Mesenchymal stem cells in rheumatology- a case study in regenerative medicine

Sino-Luso International Medical Forum

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等待考试：10人次
正在考试：10人次
考试结束：0人次
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DISCLOSURES

I received unrestricted research grants or acted as a speaker

for Abbvie, Amgen, Biogen, BMS, Janssen, Lilly, Medac, MSD, Novartis, Pfizer, Roche, UCB

Major disclosure:
This presentation is an adaptation and simplification of my annual lecture
to the Biomedical Engineering students at the University of Lisbon
This is not my specific field of research

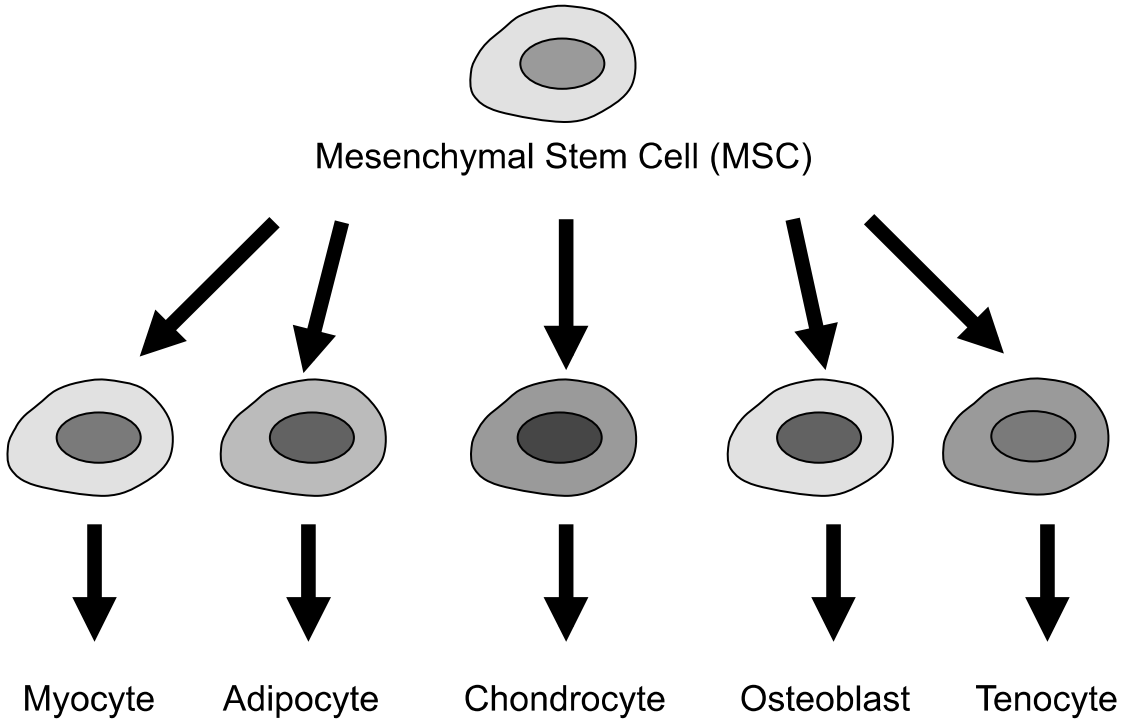
Mesenchimal Stem Cells

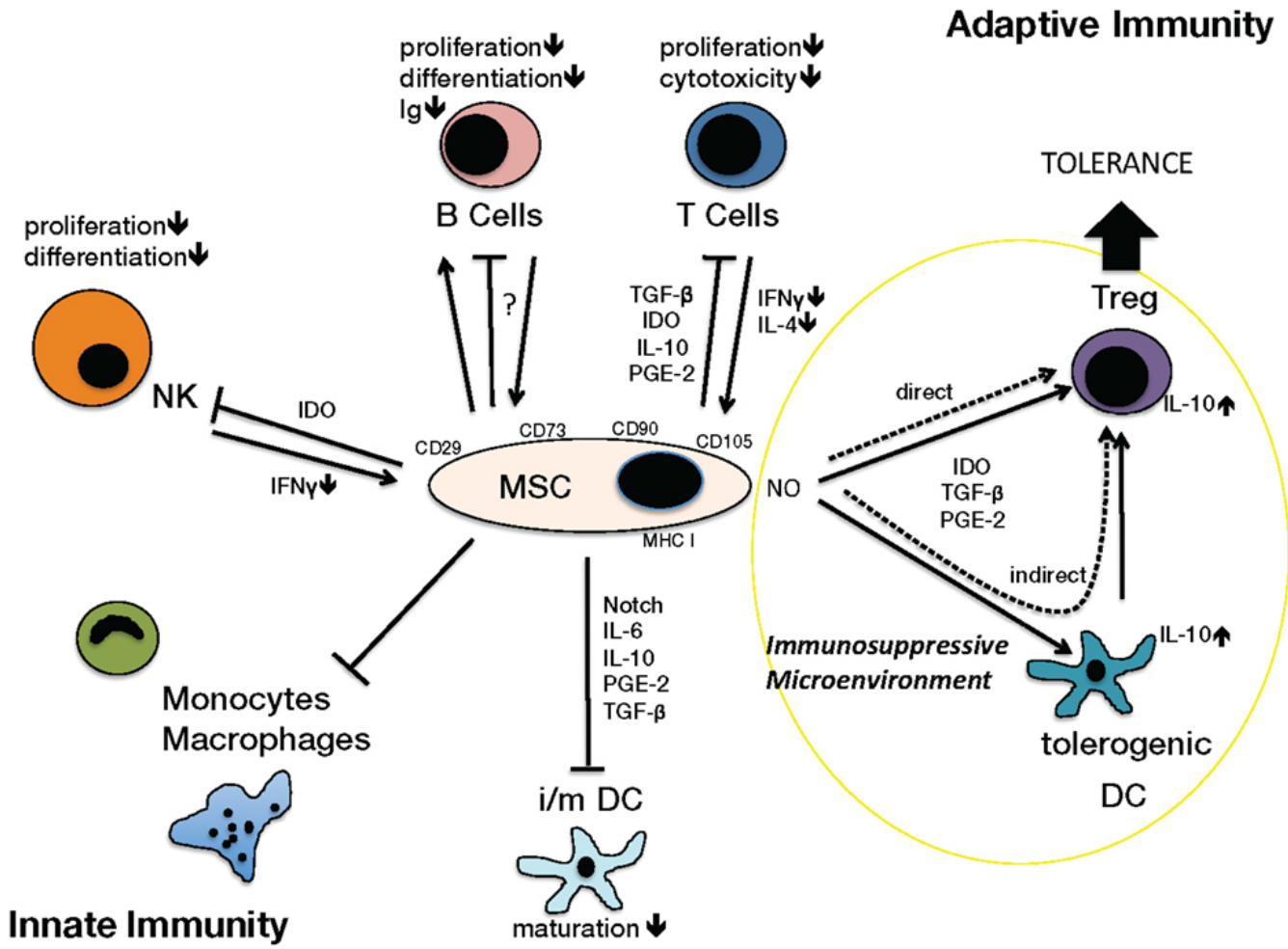
Main sources:
Umbilical Cord
Bone Marrow

