Joints. 2018 Jun 14;6(2):100-103. doi: 10.1055/s-0038-1660789. eCollection 2018 Jun.

The Effect of Three Different Suture Anchors for Rotator Cuff Repair on Primary Cultures of Human Bone Marrow Mesenchymal Stem Cells.

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Author information

Abstract

Purpose The purpose of this study is to investigate the in vitro biocompatibility of three different suture anchors (all-suture anchor, metal anchor, and polyetheretherketone anchor), commonly used for the rotator cuff repair. **Methods** To assess the biocompatibility of the anchors, the possible cytotoxicity and the immunogenicity of the devices were assessed by cell viability assay and cell count on cultures of bone marrow stem cells (BMSCs) and peripheral blood leucocytes (PBLs), respectively. The possible inhibitory effect of the devices on BMSCs osteogenic potential was evaluated by alkaline phosphatase activity and matrix deposition assay. **Results** The viability of BMSCs was slightly reduced when cultured in the presence of the devices (-24 ± 3%). Nevertheless, they were able to differentiate toward the osteogenic lineage in all culture conditions. The proliferation of PBLs and the production of interleukin-2 were not enhanced by the presence of any device. **Conclusion** The analyzed devices did not significantly affect the normal cells functions when directly cultured with human primary BMSCs or PBLs, in terms of osteogenic differentiation and inflammatory reaction. **Clinical Relevance** A deeper knowledge of the biological reactions to different devices used in rotator cuff surgeries would improve the clinical outcome of these procedures.

J Tissue Eng Regen Med. 2018 Jul 25. doi: 10.1002/term.2732. [Epub ahead of print]
Stem Cells Transl Med. 2018 Jul 23. doi: 10.1002/sctm.18-0020. [Epub ahead of print]

Intra-Articular Administration of Autologous Micro-Fragmented Adipose Tissue in Dogs with Spontaneous Osteoarthritis: Safety, Feasibility, and Clinical Outcomes.

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Abstract

Similar to the disease affecting humans, osteoarthritis (OA) is a painful musculoskeletal condition affecting 20% of the adult canine population. Several solutions have been proposed, but the results achieved to date are far from being satisfactory. New approaches, such as intra-articular delivery of cells (including mesenchymal stromal cells), have been proposed. Among the many sources, the adipose tissue is considered very promising. We evaluated the safety, feasibility, and efficacy of a

single intra-articular injection of autologous and micro-fragmented adipose tissue (MFAT) in 130 dogs with spontaneous OA. MFAT was obtained using a minimally invasive technique in a closed system and injected in the intra- and/or peri-articular space. Clinical outcomes were determined using orthopedic examination and owners' scores for up to 6 months. In 78% of the dogs, improvement in the orthopedic score was registered 1 month after treatment and continued gradually up to 6 months when 88% of the dogs improved, 11% did not change, and 1% worsened compared with baseline. Considering the owners' scores at 6 months, 92% of the dogs significantly improved, 6% improved only slightly, and 2% worsened compared with baseline. No local or systemic major adverse effects were recorded. The results of this study suggest that MFAT injection in dogs with OA is safe, feasible, and beneficial. The procedure is time sparing and cost-effective. Post injection cytological investigation, together with the clinical evidence, suggests a long-term pain control role of this treatment.

Nonunion fracture healing: evaluation of effectiveness of demineralized bone matrix and mesenchymal stem cells in a novel sheep bone nonunion model.

