28th Annual Gabor Racz Advanced Interventional Pain Conference and Workshop
Budapest, Hungary August 25-27, 2025

Comparing PRP, Stem Cells, and Exosomes: What Does the Evidence Say ?

28th Annual Gabor Racz Pain Conference
25th-27th August 2025

Dr. Matthieu Cachemaille MD, FIPP, CIPS
Médecin chef
Clinique de la douleur
Hôpital de la Tour
Meyrin
Switzerland
President Swiss Neuromodulation Society

matthieu.cachemaille@latour.ch

Conflicts of Interest

Proctoring and teaching

Boston Scientific — Advancing science for life™

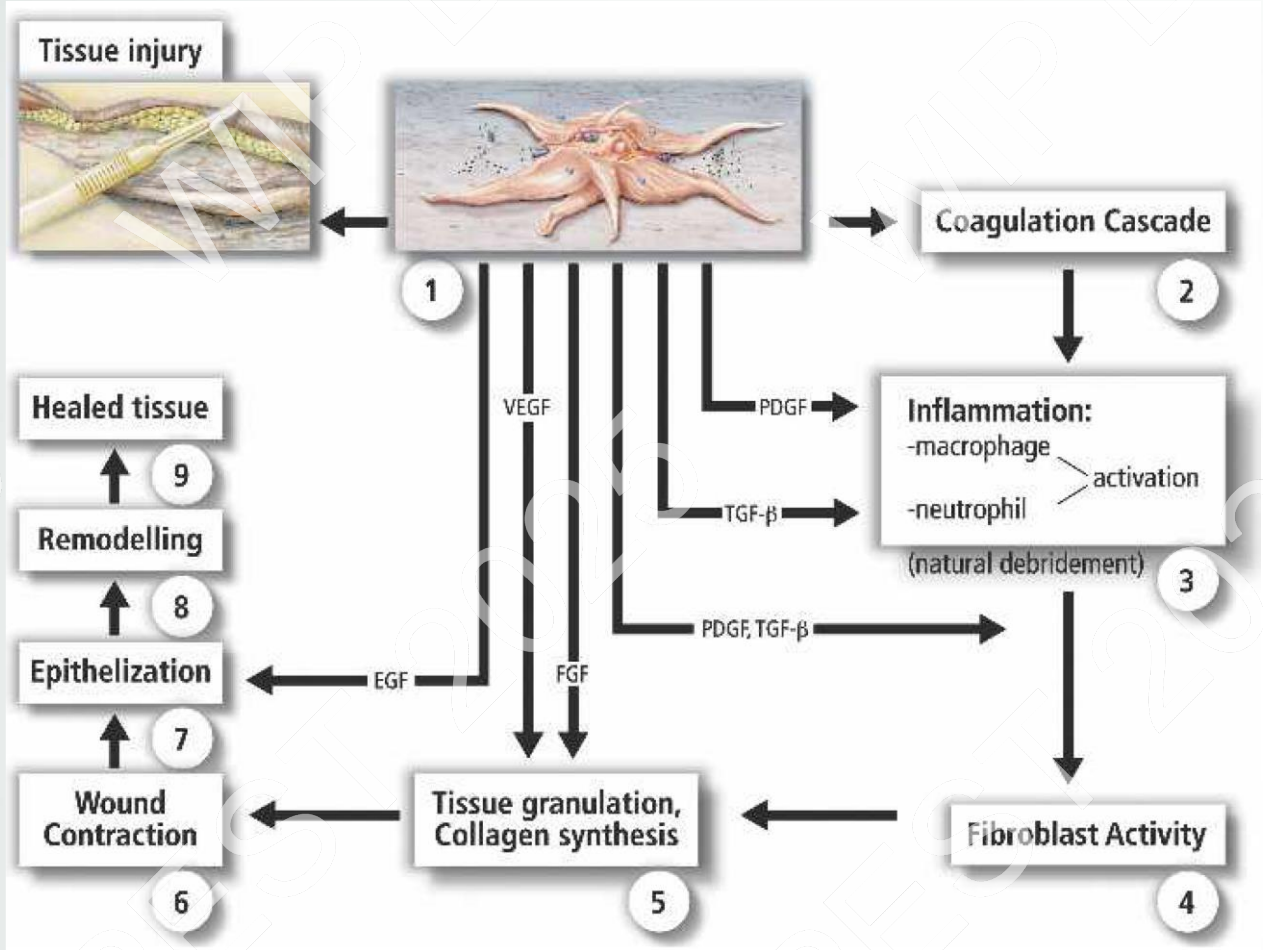
Arthrex®

Abbott

Involvement in different societies (SSIPM, WIP, ESRA, INS) as teacher and examiner to promote ultrasound, interventional pain procedures and neuromodulation

No conflict of interest in this presentation

PRP: platelets function



Everts et al, JECT, 2006

Depends on the concentration, composition and the absolute number of platelets

Ex-vivo studies

- Optimal for angiogenesis: **1.5 – 3 mio/µl** (1500-3000 G/L)

  Giusti et al, Transfusion 2009

- Inhibition and cells apoptosis: **≥ 5 mio/µl** (5000 G/L)

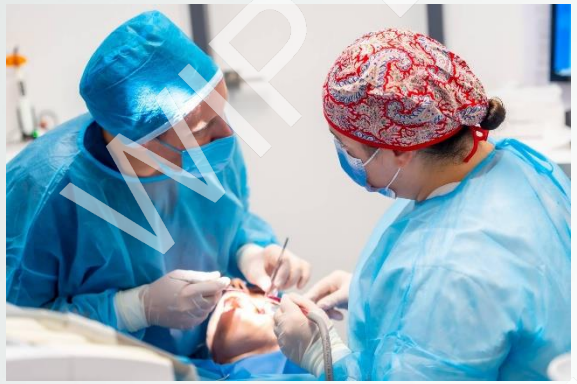
- No effects: **≤ 500 x 10^3/µl** (500 G/L). Same as platelet-poor-plasma (PPP)

