



express

BONE & JOINT INJURY CARE

CSOG is opening a NEW walk-in clinic for urgent orthopaedic needs!

Our Express care clinic will take care of:

- All Bone & Joint Injuries
- X-rays
- Casts and Splints
- Sports Injuries
- Setting Broken Bones
- and Much More!

Coming May 2018



The background of the slide is a microscopic view of blood, showing numerous red blood cells (erythrocytes) and some white blood cells (leukocytes). The cells are out of focus, creating a bokeh effect. The overall color palette is a mix of reds, pinks, and greys.

“Biologic” Treatments Stem Cells, Growth Factors

*Harnessing the Body’s Natural
Healing Capacity*

Christopher K. Jones, MD
Colorado Springs Orthopaedic
Group

www.coloradosportsdoctor.com

Hot News!!

- Scientific American 2009
- “Before playing in all four professional golf majors in 2013, Tiger Woods received four injections of PRP in his left knee following surgery.
- PRP injections in his elbow may have been the reason that Los Angeles Dodger’s pitcher Takashi Saito was able to return to the mound for the 2008 Major League Baseball playoffs.”
- “Two Pittsburg Steelers (Troy Palamalu and Hines Ward) received PRP injections prior to winning the Super Bowl.”



Hot News!!

- 2013 - “The King of Clay”, Rafael Nadal, comes back with a vengeance after a 7 month hiatus to receive PRP treatments for chronic patella tendinopathy
- Makes it to 8 straight finals and wins 6!!



Hot News!!

- 2014 Kobi Bryant goes to Germany to receive treatment for knee degeneration
- Regenokine - manipulated blood sample rich in IRAP (interleukin receptor antagonist protein)
 - Was not approved in US



Goals

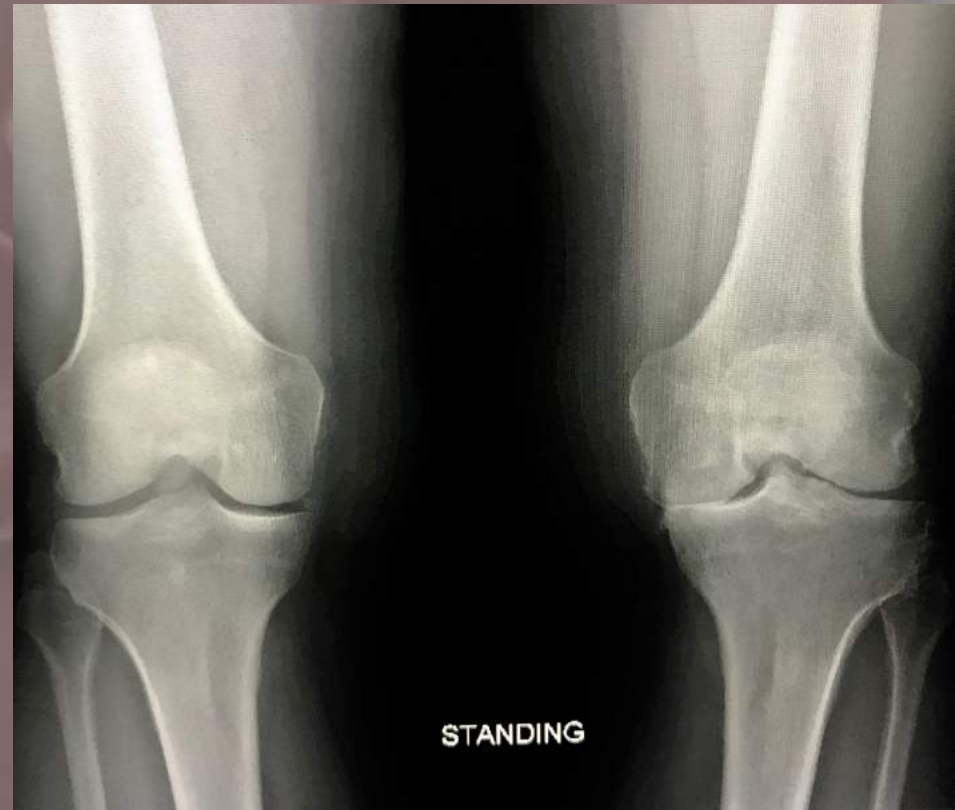
- All of the “biologic” treatments enhance healing by harnessing and amplifying the patients natural ability to heal and fight off inflammation

Goals

- Tendon, muscle and ligament injuries
 - Speed up and improve healing
- Degenerative tendon/ligament injuries
 - Promote healing in tissues without adequate blood supply
- Degenerative Arthritis
 - Inhibit inflammation
 - Stop cartilage destruction
 - Promote cartilage regrowth?

