue.

J Biol Eng. 2019 Jan 18;13:7. doi: 10.1186/s13036-019-0140-0. eCollection 2019.

Nucleic acid delivery to mesenchymal stem cells: a review of nonviral methods and applications.

Hamann A[1], Nguyen A[1], Pannier AK[1].
Author information

Abstract

BACKGROUND:

Mesenchymal stem cells (MSCs) are multipotent stem cells that can be isolated and expanded from many tissues, and are being investigated for use in cell therapies. Though MSC therapies have

demonstrated some success, none have been FDA approved for clinical use. MSCs lose stemness *ex vivo,* decreasing therapeutic potential, and face additional barriers *in vivo,* decreasing therapeutic efficacy. Culture optimization and genetic modification of MSCs can overcome these barriers. Viral transduction is efficient, but limited by safety concerns related to mutagenicity of integrating viral vectors and potential immunogenicity of viral antigens. Nonviral delivery methods are safer, though limited by inefficiency and toxicity, and are flexible and scalable, making them attractive for engineering MSC therapies.

MAIN TEXT:

Transfection method and nucleic acid determine efficiency and expression profile in transfection of MSCs. Transfection methods include microinjection, electroporation, and nanocarrier delivery. Microinjection and electroporation are efficient, but are limited by throughput and toxicity. In contrast, a variety of nanocarriers have been demonstrated to transfer nucleic acids into cells, however nanocarrier delivery to MSCs has traditionally been inefficient. To improve efficiency, plasmid sequences can be optimized by choice of promoter, inclusion of DNA targeting sequences, and removal of bacterial elements. Instead of DNA, RNA can be delivered for rapid protein expression or regulation of endogenous gene expression. Beyond choice of nanocarrier and nucleic acid, transfection can be optimized by priming cells with media additives and cell culture surface modifications to modulate barriers of transfection. Media additives known to enhance MSC transfection include glucocorticoids and histone deacetylase inhibitors. Culture surface properties known to modulate MSC transfection include substrate stiffness and specific protein coating. If nonviral gene delivery to MSCs can be sufficiently improved, MSC therapies could be enhanced by transfection for guided differentiation and reprogramming, transplantation survival and directed homing, and secretion of therapeutics. We discuss utilized delivery methods and nucleic acids, and resulting efficiency and outcomes, in transfection of MSCs reported for such applications.

CONCLUSION:

Recent developments in transfection methods, including nanocarrier and nucleic acid technologies, combined with chemical and physical priming of MSCs, may sufficiently improve transfection efficiency, enabling scalable genetic engineering of MSCs, potentially bringing effective MSC therapies to patients.

Cell Tissue Bank. 2019 Jan 23. doi: 10.1007/s10561-019-09749-8. [Epub ahead of print]

Encapsulated explant in novel low shear perfusion bioreactor improve cell isolation, expansion and colony forming unit.

Gharravi AM[1].

Author information

Abstract

One of most important issue in the field of regenerative medicine is selection of appropriate cells, scaffolds and bioreactors. The present study aimed to investigate the appropriate method for the

isolation of human UC-MSCs cells from explant cultured in alginate scaffold within novel perfusion bioreactor. MSCs were isolated with explant method and CD markers such CD73, CD31, CD90 and CD105 as were analyzed by flow cytometry. The culture chamber of the novel perfusion bioreactor was made from Plexiglas and housed the cell/scaffold constructs in the central part and the medium for the whole culture period. The flow behavior within the bioreactor chamber were performed for closed and open bypass systems. The shear stress profiles simulated using CFD modeling. The fluid flow distribution within the bioreactor chamber was performed in PBS solution containing a blue colorant. UC explants were resuspended in sodium alginate and were allowed to polymerize and placed in the perfusion bioreactor and cultured. MSCs were positive for mesenchymal markers such as CD73 and CD31. All 3D Perfusion bioreactor parts, except peristaltic pump was sterilizable by autoclaving. Results of CFD indicated very low wall shear stress on surface of culture chamber at flow rate 2 ml/min. The maximum wall shear stress was 1.10×10^{-3} m/s = 0.0110 dyne/cm^2 (1 Pa = 10 dyne/cm^2). The fluid flow distribution within the alginate gel initially exhibited oscillation. In comparison, when encapsulated explants were placed in the perfusion bioreactor, cell proliferation appeared faster ($4.6 \times 10^{11} \pm 9.2 \times 10^{11}$) than explants cultures in 2D conventional culture method ($3.2 \times 10^{11} \pm 1 \times 10^{11}$). Proliferated cell formed several colonies. Migration of chondrocytes to the periphery of the alginate bead was visible after 1 week of culture. Perfusion bioreactor with low shear stress and alginate hydrogel improve cell isolation and expansion and eliminate cell passaging and enhance colony forming unit of UC-MSCs.

