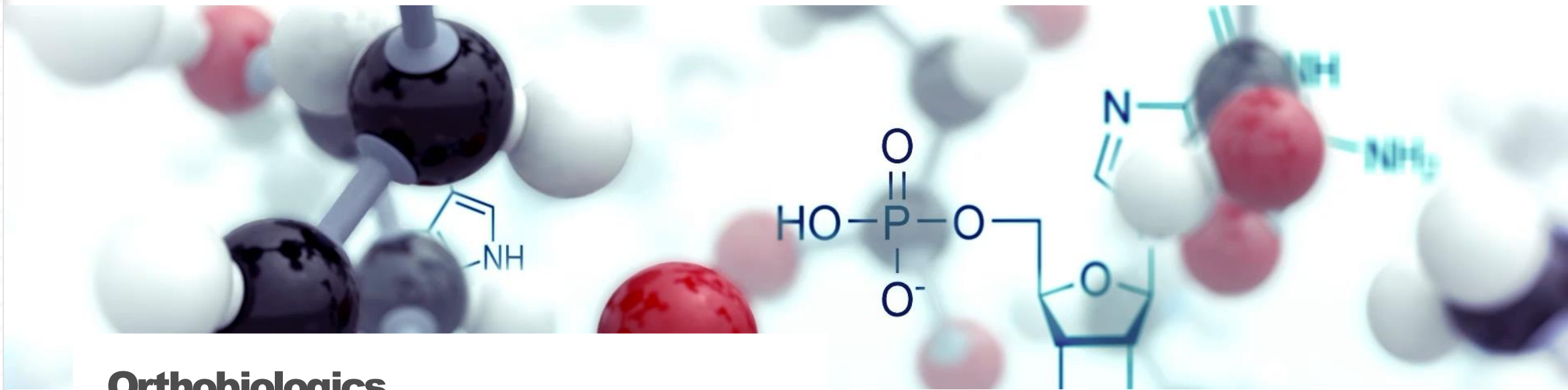




Orthobiologics Current clinical uses and controversies

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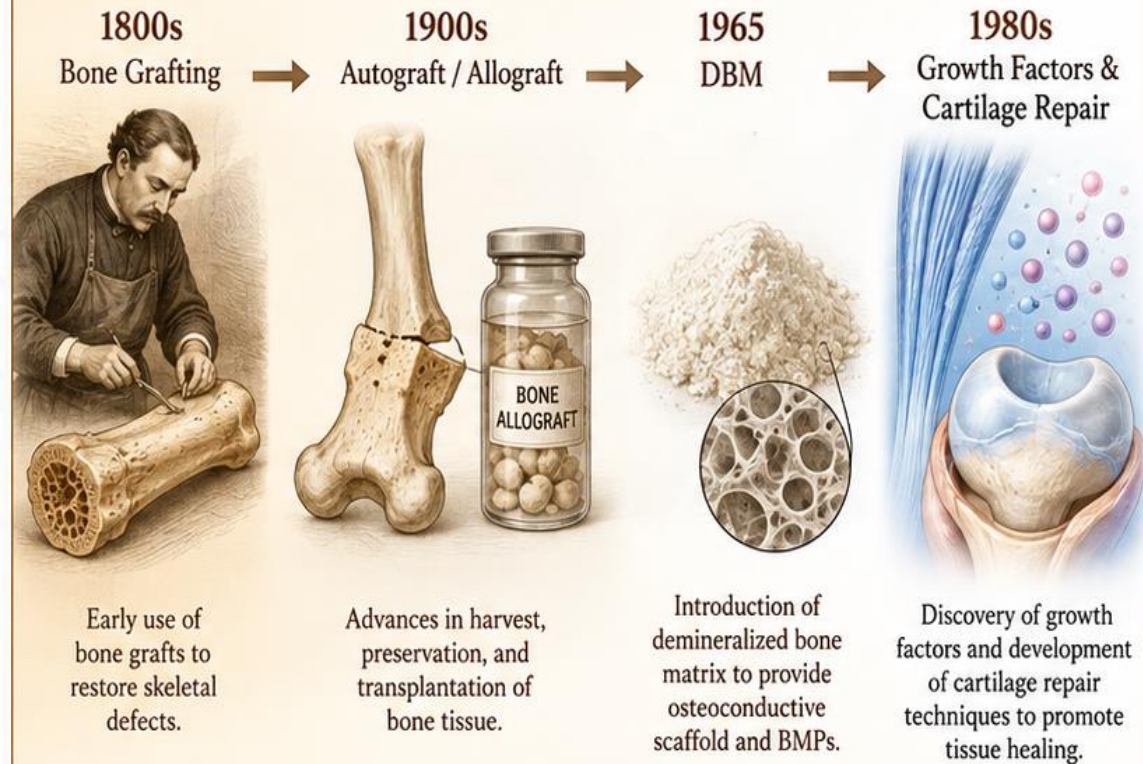
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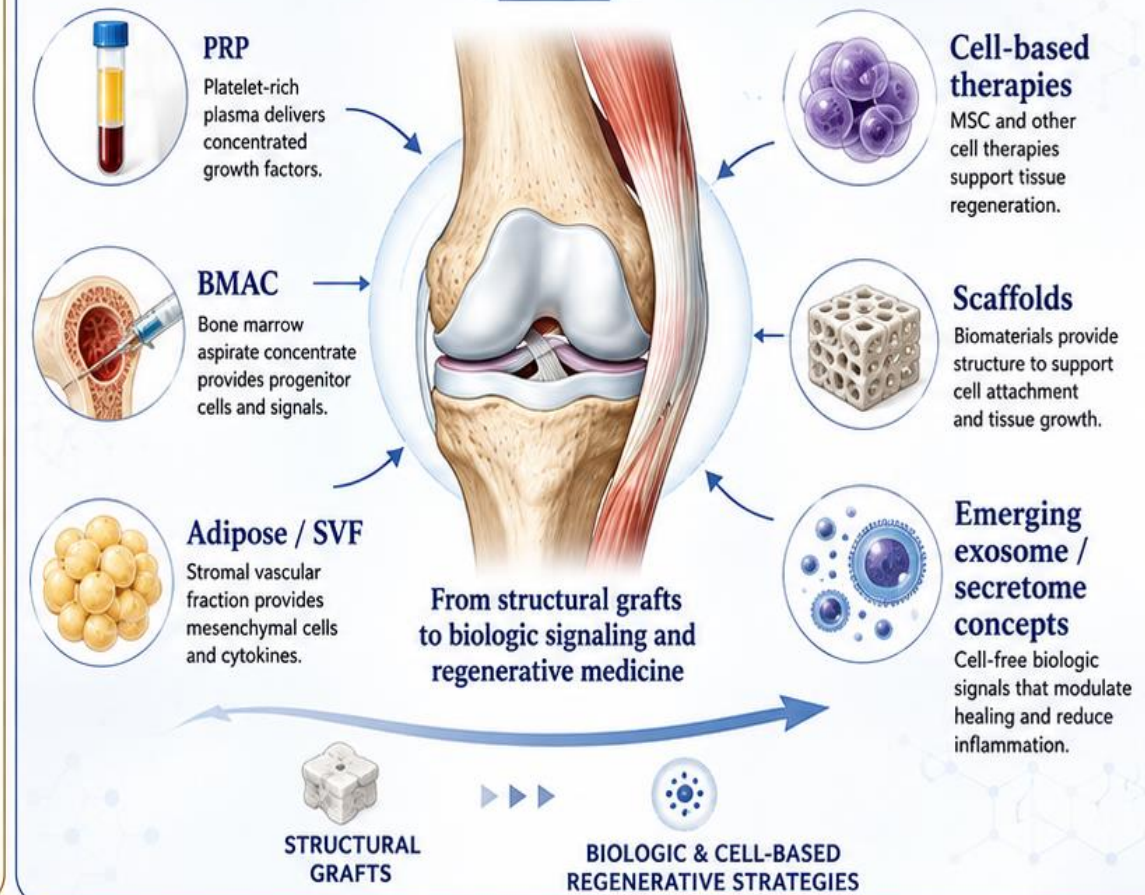
I have no relevant disclosures.