For knee OA and tendinopathy: 3-5x platelets baseline

Milants et al, Bio Med Res Int 2017

Kaux et al, Muscle Ligaments and Tendons 2015

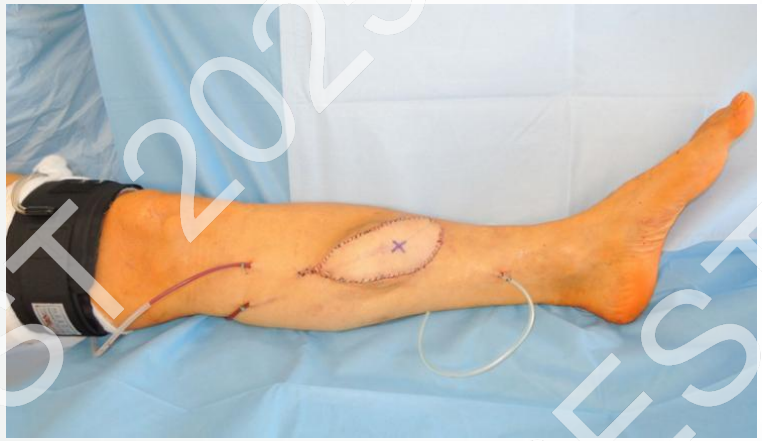
PRP indications



©Smilelakeanna

©Sonoskills

©Silverado medical clinic



©OAE publishing inc

©Eternal Hospital

Gupta et al, Exp review of hematology 2021

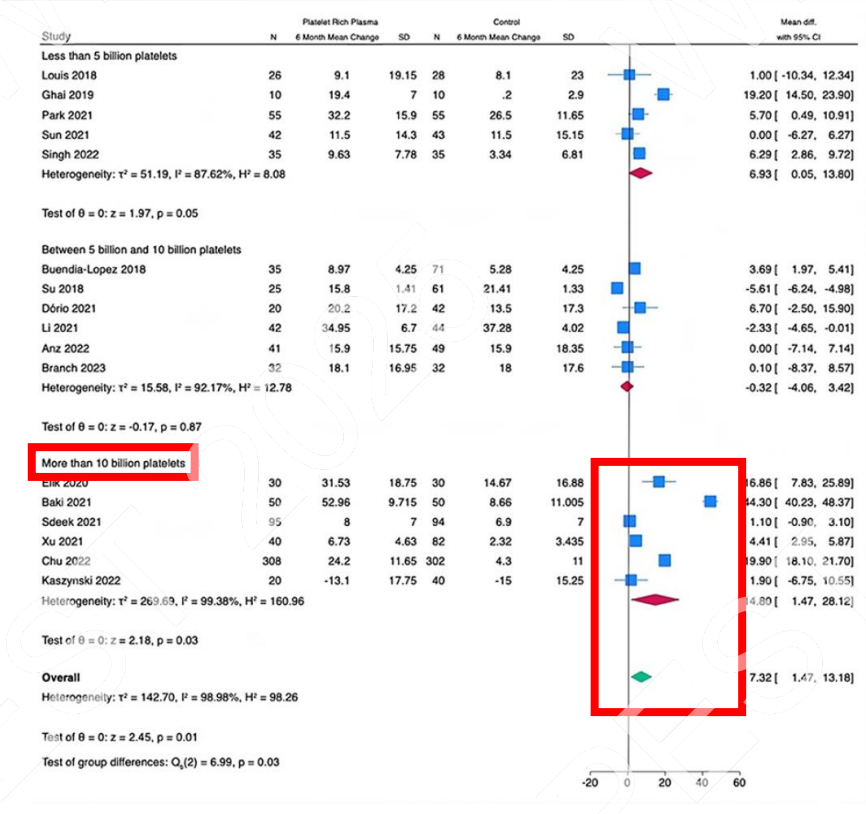
Evidence : PRP vs control (MSK)

WOMAC

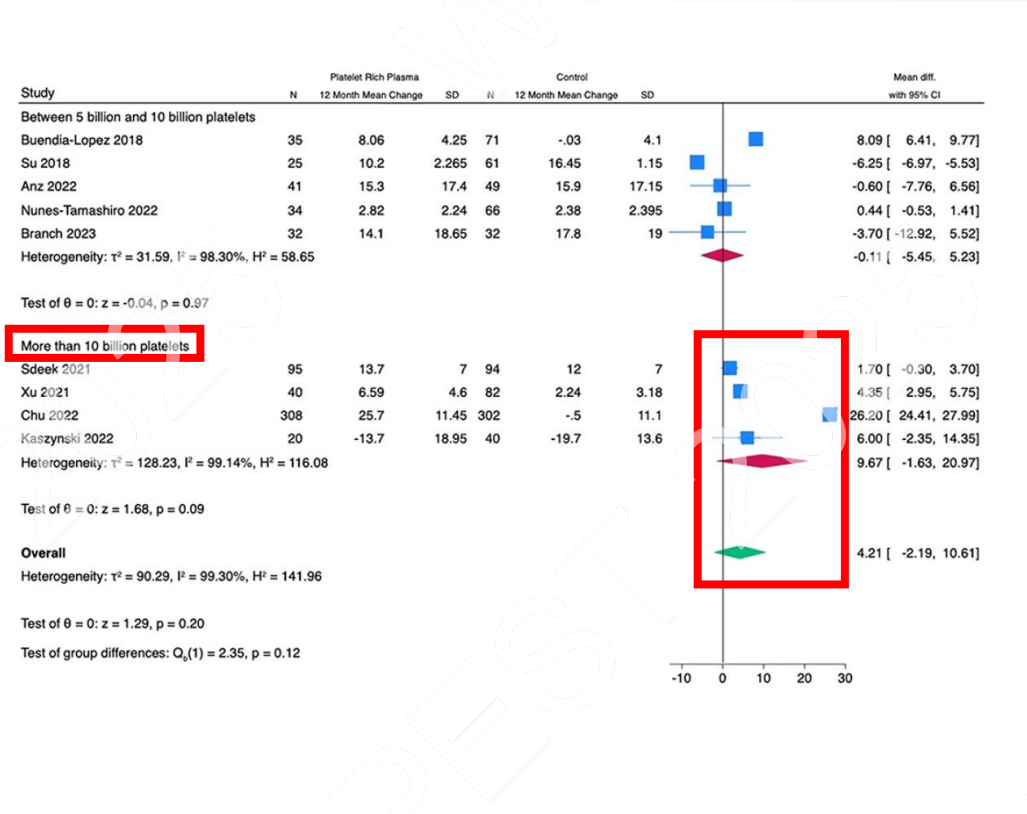
The Effect of Platelet Dose on Outcomes after Platelet Rich Plasma Injections for Musculoskeletal Conditions: A Systematic Review and Meta-Analysis

