

# Orthobiologics

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ORTHOPEDICS



# Objectives

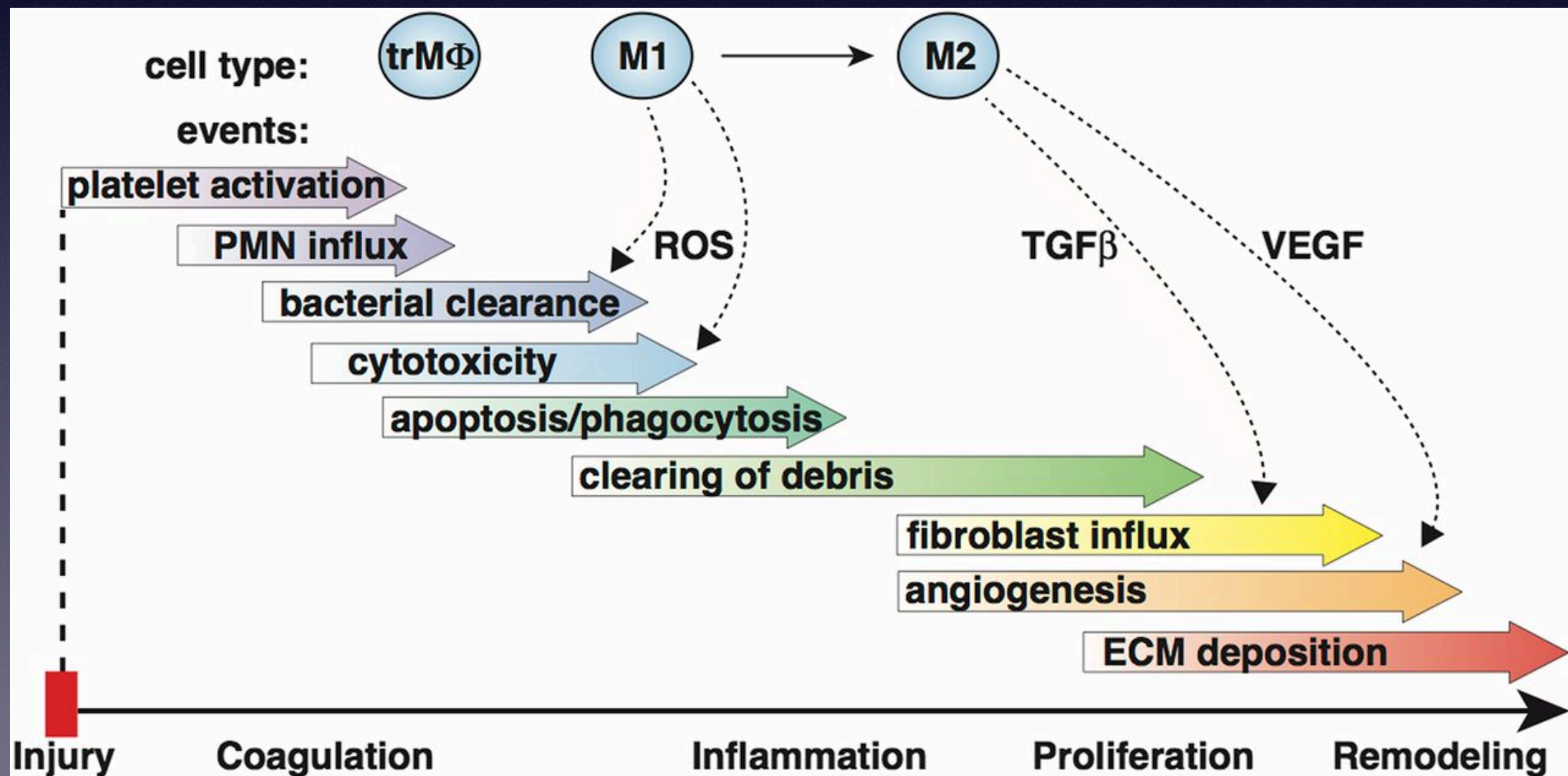
- Discuss relevance to sports medicine
- Briefly review definitions & regulatory process.
- Discuss basic science and theoretic uses.
- Review current clinical applications.
- Brief literature review and evidence.
- Summary & Questions!