Differentiate: chondrocytes, osteoblasts and adypocytes

Paracrine immunomodulation

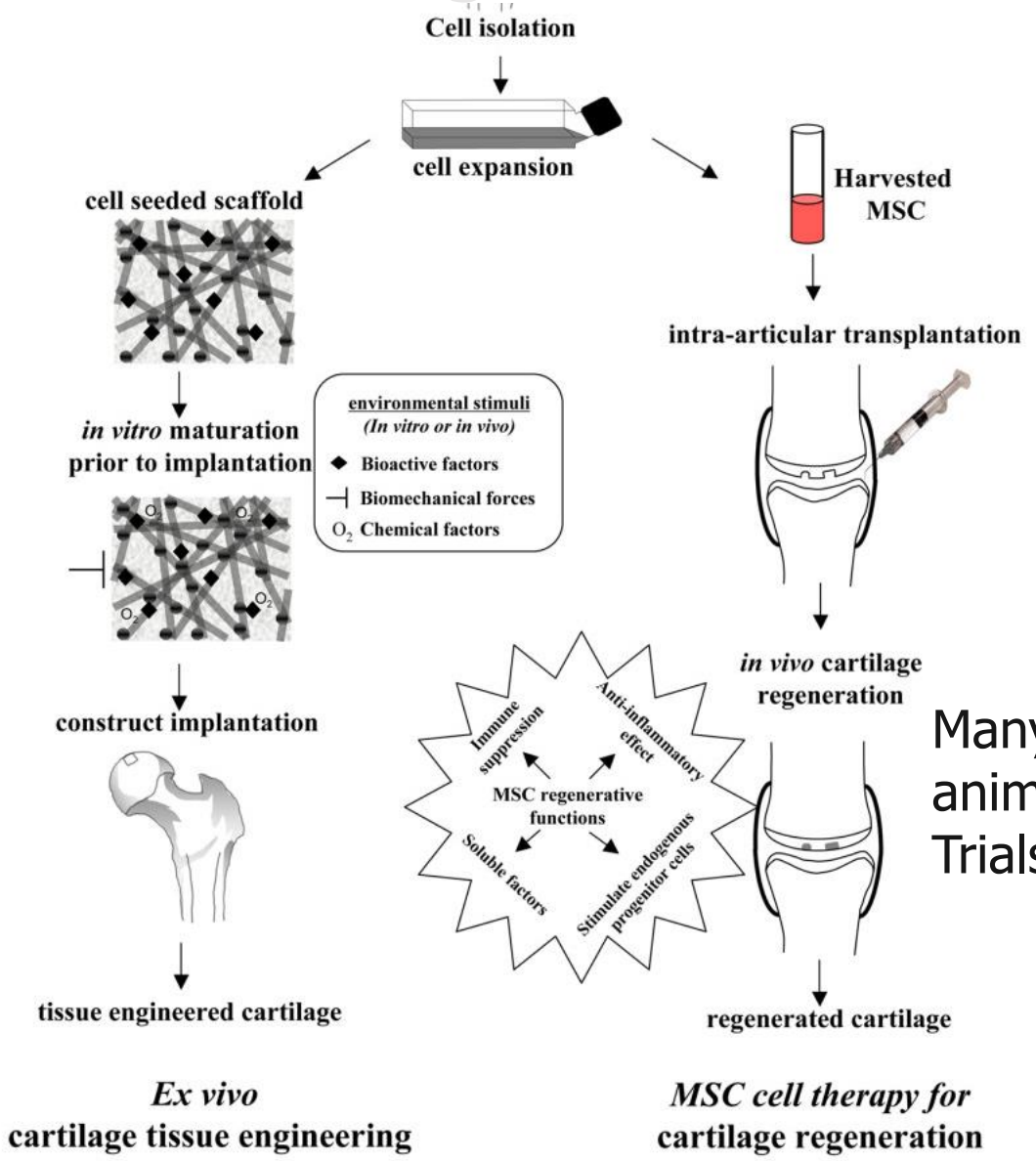
Mesenchymal Stem Cell: Potential for regenerative medicine





Mobasheri A et al. Maturitas 2014;78: 188-98

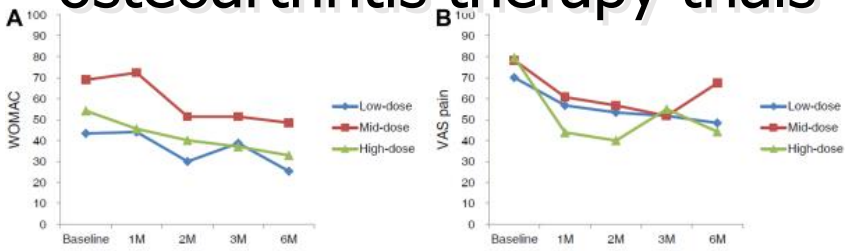
Mesenchymal Stem Cell therapy strategies for treating osteoarthritis (cartilage)