Current Reviews in Musculoskeletal Medicine (2024)

William Berrigan[1] · Frances Tao[1,2] · Joel Kopcow[3] · Anna L. Park[3] · Isabel Allen[4] · Peggy Tahir[3] · Aakash Reddy[5] · Zachary Bailowitz[1,6,7]



6 months



12 months

CLINIQUE DE LA DOULEUR

La Tour Medical Group

PRP: current evidence for spine

Responsible, Safe, and Effective Use of Biologics in the Management of Low Back Pain: American Society of Interventional Pain Physicians (ASIPP) Guidelines

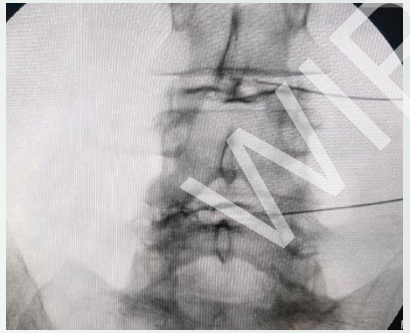
Navani et al, Pain Physician 2019

Journal of Pain Research — Dovepress
open access to scientific and medical research

Open Access Full Text Article — REVIEW

Evidence-Based Clinical Practice Guidelines on Regenerative Medicine Treatment for Chronic Pain: A Consensus Report from a Multispecialty Working Group

D'Souza et al, 2024



© Cachemaille Hôpital de la Tour 2023

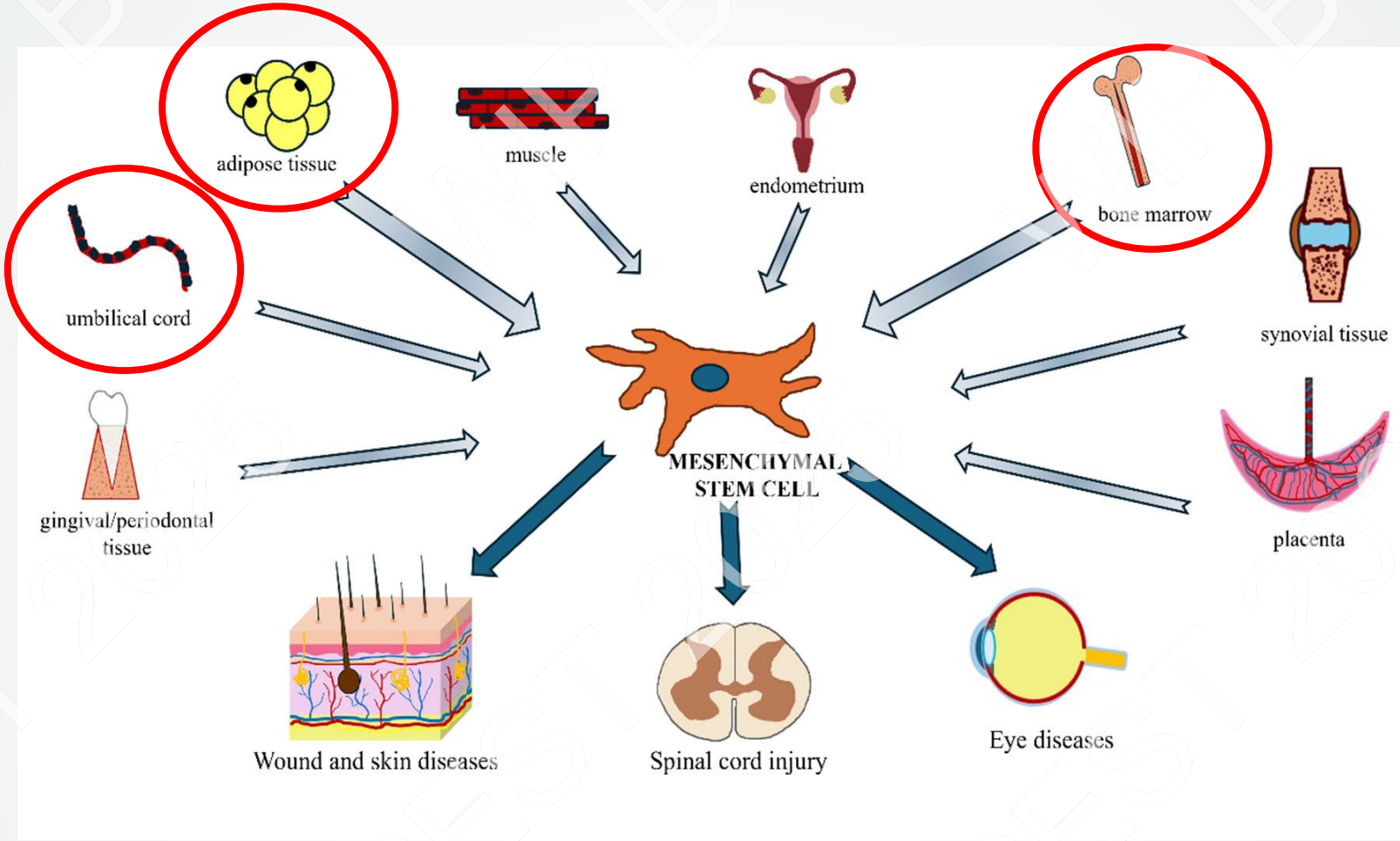
Discs and epidural injections:

Degree of recommendation: **C**
Neither recommendable nor inadvisable (at least moderate evidence that the measure is effective, but benefits are similar to harms and a general recommendation cannot be justified)