# What are Orthobiologics?

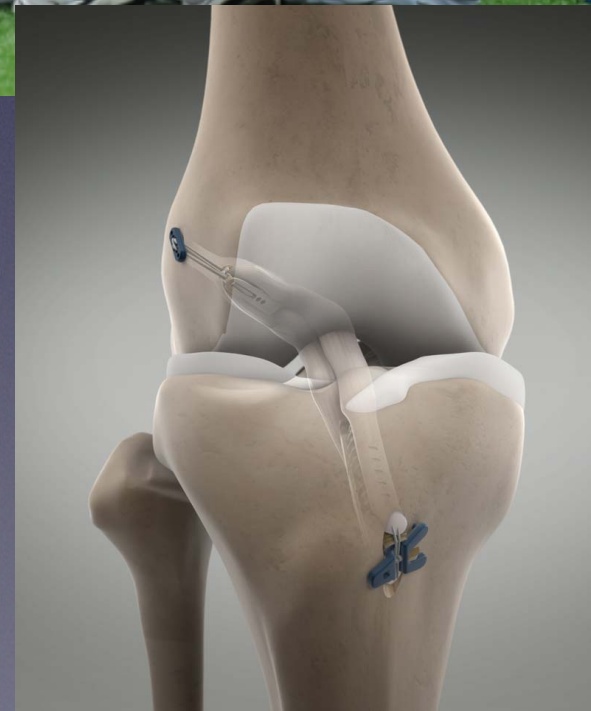
- “Biologic substances used to augment musculoskeletal healing rates and alter inflammatory pathways”





# Sports Medicine Applications

- Augment the acute healing process
- Eliminate chronic or recurrent inflammatory conditions
- Enhance soft tissue reconstructive surgery
- Joint preservation
- More rapid return to play?





# Common Use Orthobiologics

- PRP - Platelet Rich Plasma
- PPP - Platelet Poor Plasma
- Stem Cells - “Mesenchymal stem cells” (MSC)
- Growth Factors - IL-1, IL-6, PDGF, TGF-B, VEGf, TNF, \*ILRAP





