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Autologous Microfractured and Purified Adipose Tissue for Arthroscopic Management of Osteochondral Lesions of the Talus.

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Abstract

In recent years, regenerative techniques have been increasingly studied and used to treat osteochondral lesions of the talus. In particular, several studies have focused their attention on mesenchymal stem cells derived from adipose tissue. Adipose-derived stem cells (ADSCs) exhibit morphological characteristics and properties similar to other mesenchymal cells, and are able to differentiate into several cellular lines. Moreover, these cells are also widely available in the subcutaneous tissue, representing 10 - 30% of the normal body weight, with a concentration of 5,000 cells per gram of tissue. In the presented technique, the first step involves harvesting ADSCs from the abdomen and a process of microfracture and purification; next, the surgical procedure is performed entirely arthroscopically, with less soft tissue dissection, better joint visualization, and a faster recovery compared with standard open procedures. Arthroscopy is characterized by a first phase in which the lesion is identified, isolated, and prepared with microperforations; the second step, performed dry, involves injection of adipose tissue at the level of the lesion. Between January 2016 and September 2016, four patients underwent arthroscopic treatment of osteochondral lesion of the talus with microfractured and purified adipose tissue. All patients reported clinical improvement six months after surgery with no reported complications. Functional scores at the latest follow-up are encouraging and confirm that the technique provides reliable pain relief and improvements in patients with osteochondral lesion of the talus

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MSC-exosome: A novel cell-free therapy for cutaneous regeneration.

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Abstract

Cutaneous regeneration is a dynamic and complex process that requires a series of coordinated interactions involving epidermal cells, dermal cells, growth factors, the extracellular matrix (ECM), nerves and blood vessels at a damaged site. Mesenchymal stromal cells (MSCs) have been reported to participate in all afore-mentioned stages. Exosomes are one of the key secretory products of MSCs, resembling the effect of parental MSCs. They can shuttle various proteins, messenger RNA (mRNA) and microRNAs (miRNAs) to modulate the activity of recipient cells, and play important roles in

cutaneous wound healing. Compared with MSCs, exosomes are more convenient to store and transport. Moreover, they avoid many risks associated with cell transplantation. Therefore, MSC-exosome-mediated therapy may be more safe and efficient. In this review, we summarize the latest studies and observations on the role of MSC-exosome in the acute and chronic wound model and provide a comprehensive understanding of the role of exosomes in wound healing. This review can assist investigators in exploring new therapeutic strategies for enhancing the efficacy of MSC-exosome for cutaneous repair and regeneration.

Cell Stem Cell. 2018 Feb 6. pii: S1934-5909(18)30014-6. doi: 10.1016/j.stem.2018.01.014. [Epub ahead of print]

Engineering Stem and Stromal Cell Therapies for Musculoskeletal Tissue Repair.

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Abstract

Stem cells and tissue-derived stromal cells stimulate the repair of degenerated and injured tissues, motivating a growing number of cell-based interventions in the musculoskeletal field. Recent investigations have indicated that these cells are critical for their trophic and immunomodulatory role in controlling endogenous cells. This Review presents recent clinical advances where stem cells and stromal cells have been used to stimulate musculoskeletal tissue repair, including delivery strategies to improve cell viability and retention. Emerging bioengineering strategies are highlighted, particularly toward the development of biomaterials for capturing aspects of the native tissue environment, altering the healing niche, and recruiting endogenous cells.

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Pooled human serum: A new culture supplement for bioreactor-based cell therapies. Preliminary results.

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Abstract

BACKGROUND AIMS:

Bone marrow mesenchymal stromal cells (MSCs) are an appealing source for several cell-based therapies. Many bioreactors, such as the Quantum Cell Expansion System, have been developed to generate a large number of MSCs under Good Manufacturing Practice conditions by using human platelet lysate (HPL). Previously, we isolated a novel cell population in human bone marrow, mesodermal progenitor cells (MPCs), which we identified as precursors of MSCs. MPCs may represent an important cell source for regenerative medicine applications. Because HPL gives rise to a homogeneus MSC population, limiting the harvesting of other cell types, we investigated the efficacy of

pooled human AB serum (ABS) to provide clinically relevant numbers of both MSCs and MPCs for regenerative medicine applications by using the Quantum System.