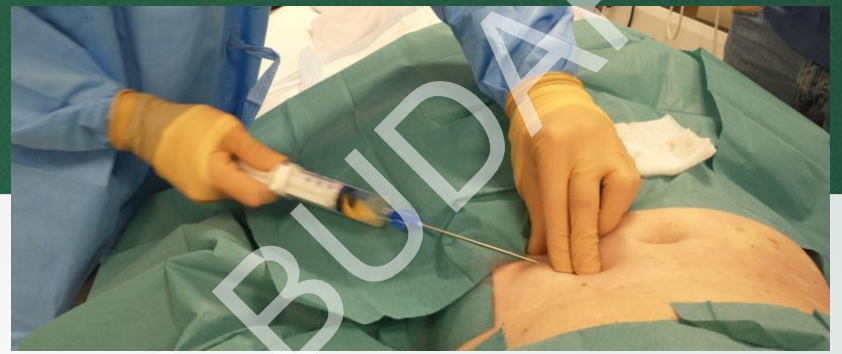
Facet joints and sacro-iliac joints:

Degree of recommendation: **B**
Recommendable (at least moderate evidence that the measure is effective and that benefits exceed harms

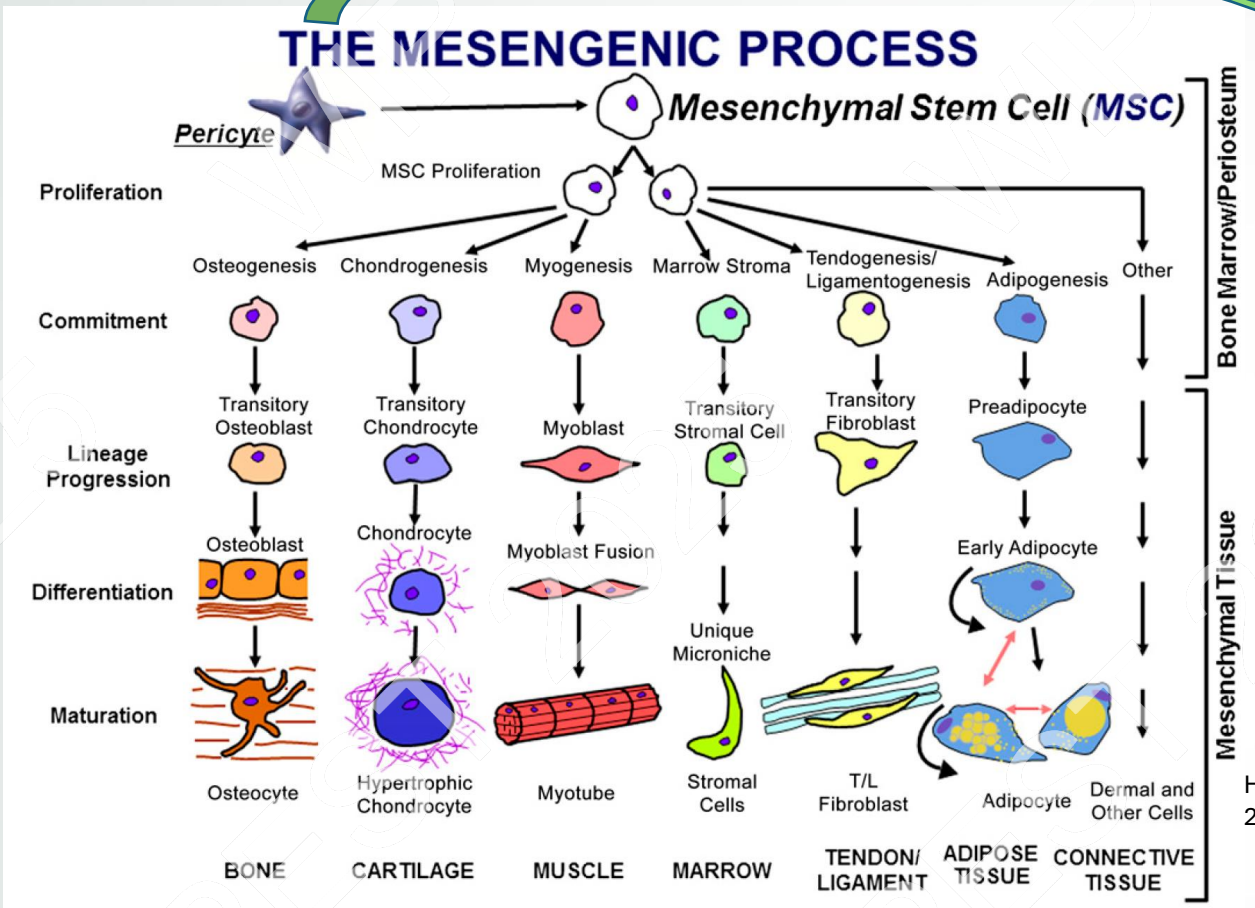
Stem cells



Picazo et al, Animals 2024



Adipose stem cells



Caplan and Hariri, Stem Cells Trans Med 2015

Present in the adipose tissue (1g = 10^3 stem cells)

