REVITASTEM
UMBILICAL CORD STEM CELLS & PEPTIDES

Umbilical Cord Tissue Mesenchymal Stem Cells

Mesenchymal Stem Cells

Umbilical Cord Tissue Offers the Greatest Number of Harvestable Mesenchymal Stem Cells for Research and Clinical Application: A Literature Review of Different Harvest Sites

C. Thomas Vangsness Jr., M.D., Hal Sternberg, M.D., and Liam Harris, B.S.

Purpose: Recent years have seen dramatic increases in the techniques used to harvest and isolate human mesenchymal stem cells. As the potential therapeutic aspects of these cells further develop, informative data on the differences in yields between tissue harvest sites and methods will become increasingly valuable. We collected and compared data on cell yields from multiple tissue harvest sites to provide insight into the varying levels of mesenchymal stem cells by tissue and offer primary and alternative tissue types for harvest and clinical application. **Methods:** The PubMed and Medline databases were searched for articles relating to the harvest, isolation, and quantification of human mesenchymal stem cells. Selected articles were analyzed for relevant data, which were categorized according to tissue site and, if possible, standardized to facilitate comparison between sites. **Results:** Human mesenchymal stem cell levels in tissue varied widely according to tissue site and harvest method. Yields for adipose tissue ranged from 4,737 cells/mL of tissue to 1,550,000 cells/mL of tissue. Yields for bone marrow ranged from 1 to 30 cells/mL to 317,400 cells/mL. Yields for umbilical cord tissue ranged from 10,000 cells/mL to 4,700,000 cells/cm of umbilical cord. Secondary tissue harvest sites such as placental tissue and synovium yielded results ranging from 1,000 cells/mL to 30,000 cells/mL. **Conclusions:** Variations in allogeneic mesenchymal stem cell harvest levels from human tissues reflect the evolving nature of the field, patient demographic characteristics, and dif-ferences in harvest and isolation techniques. At present, Wharton's jelly tissue yields the highest concentration of allogeneic mesenchymal stem cells whereas adipose tissue yields the highest levels of autologous mesenchymal stem cells per milliliter of tissue. **Clinical Relevance:** This comparison of stem cell levels from the literature offers a primer and guide for harvesting mesenchymal stem cells. Larger mesenchymal stem cell yields are more desirable for research and clinical application.

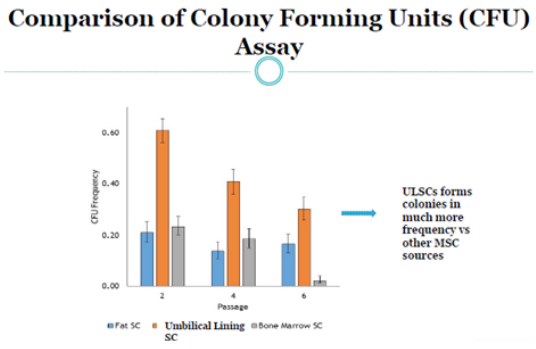
Umbilical Cord Mesenchymal Stem Cells: The New Gold Standard for Mesenchymal Stem Cell-Based Therapies?

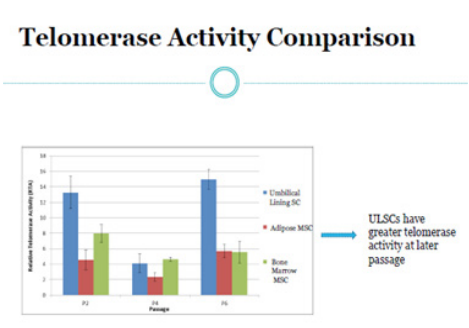
Reine El Omar,[1,*] Jacqueline Beroud,[1,*] Jean-Francois Stoltz, PhD,[1,2] Patrick Menu, PhD,[1] Emilie Velot, PhD,[1] and Veronique Decot, PharmD, PhD[1,2]

Due to their self-renewal capacity, multilineage differentiation potential, paracrine effects, and immunosup-pressive properties, mesenchymal stromal cells (MSCs) are an attractive and promising tool for regenerative medicine. MSCs can be isolated from various tissues but despite their common immunophenotypic characteristics and functional properties, source-dependent differences in MSCs properties have recently emerged and lead to different clinical applications. Considered for a long time as a medical waste, umbilical cord appears these days as a promising source of MSCs. Several reports have shown that umbilical cord-derived MSCs are more primitive, proliferative, and immunosuppressive than their adult counterparts. In this review, we aim at synthesizing the differences between umbilical cord MSCs and MSCs from other sources (bone marrow, adipose tissue, periodontal ligament, dental pulp,.) with regard to their proliferation capacity, proteic and transcriptomic profiles, and their secretome involved in their regenerative, homing, and immunomodulatory capacities. Although umbilical cord MSCs are until now not particularly used as an MSC source in clinical practice, accumulating evidence shows that they may have a therapeutic advantage to treat several diseases, especially autoimmune and neurodegenerative diseases.