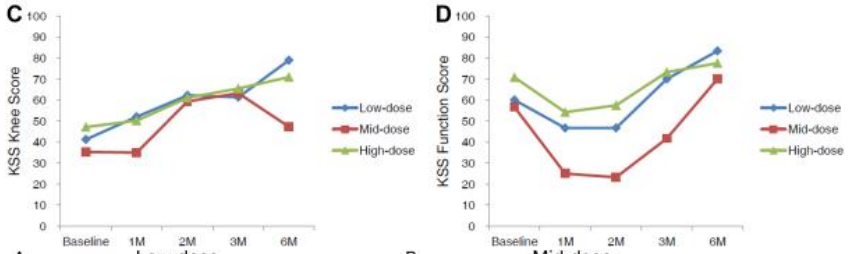


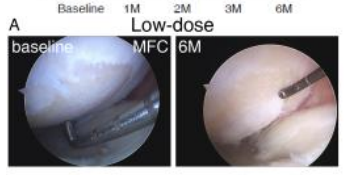
Many reports in animal models
Trials ongoing

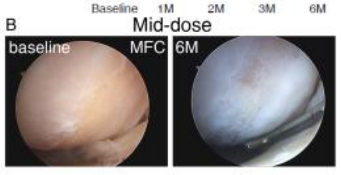
Mobasheri A et al. Maturitas 2014;78: 188-98

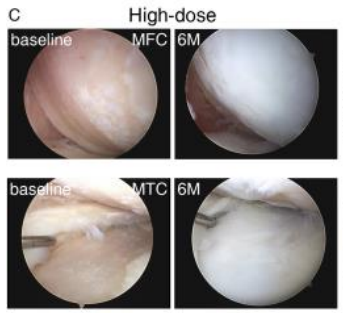
Mesenchymal Stem Cell osteoarthritis therapy trials