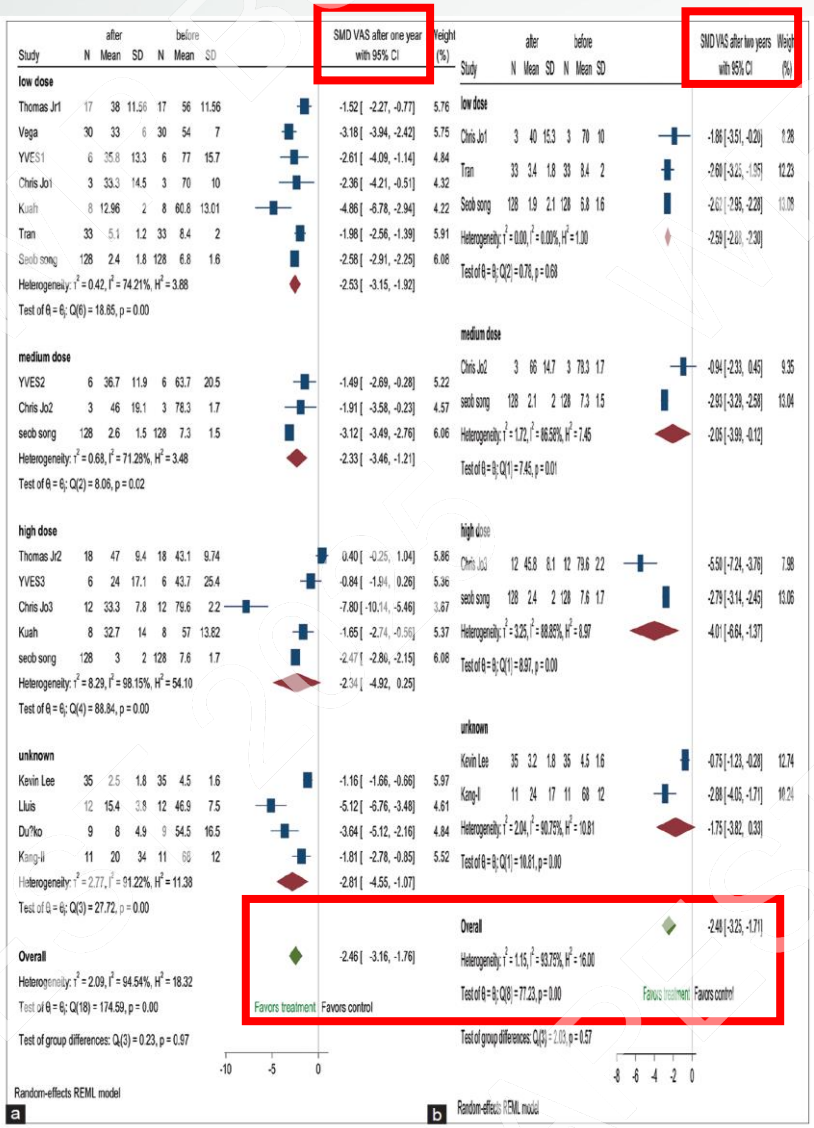
Hass et al. Cell Communication and Signaling 2011

Blood (PRP) :
1 MSC / 100'000-1'000'000 cells
Cytokins +

BMC :
1 MSC / 10'000-100'000 cells
Cytokins ++

SVF :
1 MSC / 1000-5000 cells
No cytokins

MSCs evidence for knee OA



Intra-articular injection of bone marrow aspirate concentrate (BMAC) or adipose-derived stem cells (ADSCs) for knee osteoarthritis: a prospective comparative clinical trial

Andrea Pintore[1], Donato Notarfrancesco[2], Arnaldo Zara[2], Antonio Oliviero[1,2], Filippo Migliorini[3,4*], Francesco Oliva[1] and Nicola Maffulli[1,5,6]

2023

Table 3 VAS and OKS

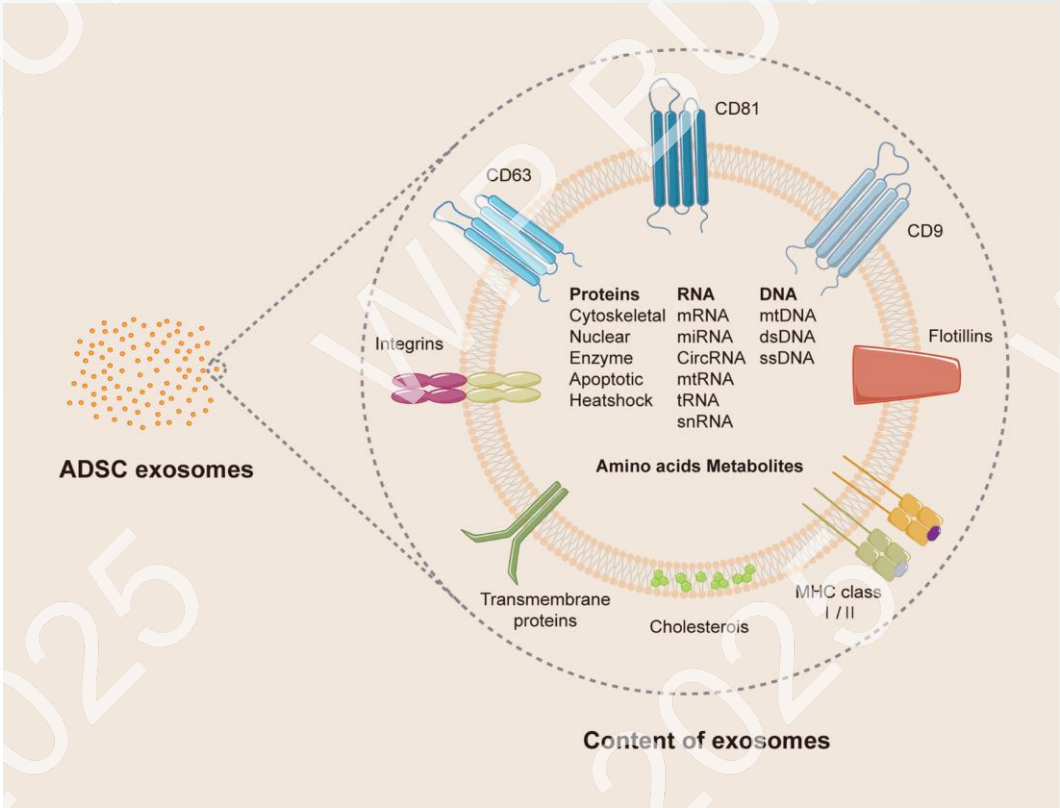
	BMAC (N = 51)	ADSCs (N = 51)	BMAC versus ADSCs (*p* value[c])
VAS score[a]			
Before	6.17 ± 1.87	6.1 ± 1.66	0.82
1 month	3.15 ± 0.78	1.84 ± 1	< 0.0001
6 months	2.98 ± 1.97	2.63 ± 1.72	0.34
p value[b]	< 0.0001	< 0.0001	
OKS score[a]			
Before	20.53 ± 5.55	20.43 ± 4.92	0.92
1 month	32.88 ± 5.94	34.58 ± 4.38	0.1
6 months	37.57 ± 10	33.35 ± 10.81	0.04
p value[b]	< 0.0001	< 0.0001	