J Mol Histol. 2019 Jan 22. doi: 10.1007/s10735-019-09812-4. [Epub ahead of print]

Melatonin preconditioning of bone marrow-derived mesenchymal stem cells promotes their engraftment and improves renal regeneration in a rat model of chronic kidney disease.

Saberi K[1], Pasbakhsh P[1], Omidi A[1], Borhani-Haghighi M[1,2], Nekoonam S[1], Omidi N[3], Ghasemi S[1], Kashani IR[4].

Author information

Abstract

Bone marrow-derived mesenchymal stem cells (BMMSCs) transplantation has shown to be effective in treating chronic kidney disease. However, the effectiveness of this strategy is constrained by low homing and survival rate of transplanted cells in the injured organs. Therefore, developing strategies to improve homing and cell survival rate and therapeutic potential in cell-based therapies seems necessary. The purpose of this study is to evaluate the effect of pretreating BMMSCs with melatonin (MT) on the prosurvival and renoprotective of transplanted cells into the irreversible model of unilateral ureteral obstruction. Adult male Sprague-Dawley rats were randomized into four groups: Sham, UUO, UUO + BMMSCs, and UUO + BMMSCs + MT. The results of our study demonstrated that preconditioning with MT enhanced homing of BMMSCs into the injured kidney. MT reduced the number of TUNEL positive transplanted cells in the UUO + BMMSCs + MT group. The UUO + BMMSCs + MT

group showed lower expressions of TGF-β1, α-SMA and TNF-α at both gene and protein levels but higher expression of E-cadherin compared with the UUO + BMMSCs group. In addition, MT preconditioned BMMSCs ameliorated basement membrane disruption and histological status of injured renal tubules and also reduced fibrosis in damaged kidneys. In conclusion, our results show that stem cells pretreated by MT may represent a feasible approach for improving the beneficial effects of stem cell therapy and significantly enhance their survival after transplantation to the injured kidney.

Stem Cell Res Ther. 2019 Jan 22;10(1):41. doi: 10.1186/s13287-019-1142-z.

Low-intensity pulsed ultrasound promotes chondrogenesis of mesenchymal stem cells via regulation of autophagy.

Wang X[1], Lin Q[1], Zhang T[1], Wang X[1], Cheng K[1], Gao M[1], Xia P[2], Li X[3].
Author information

Abstract

BACKGROUND:

Low-intensity pulsed ultrasound (LIPUS) can induce mesenchymal stem cell (MSC) differentiation, although the mechanism of its potential effects on chondrogenic differentiation is unknown. Since autophagy is known to regulate the differentiation of MSCs, the aim of our study was to determine whether LIPUS induced chondrogenesis via autophagy regulation.

METHODS:

MSCs were isolated from the rat bone marrow, cultured in either standard or chondrogenic medium, and stimulated with 3 MHz of LIPUS given in 20% on-off cycles, with or without prior addition of an autophagy inhibitor or agonist. Chondrogenesis was evaluated on the basis of aggrecan (AGG) organization and the amount of type II collagen (COL2) and the mRNA expression of AGG, COL2, and SRY-related high mobility group-box gene 9 (SOX9) genes.