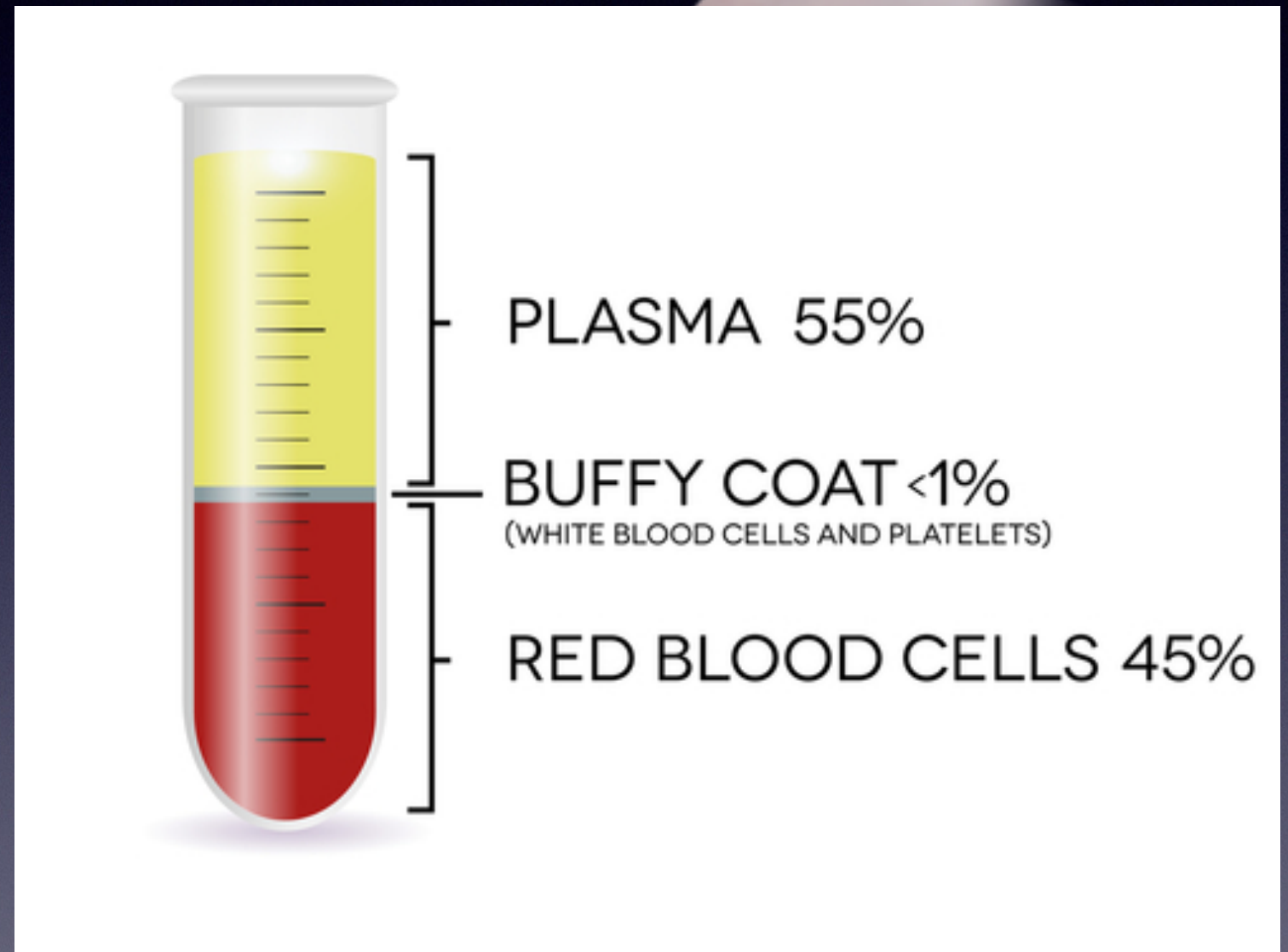
# FDA Process

- 1997 Regulations on Human Cells, Tissues, and Cellular/Tissue-Based Products (HCT/P's) intended for Human use
- Low Risk (361) vs High Risk (351)
  - Manipulation / Systemic / Homologous / Combinations
- 351 Pathway if considered High Risk: Complex pathway requiring:
  - Process development and validation / Pre-Investigational Applications / Biologic Licensing Applications / Clinical Protocol Development / Phase 1,2, and 3 Clinical Trials
  - PRP considered Low Risk - 361 Pathway (No premarket clinical trials)
  - MSC are variable and dependent on meeting the inclusion criteria for 351 pathway



# PRP

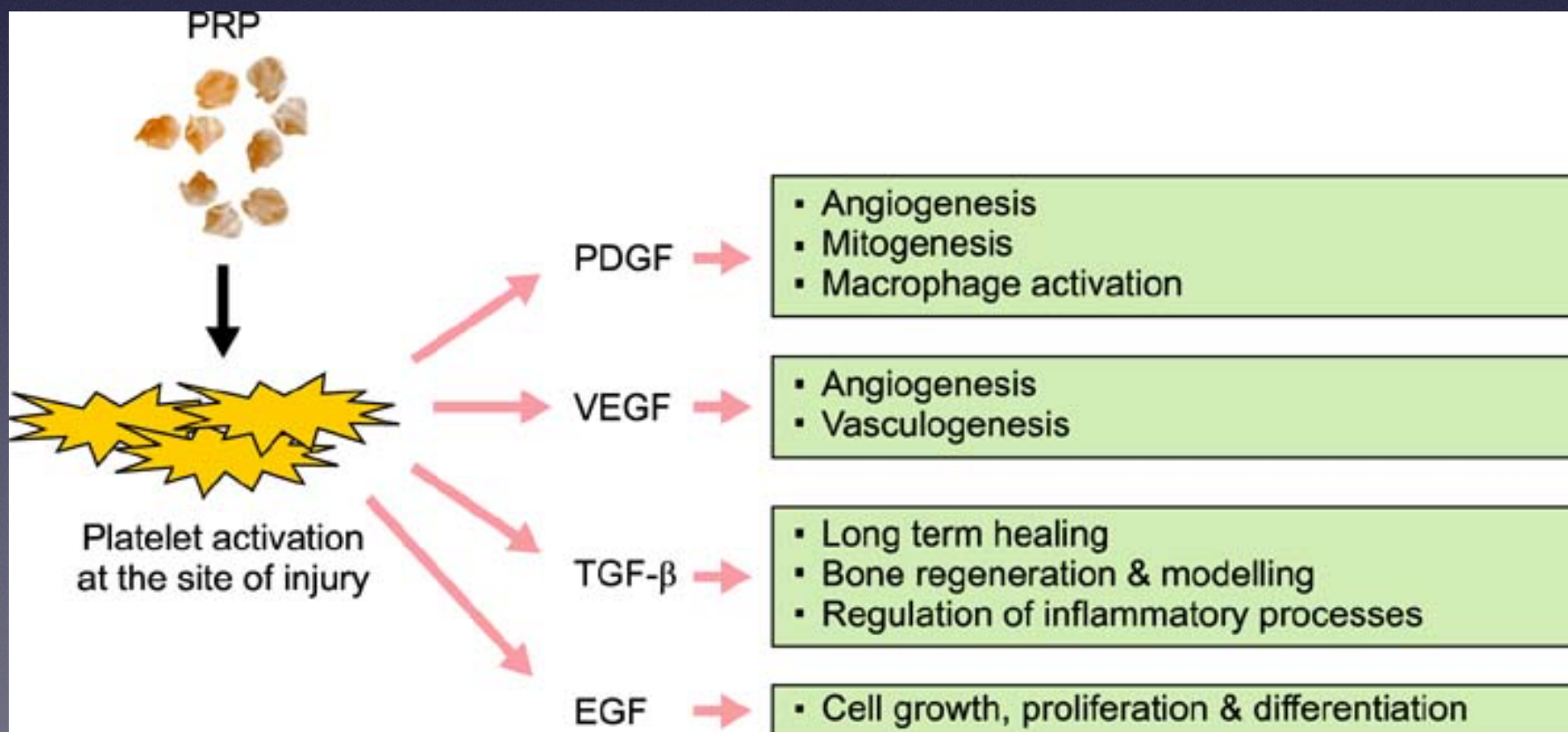
- Concentration of autologous blood w 4-8x concentration of platelets and GF's
- PRP categories:
  - Leukocyte poor (LP-PRP)
  - Leukocyte rich (LR-PRP)
- Commercial centrifuge systems used in office and operating room
- Preparation and system preferences can yield different subtypes





