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Bone marrow-derived mesenchymal stem cell-derived exosomal microRNA-208a promotes osteosarcoma cell proliferation, migration, and invasion.

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Abstract

A recent study has discovered that mesenchymal stem cells (MSCs) are recruited into tumors and MSC-derived exosomes in a novel mechanism of cell-to-cell communication in human cancers. Here, in this study, we explore the impact of the microRNA-208a (miR-208a)-enriched exosomes derived from bone marrow-derived mesenchymal stem cells (BMSCs) on osteosarcoma cells. Human osteosarcoma cells MG-63 and Saos-2 were exposed to BMSCs-derived exosomes treated with either miR-208a mimic or inhibitor. The MTT assay, transwell migration assay, and soft agar colony formation assay were used to evaluate the viability, migration, and clonogenicity of osteosarcoma cells. Bioinformatics analysis and dual-luciferase reporter gene assays validated the targeted relationship between miR-208a and PDCD4. Western blot assay was used to detect the expression of PDCD4 and related proteins in the ERK1/2 pathway in osteosarcoma cells. BMSCs communicated with osteosarcoma cells via exosomes. Ectopic expression of miR-208a was shown to increase the viability, migration, and clonogenicity of osteosarcoma cells. Analysis of the exosomal content identified miR-208a as a mediator of the exosomal effects on osteosarcoma cells in part via downregulation of PDCD4 and activating the ERK1/2 pathway. In summary, our study illuminates that BMSC-derived exosomal miR-208a enhances the progression of osteosarcoma.

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TGFBI secreted by mesenchymal stromal cells ameliorates osteoarthritis and is detected in extracellular vesicles.

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Abstract

Mesenchymal stem/stromal cells (MSCs) are of interest in the context of osteoarthritis (OA) therapy. We previously demonstrated that TGF β -induced gene product-h3 (TGFBI/BIGH3) is downregulated in human MSCs (hMSCs) from patients with OA, suggesting a possible link with their impaired regenerative potential. In this study, we investigated TGFBI contribution to MSC-based therapy in OA models. First, we showed that co-culture with murine MSCs (mMSCs) partly restored the expression of anabolic markers and decreased expression of catabolic markers in OA-like chondrocytes only upon priming by TGF β 3. Moreover, TGF β 3-primed hMSCs not only modulated the expression of anabolic and catabolic markers, but also decreased inflammatory factors. Then, we found that upon TGFBI

silencing, mMSCs partly lost their inductive effect on chondrocyte anabolic markers. Injection of hMSCs in which TGFBI was silenced did not protect mice from OA development. Finally, we showed that MSC chondroprotection was attributed to the presence of TGFBI mRNA and protein in extracellular vesicles. Our findings suggest that TGFBI is a chondroprotective factor released by MSCs and an anabolic regulator of cartilage homeostasis.

[Stem Cell Res Ther.](#) 2019 Oct 22;10(1):309. doi: 10.1186/s13287-019-1429-0.

Investigation of stemness and multipotency of equine adipose-derived mesenchymal stem cells (ASCs) from different fat sources in comparison with lipoma.

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Abstract

BACKGROUND:

Adipose tissue-derived mesenchymal stem cells (ASCs) offer a promising cell source for therapeutic applications in musculoskeletal disorders. The appropriate selection of ASCs from various fat depots for cell-based therapy is challenging. The present study aims to compare stemness and multipotency of ASCs derived from retroperitoneal (RP), subcutaneous (SC), and lipoma (LP) fat to assess their usefulness for clinical application.

METHODS:

Equine ASCs from the three fat tissue sources were isolated and characterized. The cell viability, proliferation, and self-renewal were evaluated using MTT, sulforhodamine B, and colony forming unit (CFU) assays. Stem cell relative marker CD44, CD90, and CD105 and tumor marker CA9 and osteopontin (OPN) expression were quantified using RT-qPCR. Multipotency of ASCs for adipogenic, osteogenic, and chondrogenic differentiation was examined by quantifying Oil Red O and Alizarin Red S staining, alkaline phosphatase activity (ALP), and expression of differentiation relative markers. All data were statistically analyzed using ANOVA.