Zhang et al, J of research in Medic Sciences 2024

Exosomes

Tiny vesicles that contain:

- Proteins
- Nucleic acids
- Amino acids
- Metabolites



Tang et al, International J of nanomedicine 2024

Mediate cell-cell communications + regulate cell proliferation, migration, differentiation, matrix synthesis, inflammatory reaction

- > Can be isolated by **ultrafiltration,** immunoaffinity capture, exosomal precipitation, zonal rate centrifugation, and microfluidic isolation techniques

Yang et al, Int J biol Science 2023

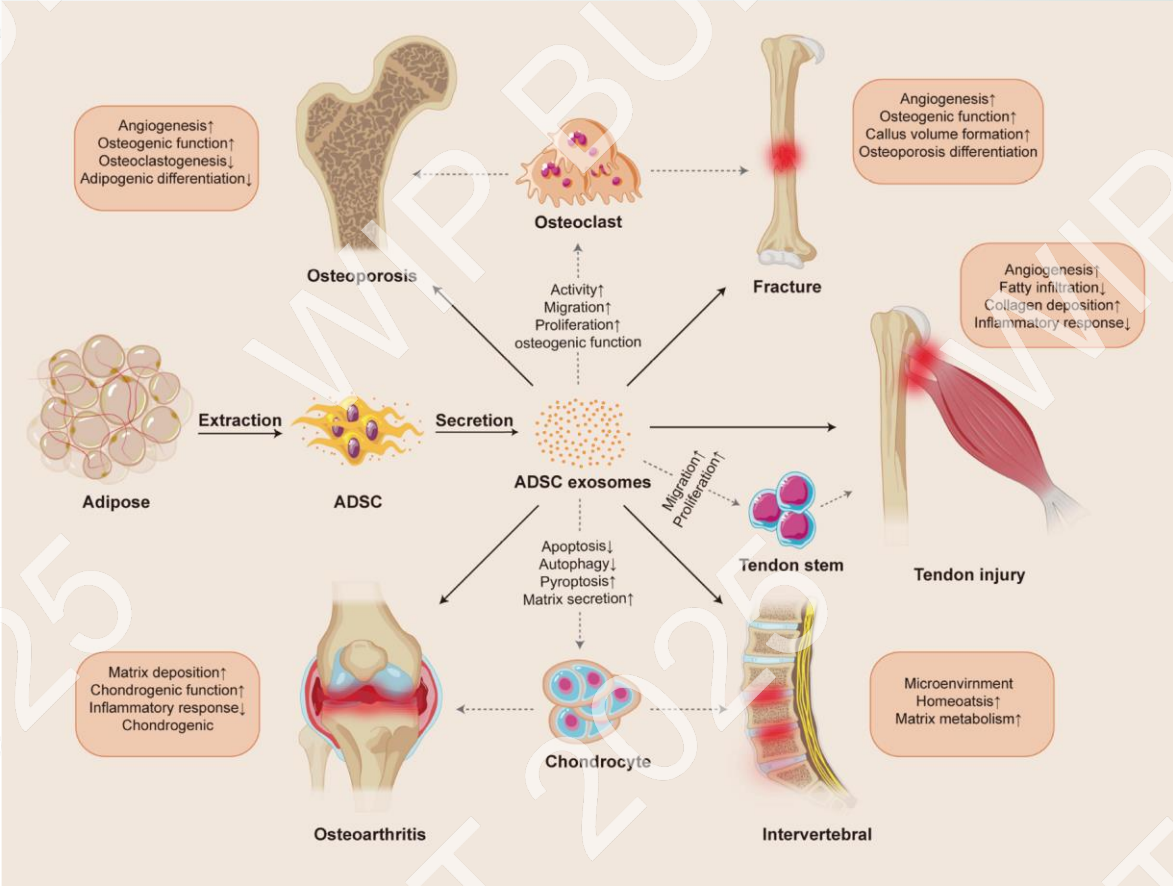
Autologous exosomes

Photothermal biomodulation

Can be detected in most biological fluids and tissues: **blood**, urine, amniotic fluid.

MSCs are a primary source of exosomes.

Tang et al, International J of nanomedicine 2024



In knee osteoarthritis:

MSC-Exos mitigate OA through stimulating cell proliferation, preventing apoptosis, triggering anti-inflammatory responses, modulating the immune system, and preserving the ECM equilibrium

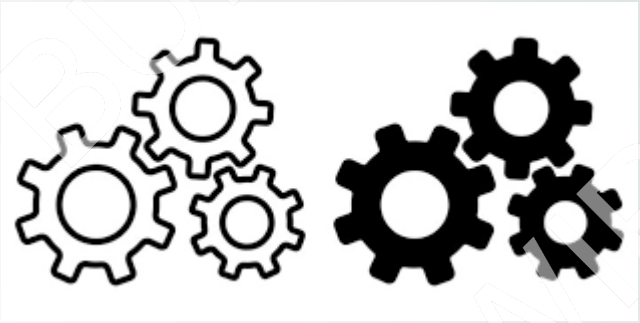
Luo et al, Frontiers in Bioengineering and Biotechnology 2024