RESULTS:

LIPUS promoted the chondrogenic differentiation of MSCs, as shown by the changes in the extracellular matrix (ECM) proteins and upregulation of chondrogenic genes, and these effects were respectively augmented and inhibited by the autophagy inhibitor and agonist.

CONCLUSIONS:

Taken together, these results indicate that LIPUS promotes MSC chondrogenesis by inhibiting autophagy.

Asian Spine J. 2019 Jan 24. doi: 10.31616/asj.2018.0215. [Epub ahead of print]

Epidural Fat-Derived Mesenchymal Stem Cell: First Report of Epidural Fat-Derived Mesenchymal Stem Cell.

Lee GW[1], Seo MS[2], Kang KK[2], Oh SK[2].
Author information

Abstract

STUDY DESIGN:

Experimental study.

PURPOSE:

To determine whether epidural fat (EF) tissue contains mesenchymal stem cells (MSC).

OVERVIEW OF LITERATURE:

Spine surgeons are unaware of the contents of EF tissue and the reason for its presence between the ligamentum flavum and the dura mater; therefore, EF tissues are routinely eliminated during surgical procedures. However, EF removal causes certain postoperative problems, such as post-laminectomy syndrome. We hypothesized that the EF tissue may play a significant supportive role for the neural structures and other nearby conditions.

METHODS:

EF tissues were obtained from consenting patients (n=3) during posterior decompression surgery of the lumbar spine. The primary cells were isolated and cultured as per previously described methods with some modifications, and the cell morphology and cumulation were examined. Thereafter, reverse transcription-polymerase chain reaction (RT-PCR), a fluorescence-activated cell sorting (FACS) analysis, and differentiation potency for differentiation into osteoblasts, chondroblasts, and adipocytes were investigated to identify whether the cells derived from EF are MSC.

RESULTS:

The cells from the EF tissue had a fibroblast or neuron-like morphology that persisted until the senescence at p18. MSCspecific genes, such as OCT4, SOX2, KLF4, MYC, and GAPDH were expressed in the RT-PCR study, while MSC-specific surface markers such as CD105, CD90, and CD73 were exhibited in the FACS analysis. The differentiation properties of EF-MSC for differentiation into the three types of cells (osteoblast, chondroblast, and adipocyte) were also confirmed.

CONCLUSIONS:

Based on the cell culture, FACS analysis, RT-PCR analysis, and differentiation potent outcomes, all the features of the cells corresponded to MSC. This is the first study to identify EF-MSC derived from the EF tissue.

Int J Nanomedicine. 2019 Jan 14;14:573-589. doi: 10.2147/IJN.S184920. eCollection 2019.

Iron oxide nanoparticles promote the migration of mesenchymal stem cells to injury sites.

Li X[1], Wei Z[1], Lv H[1], Wu L[1], Cui Y[1], Yao H[1], Li J[1], Zhang H[2], Yang B[2], Jiang J[1].

Author information

Abstract

BACKGROUND:

Developing new methods to deliver cells to the injured tissue is a critical factor in translating cell therapeutics research into clinical use; therefore, there is a need for improved cell homing capabilities.

MATERIALS AND METHODS:

In this study, we demonstrated the effects of labeling rat bone marrow-derived mesenchymal stem cells (MSCs) with fabricated polydopamine (PDA)-capped Fe_3O_4 (Fe_3O_4@PDA) superparticles employing preassembled Fe_3O_4 nanoparticles as the cores.

RESULTS:

We found that the Fe_3O_4@PDA composite superparticles exhibited no adverse effects on MSC characteristics. Moreover, iron oxide nanoparticles increased the number of MSCs in the S-phase, their proliferation index and migration ability, and their secretion of vascular endothelial growth factor relative to unlabeled MSCs. Interestingly, nanoparticles not only promoted the expression of C-X-C chemokine receptor 4 but also increased the expression of the migration-related proteins c-Met and C-C motif chemokine receptor 1, which has not been reported previously. Furthermore, the MSC-loaded nanoparticles exhibited improved homing and anti-inflammatory abilities in the absence of external magnetic fields in vivo.