RESULTS:

RP fat-derived ASCs showed a higher cell proliferation rate compared to SC and LP derived cells. In contrast, ASCs from lipoma displayed a lower proliferation rate and impaired CFU capacities. The expression of CD44, CD90, and CD105 was upregulated in RP and SC derived cells but not in LP cells. RP fat-derived cells displayed a higher adipogenic potential compared to SC and LP cells. Although ASCs from all fat sources showed enhanced ALP activity following osteogenic differentiation, SC fat-derived cells revealed upregulated ALP and bone morphogenetic protein-2 expression together with a higher calcium deposition. We found an enhanced chondrogenic potency of RP and SC fat-derived cells as shown by Alcian blue staining and upregulation of aggrecan (Aggre), cartilage oligomeric matrix protein precursor (COMP), and collagen 2a1 (Col2a1) expression compared to LP. The expression of OPN and CA9 was exclusively upregulated in the ASCs of LP.

CONCLUSIONS:

The results provide evidence of variation in ASC performance not only between normal fat depots but also compared to LP cells which suggest a different molecular regulation controlling the cell fate. These data provided are useful when considering a source for cell replacement therapy in equine veterinary medicine.

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Subcutaneous and Visceral Adipose-Derived Mesenchymal Stem Cells: Commonality and Diversity.

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Abstract

Adipose-derived mesenchymal stem cells (ASCs) are considered to be a useful tool for regenerative medicine, owing to their capabilities in differentiation, self-renewal, and immunomodulation. These cells have become a focus in the clinical setting due to their abundance and easy isolation. However, ASCs from different depots are not well characterized. Here, we analyzed the functional similarities and differences of subcutaneous and visceral ASCs. Subcutaneous ASCs have an extraordinarily directed mode of motility and a highly dynamic focal adhesion turnover, even though they share similar surface markers, whereas visceral ASCs move in an undirected random pattern with more stable focal adhesions. Visceral ASCs have a higher potential to differentiate into adipogenic and osteogenic cells when compared to subcutaneous ASCs. In line with these observations, visceral ASCs demonstrate a more active sonic hedgehog pathway that is linked to a high expression of cilia/differentiation related genes. Moreover, visceral ASCs secrete higher levels of inflammatory cytokines interleukin-6, interleukin-8, and tumor necrosis factor α relative to subcutaneous ASCs. These findings highlight, that both ASC subpopulations share multiple cellular features, but significantly differ in their functions. The functional diversity of ASCs depends on their origin, cellular context and surrounding microenvironment within adipose tissues. The data provide important insight into the biology of ASCs, which might be useful in choosing the adequate ASC subpopulation for regenerative therapies.

[Stem Cells Int](#). 2019 Sep 17;2019:5924878. doi: 10.1155/2019/5924878. eCollection 2019.

Molecular Profiles of Cell-to-Cell Variation in the Regenerative Potential of Mesenchymal Stromal Cells.

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Abstract

Cell-to-cell variation in the regenerative potential of mesenchymal stromal cells (MSCs) impedes the translation of MSC therapies into clinical practice. Cellular heterogeneity is ubiquitous across MSC cultures from different species and tissues. This review highlights advances to elucidate molecular profiles that identify cell subsets with specific regenerative properties in heterogeneous MSC cultures.

Cell surface markers and global signatures are presented for proliferation and differentiation potential, as well as immunomodulation and trophic properties. Key knowledge gaps are discussed as potential areas of future research. Molecular profiles of MSC heterogeneity have the potential to enable unprecedented control over the regenerative potential of MSC therapies through the discovery of new molecular targets and as quality attributes to develop robust and reproducible biomanufacturing processes. These advances would have a positive impact on the nascent field of MSC therapeutics by accelerating the development of therapies with more consistent and effective treatment outcomes.