History and Development of Orthobiologics

Historical Foundations



Modern Orthobiologics



Orthobiologics evolved from structural grafting to biologic and cell-based approaches aimed at enhancing musculoskeletal healing.



Recent Publication Regarding Orthobiologics

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REVIEW ARTICLES
HEALTH CARE RECOMMENDATIONS

An International Expert Consensus Statement Defining the Best Practices and Areas of Uncertainty Concerning the Use of Orthobiologics

Kyle N. Kunze, MD, Jacob T. Morgan, BA, Cameron Gerhold, MD, Tanner Nishioka, BS, Nicolas S. Piuze, MD, Jorge Chahla, MD, PhD, and the Delphi Study Group*

Investigation performed at Midwest Orthopaedics at Rush, Chicago, Illinois

Published in the Journal of Bone and Joint Surgery on 9/2/2026

“Despite high levels of agreement across most categories, experts contended that dosing, preparation methods, and quality control remain areas of uncertainty and inconsistency that require standardization in order to allow for reproducible and meaningful treatment effects.”



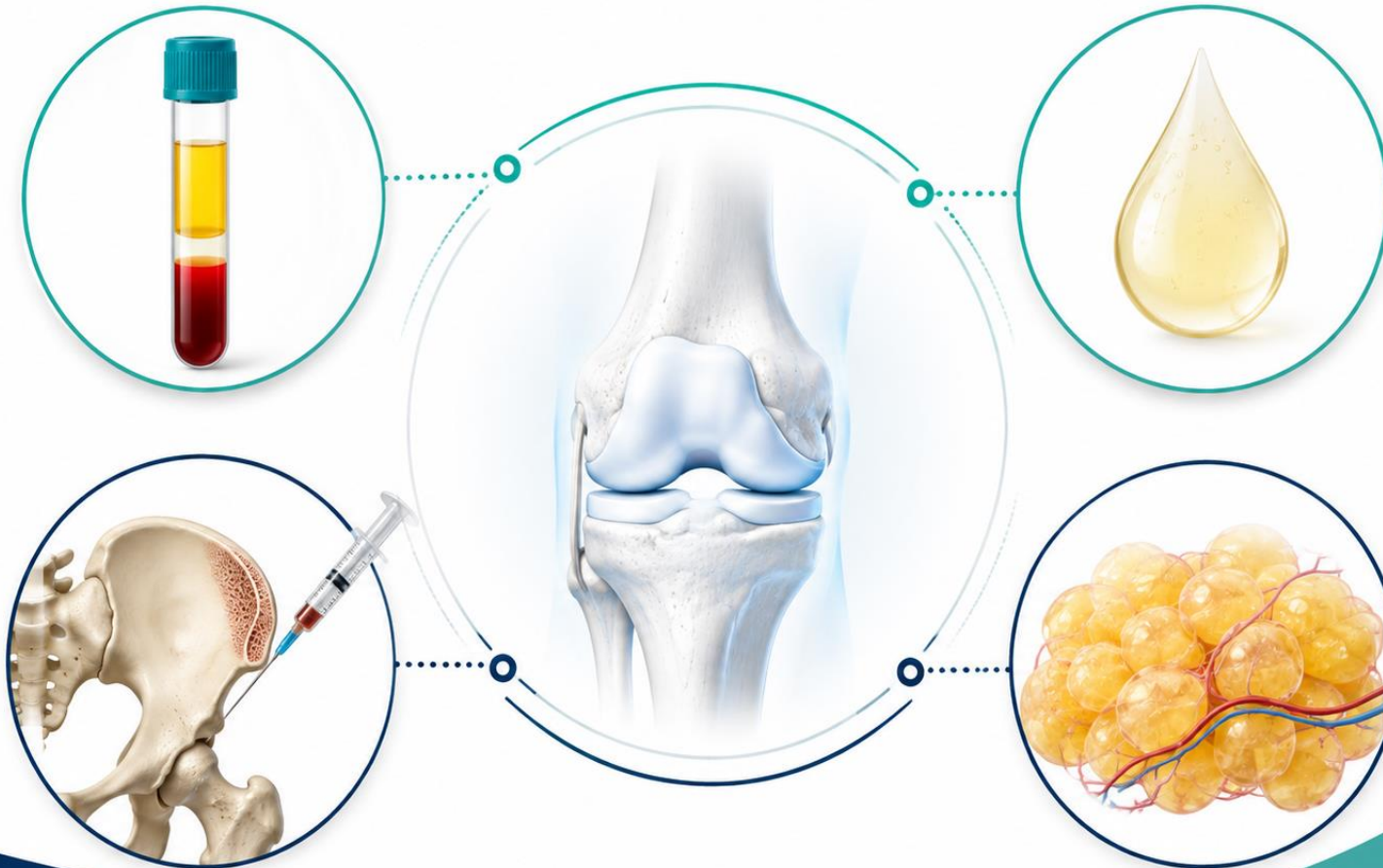
Summary

- Selectively targeted use of orthobiologics can help improve the symptoms of many musculoskeletal problems.
- However, current treatments are unlikely to change the structure of the treated architecture.



Orthobiologic Ingredients

A visual orientation to PRP, PPP, bone marrow aspirate/concentrate, and stromal vascular fraction



Core idea

These are not single, uniform drugs. They are patient-derived biologic mixtures whose composition changes with harvest site, processing method, and target tissue.

blood → PRP / PPP

marrow → BMAC

fat → SVF

Practical lens: ask “what cells, platelets, plasma proteins, leukocytes, and red cells are being used in the final product



Platelet-Rich Plasma (PRP)

Concentrated platelet signaling in a plasma carrier

What is in it?

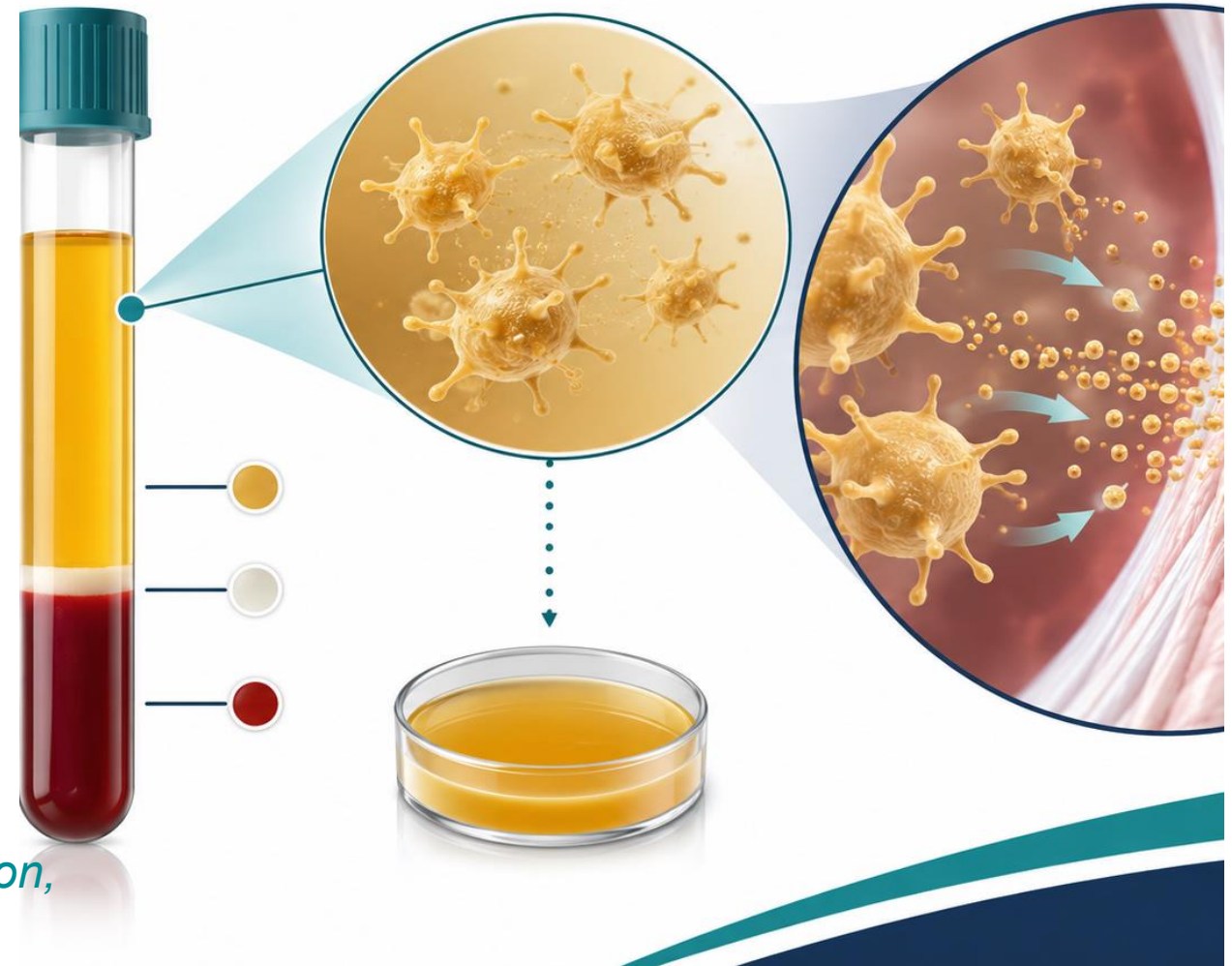
Source: autologous whole blood separated by centrifugation.

Key ingredient: platelets, with variable leukocytes and residual red cells.

Payload: alpha-granule growth factors, cytokines, chemokines, and adhesive proteins.