Ex vivo evidence for adipose derived stem cells exosomes

Origin of Exosomes	Cargo	Target Cells	Mechanism of Action	Effects	Reference
ADSC-EVs	miR-486-5p	HDF and HMECs	Neoangiogenesis	Improved healing	[57]
ADSC-exos	miR-125a, miR-31	HUVECs	The enhancement of pro-angiogenic activity by targeting FIH1 in endothelial cells	Angiogenesis	[58,59]
ADSC-exos	lncRNA MALAT1	HDF/HaCaT	HDF proliferation and migration, Wnt/β-catenin activation through miR-124 binding, and the inhibition of oxidative stress	Improved healing	[60,61]
ADSC-exos	-	EPCs	Nrf2 expression and the inhibition of oxidative stress	Neoangiogenesis/improved healing in the hyperglycemic state	[62]
ADSC-exos	-	HDF	Increase in TGF-β3, collagen III, and MMP-3 through the ERK/MAPK pathway	Improved healing	[65]
ADSC-exos	miR-21	HaCaT	The activation of keratinocyte proliferation and induction of MMP-9	Improved healing in tissue deficits	[67,68]
ADSC-exos	CD9, CD63, AGO2 (as surface molecules)	HDF	The expression of VEGF-A, FGF-2, HGF, and PDGF-BB, and the conversion of fibroblasts to myofibroblasts	Improved healing	[69]
ADSC-EVs	miR-23a, miR-23b, miR-let7, miR-24, miR-125b miR-16	Macrophages	Proangiogenesis, M2 macrophage polarity, and the downregulation of MYD88/NF-κB, IL-6/TNF-α, and IKK-α	Muscle regeneration	[72,73]
ADSC-exos	miR-145, miR-221	Periosteal cells and ADSCs	Guiding cells to differentiate, KGN-induced ADSC-exos promote ADSCs into chondrocytes	Chondrogenesis	[74,78]
ADSC-exos	miR-130a-3p	ADSCs	Increase in Runx2 and ALP and the osteogenic differentiation of ADSCs via SIRT7/Wnt/β-catenin	Osteogenesis	[75,76]
AT-EVs	miR-450a-5p	ADSCs	The differentiation of ADSCs to mature adipose tissue through WISP2 inhibition	Lipogenesis	[81]
ADSC-exos	-	Schwann cells	The overexpression of Ccnd1, Ccna2, Rac1, Cthrc1, and MMP-9	Neural regeneration	[82]
ADSC-exos	miR-21	HUVECs	The promotion of endothelial cells towards angiogenesis	Angiogenesis	[85]
MSC-exos	miR-1, miR-133, miR-206, miR-494	Muscle cells	Increase in VEGF and IL-6	Muscle regeneration and angiogenesis	[86]

Papadopoulos et al, International J of molecular sciences 2024

Mechanisms of action



PRP

Indirect effect:

Platelets release **PDGF, VEGF, TGF-β, IGF-1** → stimulate tissue repair

Modulates inflammatory cytokines in joints, tendons, discs

For degenerative or micro-trauma conditions

Everts et al, JECT, 2006

Stem Cells

Direct effect: Differentiate into cartilage, bone, tendon cells

Indirect effect: Paracrine signaling → anti-inflammatory cytokines, recruitment of repair cells

Neuropathic pain modulation via immune regulation (BMC) ?

Picazo et al, Animals 2024

Exosomes

"Messenger packages" carrying microRNAs, proteins

Can cross biological barriers

Anti-inflammatory + pro-healing without introducing whole cells

Tang et al, International J of nanomedicine 2024

Wang et al, Cellular reprogramming 2020

Comparing potential efficiency

PRP vs stem cells

Both release cytokines and exosomes (paracrine mechanism) ….
after platelet degranulation, no further therapeutic benefit
➔ **More robust and dynamic results with stem cells** D'Souza et al, J Pain res 2024

Exosomes vs PRP

Exosomes tend to be more potent and consistent (laboratory controlled)
Exosomes can target more specifically recipient cells Goulian et al, J of clinical med 2025
Exosomes may lead to faster recovery time with less 1st stage inflammation

Exosomes vs stem cells

Exosomes cannot replicate (no potential tumor formation and immune response)
More stability. Can be administered by several routes. Zhang and Cheng, Nature reviews 2023

Comparison PRP-Stem cells-peptides in orthopedics

Review

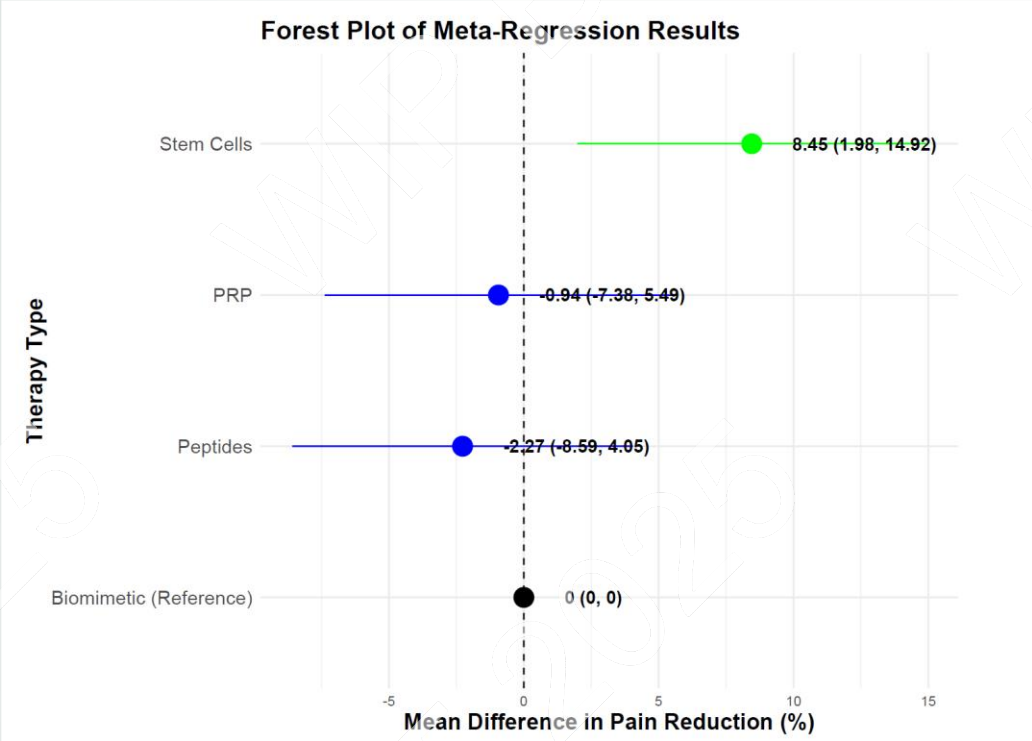
Advancements in Regenerative Therapies for Orthopedics: A Comprehensive Review of Platelet-Rich Plasma, Mesenchymal Stem Cells, Peptide Therapies, and Biomimetic Applications