CONCLUSION:

These results indicated that iron oxide nanoparticles rendered MSCs more favorable for use in injury treatment with no negative effects on MSC properties, suggesting their potential clinical efficacy.

Acta Biomater. 2019 Jan 18. pii: S1742-7061(19)30059-5. doi: 10.1016/j.actbio.2019.01.039. [Epub ahead of print]

Platelet Rich Plasma Hydrogels Promote in vitro and in vivo Angiogenic Potential of Adipose-Derived Stem Cells.

Samberg M[1], Stone R 2nd[1], Natesan S[1], Kowalczewski A[1], Becerra S[1], Wrice N[1], Cap A[2], Christy R[3].

Author information

Abstract

Despite great advances in skin wound care utilizing grafting techniques, the resulting severe scarring, deformity and ineffective vascularization remains a challenge. Alternatively, tissue engineering of new skin using patient-derived stem cells and scaffolding materials promises to greatly increase the functional and aesthetic outcome of skin wound healing. This work focused on the optimization of a polyethylene glycol modified (PEGylated) platelet-rich plasma (PRP) hydrogel for the protracted release of cytokines, growth factors, and signaling molecules and also the delivery of a provisional physical framework for stem cell angiogenesis. Freshly collected whole blood was utilized to synthesize PEGylated PRP hydrogels containing platelet concentrations ranging from 0 to 200,000 platelets/µl. Hydrogels were characterized using thromboelastography and impedance aggregometry for platelet function and were visualized using scanning electron microscopy. To assess the effects of PEGylated PRP hydrogels on cells, PRP solutions were seeded with human adipose-derived stem cells (ASCs) prior to gelation. Following 14 days of incubation in vitro, increased platelet concentrations resulted in higher ASC proliferation and vascular gene and protein expression (assessed via RT-PCR, ELISA, and immunochemistry). Using a rat skin excision model, wounds treated with PRP + ASC hydrogels increased the number of vessels in the wound by day 8 (80.2 vs. 62.6 vessels/mm^2) compared to

controls. In conclusion, the proposed PEGylated PRP hydrogel promoted both in vitro and transient in vivo angiogenesis of ASCs for improved wound healing. STATEMENT OF SIGNIFICANCE: Our findings support an innovative means of cellular therapy intervention to improve surgical wound healing in a normal wound model. ASCs seeded within PEGylated PRP could be an efficacious and completely autologous therapy for treating patients who have poorly healing wounds caused by vascular insufficiency, previous irradiation, or full-thickness burns. Because wound healing is a dynamic and complex process, the application of more than one growth factor with ASCs demonstrates an advantageous way of improving healing.

Dis Colon Rectum. 2019 Jan 18. doi: 10.1097/DCR.0000000000001333. [Epub ahead of print]

Early Results of a Phase I Trial Using an Adipose-Derived Mesenchymal Stem Cell-Coated Fistula Plug for the Treatment of Transsphincteric Cryptoglandular Fistulas.

Dozois EJ, Lightner AL, Mathis KL, Chua HK, Kelley SR, Fletcher JG, Dietz AB, Friton JJ, Butler GW, Faubion WA.

Abstract

BACKGROUND:

Management of transsphincteric cryptoglandular fistulas remains a challenging problem and the optimal surgical approach remains elusive. Mesenchymal stem cells, increasingly being utilized for perianal Crohn's disease, offer a novel therapy to treat cryptoglandular fistulas.

OBJECTIVES:

This study aimed to determine safety and feasibility of using an autologous mesenchymal stem cell-coated fistula plug in patients with transsphincteric cryptoglandular fistulas.

DESIGN:

This study is a phase I clinical trial.

SETTING:

This study was conducted at a tertiary academic medical center.

PATIENTS:

Adult (>18 years) male and female patients with transsphincteric cryptoglandular fistulas were selected.

MAIN OUTCOMES MEASURES:

The primary outcomes measured were the safety, feasibility, and efficacy of a mesenchymal stem cell-coated fistula plug in patients with transsphincteric fistulas.

