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Human adipose-derived stem cells loaded with drug-coated magnetic nanoparticles for in-vitro tumor cells targeting.

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Abstract

Magnetic nanoparticles (MNPs) functionalized with different therapeutics delivered by mesenchymal stem cells represent a promising approach to improve the typical drug delivery methods. This innovative method, based on the "Trojan horse" principle, faces however important challenges related to the viability of the MNPs-loaded cells and drug stability. In the present study we report about an in vitro model of adipose-derived stem cells (ADSCs) loaded with palmitate-coated MNPs (MNPsPA) as antitumor drug carriers targeting a 3D tissue-like osteosarcoma cells. Cell viability, MNPsPA-drug loading capacity, cell speed, drug release rate, magnetization and zeta potential were determined and analysed. The results revealed that ADSCs loaded with MNPsPA-drug complexes retained their viability at relatively high drug concentrations (up to 1.22 pg antitumor drug/cell for 100% cell viability) and displayed higher speed compared to the targeted tumor cells in vitro. The magnetization of the sterilized MNPsPA complexes was 67 emu/g within a magnetic field corresponding to induction values of clinical MRI devices. ADSCs payload was around 9 pg magnetic material/cell, with an uptake rate of 6.25 fg magnetic material/min/cell. The presented model is a proof-of-concept platform for stem cells-mediated MNPs-drug delivery to solid tumors that could be further correlated with MRI tracking and magnetic hyperthermia for theranostic applications

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Mesenchymal stem cells as adjuvant therapy for limb lengthening in achondroplasia.

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Abstract

Staged leg lengthening allows achondroplastic dwarfs to reach nearly normal height, but it takes long periods of external fixation and it can be burdened by delayed unions. Between 2009 and 2013, eight achondroplastic dwarfs showed delayed unions in the callus formation during femoral lengthening stages in our institute. We performed in-situ injections of bone marrow-derived stem cell concentrates. Patients underwent monthly clinical and radiographic assessment for determination of the healing rate. All eight patients showed an improvement in the regenerated bone, with an average healing index of 23.1 days/cm (range: 18.7-23.8 days/cm). The complete recovery of the delayed consolidation took on an average of 5.2 months (range: 2-10 months). The use of cellular therapy in these patients could represent an innovative application

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Comparison of Oxidative Stress Effects on Senescence Patterning of Human Adult and Perinatal Tissue-Derived Stem Cells in Short and Long-term Cultures.

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Abstract

Human Mesenchymal Stem Cells (hMSCs) undergo senescence in lifespan. In most clinical trials, hMSCs experience long-term expansion *ex vivo* to increase cell number prior to transplantation, which unfortunately leads to cell senescence, hampering post-transplant outcomes. Hydrogen peroxide (H_2O_2) *in vitro* represents a rapid, time and cost-effective tool, commonly used as oxidative stress tantalizing the stem cell ability to cope with a hostile environment, recapitulating the onset and progression of cellular senescence. Here, H_2O_2 at different concentrations (ranging from 50 to 400 μM) and time exposures (1 or 2 hours - h), was used for the first time to compare the behavior of human Adipose tissue-derived Stem Cells (hASCs) and human Wharton's Jelly-derived MSCs (hWJ-MSCs), as representative of adult and perinatal tissue-derived stem cells, respectively. We showed timely different responses of hASCs and hWJ-MSCs at low and high subculture passages, concerning the cell proliferation, the cell senescence-associated β-Galactosidase activity, the capability of these cells to undergo passages, the morphological changes and the gene expression of *tumor protein p53* (*TP53*, alias *p53*) and *cyclin dependent kinase inhibitor 1A* (*CDKN1A*, alias *p21*) post H_2O_2 treatments. The comparison between the hASC and hWJ-MSC response to oxidative stress induced by H_2O_2 is a useful tool to assess the biological mechanisms at the basis of hMSC senescence, but it could also provide two models amenable to test *in vitro* putative anti-senescence modulators and develop anti-senescence strategies.

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Safety analysis in patients with autoimmune disease receiving allogeneic mesenchymal stem cells infusion: a long-term retrospective study.

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Abstract

OBJECTIVE:

The aim of this study was to evaluate the safety of mesenchymal stem cell infusion in patients with autoimmune diseases.

METHODS:

A total of 404 patients with autoimmune diseases who received mesenchymal stem cell infusion between 2007 and 2016 were included in this study. Adverse events in these patients were collected, mainly including infections and malignancies. Sources of information included hospitalization records and data from outpatient visits and each follow-up.