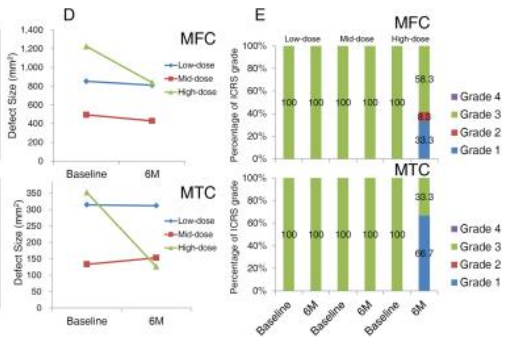


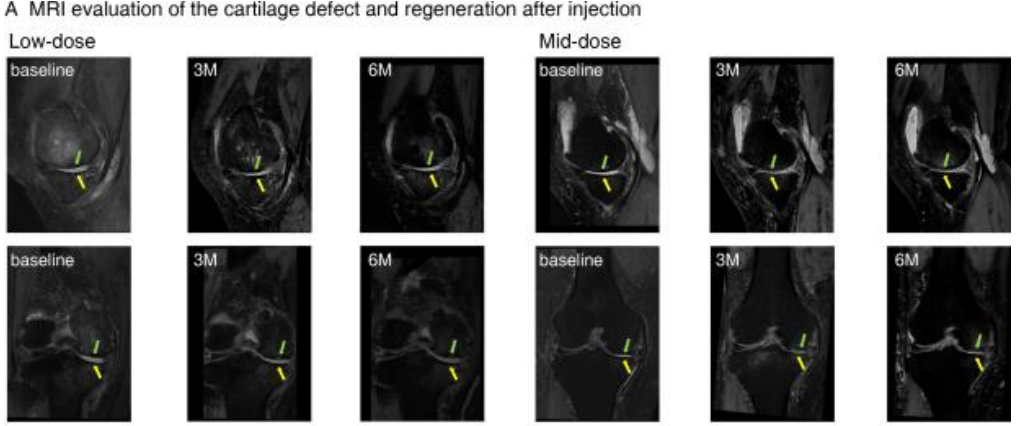


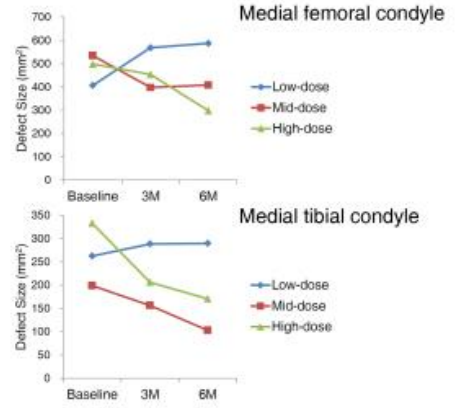


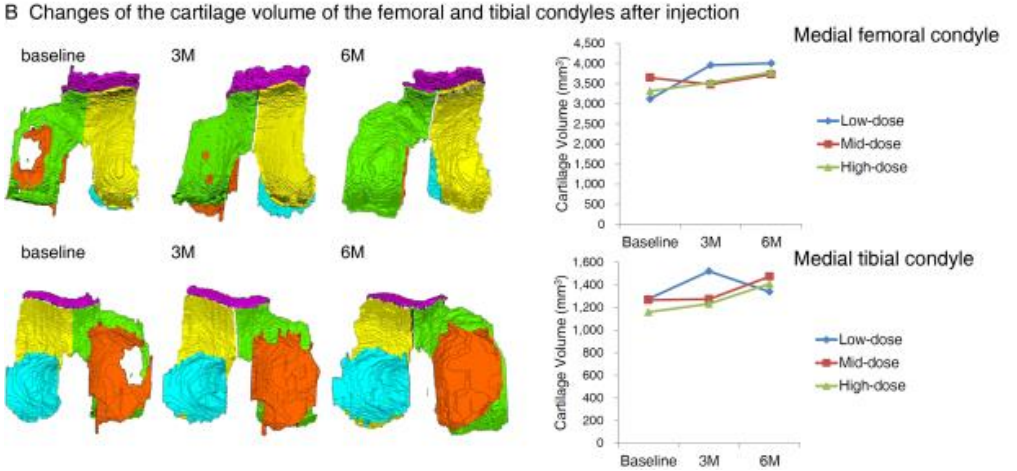






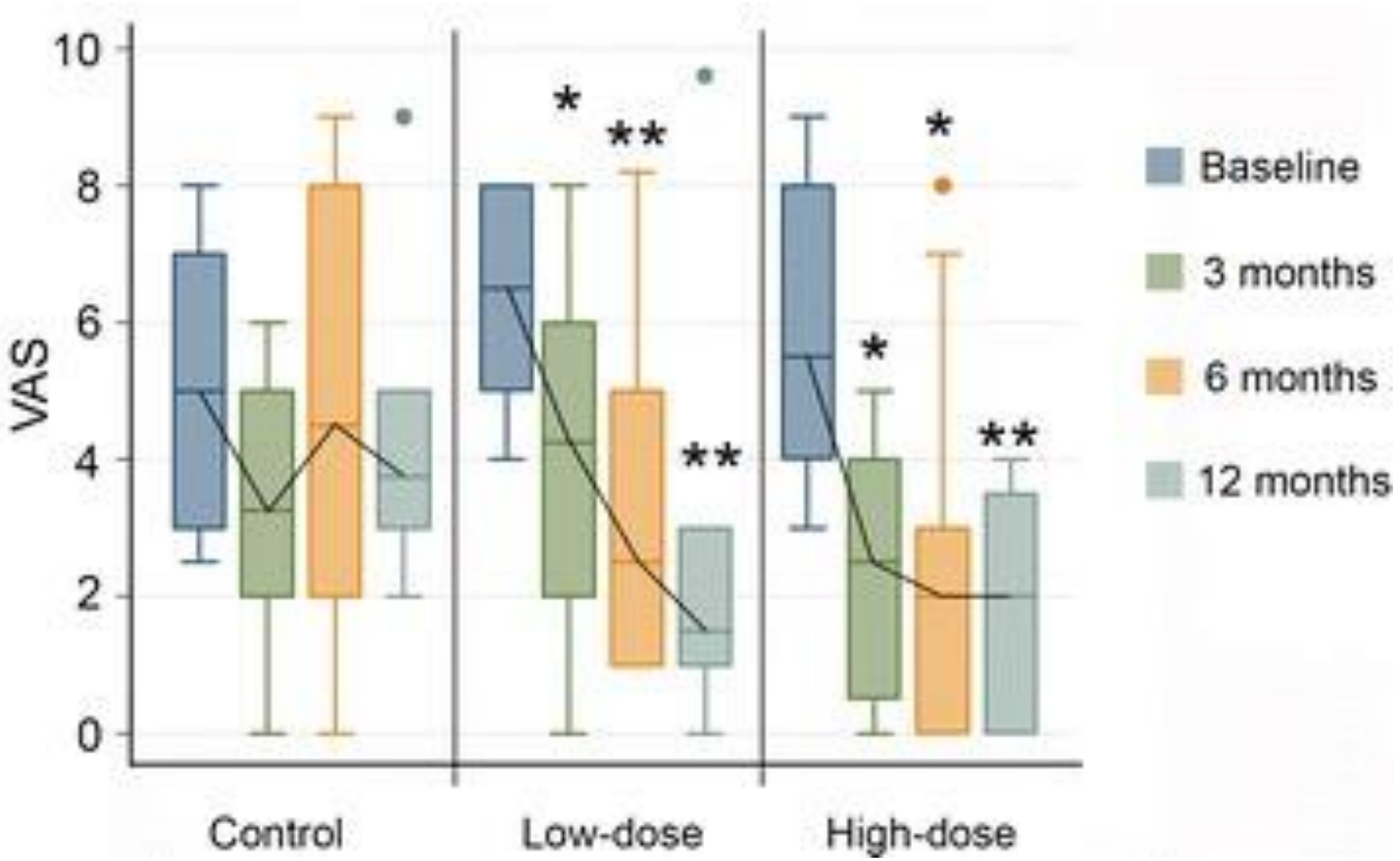






Jo CH et al. Stem Cells 2014;32: 1254-66; Vega A et al. Transplantation 2015;99: 1681-90; Wonk KLet al. Arthroscopy 2013;12: 2020-8; Orozco L et al. Transplantation 2013;95: 1535-41