# PRP - Mechanism of action

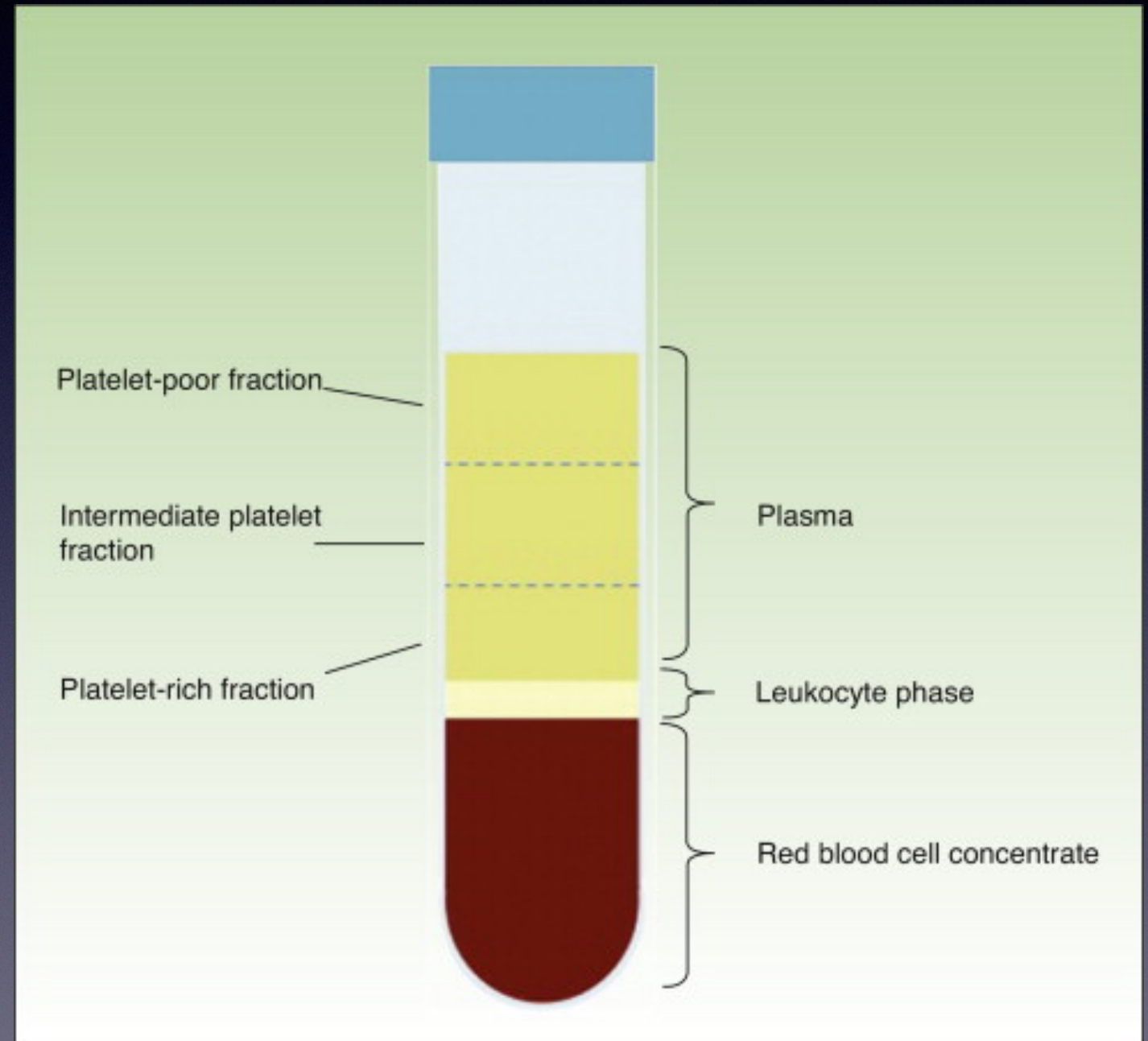
- Attraction of MSC's / Macrophages / Fibroblasts / \*Alters Inflammatory environment
- Stimulation of cell proliferation and extracellular matrix protein production
- Promotes healing