Andrew J. Goulian [1], Brielle Goldstein [1] and Maarouf A. Saad [2,*]

Journal of clinical medicine 2025

Therapy Type	Number of Studies	Mean Sample Size	Pain Reduction Percent (Mean ± SD, 95% CI)	Functional Improvement	Cochrane RoB Summary	ROBINS-I Summary	Statistical Comparisons (p-Values)	Meta-Regression (β, p-Value)
PRP	20	2022 (101)	41.0 ± 6.36% (36.5–45.5)	Observed in most studies but inconsistent in long-term follow-ups.	Low Risk: 5 studies (25%) (Cochrane RoB); Moderate Risk: 9 studies (45%) (Cochrane RoB); Serious Risk: 4 studies (20%) (Cochrane RoB)	Serious Risk: 2 studies (10%) (ROBINS-I)	PRP vs. Biomimetic: $p > 0.05$ PRP vs. Peptides: $p > 0.05$ PRP vs. Stem Cells: $p > 0.05$	β = −0.94, $p > 0.05$
Stem Cells	20	1579 (78)	45.0 ± 3.85% (43.3–46.8)	Observed in most studies, superior in cartilage regeneration and tendon healing.	Low Risk: 12 studies (60%) (Cochrane RoB); Moderate Risk: 1 study (5%) (Cochrane RoB); Serious Risk: 2 studies (10%) (Cochrane RoB)	Serious Risk: 4 studies (20%) (ROBINS-I); Moderate Risk: 1 study (5%) (ROBINS-I)	PRP vs. Stem Cells: $p > 0.05$ Stem Cells vs. Peptides: $p < 0.001$ *** Stem Cells vs. Biomimetic: $p < 0.001$ ***	β = 8.45, $p < 0.05$ *
Peptides	10	738 (73)	35.5 ± 3.03% (33.3–37.7)	Improvement seen in tendon healing and pain management but limited long-term evidence.	Low Risk: 6 studies (60%) (Cochrane RoB); Moderate Risk: 1 study (10%) (Cochrane RoB); Serious Risk: 1 study (10%) (Cochrane RoB)	Serious Risk: 1 study (10%) (ROBINS-I); Moderate Risk: 1 study (10%) (ROBINS-I)	PRP vs. Peptides: $p > 0.05$ Stem Cells vs. Peptides: $p < 0.001$ *** Peptides vs. Biomimetic: $p > 0.05$	β = −2.27, $p > 0.05$
Biomimetic	7	530 (75)	37.4 ± 2.82% (34.8–40.0)	Notable in ACL healing, meniscus repair, and cartilage regeneration, but mixed long-term durability.	Low Risk: 4 studies (57%) (Cochrane RoB)	Serious Risk: 3 studies (43%) (ROBINS-I)	PRP vs. Biomimetic: $p > 0.05$ Peptides vs. Biomimetic: $p > 0.05$ Stem Cells vs. Biomimetic: $p < 0.001$ ***	Reference (β = 0.00)

Note: *** $p < 0.001$ indicates a very highly significant difference, * $p < 0.05$ indicates a statistically significant difference.



Goulian et al, J of clinical medicine 2025

Stem cells: highest relative pain reduction
PRP: highest proportion of serious-risk studies (30%)

PRP provides :

- Short-term symptomatic relief
- For tendons + ligament injuries
- Long-term efficacy ?

MSC-based therapies demonstrate :

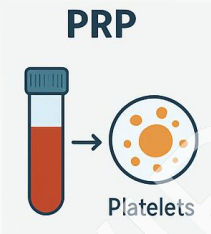
- Superior in cartilage repair and osteoarthritis
- High costs and regulatory barriers

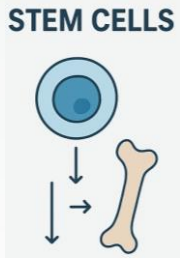
Evidence in Pain-Related Conditions

Condition	PRP	Stem Cells	Exosomes
Knee OA	Several RCTs show benefit vs placebo & HA	Multiple small RCTs & case series show cartilage repair potential	Limited early human data; promising in animal OA models
Tendinopathy	Good for lateral epicondylitis, patellar tendinopathy	Rarely used	No robust data yet
Discogenic Low Back Pain	Some pilot trials with mixed results	MSC injections show improvement in small trials	Preclinical spine studies only
Neuropathic Pain	Weak evidence	Some animal & pilot human data (peripheral nerve injury)	Early animal studies; possible neuroprotective effects

D'Souza et al, J Pain res 2024

Summary of comparison





Regenerative Capacity	Moderate (enhances repair but limited to growth factor effect)	High (tissue regeneration potential + signaling)	Indirect regeneration (signal modulation without cells)
Evidence in Pain Medicine	Moderate for tendinopathies, OA, spine pain	Promising for OA, disc degeneration, cartilage repair (early to mid-stage trials)	Emerging; mostly preclinical + small human studies
Onset of Effect	Weeks	Weeks–months	Possibly faster (days–weeks) but limited data
Duration	Months to >1 year	Potentially long-lasting if tissue regeneration occurs	Variable; may need repeated dosing
Regulatory Status	Widely allowed (autologous, minimal manipulation)	Restricted in many countries; often research/experimental	Largely experimental; unclear regulatory path
Cost	Low–moderate	High	High
Risks	Minimal (infection, pain at injection)	Harvest site pain, infection, theoretical tumor risk (very low)	Unknown long-term risks, immune reaction possible if allogenic

Conclusion
Practically what do I chose ?

If the goal is symptom modulation in mild-to-moderate degeneration:
➔ **PRP** (cost-effective and widely accepted)

If the goal is to attempt structural regeneration in advanced disease:
➔ **Stem cells** (but cost and regulations as barriers)

If aiming for potent, targeted signaling without cells:
➔ **Exosomes** (promising, but still under research-stage)

matthieu.cachemaille@latour.ch

WORLD INSTITUTE OF PAIN®

28th Annual Gabor Racz Advanced Interventional Pain Conference and Workshop

Budapest, Hungary August 25-27, 2025