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J Biol Regul Homeost Agents. 2019 Jul-Aug;33(4):1019-1022.

# Mesenchymal stem cells and IL-37: a powerful combination.

Gugliandolo A[1], Caraffa AL[2], Gallenga CE[3], Kritas SK[4], Ronconi G[5], Trubiani O[6], Conti P[7], Di Emidio P[8], Mazzon E[1].
**Author information**

**Abstract**

Mesenchymal stem cells (MSCs) are able to exert immunomodulatory and anti-inflammatory actions. Thanks to these properties, MSCs may be a promising alternative approach for the treatment of inflammatory disease. Important cytokines involved in inflammation are those included in the IL-1 family. Interleukin-37 (IL-37) is one of the member able to suppress both innate and adaptive immunity. Recently, it was found that MSCs and their derivatives can modulate IL-37, and MSCs expressing IL-37 seem to have an enhanced therapeutic efficacy.

Intensive Care Med Exp. 2019 Jul 25;7(Suppl 1):41. doi: 10.1186/s40635-019-0235-4.

# Modulating the distribution and fate of exogenously delivered MSCs to enhance therapeutic potential: knowns and unknowns.

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**Abstract**

Mesenchymal stem/stromal cells (MSCs) are undergoing intensive translational research for several debilitating conditions, including critical illnesses such as ARDS and sepsis. MSCs exert diverse biologic effects via their interaction with host tissues, via mechanisms that require the MSC to be in close proximity to the area of injury. Fully harnessing the therapeutic potential of advanced medicinal therapeutic products such as MSCs and their successful translation to clinical use requires a detailed understanding of MSC distribution and persistence in the injured tissues.Key aspects include understanding MSC distribution within the body, the response of the host to MSC administration, and the ultimate fate of exogenously administered MSCs within the host. Factors affecting this interaction include the MSC tissue source, the in vitro MSC culture conditions, the route of MSC administration and the specific issues relating to the target disease state, each of which remains to be fully characterised. Understanding these factors may generate strategies to modify MSC distribution and fate that may enhance their therapeutic effect.This review will examine our understanding of the mechanisms of action of MSCs, the early and late phase distribution kinetics of MSCs following in vivo administration, the ultimate fate of MSCs following administration and the potential importance of these MSC properties to their therapeutic effects. We will critique current cellular imaging and tracking methodologies used to track exogenous MSCs and their suitability for use in patients, discuss the insights they provide into the distribution and fate of MSCs after administration, and suggest strategies by which MSC biodistribution

and fate may be modulated for therapeutic effect and clinical use.In conclusion, a better understanding of patterns of biodistribution and of the fate of MSCs will add important additional safety data regarding MSCs, address regulatory requirements, and may uncover strategies to increase the distribution and/or persistence of MSC at the sites of injury, potentially increasing their therapeutic potential for multiple disorders.

Cells. 2019 Jul 23;8(7). pii: E764. doi: 10.3390/cells8070764.

# Mesenchymal Stem Cells for Perianal Crohn's Disease.

Carvello M[1], Lightner A[2], Yamamoto T[3], Kotze PG[4], Spinelli A[5,6].
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**Abstract**

Perianal fistulizing Crohn's disease (PFCD) is associated with significant morbidity and might negatively impact the quality of life of CD patients. In the last two decades, the management of PFCD has evolved in terms of the multidisciplinary approach involving gastroenterologists and colorectal surgeons. However, the highest fistula healing rates, even combining surgical and anti-TNF agents, reaches 50% of treated patients. More recently, the administration of mesenchymal stem cells (MSCs) have shown notable promising results in the treatment of PFCD. The aim of this review is to describe the rationale and the possible mechanism of action of MSC application for PFCD and the most recent results of randomized clinical trials. Furthermore, the unmet needs of the current administration process and the expected next steps to improve the outcomes will be addressed.

Eur Cell Mater. 2019 Jul 23;38:14-22. doi: 10.22203/eCM.v038a02.

