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Antioxidants inhibit cell senescence and preserve stemness of adipose tissue-derived stem cells by reducing ROS generation during long-term in vitro expansion.

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BACKGROUND:

Adipose tissue-derived mesenchymal stem cells (ADSCs) are promising candidates for regenerative medicine. However, long-term in vitro passaging leads to stemness loss and cell senescence of ADSCs, resulting in failure of ADSC-based therapy.

METHODS:

In this study, ADSCs were treated with low dose of antioxidants (reduced glutathione and melatonin) with anti-aging and stem cell protection properties in the in vitro passaging, and the cell functions including stem cell senescence, cell migration, cell multidirectional differentiation potential, and ROS content were carefully analyzed.

RESULTS:

We found that GSH and melatonin could maintain ADSC cell functions through reducing cell senescence and promoting cell migration, as well as by preserving stemness and multidirectional differentiation potential, through inhibiting ROS generation during long-term expansion of ADSCs.

CONCLUSIONS:

Our results suggested that antioxidant treatment could efficiently prevent the dysfunction and preserve cell functions of ADSCs after long-term passaging, providing a practical strategy to facilitate ADSC-based therapy.

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Cell detachment rapidly induces changes in noncoding RNA expression in human mesenchymal stromal cells.

<u>Della Bella E</u>¹, <u>Stoddart MJ</u>¹. <u>Author information</u>

AO Research Institute, AO Foundation, Davos, Switzerland. Abstract

Aims: To identify differential expression of noncoding RNAs after trypsinization in human mesenchymal stromal cells (hMSCs), focusing on miRNAs, piRNAs and circRNAs. **Methods:** hMSCs from the bone marrow of three donors were collected for RNA extraction, either lysed directly in monolayer or trypsinized and lysed within 30 min. Total RNA was isolated and sequenced for the evaluation of

miRNA and piRNA expression or RNaseR treated and labeled for circRNA array hybridization. RTqPCR was performed to evaluate the stability of candidate reference genes. **Results & conclusions:** Alterations in levels of several noncoding RNAs are rapidly induced after trypsinization of hMSCs, affecting critical pathways. This should be carefully considered for a proper experimental design

Stem Cell Investig. 2019 Sep 25;6:34. doi: 10.21037/sci.2019.08.11. eCollection 2019.

A revealing review of mesenchymal stem cells therapy, clinical perspectives and Modification strategies.

<u>Saeedi P</u>¹, <u>Halabian R</u>¹, <u>Imani Fooladi AA</u>¹. <u>Author information</u> <u>Abstract</u>

Multipotent mesenchymal stem cells (MSCs) have been considerably inspected as effective tool for cell-based therapy of inflammatory, immune-mediated, and degenerative diseases, attributed to their immunomodulatory, immunosuppressive, and regenerative potentials. In the present review, we focus on recent research findings of the clinical applications and therapeutic potential of this cell type, MSCs' mechanisms of therapy, strategies to improve their therapeutic potentials such as manipulations and preconditioning, and potential/unexpected risks which should be considered as a prerequisite step before clinical use. The potential risks would probably include undesirable immune responses, tumor formation and the transmission of incidental agents. Then, we also review some of the milestones in the field, briefly discuss challenges and highlight the new guideline suggested for future directions and perspectives.

Arch Dermatol Res. 2019 Oct 15. doi: 10.1007/s00403-019-01997-8. [Epub ahead of print]

Extracellular matrix deposition by adipose-derived stem cells and fibroblasts: a comparative study.

Paganelli A¹, Benassi L², Rossi E², Magnoni C². Author information Abstract

Cell-based strategies are today widely studied as possible therapies for wound healing. In this setting, fibroblasts play a key role since they are the main dermal cellular component and are responsible for extracellular matrix secretion. Several works report on the possibility of using fibroblast-derived extracellular matrix scaffolds for wound healing in skin injuries. While fibroblast-based substitutes have already been intensively studied by other groups, we focused our attention on the possibility of creating an adipose-derived stem cell (ADSC)-induced dermal scaffold for wound healing. ADSCs are a particular subset of mesenchymal stem cells present in the stromal vascular fraction of the adipose tissue. The aim of our work was to compare the ability of ADSCs and fibroblast to produce in vitro a scaffolding material, both in terms of collagen and fibronectin-containing dermal matrix upon stimulation with ascorbic acid. We observed fibronectin and collagen production by ADSCs to be even more

abundant when compared to fibroblasts'. Our results support the use of ADSC-induced sheets instead of fibroblast-based dermal substitutes as wound-healing strategies in full-thickness skin injuries.

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J Pathol. 2019 Oct 14. doi: 10.1002/path.5357. [Epub ahead of print]

Mesenchymal stromal cells in cancer: A review of their immunomodulatory functions and dual effects on tumor progression.

<u>Galland S</u>¹, <u>Stamenkovic I</u>¹. <u>Author information</u> Abstract

Mesenchymal stem or stromal cells (MSCs) are pluripotent cells implicated in a broad range of physiological events, including organogenesis and maintenance of tissue homeostasis as well as tissue regeneration and repair. Because their current definition is somewhat loose - based primarily on their ability to differentiate into a variety of mesenchymal tissues, adhere to plastic and express, or lack, a handful of cell surface markers - MSCs likely encompass several subpopulations, which may have diverse properties. Their diversity may explain, at least in part, the pleiotropic functions that they display in different physiological and pathological settings. In the context of tissue injury, MSCs can respectively promote and attenuate inflammation during the early and late phases of tissue repair. They may thereby act as sensors of the inflammatory response and secrete mediators that boost or temper the response as required by the stage of the reparatory and regenerative process. MSCs are also

implicated in regulating tumor development, in which they are increasingly recognized to play a complex role. Thus, MSCs can both promote and constrain tumor progression by directly affecting tumor cells via secreted mediators and cell-cell interactions and by modulating the innate and adaptive immune response. This review summarizes our current understanding of MSC involvement in tumor development and highlights the mechanistic underpinnings of their implication in tumor growth and progression.