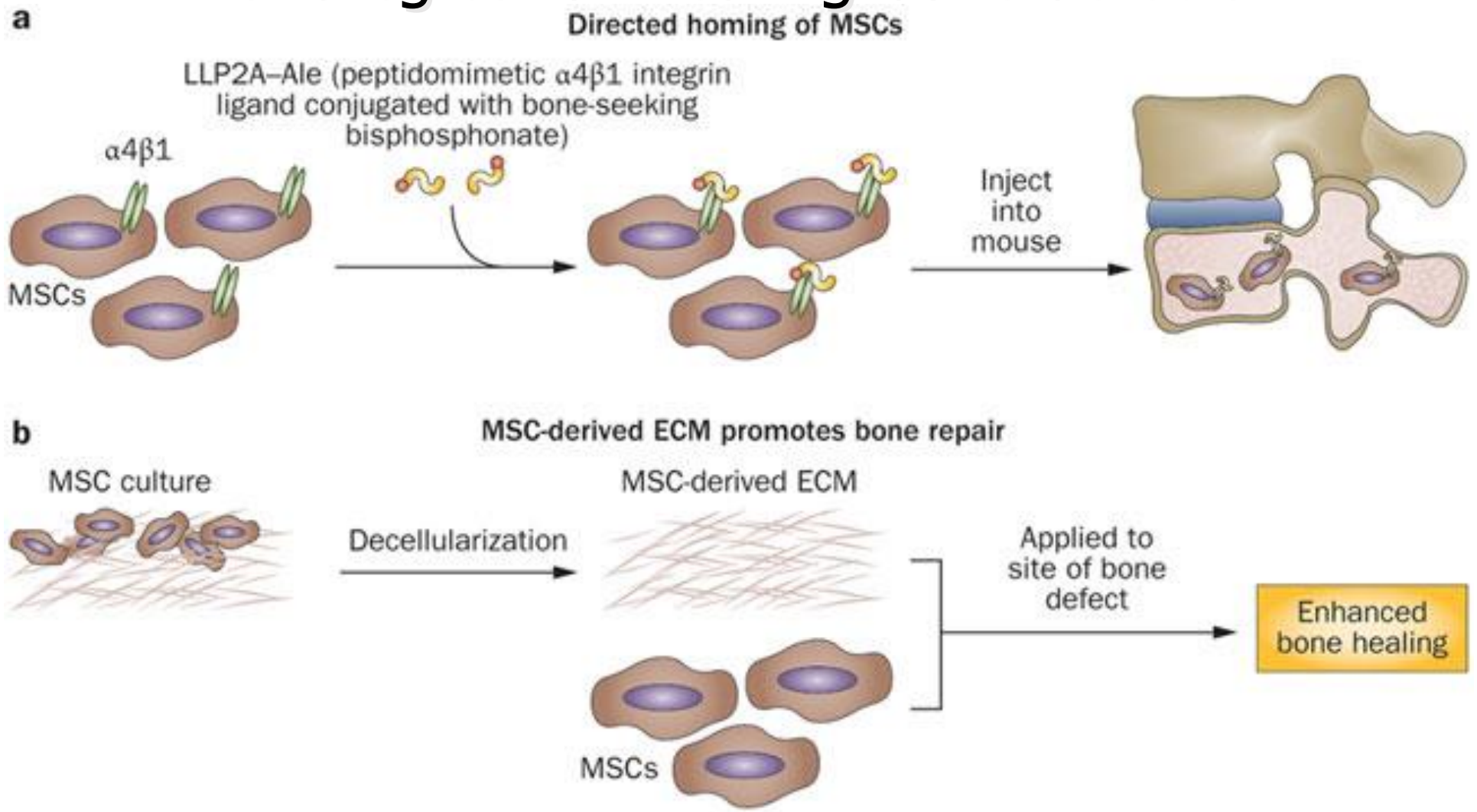
Mesenchymal Stem Cell therapy phase I-II trial in osteoarthritis
Comparing hyaluronic acid with MSC



Hyaluronic acid

Lamos-Espinosa JM et al J Transl Med 2016; 14: 246.

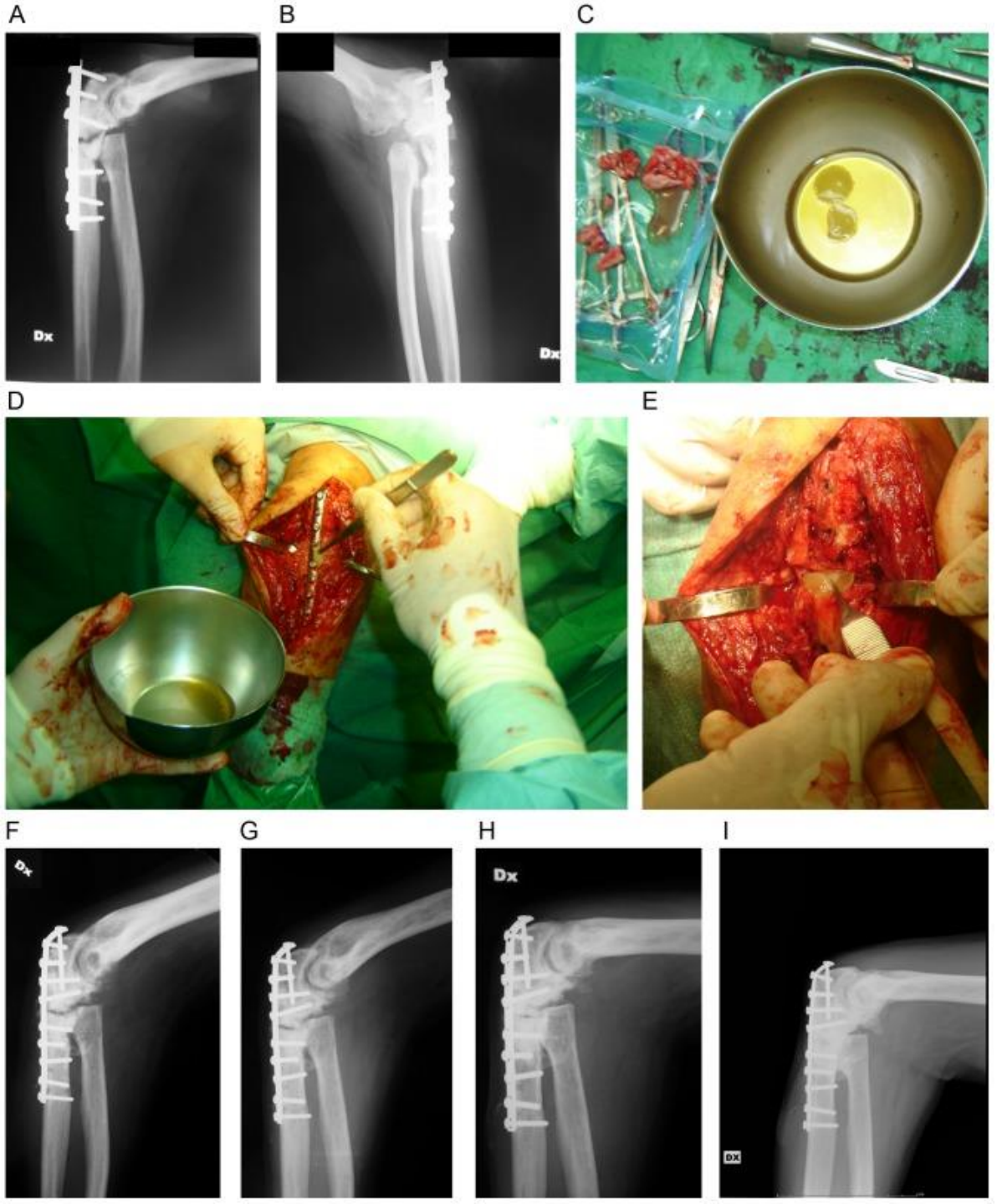
Mesenchymal Stem Cell therapy strategies for treating bone defects