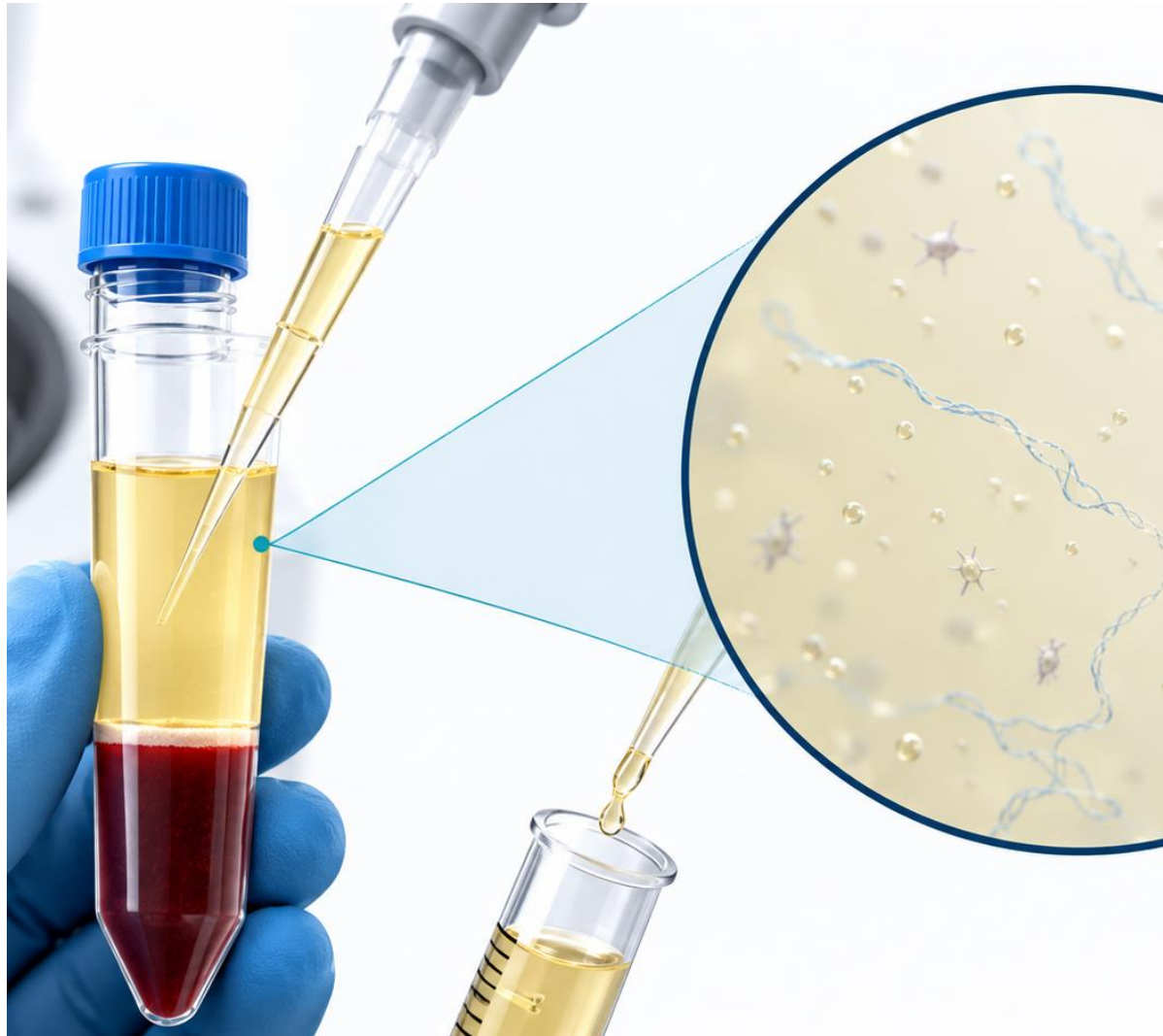
Main variable: leukocyte-rich vs leukocyte-poor PRP; platelet dose is system-dependent.

Clinical implication: document the preparation, not just “PRP.”



Platelet-Poor Plasma (PPP)

Plasma proteins with a low platelet concentration



How to think about PPP

Source: the plasma fraction after whole blood processing.

Content: fewer platelets than PRP; mostly plasma proteins such as fibrinogen and albumin.

Common role: carrier/diluent; fibrin-rich matrix or sealant-style applications depending on preparation.

Caution: not a platelet-concentrated product; terminology is often inconsistent.

Useful question: is PPP being used as a scaffold, an adjunct, or simply the leftover fraction?



Bone Marrow Aspirate / BMAC

A marrow-derived mixture of platelets, nucleated cells, and rare stromal cells

What changes with processing?