RESULTS:

Fifteen patients (8 women, mean age 39.8 years) with a single-tract transsphincteric fistula received a mesenchymal stem cell-loaded fistula plug and were followed for 6 months. Duration of disease at the time of study enrollment was a median of 3.0 years (range, 1-13 years) with a median of 3.5 (range, 1-20) prior surgical interventions. Adverse events included 1 plug extrusion, 1 abdominal wall seroma, 3

perianal abscesses requiring drainage, and 1 patient with perianal cellulitis. There were no serious adverse events. At 6 months, 3 patients had complete clinical healing, 8 had partial healing, and 4 patients showed no clinical improvement. Radiographic improvement was seen in 11 of 15 patients.

LIMITATIONS:

This study was limited by the small cohort and short follow-up.

CONCLUSIONS:

Autologous mesenchymal stem cell-coated fistula plug treatment of transsphincteric cryptoglandular fistulas was safe and feasible and resulted in complete or partial healing in a majority of patients. See Video Abstract at http://links.lww.com/DCR/A897.

Mol Med Rep. 2019 Jan 10. doi: 10.3892/mmr.2019.9842. [Epub ahead of print]

Effects of storage culture media, temperature and duration on human adipose-derived stem cell viability for clinical use.

Wu YD[1], Li M[1], Liao X[1], Li SH[1], Yan JX[1], Fan L[2], She WL[1], Song JX[3], Liu HW[1].
Author information

Abstract

Adipose-derived stem cells (ADSCs) are mesenchymal stem cells that are often used in regenerative medicine. Maintaining ADSC viability is important, as this optimizes the curative effects of cell therapy. However, the optimal conditions for cell viability preservation remain unknown. The present study aimed to acquire a better protocol for ADSC storage by comparing the effects of various solutions and temperatures for ADSC preservation, in order to suggest the most effective methods of short-term ADSC preservation for clinical use. ADSCs from passage 2 were suspended in solutions comprising 0.9% NaCl, 10% human serum (HS) or 10% platelet-rich plasma (PRP). Suspended cells were maintained at 4˚C or room temperature (~26˚C) for 2, 4 and 6 h. The differentiation capacity, apoptosis and proliferation of ADSCs were determined by oil red O/alizarin red S staining, flow cytometry, and a cell counting kit-8 cell proliferation assay, respectively. In addition, reverse transcription-quantitative polymerase chain reaction and western blot analysis was performed. The results revealed that proliferation of ADSCs decreased with time. The optimal time for ADSC use was ~2 h, and 4 h was determined to be the latest time that ADSCs should be used. The 10% HS group had the highest survival rate, followed by the 10% PRP group; these two groups had higher survival rates than the 0.9% NaCl group ($P<0.05$). HS and PRP at 4˚C enhanced the ADSC proliferation rate ($P<0.05$), although the difference between these two groups was insignificant ($P>0.05$). In conclusion, the optimal time to use ADSCs was <2 h, and should not exceed 4 h. It was recommended that, for the transportation and short-term storage of ADSCs during clinical use, they should be stored with 10% HS at 4˚C to maintain ADSC viability. In addition, this was a cost-effective and safe method.

Send to

J Vis Exp. 2019 Jan 7;(143). doi: 10.3791/58825.

Mesenchymal Stem Cell Isolation from Pulp Tissue and Co-Culture with Cancer Cells to Study Their Interactions.

Doğan A[1], Demirci S[2], Apdik H[1], Apdik EA[1], Şahin F[1].
Author information

Abstract

Cancer as a multistep process and complicated disease is not only regulated by individual cell proliferation and growth but also controlled by tumor environment and cell-cell interactions. Identification of cancer and stem cell interactions, including changes in extracellular environment, physical interactions, and secreted factors, might enable the discovery of new therapy options. We combine known co-culture techniques to create a model system for mesenchymal stem cells (MSCs) and cancer cell interactions. In the current study, dental pulp stem cells (DPSCs) and PC-3 prostate cancer cell interactions were examined by direct and indirect co-culture techniques. Condition medium (CM) obtained from DPSCs and 0.4 μm pore sized trans-well membranes were used to study paracrine activity. Co-culture of different cell types together was performed to study direct cell-cell interaction. The results revealed that CM increased cell proliferation and decreased apoptosis in prostate cancer cell cultures. Both CM and trans-well system increased cell migration capacity of PC-3 cells. Cells stained with different membrane dyes were seeded into the same culture vessels, and DPSCs participated in a self-organized structure with PC-3 cells under this direct co-culture condition. Overall, the results indicated that co-culture techniques could be useful for cancer and MSC interactions as a model system.