Umbilical Cord Stem Cells

- No invasive harvesting procedure needed
- UCTMSCs are immune privileged due to low MHC-1 level and absence of MHC-II expression which protects against immune mediated lysis and GVHD.
- Studies show that non-cross matched cells perform as well or better than using a matched donor.
- Risk of chronic infection is also lower with donated UCTMSCs compared to autologous from bone marrow and adipose





(fig 1 & 2) Gonzolez R. Properties of Umbilical Cord Tissue Stem Cells A4M Stem Cell Fellowship., Las Vegas, NV 2017

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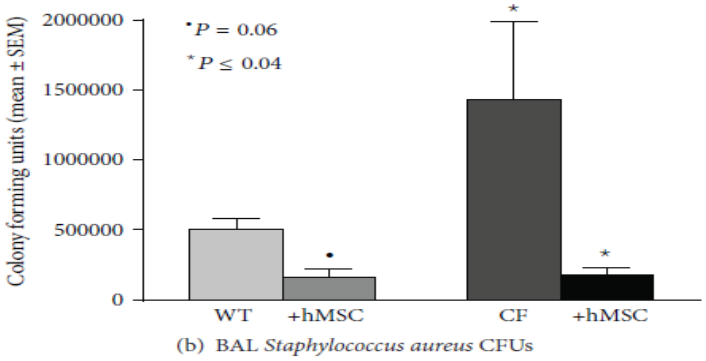
MSCs for Chronic Infection

"We have previously shown that human MSCs (hMSCs) decrease inflammation and infection in the in vivo murine model of CF. Our studies show that hMSCs secrete bioactive molecules which are antimicrobial in vitro against Pseudomonas aeruginosa, Staphylococcus aureus, and Streptococcus pneumonia, impacting the rate of bacterial growth and transition into colony forming units regardless of the pathogen."

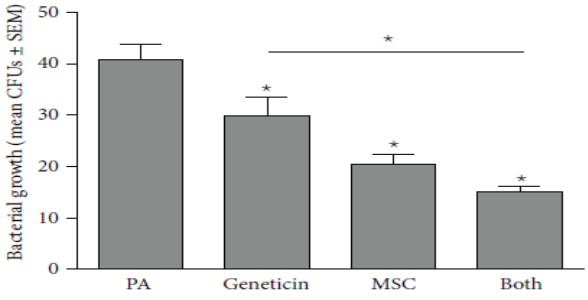
"Further, we show that the hMSCs have the capacity to enhance antibiotic sensitivity, improving the capacity to kill bacteria. We present data which suggests that the antimicrobial effectiveness is associated with the capacity to slow bacterial growth and the ability of the hMSCs to secrete the antimicrobial peptide LL-37."

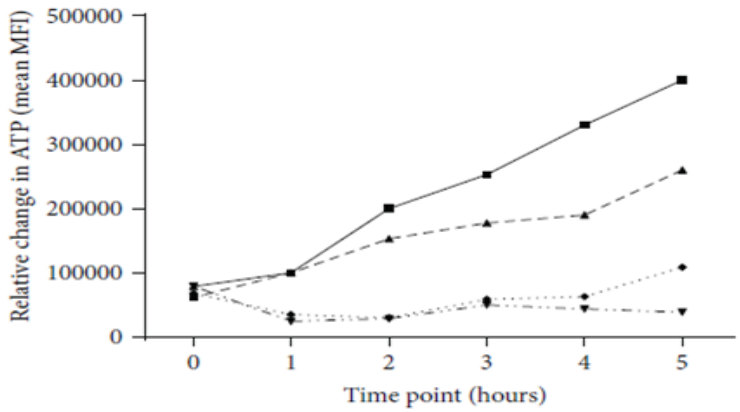
Sutton MT, Fletcher D, Ghosh SK, et al. Antimicrobial Properties of Mesenchymal Stem Cells: Therapeutic Potential for Cystic Fibrosis Infection, and Treatment. Stem Cells Int 2016; 2016:5303048:1-10.

Antimicrobial Effects of MSCs

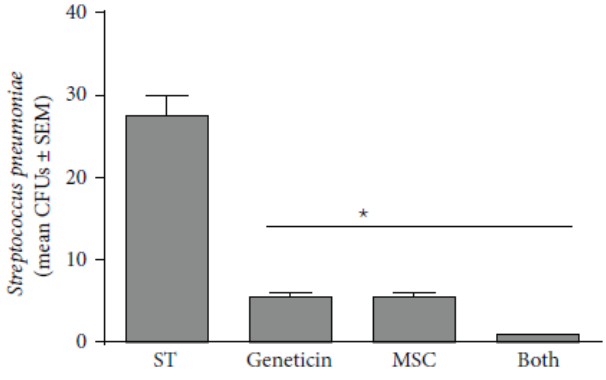


(b) BAL *Staphylococcus aureus* CFUs





(b) *Pseudomonas aeruginosa* growth rate



Sutton MT, Fletcher D, Ghosh SK, et al. Antimicrobial Properties of Mesenchymal Stem Cells: Therapeutic Potential for Cystic Fibrosis Infection, and Treatment. Stem Cells Int 2016; 2016:5303048:1-10.

Stem Cell and Peptide Synergy

"Conclusions: Taken together, our observations may serve as groundwork for the development of new therapeutic strategies based on the combined use of LL-37 and MSCs, which may provide patients not only with an enhanced immunosuppression regime, but also with an agent to prevent opportunistic infections… These results may also be of great relevance and open the possibility for a new therapeutic strategy for a highly efficient MSC-based therapy."[77]

"Extended-release TB4 administration improves the retention, survival, and regenerative potency of transplanted sMSCs after myocardial injury."[99]

99. Ye L, Shang P, Duval S, et al. Thymosin B4 Increases the Potency of TransplantedMesenchymal Stem Cells for Myocardial Repair. Circulation. 2013;128:S32-S41.
77. Oliveria-Bravo M, Sanglorgi BB, Schavinato S, et al. LL-37 boosts immunosuppressive function of placenta-derived mesenchymal stromal cells. Stem Cell Resch & Ther 2016;7-189