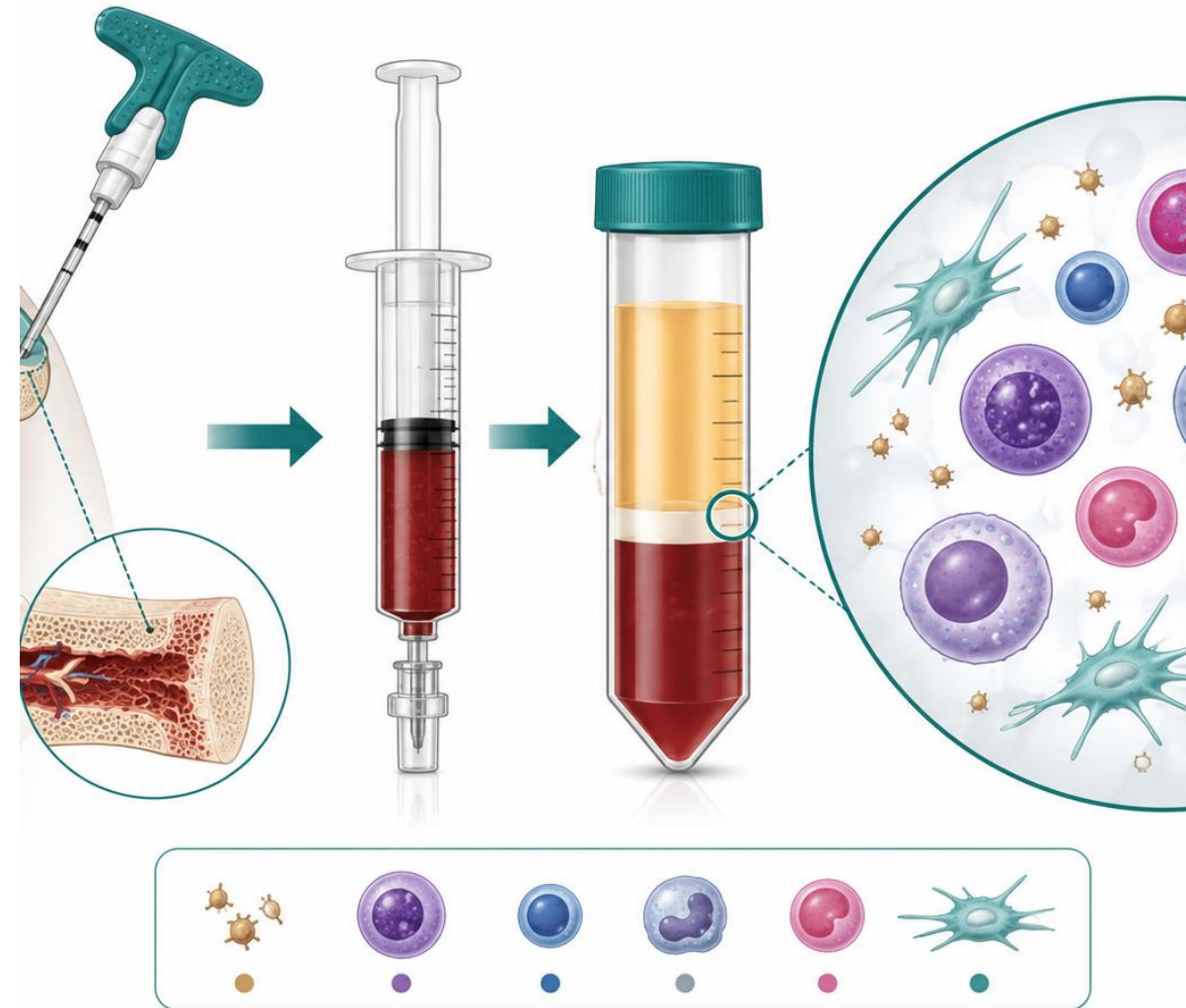
Harvest: usually iliac crest aspirate; technique affects dilution by peripheral blood.

Concentrate: nucleated cell-rich buffy coat plus platelets; red cell carryover varies.

Cells: hematopoietic cells, monocytes/macrophages, endothelial-associated cells, and rare MSC-like colony-forming cells.

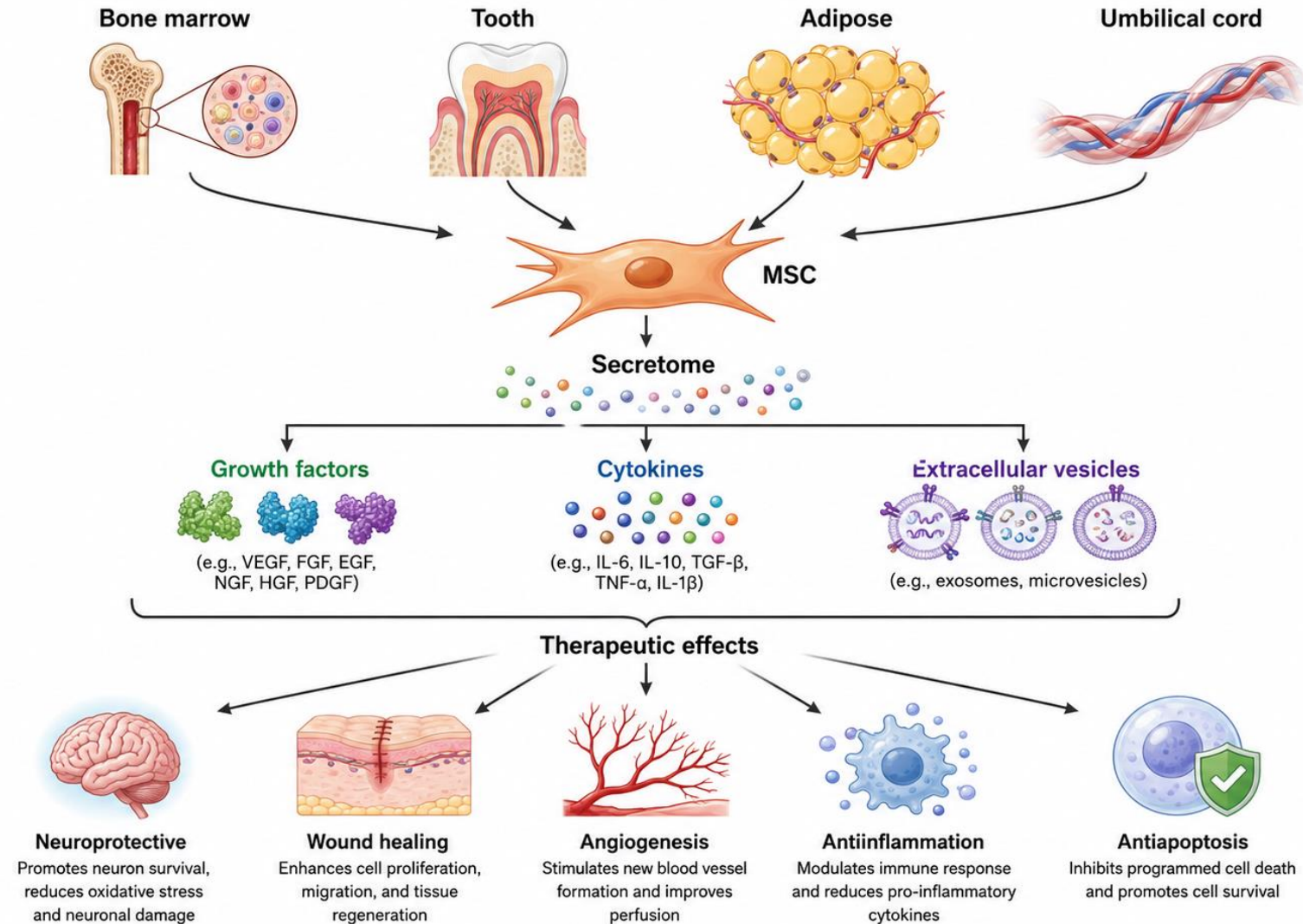
Variables: total nucleated cell count, CFU-F, platelet concentration, and viability.