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Abstract

Nonunion treatment has a high rate of success, although recalcitrant nonunion may determine the need for amputation. Therefore, new treatment options are continuously investigated in order to further reduce the risk of nonunion recurrence. This study aimed to (i) develop a new large animal model for bone atrophic nonunion and (ii) compare the efficacy of demineralized bone matrix (DBM) and DBM in combination with mesenchymal stem cells (MSC) in the new nonunion model. The new model consists of a non-critical, full-thickness segmental defect created in the sheep tibia, stabilized by an intramedullary nail, and involves the creation of a locally impaired blood supply achieved through periosteum excision and electrocauterization of the stump ends. Six weeks after defect creation, lack of hard tissue callus and established nonunion was observed in all operated tibiae both by radiographic and clinical evaluation. Nonunion was treated with allogeneic DBM or autologous MSC cultivated on DBM particles (DBM+MSC) for one day before implantation. Twelve weeks after treatment, radiographic, microtomographic, histologic and histomorphometric analysis showed the formation of bone callus in DBM group, while the fracture healing appeared at an early stage in DBM+MSC group. Torsional strength and stiffness of the DBM group appeared higher than those of DBM+MSC group, although the differences were not statistically significant. In conclusion, a new sheep bone nonunion model resembling the complexity of the clinical condition was developed. DBM is an effective option for nonunion treatment, while MSC do not improve the healing process when cultivated on DBM particles before implantation.

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Manufacturing mesenchymal stromal cells for the treatment of graft-versus-host disease: a survey amongst centers affiliated to the European Group of Blood and Marrow Transplantation.

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Abstract

BACKGROUND:

The immunosuppressive properties of mesenchymal stromal cells (MSC) have been successfully tested to control clinical severe graft-versus host disease (GvHD) and improve survival. However, clinical studies have not yet provided conclusive evidence of their efficacy largely because of lack of patients' stratification criteria. The heterogeneity of MSC preparations is also a major contributing factor, as manufacturing of therapeutic MSC is performed according to different protocols amongst different centers. Understanding the variability of the manufacturing protocol would allow a better comparison of the results obtained in the clinical setting amongst different centers. In order to acquire information on MSC manufacturing we have sent a questionnaire to the European Group for Blood and Marrow Transplantation (EBMT) centers registered as producing MSC.

METHODS:

Data from 17 centers were obtained and analyzed by means of a two-phase questionnaire specifically focused on product manufacturing. Gathered information included MSC tissue sources, MSC donor matching, medium additives for ex-vivo expansion, data on MSC product specification for clinical release.

RESULTS:

The majority of centers manufactured MSC from bone marrow (88%), whilst only two centers produced MSC from umbilical cord blood or cord tissue. One of the major changes in the manufacturing process has been the replacement of fetal bovine serum with human platelet lysate as medium supplement. 59% of centers used only third-party MSC, whilst only one center manufactured exclusively autologous MSC. The large majority (71%) of these facilities administered MSC exclusively from frozen batches. Aside from variations in the culture method, we found large heterogeneity also regarding product specification, particularly in the markers used for phenotypical characterization and their threshold of expression, use of potency assays to test MSC functionality and karyotyping.

DISCUSSION:

The initial data collected from this survey highlight the variability in MSC manufacturing as clinical products and the need for harmonization. Until more informative potency assays become available, a more homogeneous approach to cell production may at least reduce variability in clinical trials and improve interpretation of results.

Stem Cells Dev. 2018 Jul 25. doi: 10.1089/scd.2017.0241. [Epub ahead of print]

Comparison of antibacterial and immunological properties of Mesenchymal Stem/Stromal cells from equine Bone Marrow, Endometrium and Adipose tissue.

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Abstract

Equine Mesenchymal stem/stromal cells (MSCs) are multipotent cells that are widely used for treatment of musculoskeletal injuries, and there is significant interest in expanding their application to non-orthopedic conditions. MSCs possess antibacterial and immunomodulatory properties which may be relevant for combatting infection, however, comparative studies using MSCs from different origins have not been carried out in the horse, and this was the focus of the present study. Our results showed that MSC-conditioned media attenuated the growth of Escherichia coli, and that this effect was, on average, more pronounced for endometrium (EM)- and adipose tissue (AT)- than for bone marrow (BM)-derived MSCs. In addition, the antimicrobial Lipocalin-2 was expressed at mean higher levels in EM- compared to AT- and BM-MSCs, and the bacterial product lipopolysaccharide (LPS) stimulated its production by all three MSC types. We also show that MSCs express IL-6, IL-8, MCP-1, CCL5 and TLR4, and that, in general, these cytokines were induced in all cell types by LPS. Low expression levels of the macrophage marker CSF1-R were detected in BM- and EM-MSCs, but not in AT-MSCs. Altogether, these findings suggest that equine MSCs from endometrium, adipose tissue and bone marrow have both direct and indirect antimicrobial properties which may vary between MSCs from different origins and could be exploited towards improvement of regenerative therapies for horses.

