ML 34-20 (07/09/2020)

Dermatol Ther

. 2020 Sep 5;e14277.
doi: 10.1111/dth.14277. Online ahead of print.

Adipose Tissue Stromal Vascular Fraction and Adipose Tissue Stromal Vascular Fraction Plus Platelet-Rich Plasma Grafting: New Regenerative Perspectives in Genital Lichen Sclerosus

Marinella Tedesco[#1], Barbara Bellei[#2], Valentina Garelli[1], Silvia Caputo[2], Alessandra Latini[3], Massimo Giuliani[3], Carlo Cota[4,5], Giuseppina Chichierchia[6,7], Claudia Romani[1], Maria Laura Foddai[6], Antonio Cristaudo[3], Aldo Morrone[8], Emilia Migliano[1]
Affiliations expand

- PMID: 32888384

- DOI: 10.1111/dth.14277

Abstract

Lichen sclerosus (LS) is a chronic relapsing, inflammatory skin disorder usually involving the anogenital region of both sexes lacking a resolutive therapy. This study compared adipose tissue derived-stromal vascular fraction (AD-SVF) and AD-SVF-enriched platelet-rich plasma (PRP) therapy in the management of genital LS patients. Additionally, in vitro evaluation of cells and growth factors contained in the injected SVF have been evaluated as possible predictive factors for treatment outcome. The study population was 40 patients diagnosed with LS who were symptomatic despite medical treatment. Patients (age 43-78 years) randomized into two groups using a 1:1 allocation ratio, were evaluated clinically and assessing Dermatology Life Quality Index (DLQI) before and 6 months after treatment. Both procedures demonstrated a strong safety profile with no complications linked to the therapy. After 6 months, both treatments allowed for a significant improvement respect to baseline. Combinatory therapy demonstrated decreased efficacy in late stage patients. No correlations have been found between clinical and biological findings. AD-SVF and AD-SVF plus PRP are safe and effective regenerative approaches for genital LS patients. Clinical

results support the preferential use of combinatory therapy for early stage patients confirming a synergic effect of AD-SVF and PRP. In contrast, AD-SVF plus PRP is discouraged for late stage patients.

J Cell Physiol

. 2020 Sep 4.
doi: 10.1002/jcp.30042. Online ahead of print.

Effects of biophysical cues of 3D hydrogels on mesenchymal stem cells differentiation

Yutong Guo[1], Shufang Du[1], Shuqi Quan[1], Fulin Jiang[1], Cai Yang[1], Juan Li[1]
Affiliations expand

- PMID: 32885847

- DOI: 10.1002/jcp.30042

Abstract

For stem cell research, three-dimensional (3D) hydrogels are increasingly recognized as more physiological systems than two-dimensional culture plates due to bidirectional and 3D interaction of stem cells and surrounding matrix. Among various stem cells, mesenchymal stem cells (MSCs) are one of the most widely applied from bench to bedside. In 3D hydrogels, MSCs are allowed to actively remodel the surrounding matrix through proteolytic degradation and cell-exerted force, which highly resembles in vivo situation. Notably, factors affecting hydrogel modifiability including matrix viscoelasticity and matrix degradability have been found to regulate adhesion, morphology, and fate decision of MSCs. In addition, MSCs within 3D hydrogels have been found to employ multiple mechanotransduction mechanisms including not only the classic integrin-actomyosin cytoskeleton system but also ion channels, microtubule cytoskeleton, and self-secreted proteinaceous matrix. This review summarizes the effects of biophysical cues on MSCs differentiation in 3D hydrogels and underlying mechanobiology in a hope to update our readers' understanding of stem cell biology and guide tissue engineering

J Cell Mol Med

. 2020 Sep 3.
doi: 10.1111/jcmm.15797. Online ahead of print.