Not simply “stem cells”: MSC-like cells are rare in aspirate products.



MSC Sources, Secretome, and Therapeutic Effects

Stem-cell secretory products are proposed to act through growth factors, cytokines, and extracellular vesicles.



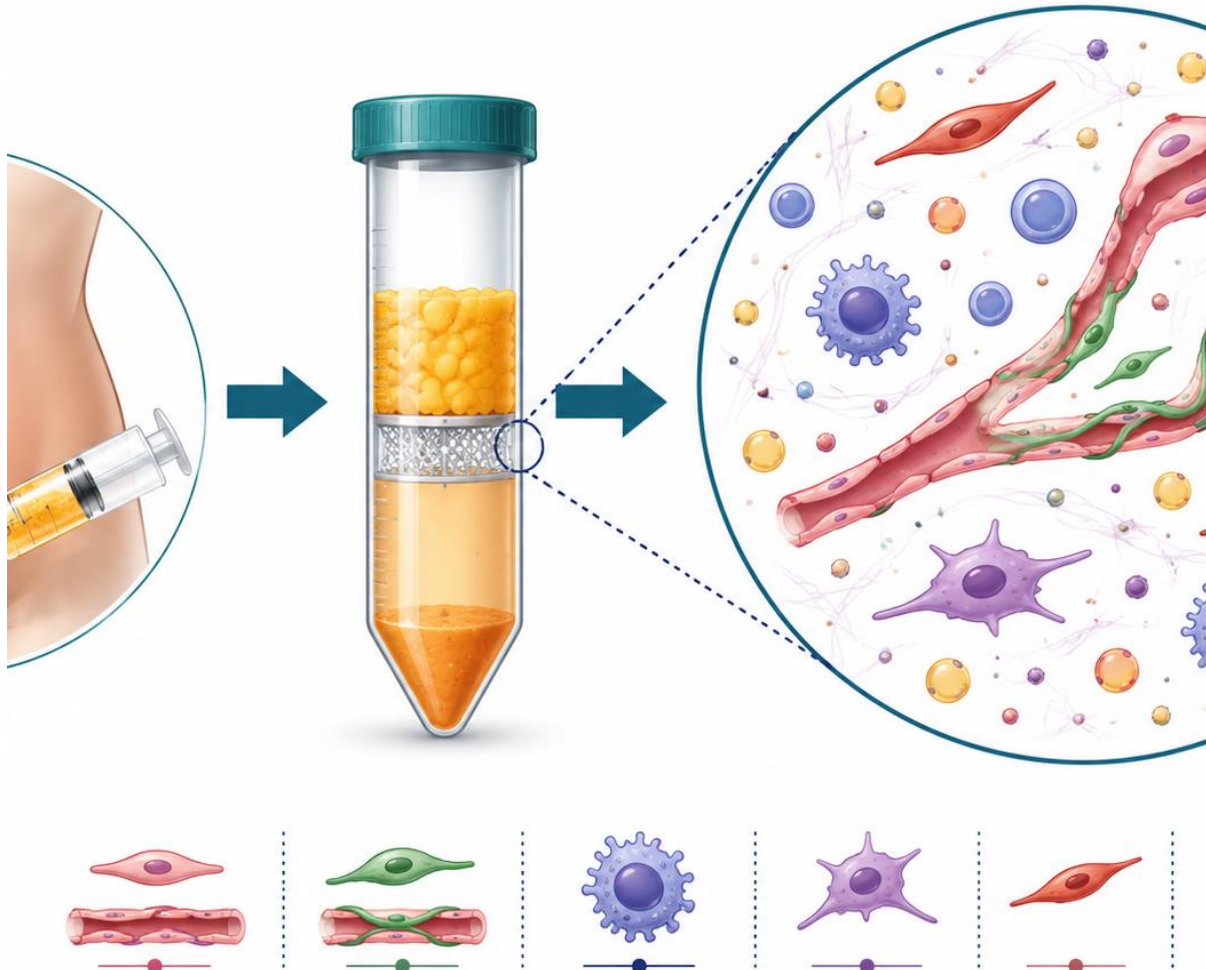
Clinical interpretation: MSC benefit is increasingly viewed as a paracrine / "secretome" effect rather than durable engraftment alone.

Adapted from Foo JB et al. Stem Cells International. 2021;2616807. Figure 3. DOI: 10.1155/2021/2616807.



Stromal Vascular Fraction (SVF)

Adipose-derived heterogeneous cellular fraction, not cultured MSCs



What is in it?

Source: lipoaspirate or adipose tissue processed mechanically or enzymatically.

Cell mix: perivascular stromal cells, endothelial cells, immune cells, adipose-lineage cells, and extracellular matrix fragments.

Distinction: SVF is not the same as expanded/cultured MSC products.

Practical caution: evidence and regulation vary by processing method and indication.

Bottom line: ingredient labels matter—PRP, PPP, BMAC, and SVF are different biologic mixtures.

Key sources in notes: AAOS OrtholInfo and Technology Overviews; Lana 2019/2021; Pavlovic 2016; EFORT Open Reviews 2021.



How PRP could help

Patellar tendinosis = chronic degenerative change at the proximal tendon, not simply “acute inflammation.”

1

Target the lesion

Ultrasound-guided PRP is placed at the degenerative tendon zone.

2

Activate platelets

Platelets release PDGF, TGF- β , VEGF, IGF-1 and other bioactive signals.

3

Shift the environment

Signals may modulate inflammation and recruit tenocytes / fibroblasts.

4

Remodel collagen

Tendon cells lay down and organize extracellular matrix over weeks to months.

5

Load guides healing

Progressive eccentric/heavy-slow resistance loading helps align collagen and restore capacity.

Clinical evidence is mixed; this slide shows the biologic rationale, not a promise of outcome.