# PPP - Platelet Poor Plasma

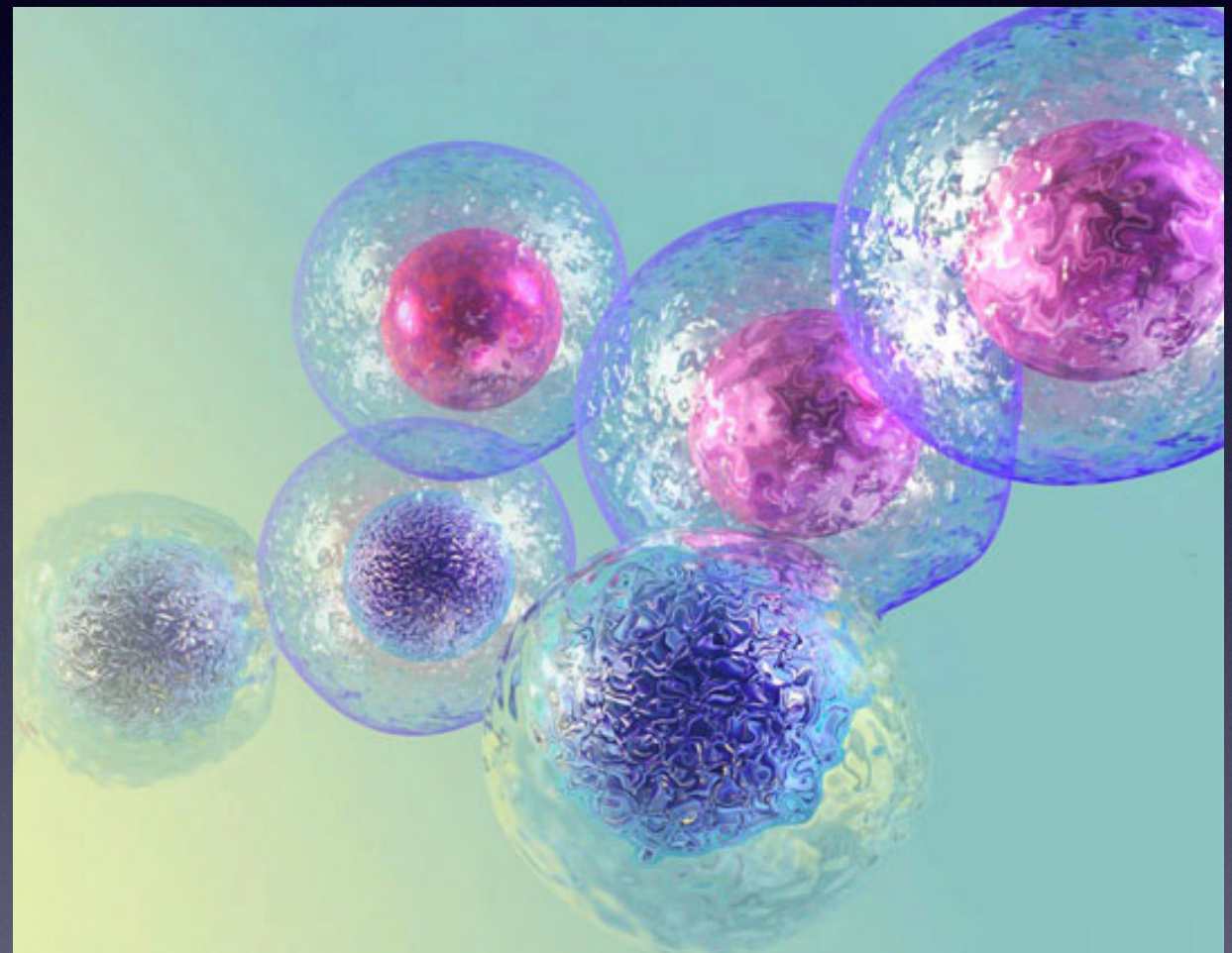
- PPP - The result of a second centrifuge spin of LP-PRP which removes Platelets
- Aids in Myoblast differentiation vs. proliferation
- May be most useful in muscle injury vs PRP