Am J Transl Res. 2018 Nov 15;10(11):3555-3566. eCollection 2018.

Gene expression profiling: identification of gene expression in human MSC chondrogenic differentiation.

Gong M[1,2], Liang T[3], Zhang H[1], Chen S[1], Hu Y[1], Zhou J[1], Zhang X[1], Zhang W[1], Geng X[4], Zou X[2].
Author information

Abstract

Understanding the mechanisms that govern cell fate will lead to the development of techniques for the induction of human mesenchymal stem cell differentiation into desired cell outcomes and the production of an autologous source of tissue for regenerative medicine. Here, we demonstrate that stem cells derived from adult bone marrow grown with 3D pellets take on characteristics similar to human cartilage. The NFAT signaling pathway is primarily linked to cell differentiation and influences chondrogenic differentiation. Based on our previous results that alterations in the expression of the NFATc1 gene affect chondrogenesis, we screened a microarray and identified 29 genes with altered expression, including 13 up-regulated (fold change ≥ 2) and 16 down-regulated (fold change ≤ 2) genes, compared with the control group. We then used RT-PCR to validate the chip data. Gene ontology and pathway analyses were performed on these altered genes. We found that these altered genes function in the complement and coagulation cascades, metabolism, biosynthesis, transcriptional regulation, proteolysis, and intracellular signaling pathways, such as the cytoplasmic calcineurin-dependent signaling pathway, the cyclin-dependent kinase inhibitor 2C signaling pathway, the MAPK

signaling pathway, and the insulin signaling pathway. Our study suggests that these pathways may play important roles in chondrogenesis, which could be useful in the design of biomaterials.

Asian Pac J Cancer Prev. 2019 Jan 25;20(1):263-267.

Novel Combination of Mesenchymal Stem Cell-Conditioned Medium with Sorafenib Have Synergistic Antitumor Effect of Hepatocellular Carcinoma Cells

Seyhoun I[1], Hajighasemlou S, Ai J, Hosseinzadeh F, Mirmoghtadaei M, Seyhoun SM, Parseh B, Abdolahi S, Ghazvinian Z, Shadnoush M, Verdi J.

Author information

Abstract

OBJECTIVE:

Hepatocellular carcinoma (HCC) is the most common liver malignancy. Sorafenib is the first-line systemic treatment for advanced HCCs. However, due to safety concerns, researchers are now looking for ways to boost the efficacy of the medication. One approach for reducing toxicity is combining sorafenib with other agents so that a lower dose of sorafenib is required. Mesenchymal stromal cells (MSCs) can have an inhibitory effect on HCC tumor growth. Mesenchymal Stem Cell-Conditioned Medium (MSC-CM) is the substance extracted from MSC culture and contains most of the potential cytokines secreted by MSCs. We, therefore, anticipated a synergistic Antitumor Effect of sorafenib in Combination with MSC-CM. In this study, we used HepG2 as our target cell lines.

METHODS:

HepG2 cells were treated with sorafenib alone and with sorafenib + MSC-CM. CCK-8 assay was used to evaluate and compare the inhibition of cell growth between the two groups with different treatments.

RESULTS:

The combination treatment of cell lines with sorafenib and MSC-CM had significantly reduced the values of IC50 compared to the use of sorafenib alone (3.4 vs. 2.7 respectively).

CONCLUSION:

This study suggests that a combination of sorafenib with MSC-CM can synergistically suppress the growth of HCC cells.