Data

- According to Dr. Constance Chu at Stanford, “there is no good science on the clinical use of PRP.”
 - PRP is highly variable and depends upon:
 - Preparation
 - Stress level
 - Activity level
 - Genetics
 - Biology
 - Better with nutritional support
 - PRP in randomized controlled trials
 - Expensive, limited, not informative
 - VA Merit Study – Chu
 - pain, stiffness, function improved
- MRI - UTE – T2* (gradient-echo-based) quantification - still a research tool – may serve as biomarker of early degeneration

Evidence of Efficacy

Lateral elbow and rotator cuff
tendinopathy – strongest evidence
Fitzpatrick 2017, Chen 2018 AJSM

Knee osteoarthritis
PRP helpful for pain in meta-analysis
Bensa, AJSM 2025, Chu 2022
(RESTORE trial 2021 – no benefit)

Low back pain –discogenic, chronic
PRP and BMAC better for
pain/function than placebo at 12
months
Navani 2024,



How Platelet-Poor Plasma May Help Muscle Heal

Proposed mechanism: guide repair toward organized muscle regeneration rather than scar-dominant healing.

1 Fibrinogen/thrombin form a biologic scaffold

gives myogenic cells a temporary matrix to bridge the defect

2 Lower platelet cytokine load may temper inflammation

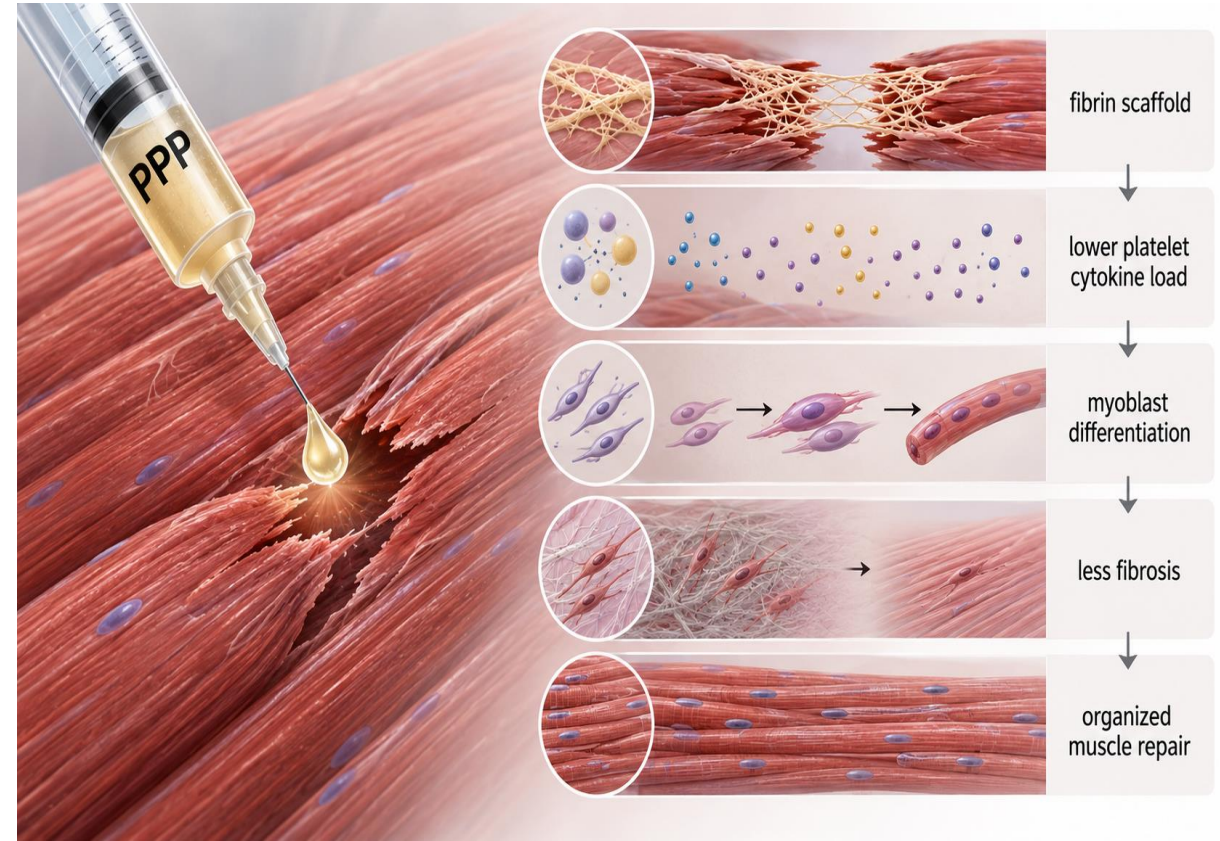
less platelet-driven signaling may reduce fibrosis risk

3 Promotes myoblast differentiation

helps satellite cells mature into contractile muscle fibers

Clinical takeaway

PPP is best framed as a biologic “repair modulator,” not a proven stand-alone accelerator. Pair with progressive rehab and objective return-to-sport criteria.



Evidence note: basic-science rationale is promising; high-quality comparative clinical trials remain limited. Sources: Chellini et al., IJMS 2019; Raum et al., Curr Sports Med Rep 2024.





Stem Cells - FDA

- FDA has sought permanent injunctions against stem cell providers ● “the FDA will continue to take enforcement actions against clinics that abuse the trust of patients and endanger their health with inadequate manufacturing conditions or by purporting to have treatments that are being manufactured and used in ways that make them drugs under the existing law but have not been proven safe or effective for any use.”
(<https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm607257.htm>) ● Recognize that the entity that turns you in will usually be your local orthopedist



Medical Tourism

- Clínica de Artrosis
 - Medellín, Colombia
 - Use of Wharton's jelly – rich source of mesenchymal stem cells (MSCs)
 - 90% success rate at 1-year mark? – British Medical Bulletin, 2024
- Why travel?
 - U.S. regulations block use of many products (SVF, chemically manipulated tissues)
 - NFL and MLB team physician estimate that 15 percent of their athletes seek care outside of the US, most commonly Panama, South Korea and Europe



What do we do?

- 1 PRP – leukocyte rich – lateral elbow(epicondylitis), patellar tendinosis, rotator cuff tendinosis
- 2 PRP – leukocyte poor – osteoarthritis (knee, hip, shoulder)
- 3 PPP - (platelet poor plasma) – muscle injury
- 4 BMAC – (bone marrow aspirate) – achilles tendinosis
- 5 Stromal Vascular Fraction – coming?