Comparative proteomic analysis of osteogenic differentiated human adipose tissue and bone marrow-derived stromal cells

Mehran Dadras[1], Caroline May[2], Johannes Maximilian Wagner[1], Christoph Wallner[1], Mustafa Becerikli[1], Stephanie Dittfeld[1], Bettina Serschnitzki[2], Lukas Schilde[2], Annika Guntermann[2], Christina Sengstock[3], Manfred Köller[3], Dominik Seybold[3], Jan Geßmann[3], Thomas Armin Schildhauer[3], Marcus Lehnhardt[1], Katrin Marcus[2], Björn Behr[1]
Affiliations expand

- PMID: 32885592

- DOI: 10.1111/jcmm.15797

Free article

Abstract

Mesenchymal stromal cells are promising candidates for regenerative applications upon treatment of bone defects. Bone marrow-derived stromal cells (BMSCs) are limited by yield and donor morbidity but show superior osteogenic capacity compared to adipose-derived stromal cells (ASCs), which are highly abundant and easy to harvest. The underlying reasons for this difference on a proteomic level have not been studied yet. Human ASCs and BMSCs were characterized by FACS analysis and tri-lineage differentiation, followed by an intraindividual comparative proteomic analysis upon osteogenic differentiation. Results of the proteomic analysis were followed by functional pathway analysis. 29 patients were included with a total of 58 specimen analysed. In these, out of 5148 identified proteins 2095 could be quantified in >80% of samples of both cell types, 427 in >80% of ASCs only and 102 in >80% of BMSCs only. 281 proteins were differentially regulated with a fold change of >1.5 of which 204 were higher abundant in BMSCs and 77 in ASCs. Integrin cell surface interactions were the most overrepresented pathway with 5 integrins being among the proteins with highest fold change. Integrin 11a, a known key protein for osteogenesis, could be identified as strongly up-regulated in BMSC confirmed by Western blotting. The integrin expression profile is one of the key distinctive features of osteogenic differentiated BMSCs and ASCs. Thus, they represent a promising target for modifications of ASCs aiming to improve their osteogenic capacity and approximate them to that of BMSCs.

Sci Rep

. 2020 Aug 31;10(1):14257.
doi: 10.1038/s41598-020-71224-2.

A highly efficient non-viral process for programming mesenchymal stem cells for gene directed enzyme prodrug cancer therapy

Yoon Khei Ho[1], Jun Yung Woo[2], Geraldine Xue En Tu[2], Lih-Wen Deng[2], Heng-Phon Too[3]
Affiliations expand

- PMID: 32868813

- PMCID: PMC7458920

- DOI: 10.1038/s41598-020-71224-2

Free PMC article

Abstract

Mesenchymal stem cells (MSCs) driven gene-directed enzyme prodrug therapy has emerged as a potential strategy for cancer treatment. The tumour-nesting properties of MSCs enable these vehicles to target tumours and metastases with effective therapies. A crucial step in engineering MSCs is the delivery of genetic material with low toxicity and high efficiency. Due to the low efficiency of current transfection methods, viral vectors are used widely to modify MSCs in preclinical and clinical studies. We show, for the first time, the high transfection efficiency (> 80%) of human adipose tissue derived-MSCs (AT-MSCs) using a cost-effective and off-the-shelf Polyethylenimine, in the presence of histone deacetylase 6 inhibitor and fusogenic lipids. Notably, the phenotypes of MSCs remained unchanged post-modification. AT-MSCs engineered with a fused transgene, yeast cytosine deaminase::uracil phosphoribosyltransferase (CDy::UPRT) displayed potent cytotoxic effects against breast, glioma, gastric cancer cells in vitro. The efficiency of eliminating gastric cell lines were effective even when using 7-day post-transfected AT-MSCs, indicative of the sustained expression and function of the therapeutic gene. In addition, significant inhibition of temozolomide resistant glioma tumour growth in vivo was observed with a

single dose of therapeutic MSC. This study demonstrated an efficient non-viral modification process for MSC-based prodrug therapy.

Stem Cells Transl Med

. 2020 Aug 31.
doi: 10.1002/sctm.19-0431. Online ahead of print.