Bone marrow MSCs isolated from 8 patients were expanded *ex vivo.*

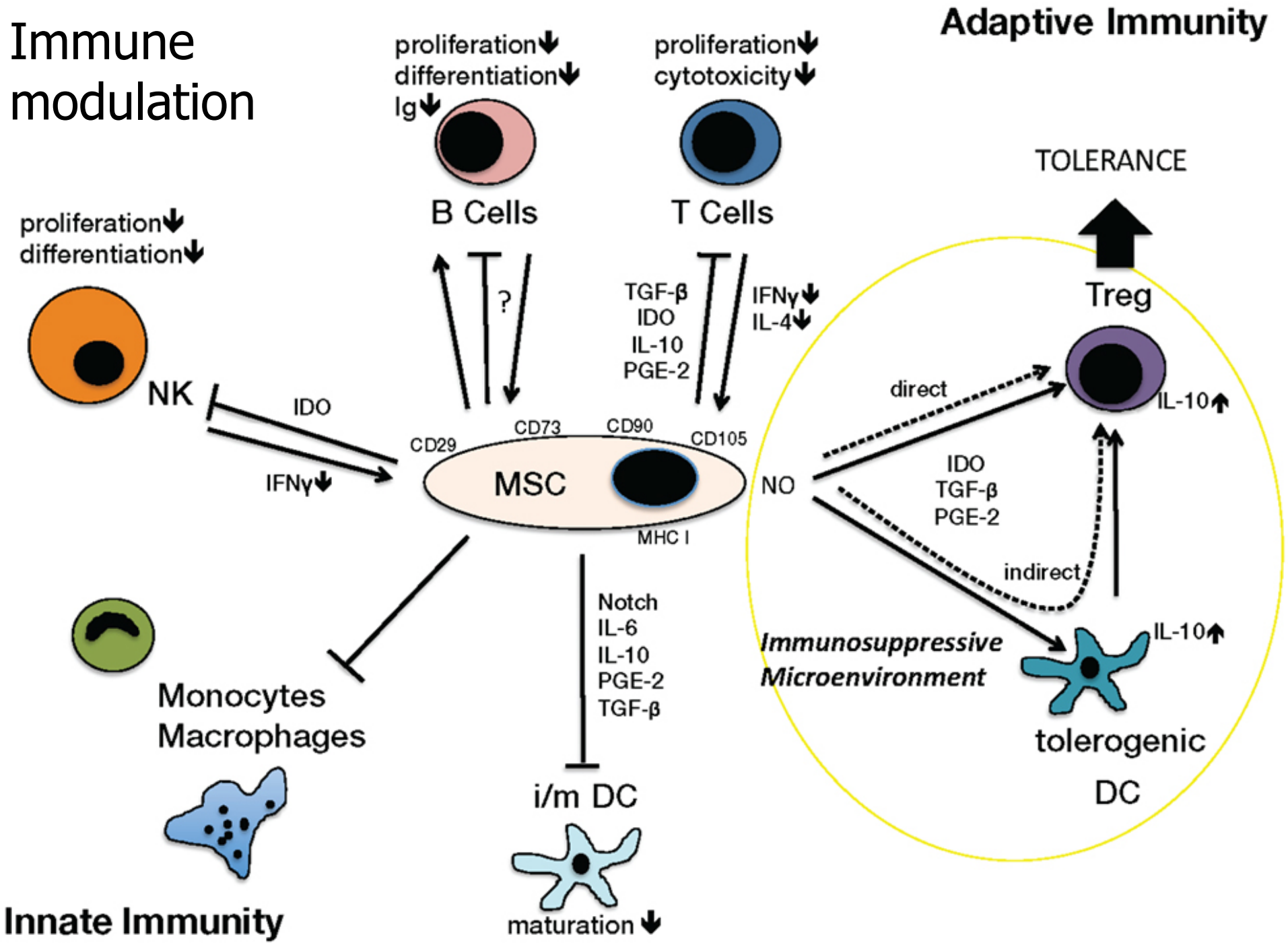
Embed MSCs in autologous fibrin clots were locally implanted with bone grafts, calibrating their number on the extension of bone damage.

All patients recovered limb function, with no evidence of tissue overgrowth or tumor formation.



Stefano Giannotti et al
PLoS One. 2013; 8(8): e73893.
Use of Autologous Human mesenchymal Stromal Cell/Fibrin Clot Constructs in Upper Limb Non-Unions: Long-Term Assessment