RESULTS:

The mean follow-up period of all patients was 43.4 ± 25.9 months (range 1-109). Majority of stem cells were from the umbilical cord. The most common indications for mesenchymal stem cell infusion were systemic lupus erythematosus, Sjögren's syndrome, and systemic sclerosis. The median age at infusion was 38.7 ± 15.7 years. The 5-year and 8-year survival rates were 90.4% and 88.9%, respectively. Median follow-up of survivors was 45.1 ± 25.7 months. The incidence rate of infections was 29.5% (119/404), and that of serious infections was 12.9% (52/404). Five patients (1.2%) experienced malignancies. Deaths occurred in 45 patients, and transplantation-related mortality was 0.2%. The most common causes of deaths in our study were disease relapse and complications associated with the underlying disease.

CONCLUSION:

Autoimmune disease is an emerging indication for mesenchymal stem cell infusion. Our data shows that mesenchymal stem cell infusion is a safe therapy for patients with autoimmune diseases. The incidences of adverse events, whether infections or malignancies, are acceptable in these patients.

TRIAL REGISTRATION:

ClinaicalTrials.gov, NCT00698191

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Characterization and Therapeutic Uses of Exosomes: A New Potential Tool in Orthopedics.

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Abstract

In recent years, regenerative medicine has directed its interests onto the use of stem cells to heal human tissue. One specific class of cells that has been employed in this field of research is mesenchymal stem cells. Due to difficulties with the usage of whole stem cells, researchers have turned to an alternative, the secretome of these mesenchymal stem cells. In recent years, research has explored numerous aspects of the mesenchymal stem cell secretome, especially the most promising aspect, exosomes. This review explores a variety of interest in exosomes including the classification and molecular composition, mechanisms for isolation, and the various biological functions. As more is discovered about these exosomes different diagnostic and therapeutic uses in the medical field have also been explored. A new field attempting to exploit these exosomes in clinical practice is orthopedics. While a significant deal of research has been carried out, even more is being discovered to allow utilization of these vesicles in clinical practice.

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High Throughput screening reveals no significant changes in protein synthesis, processing and degradation machinery during passaging of mesenchymal stem cells.

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Abstract

Increasing reports of successful and safe application of bone marrow derived mesenchymal stem cells (MSCs) for cell therapy are pouring in through numerous studies. However, poor survival of transplanted cells in the recipient has impaired the benefits of MSCs based therapies. Therefore, cell product preparation procedures pertaining to MSC therapy need to be optimized to improve the survival of transplanted cells. One of the important ex vivo procedures in the preparation of cells for therapy is passaging of MSCs to ensure suitable number of cells for transplantation, which may affect the turn-over of proteins involved in regulation of cell survival/death pathways. In the current study, we investigated the effect of increase in passage number of MSCs in cell culture on the intracellular protein turn over (protein synthesis, processing and degradation machinery). We performed proteomic analysis of MSCs at different passages. There was no significant difference observed in the ribosomal, protein processing and proteasomal pathways related proteins in MSCs with an increase in passage number from P3 to P7. Therefore, expansion of MSCs in the cell culture wi

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Fusion with mesenchymal stem cells differentially affects tumorigenic and metastatic abilities of lung cancer cells.

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Abstract

Cell fusion plays a crucial role in cancer progression and leads to massive aberrant changes in chromosome and gene expression involved in tumor metastasis. Cancer cells can fuse with many cell types, including stromal cells, epithelial cells, macrophages, and endothelial cells. Mesenchymal stem cells (MSCs) have been reported to migrate and incorporate into tumor sites during cancer progression. However, the underlying mechanism of stem cell fusion in tumor metastasis has not been fully deciphered. In this research, we established a cell fusion model between lung cancer cells and MSCs in vitro. We found that the hybrid cells showed enhanced metastatic capacity with increased expression of MMP-2 and MMP-9, whereas the proliferation ability was inhibited and cell cycle was blocked in the G_0 /G_1 phase with elevated expression of p21, p27, and p53. Moreover, the hybrid cells lost epithelial morphology and exhibited an epithelial-mesenchymal transition (EMT) change with downregulation of E-cadherin and upregulation of N-cadherin, Vimentin, α-SMA and Fibronectin1. Meanwhile, the expressions of EMT transcription factors, including Snail1, Slug, Twist1, Zeb1, and Zeb2, were also increased in hybrid cells. More important, the fusion hybrids acquired stem cell-like properties, which exhibited increased expression stem cell transcription factors Oct4, Sox2, Nanog, Kif4 as well as Bmi1. Taken together, our results suggested that cell fusion between lung cancer cells and MSCs offered enhanced metastatic capacity and characteristics of cancer stem cell by undergoing EMT. This study will contribute to explaning the origin of lung cancer stem cells and to elucidate the role of cell fusion in cancer metastasis.