Two phase I/II clinical trials for the treatment of urinary incontinence with autologous mesenchymal stem cells

Mariano Garcia-Arranz[1,2], Sergio Alonso-Gregorio[3], Pamela Fontana-Portella[4], Elena Bravo[5], Jesus Diez Sebastian[6], María Eugenia Fernandez-Santos[7], Damian Garcia-Olmo[1,2]
Affiliations expand

- PMID: 32864818

- DOI: 10.1002/sctm.19-0431

Free article

Abstract

We proposed to evaluate the safety and feasibility of adipose-derived mesenchymal stem cells to treat endoscopically urinary incontinence after radical prostatectomy in men or female stress urinary. We designed two prospective, nonrandomized phase I-IIa clinical trials of urinary incontinence involving 9 men (8 treated) and 10 women to test the feasibility and safety of autologous mesenchymal stem cells for this use. Cells were obtained from liposuction containing 150 to 200 g of fat performed on every patient. After 4 to 6 weeks and under sedation, endoscopic intraurethral injection of the cells was performed. On each visit (baseline, 1, 3, 6, and 12 months), clinical parameters were measured, and blood samples, urine culture, and uroflowmetry were performed. Every patient underwent an urethrocystoscopy and urodynamic studies on the first and last visit. Data from pad test, quality-of-life and incontinence questionnaires, and pads used per day were collected at every visit. Statistical analysis is made by Wilcoxon signed-rank test. No adverse effects have been collected. Three men (37.5%) and five women (50%) showed an objective improvement of >50% ($P < .05$) and a subjective improvement of 70% to 80% from baseline. In conclusion, intraurethral application of stem cells derived from adipose

tissue is a safe and feasible procedure to treat urinary incontinence after radical prostatectomy or in female stress urinary incontinence. A statistically significant difference was obtained for pad-test improvement in 3/8 men and 5/10 women. Our results encourage studies to confirm safety and to analyze efficacy.

Life Sci

. 2020 Aug 31;261:118369.
doi: 10.1016/j.lfs.2020.118369. Online ahead of print.

Targeted doxorubicin-loaded mesenchymal stem cells-derived exosomes as a versatile platform for fighting against colorectal cancer

Elnaz Bagheri[1], Khalil Abnous[2], Sara Amel Farzad[3], Seyed Mohammad Taghdisi[4], Mohammad Ramezani[5], Mona Alibolandi[6]
Affiliations expand

- PMID: 32882265

- DOI: 10.1016/j.lfs.2020.118369

Abstract

Exosomes hold great potential for cancer treatment to deliver therapeutics due to its inherent low immunogenicity. Exosomes are biocompatible cell-exocytosed secreted vesicles by most cell types, which can be used to construct novel biomanufacturing platform for drug delivery and cancer therapy. In this study, we implemented nano-sized vesicles which were secreted by mesenchymal stem cell (MSC), to encapsulate doxorubicin (DOX) through electroporation method (DOX@exosome). DOX was loaded into exosomes, with an encapsulation efficiency of up to 35% and separated by ultracentrifugation. Subsequently, carboxylic acid-end MUC1 aptamer was used to covalently decorate the surface amine groups of the exosomes via amide bond formation to provide selective guided drug delivery (DOX@exosome-apt). The data showed that the DOX@exosome-apt provided highly efficient DOX transportation to MUC1-positive cancer cells in vitro as confirmed by MTT and flow cytometry experiments. Moreover, in vivo study on ectopic model of C26 (mouse colon adenocarcinoma) in BALB/c mice indicated that the single dose intravenous injection of DOX@exosome-apt significantly suppress tumor growth in comparison with free DOX. Ex vivo fluorescent imaging also verified the desirable

biodistribution of DOX@exosome-apt by exhibiting higher tumor accumulation and faster liver clearance in comparison with DOX@exosome and free DOX. It could be concluded that MUC1 aptamer-decorated exosomes can be implemented therapeutically for the safe and versatile delivery of DOX to colon adenocarcinoma, thus offering valuable platform for clinical applications.