International Expert Consensus

Table 1. Final Expert Consensus, with Levels of Agreement and Disagreement, for All Round-3 Statements*

Statement	% Disagreement	% Agreement
General orthobiologics statements		
1. Contemporary evidence suggests that the use of orthobiologics for cartilage, ligament, tendon, and muscle injuries is generally beneficial and should be considered as part of nonoperative treatment plans; however, treatment should be individualized on a case-by-case basis considering patient factors and specific pathology.	0.0	95.8
2. There are no established guidelines outlining which specific patient profiles and conditions can expect to predictably experience clinical benefits from orthobiologic use.	12.5	83.3
3. Currently no treatment guidelines exist explaining at which point it is most effective to incorporate orthobiologics as part of a treatment plan.	12.5	83.3
4. Anatomic (structure-modifying) changes following the use of orthobiologics have not been consistently proven in vivo.	4.2	87.5
5. Positive structure-modifying effects of orthobiologics on tendons and ligaments (i.e., thickness, neo-vascularity) are more often reported compared with cartilage, though these changes may not correlate with patient reported outcomes.	0.0	91.7



Future outlook : eg. Cartistem[®] (South Korea): how it is thought to work

Allogeneic human umbilical cord blood–derived MSCs + hyaluronate hydrogel for severe knee cartilage defects

Core concept

Cartistem is not simply “stem cells become cartilage.” The biologic effect is generally thought to be a local repair niche created by cells + HA scaffold.

1 Delivery & retention

HA hydrogel holds hUCB-MSCs in the chondral defect and mimics cartilage extracellular matrix.

2 Paracrine signaling

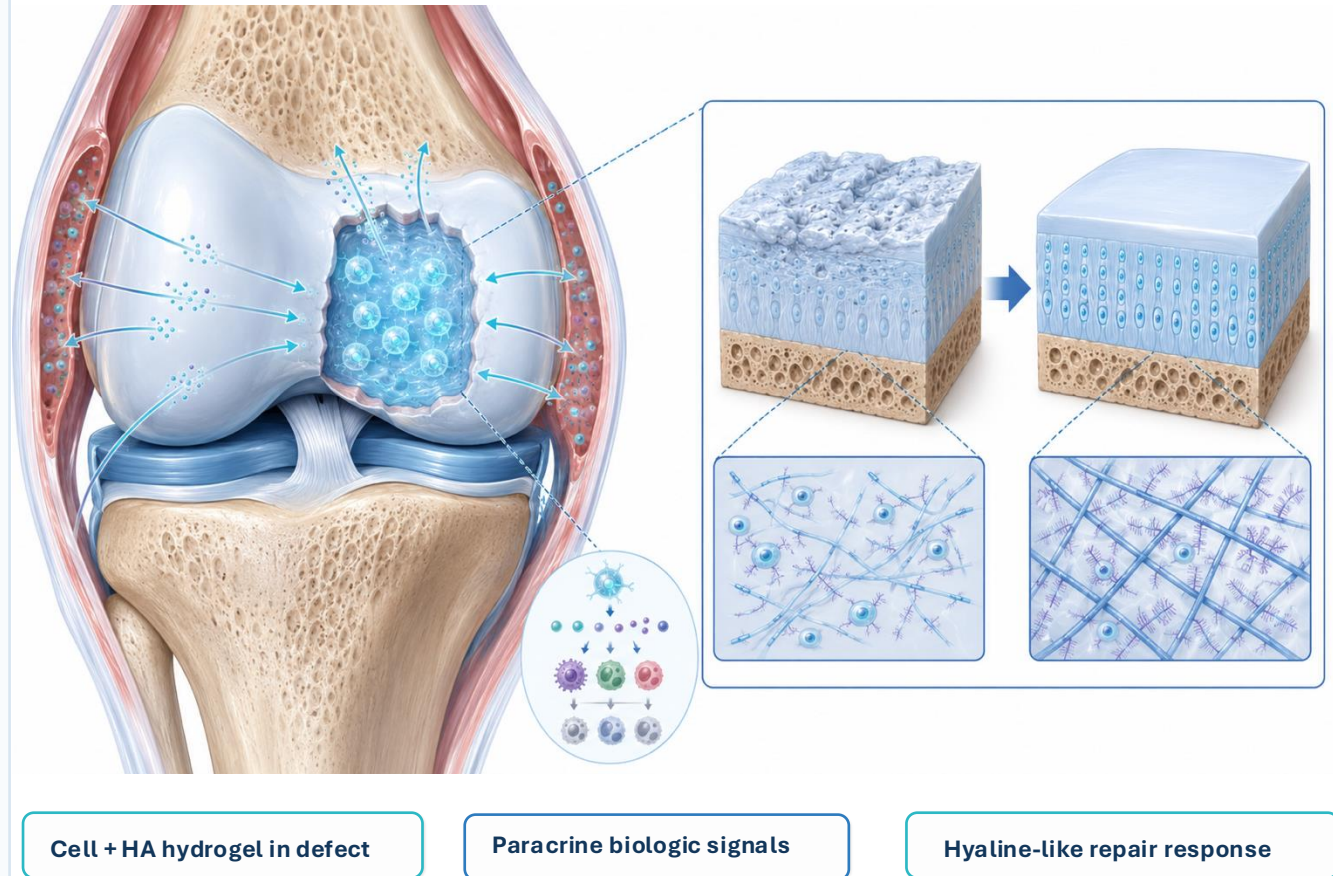
MSCs release trophic and immunomodulatory mediators that may dampen OA inflammation and catabolic activity.

3 Repair response

Signals may recruit/protect local cells, support chondrocyte activity, and increase matrix deposition.

4 Tissue outcome

Goal is durable hyaline-like repair tissue; direct MSC chondrogenesis may contribute but is not proven dominant.



Mechanism remains incompletely defined: clinical and translational literature suggests a combined paracrine, anti-inflammatory, scaffold, and local matrix-support effect.



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