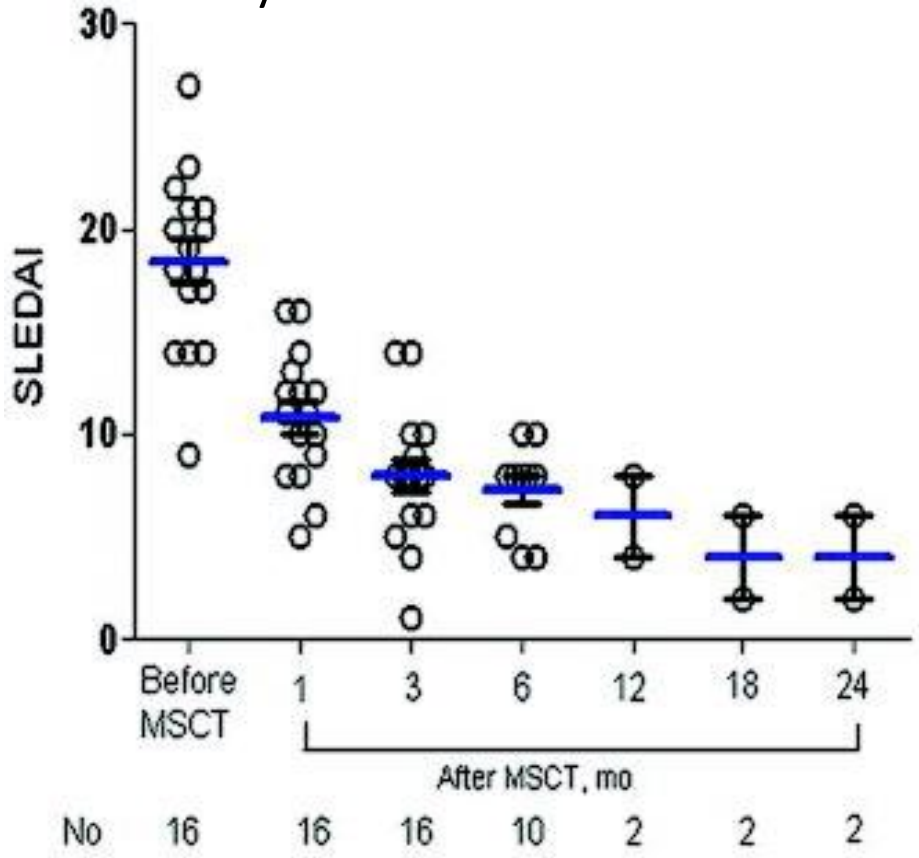
Immune modulation

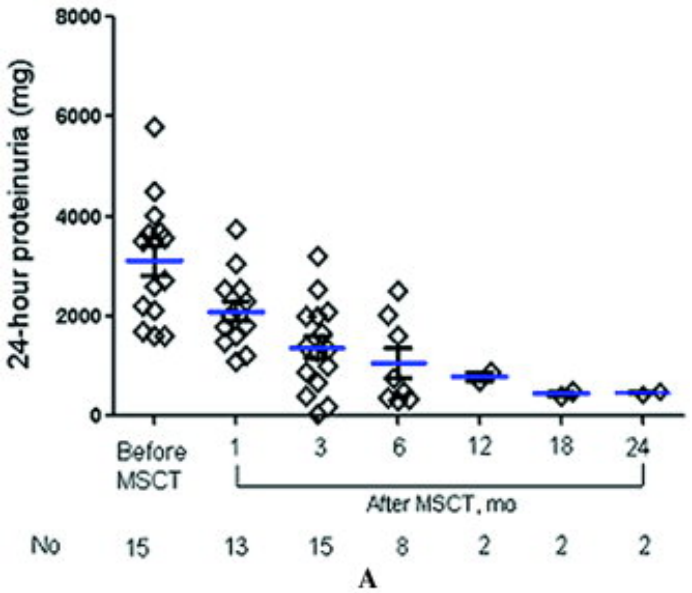


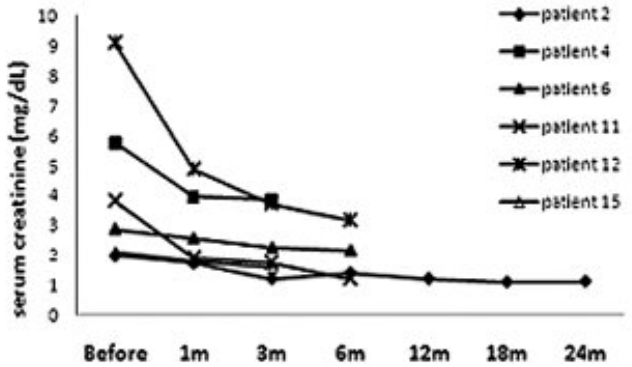
16 patients with active SLE were enrolled
The median follow-up time after MSCT was 8.25 months

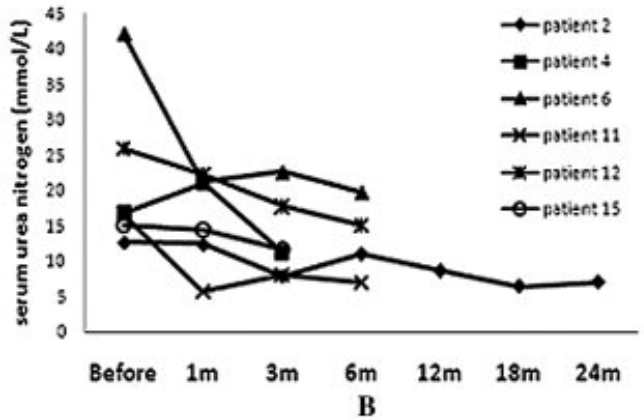
Significant improvements levels of serum ANA, anti-dsDNA, C3.

Increase in peripheral Treg cells and a re-established balance between Th1- and Th2-related cytokines.









Sun L1 et al
Arthritis Rheum. 2010 Aug;62(8):2467-75.
Umbilical cord mesenchymal stem cell transplantation in severe and refractory systemic lupus erythematosus.

A randomised double-blind, placebo-controlled trial of allogeneic umbilical cord-derived mesenchymal stem cell for lupus nephritis

No additional effect over standard immunosuppression with cyclophosphamide and corticosteroids

DanQi Deng, Peilian Zhang, Yun Guo1, Teck Onn Lim
Ann Rheum Dis 2017; 76: 1436-39.