# Paracrine effects of living human bone particles on the osteogenic differentiation of mesenchymal stem cells.

Atasoy-Zeybek A[1], Ivkovic A, Beyzadeoglu T, Ona A, Evans CH, Kose GT.
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**Abstract**

Bone autografting remains the clinical model of choice for resolving problematic fractures. The precise mechanisms through which the autograft promotes bone healing are unknown. The present study examined the hypothesis that cells within the autograft secrete osteogenic factors promoting the differentiation of mesenchymal stem cells (MSCs) into osteoblasts. Particles of human bone ("chips") were recovered at the time of joint replacement surgery and placed in culture. Then, conditioned media were added to cultures of human, adipose-derived MSCs under both basal and osteogenic conditions. Contrary to expectation, medium conditioned by bone chips reduced the expression of alkaline phosphatase and strongly inhibited mineral deposition by MSCs cultured in osteogenic medium. Real time PCR revealed the inhibition of collagen type I alpha 1 chain (Col1A1) and osteopontin (OPN) expression. These data indicated that the factors secreted by bone chips inhibited the osteogenic differentiation of MSCs. However, in late cultures, bone morphogenetic protein-2 (BMP-2) expression was stimulated, suggesting the possibility of a delayed, secondary osteogenic effect.

PLoS One. 2019 Jul 22;14(7):e0220055. doi: 10.1371/journal.pone.0220055. eCollection 2019.

# A non-traditional approach to cryopreservation by ultra-rapid cooling for human mesenchymal stem cells.

Irdani T[1], Mazzanti B[2], Ballerini L[2], Saccardi R[3], Torre R[4].
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**Abstract**

Cryopreservation is the most common method for long-term cell storage. Successful cryopreservation of cells depends on optimal freezing conditions, freezer storage and a proper thawing technique to minimize the cellular damage that can occur during the cryopreservation process. These factors are especially critical for sensitive stem cells with a consequential and significant impact on viability and functionality. Until now, slow-freezing has been the routine method of cryopreservation but, more recently rapid-cooling techniques have also been proposed. In this study, an ultra-rapid cooling technique [1] was performed for the first time on human mesenchymal stem cells and the effectiveness evaluated in comparison with the conventional slow-freezing procedure. A thin nylon-membrane carrier was used combined with different cryoprotective agents: dimethyl sulfoxide, ethylene glycol and/or trehalose. Various aspects of the low cryoprotective doses and the ultra-rapid cooling procedure of the human mesenchymal stem cells were examined including: the physical properties of the nylon-support, cells encumbrance, viability, proliferation and differentiation. The expression of cell surface markers and apoptosis were also investigated. The study used an ultra-rapid cooling/warming method and showed an overall cell integrity preservation (83-99%), with no significant differences between dimethyl sulfoxide or ethylene glycol treatment (83-87%) and a substantial cell viability of 68% and 51%, respectively. We confirmed a discrepancy also observed by other authors in cell viability and integrity, which implies that caution is necessary when assessing and reporting cell viability data.

J Control Release. 2019 Jul 18;309:11-24. doi: 10.1016/j.jconrel.2019.07.022. [Epub ahead of print]

# Mesenchymal stem/stromal cell secretome for lung regeneration: The long way through "pharmaceuticalization" for the best formulation.

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**Abstract**

Pulmonary acute and chronic diseases, such as chronic obstructive pulmonary disease, pulmonary fibrosis and pulmonary hypertension, are considered to be major health issues worldwide. Cellular therapies with Mesenchymal Stem Cells (MSCs) offer a new therapeutic approach for chronic and acute lung diseases related to their anti-inflammatory, immunomodulatory, regenerative, pro-angiogenic and anti-fibrotic properties. Such therapeutic effects can be attributed to MSC-secretome, made of free soluble proteins and extracellular vesicles (EVs). This review summarizes the recent findings related to the efficacy and safety of MSC-derived products in pre-clinical models of lung diseases, pointing out the biologically active substances contained into MSC-secretome and their mechanisms involved in tissue regeneration. A perspective view is then provided about the missing steps required for the secretome

"pharmaceuticalization" into a high quality, safe and effective medicinal product, as well as the formulation strategies required for EV non-invasive route of administration, such as inhalation.