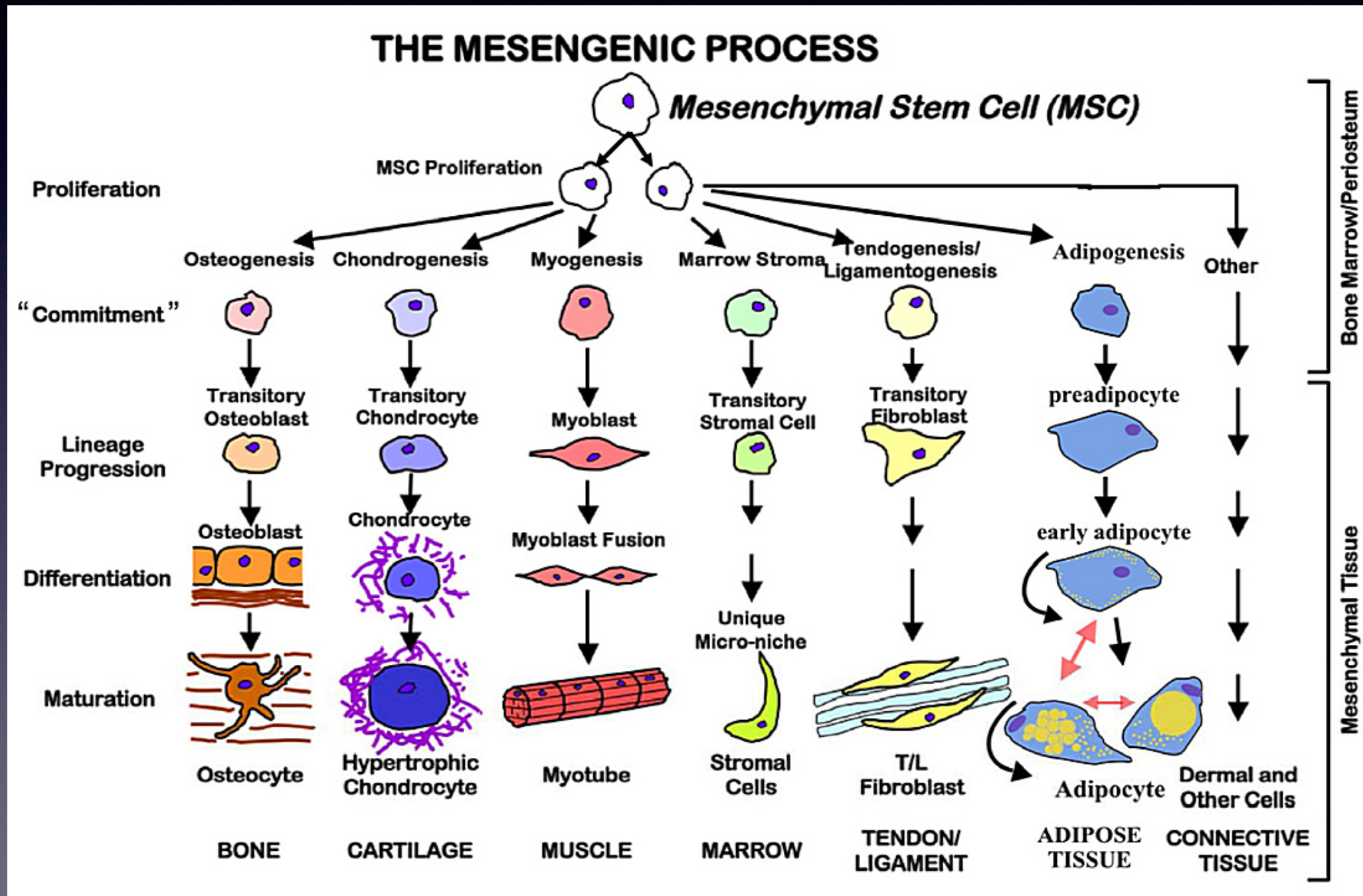
# ”Stem Cells”

- Should be referred to as Mesenchymal Stem Cells for our purposes
- NOT Pluripotent!
- Common sources are Adipose, Bone Marrow, Amniotic tissue, and banked Placental tissue
- They are very safe, but still poorly understood!