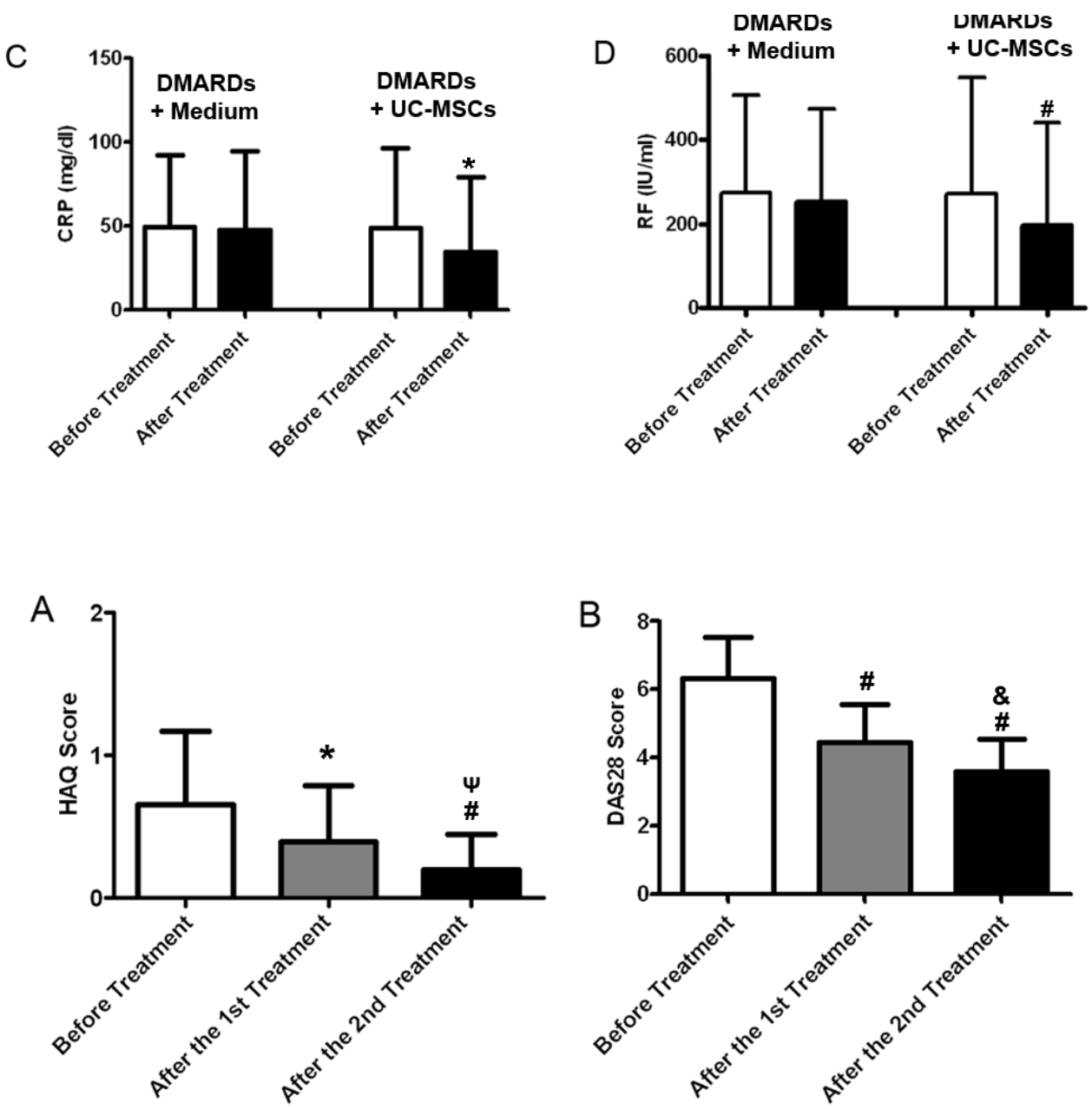
172 patients with active rheumatoid arthritis who had inadequate responses to traditional medication were enrolled.

Patients were divided into two groups for different treatment:
disease-modifying anti-rheumatic drugs (DMARDs) plus medium without UC-MSCs, or DMARDs plus UC-MSCs group

No serious adverse effects were observed during or after infusion.

The serum levels of TNF and IL6 decreased after the first UC-MSCs treatment ($P<0.05$).

The percentage of CD4(+)CD25(+)Foxp3(+) regulatory T cells of peripheral blood was increased ($P<0.05$).



Wang L1 et al
Stem Cells Dev. 2013 Dec 15;22(24):3192-202..
Human umbilical cord mesenchymal stem cell therapy for patients with active rheumatoid arthritis: safety and efficacy.

Intravenous administration of expanded allogeneic adipose-derived mesenchymal stem cells in refractory rheumatoid arthritis (Cx611): results of a multicentre, dose escalation, randomised, single-blind, placebo-controlled phase Ib/IIa clinical trial

Safe. A trend for clinical efficacy was observed

Alvaro-Gracia JM et al. Ann Rheum Dis 2017; 76: 196-200

MSC works better with IFN-γ in rheumatoid arthritis

Wild-type MSCT treated mice significantly improved the clinical severity of a murine model of collagen-induced arthritis (CIA),
while IFN-γR$^{-/-}$ MSCT treated aggravated synovitis, and joint and cartilage damage.

a phase 1/2 randomised controlled study was conducted in 63 patients with RA who responded poorly to regular clinical treatments.

MSCT monotherapy group (n=32)
or an MSCT plus recombinant human IFN-γ treatment group (n=31),
with 1 year of follow-up.

The 3-month follow-up results showed that the efficacy and ACR20 response rates were attained in 53.3% patients with MSCT monotherapy and in 93.3% patients with MSCT combined with IFN-γ treatment ($p<0.05$).

No new or unexpected safety issues were encountered in 1-year follow-up for either treatment group.

Xiao He et al
Ann Rheum Dis2020 Oct;79(10):1298-1304.

Mesenchimal Stem Cells and regenerative medicine- Conclusion

Main sources:
Umbilical Cord
Bone Marrow

Differentiate into chondrocytes and osteoblasts:
promising in osteoarthritis and fracture malunion

Paracrine immunomodulation:
Promising in rheumatoid arthritis
Promising in Lupus?

SAFE!! Unexpensive, but no patent protection possible – orphan drugs

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