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Lung resident mesenchymal cells isolated from patients with the Bronchiolitis Obliterans Syndrome display a deregulated epigenetic profile.

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Abstract

Bronchiolitis Obliterans Syndrome is the major determinant of the graft function loss after lung transplantation, but its pathogenesis is still incompletely understood and currently available therapeutic strategies are poorly effective. A deeper understanding of its pathogenic mechanisms is crucial for the

development of new strategies to prevent and treat this devastating complication. In this study, we focused on the mesenchymal stromal cells, recently recognized as BOS key effectors, and our primary aim was to identify their epigenetic determinants, such as histone modifications and non-coding RNA regulation, which could contribute to their differentiation in myofibroblasts. Interestingly, we identified a deregulated expression of histone deacetylases and methyltransferases, and a microRNA-epigenetic regulatory network, which could represent novel targets for anti-fibrotic therapy. We validated our results in vitro, in a cell model of fibrogenesis, confirming the epigenetic involvement in this process and paving the way for a new application for epigenetic drugs.

Curr Protoc Stem Cell Biol. 2018 May;45(1):e52. doi: 10.1002/cpsc.52. Epub 2018 May 4.

Fluorescence Endomicroscopy Imaging of Mesenchymal Stem Cells in the Rat Lung.

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Abstract

Stem cell therapy has shown great promise for organ repair and regeneration. In the context of lung disease, such as radiation-induced lung damage (RILD) in cancer radiotherapy, mesenchymal stem cells (MSCs) have shown the ability to reduce damage possibly due to their immunomodulatory properties and other unknown mechanisms. However, once MSCs are transplanted into the body, little is known as to their localization or their mechanisms of action. In this work, we proposed, implemented, and validated a fluorescence endomicroscopy (FE) imaging technique that allows for the real-time detection and quantification of transplanted pre-labeled MSCs in vivo and tracking in a rat model. This protocol covers aspects related to MSCs extraction, labeling, FE imaging, and image analysis developed in a RILD rat model but applicable to other biological systems.

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Temporary storage solution for adipose derived mesenchymal stem cells.

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Author information

Abstract

BACKGROUND:

We have developed a simple lipoaspirate washing method using a coffee filter to eliminate liposuction noxious material before isolating adipose tissue derived mesenchymal stem cells (AT-MSCs), and used them in clinical trials. Before administration to patients, MSCs are usually suspended in physiologic saline. However, MSCs only survive for a limited time in physiologic saline. Therefore, alternative solution that can preserve MSC survival will be beneficial. Therefore, the purpose of this study was to

compare the use of physiologic saline and Dulbecco's modified Eagle's Medium (DMEM) as temporary storage solution for our AT-MSCs.

METHODS:

We did viability assessments of AT MSCs after 0, 3, 6, 24, 48, 72, and 96 hours suspended in physiologic saline compared to DMEM, and stored at 4 ℃. Further proliferation capacities of the cells after various suspension times were assessed. All viability and proliferation capacity assessments were done in four replications. Differences between the various suspension time in terms of viability and proliferation capacity were compared and tested by ANOVA or Kruskal-Wallis test.

RESULTS:

Viability was >70% after 48 hours in physiologic saline and 24 hours in DMEM, which showed that physiologic saline was superior compared to DMEM. Increase in PDT began to be significant compared to initial PDT after 24 hours in both physiologic saline, and DMEM.

CONCLUSIONS:

For our AT-MSCs, physiologic saline was superior to DMEM, and storage should not exceed 24 hours.