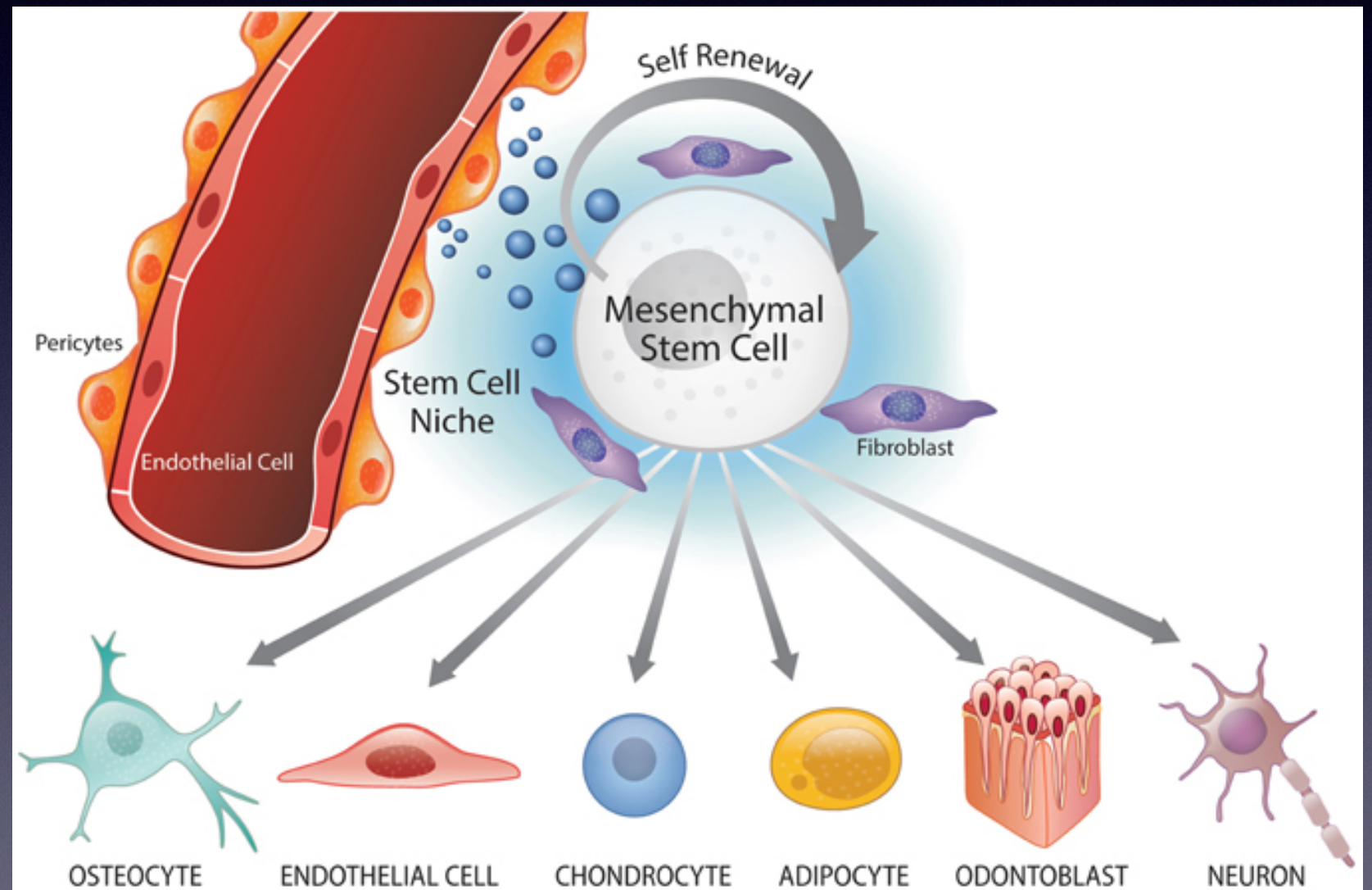
# MSC Mechanism of action





# MSC Mechanism of action

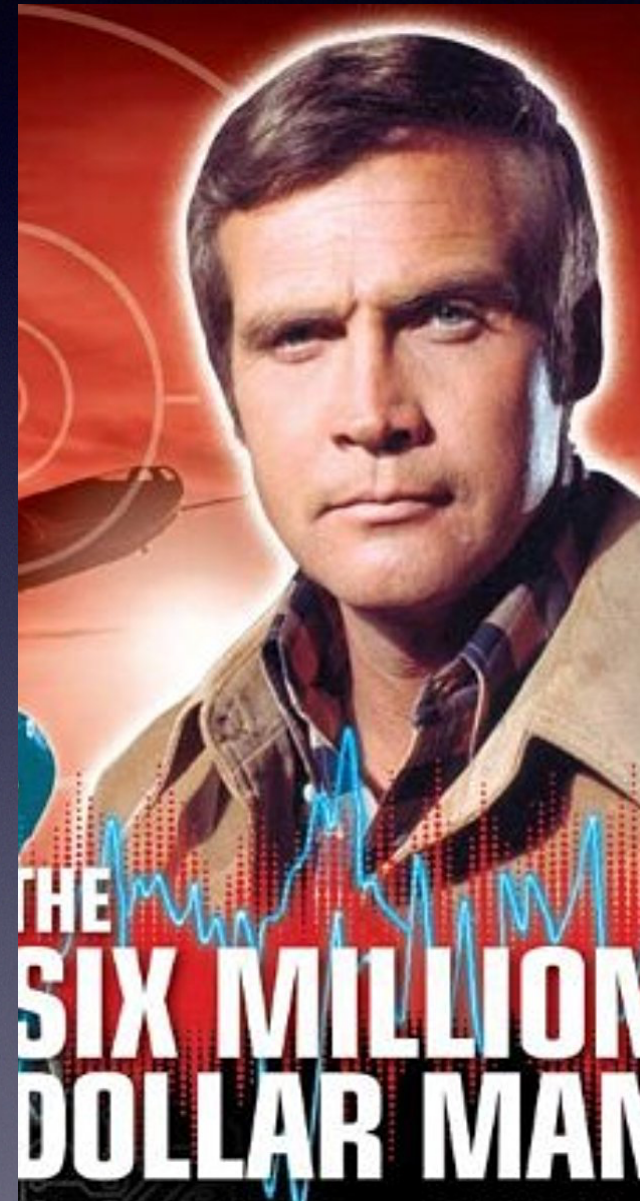
- Differentiate into terminal cells
- Secrete growth factors
- Encourage cell migration and tissue repair
- Reduces inflammation





