







Cell Based Therapies: How are they Being Optimized?

UCSF Trauma Course 6-2023

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U.S. OLYMPIC & PARALYMPIC NATIONAL MEDICAL CENTER

There is no one MSC

tSNE_1

Single-cell RNA sequencing deconvolutes the in vivo heterogeneity of human bone marrow-derived mesenchymal stem cells

Zun Wang, Xiaohua Li, Junxiao Yang, Yun Gong, Huixi Zhang, A Jonathan Greenbaum, Liang Cheng, Yihe Hu, Jie Xie, Xucheng Si-Yuan Tang, Hui Shen, Hong-Mei Xiao, Hong-Wen Deng doi: https://doi.org/10.1101/2020.04.06.027904

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Clinical Application of "MSCs"



The FDA is going after stem cell clinics that peddle unproven treatments The clinics claim they can treat serious diseases with stem cells from fat. The

The clinics claim they can treat serious diseases with stem cells from fat. The FDA doesn't buy it.

By Max Levy | Updated Jan 13, 2019, 9:17am EST



Bone Joint J. 2020 Feb; 102-B(2): 148–154. Published online 2020 Feb 1. doi: <u>10.1302/0301-620X.102B2.BJJ-2019-1104.R1</u>

PMCID: PMC7002842 PMID: <u>32009438</u>

Rogue stem cell clinics

<u>Iain R. Murray</u>, MD, PhD, Clinical Lecturer of Orthopaedic Surgery,¹ <u>Jorge Chahla</u>, MD, PhD, Assistant Professor of Orthopaedic Surgery,² <u>Rachel M. Frank</u>, MD, Assistant Professor of Orthopaedic Surgery,³ <u>Nicolas S. Piuzzi</u>, MD, Assistant Professor of Orthopaedic Surgery,⁴ <u>Bert R. Mandelbaum</u>, MD, Co-Chair of Medical Affairs,⁵ <u>Jason L. Dragoo</u>, MD, Professor of Orthopaedic Surgery,⁶ and Members of the Biologics Association^{*}



Stem Cells and Age – Are These Effective When we Need Them?





K Miclau et al. Aging Cell 2022

Aging and Senescence



Aging and Senescence: Impact on Orthobiologics



Senolytics to Optimize Orthobiologics

un2nt in one

Treatment

control





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TKR/GFR/EFNB1 Dasatinib 20 Navitoclax A1331852 BCL-2 family SRC A1155463 **Procyanidin C1** BAX/BAK Quercetin Proteasome **PI3K** Fisetin Luteolin Enzastaurin AKT Mitochondria Piperlongumine HSP90 (17-DMAG) Ansamycin Caspase activation Survival Resorcinol FOXO4-DRI pyrimidine-Apoptosis Na⁺/K⁺ inhibitors Lysosomes **ATPase** p53-FOXO4 pump membrane proteins Nanoparticles/ prodrugs Cardiac glycosides Senomorphics



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How do MSCs Impart a Regenerative Function?



https://www.nature.com/articles/s41585-019-0169-3 https://www.mdpi.com/1422-0067/20/12/2853

nature medicine

Article | Published: November 2000

Human mesenchymal stem cells engraft and demonstrate site-specific differentiation after *in utero* transplantation in sheep

Kenneth W. Liechty, Tippi C. MacKenzie, Aimen F. Shaaban, Antoneta Radu, AnneMarie B. Moseley, Robert Deans, Daniel R. Marshak & Alan W. Flake 🖂



International Journal of *Molecular Sciences*



Review

Mesenchymal Stem Cell Secretome: Toward Cell-Free Therapeutic Strategies in Regenerative Medicine

Francisco J. Vizoso ^{1,*}, Noemi Eiro ¹, Sandra Cid ¹, Jose Schneider ² and Roman Perez-Fernandez ^{3,*}

How do MSCs Impart a Regenerative Function?



Exercise Maintains Stem Cell Health & Regeneration



The Impact of Aerobic Exercise on the Muscle Stem Cell Response

OPEN a ACCESS Freely available online

The Acute Satellite Cell Response and Skeletal Muscle Hypertrophy following Resistance Training

Leeann M. Bellamy^{1®}, Sophie Joanisse^{1®}, Amanda Grubb^{1®}, Cameron J. Mitchell¹, Bryon R. McKay¹, Stuart M. Phillips¹, Steven Baker³, Gianni Parise^{1,2}*







Mechanical Stimulus Improves Exosome Production



October 2022, DOI: (10.1002/jor.25467)

Mechanical Stimulus Enhances Effect on Proliferation





Mechanical Stimulus Enhances Effect on Myogenesis







+ LSLD Exo

Problem with exosomes: We don't know what is in them (yet!)



Exosomes – Next Generation of Cell Therapy?

- Exercise improves exosome output from muscle cells
- > Exercise stimulates proliferation of recipient cells
- Exercise enhances repair/regeneration
- > Exosomes have relatively long storage capacity