METHODS:

Bone marrow aspirates were obtained from healthy adults undergoing routine total hip replacement surgery. The aspirates were used to generate primary cultures in the bioreactor. HPL and ABS were tested as supplements to culture medium. Morphological observations, cytofluorimetric analysis and lactate and glucose level assessments were performed.

RESULTS:

ABS gave rise to both heterogeneous MSC and MPC populations. About 95% of cells cultured in HPL showed a fibroblast-like morphology and typical mesenchymal surface markers, but MPCs were scarcely represented.

DISCUSSION:

The use of ABS appeared to sustain large-scale MSC production, as well as promote the recovery of a subset of MPCs, resulting in a suitable alternative to HPL in the cell generation based on the Quantum System.

Biochem Biophys Res Commun. 2018 Feb 8. pii: S0006-291X(18)30299-7. doi: 10.1016/j.bbrc.2018.02.076. [Epub ahead of print]

Co-transplantation of exosomes derived from hypoxia-preconditioned adipose mesenchymal stem cells promotes neovascularization and graft survival in fat grafting.

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Abstract

BACKGROUND:

Adipose-derived stromal cells (ADSCs)-derived exosomes (ADSC-Exos) account for the proangiogenic potential of stem cell. This study aimed to investigate the effect of ADSC-derived exosomes (ADSC-Exos) on the survival in fat grafting.

METHODS:

A nude mouse model of subcutaneous fat grafting was adopted. Hypoxic preconditioned ADSC-Exos and ADSC-Exos were injected around the grafted tissue. The fat graft sample was weighed and examined by hematoxylin and eosin (H&E) staining and immunohistochemistry. Laser Doppler flowmetry and CD31 immunofluorescence staining were used to analyze neovascularization.

RESULTS:

ADSC-Exo and hypoxic ADSC-Exo groups had a significantly higher weight of fat graft and more perilipin-positive adipocytes than the control groups from 2 to 8 weeks after grafting, and the hypoxic ADSC-Exo group had better outcomes (all $P < 0.05$). H&E staining showed that ADSC-Exos attenuated

infiltration of inflammatory cells around the fat grafts. Laser Doppler flowmetry showed that the two ADSC-Exo groups had better blood perfusion in the graft tissue than the control groups (all $P < 0.05$). Immunofluorescence demonstrated that the hypoxic ADSC-Exo group had significantly more CD31-positive cells than the ADSC-Exo group. In vitro study showed that hypoxic ADSC-Exos treatment significantly increased the migration (at 12 and 24 h) and in vitro capillary network formation (at 12 h) in the human umbilical vein endothelial cells (HUVECs) as compared with the ADSC-Exo group and control group (all $P < 0.05$).

CONCLUSIONS:

Co-transplantation of ADSC-Exos can effectively promote the survival of graft, neovascularization and attenuated inflammation in the fat grafts. Hypoxia treatment can further enhance the beneficial effect of ADSC-Exos.

Cell Death Dis. 2018 Feb 13;9(2):218. doi: 10.1038/s41419-018-0323-5.

Human umbilical cord mesenchymal stem cell-derived extracellular vesicles promote lung adenocarcinoma growth by transferring miR-410.

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Abstract

Although accumulating evidence has linked mesenchymal stem cells (MSCs) with tumor growth, the underlying mechanisms are poorly understood. Here, we demonstrated for the first time that human umbilical cord MSCs (hUCMSCs) dramatically increased the growth of lung adenocarcinoma (LUAD) cancer cells in a xenograft tumor model. Then, we observed that hUCMSC-derived extracellular vesicles (hUCMSC-EVs) contribute to the hUCMSC-promoted LUAD cell growth through a direct effect on LUAD cells. Furthermore, we showed that hUCMSC-EV-mediated LUAD growth is associated with increased proliferation and decreased apoptosis in LUAD cells, concomitant with reduced PTEN expression mediated by the hUCMSC-EV-transmitted miR-410. Our findings provide novel insights into the intercellular communications between cancer cells and MSCs through MSC-EV-miRNA and suggest that modification of hUCMSC-EVs might be an attractive therapeutic option for the clinical application of hUCMSC-EVs that would reduce unwanted side effects.