# PRP & MSC Ortho Applications

- Articular Cartilage Injury
- \*Osteoarthritis symptom relief
- Meniscus & ACL surgery
- Rotator Cuff Repair
- Chronic Tendinopathies
- Muscle Injury






# Literature Review

## Paper 5: The Effect of Platelet Enriched Plasma on Early Clinical Outcomes in Patients With Femoroacetabular Impingement Following Arthroscopic Labral Repair and Femoral Neck Osteoplasty

[Brian D. Giordano](#), MD, USA (Presenting Author), [Jason Snibbe](#), MD, USA  
Kerlan Jobe Orthopaedic Clinic

## The Effect of Platelet-Rich Plasma on Clinical Outcomes in Lateral Epicondylitis

[Zafar Ahmad](#), M.Phil., M.R.C.S., M.B.B.S., B.Sc. , [Roger Brooks](#), Ph.D., [Sertaz-Niel Kang](#), F.R.C.S., [Holly Weaver](#), B.A., [Ian Nunney](#), M.Sc., B.Sc., [Graham Tytherleigh-Strong](#), M.D., F.R.C.S., [Neil Rushton](#), M.D., F.R.C.S

## Biological Treatment for Osteoarthritis of the Knee: Moving from Bench to Bedside—Current Practical Concepts

[Jorge Chahla](#), M.D., Ph.D. , [Bert R. Mandelbaum](#), M.D., D.H.L. (hon.)  
Santa Monica Orthopaedic and Sports Medicine Group, Santa Monica, California, U.S.A.

## Properties of Biologic Scaffolds and Their Response to Mesenchymal Stem Cells

Presented at the 2013 Congress of the International Society of Arthroscopy, Knee Surgery & Orthopaedic Sports Medicine, Toronto, Canada, May 2013.

[Knut Beitzel](#), M.A., M.D., [Mary Beth McCarthy](#), B.S., [Mark P. Cote](#), P.T., D.P.T., [Ryan P. Russell](#), M.A., [John Apostolakos](#), B.S., [Daisy M. Ramos](#), B.S., [Sangamesh G. Kumbar](#), Ph.D., [Andreas B. Imhoff](#), M.D., [Robert A. Arciero](#), M.D., [Augustus D. Mazzocca](#), M.S., M.D. 

## Plasma Rich in Growth Factors in Arthroscopic Rotator Cuff Repair: A Randomized, Double-Blind, Controlled Clinical Trial

[Pedro Ruiz-Moneo](#), M.D., [Jorge Molano-Muñoz](#), M.D., [Estrella Prieto](#), M.D., [Jaime Algorta](#), M.D., Ph.D. 

## Prospective Evaluation of Osteochondral Defects in the Knee Treated with Biodegradable Scaffolds (SS-45)

[Philip A. Davidson](#), MD, [Dennis W. Rivenburgh](#), PA-C, ATC



# Articular Cartilage & Osteoarthritis

- \*LP-PRP improves clinical outcomes in OA Knee 3-12 months in 75%
- Prevention of cartilage damage and disease modification through GF alteration
- MSC's may further improve results, but more costly and assoc. w/ harvest morbidity
- Surgical cartilage restoration w PRP & MSC's shown to increase healing rates and quality of tissue
- \*Scaffold and matrix delivery systems are a rapid growing area of research



# ACL & Meniscus Preservation

- Early studies showing promise for scaffold augmentation of ACL
- Improved ACL Graft maturation up to 40% faster
- Small patient populations and poor study design
- \*PRP trend toward increased healing rates in current studies
- Meniscal preservation surgery increasing in frequency
- PRP & MSC augmentation may improve healing rates and aid in prevention of OA
- Early studies with small patient populations and fair study design



# Rotator Cuff Repair

- Animal studies have shown MSC's in addition to scaffold or matrix delivery systems to be successful
- Improved healing rates / decreased muscular atrophy / decreased fatty infiltration of muscle
- PRP has not shown the same potential in the shoulder with Animal studies
- PRP may be beneficial in non-op management of rotator cuff tears
- \*Improves the inflammatory environment and decreases pain



# Chronic Tendinopathy

- \*LR-PRP strongly favored for these applications
- Excellent clinical outcomes for PRP in Tennis Elbow and Patellar Tendinosis
- Plantar Fasciitis showing moderately successful outcomes
- Less favorable for other anatomic tendinopathies: Achilles, Rotator Cuff, Hamstring...



# Muscle Injury

- PRP & MSC have a limited role in muscle regeneration
- PPP appears to have the most promise
- \*Favors myoblast differentiation which results in muscle regeneration
- Limits scar tissue formation
- Improved pain relief during healing



# Summary





Questions?



# Thank You!



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