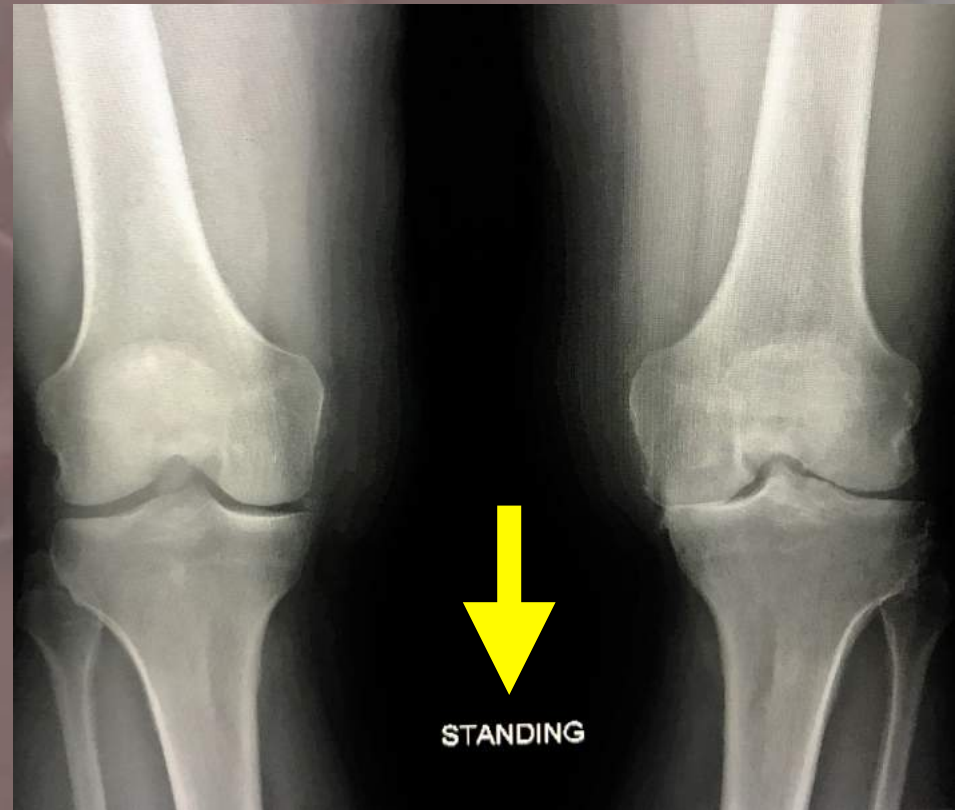
Promote Cartilage Growth?

- No evidence that will reverse damage caused by osteoarthritis
- Has shown benefit in healing of isolated cartilage defects
- Studies have shown “some” cartilage regrowth
 - Mostly in lab models



Promote Cartilage Growth?

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- Has shown benefit in healing of isolated cartilage defects
- Studies have shown “some” cartilage regrowth
 - Mostly in lab models
 - But...DOES NOT CHANGE XRAY



Promote Cartilage Growth?

Actual Patient | 63 Years Old, 8 Months After Regenerative Stem Cell Therapy

Before

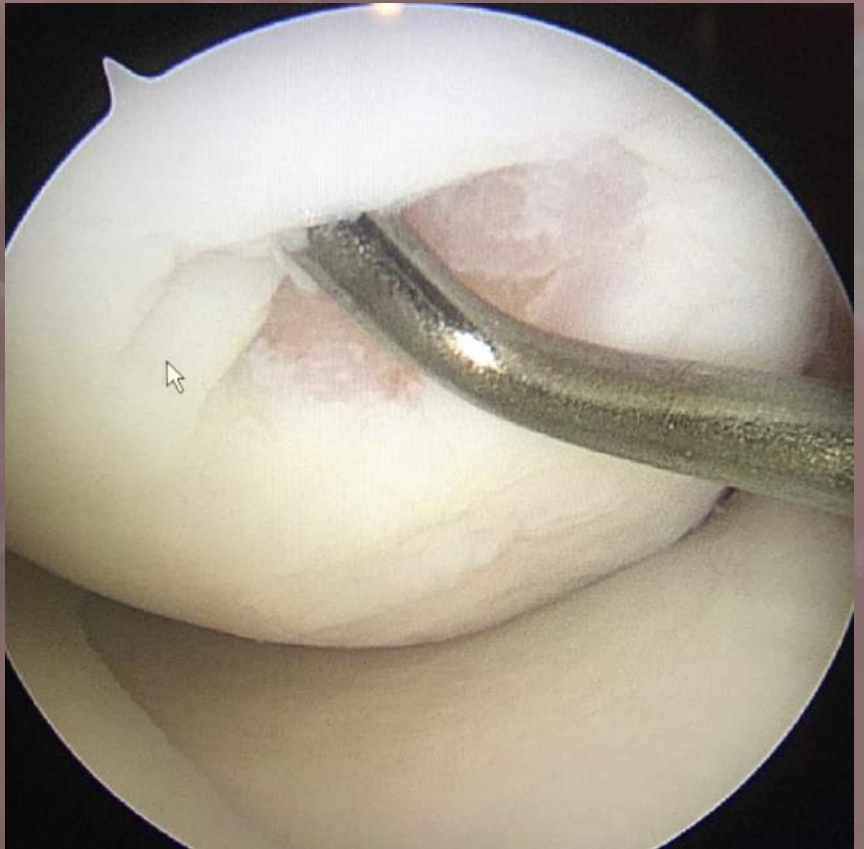


After



Promote Cartilage Growth?

- Has shown benefit in healing of isolated cartilage defects
- This is one of the most exciting treatments on horizon



AVOID SURGERY?

- This is a promise made by “stem cell clinics”
- May be an alternative for many patients
- Unlikely to prevent need for joint replacement
- Can delay need!!
- Many patients need surgery to clean up prior to biologics



STEM CELL INSTITUTE OF AMERICA

FREE Educational Seminars
STOP THE PAIN!
Get Relief without Surgery!

Do you SUFFER from...

- Knee Pain
- Lower Back Pain
- Shoulder Pain
- Foot Pain
- Joint Pain
- Plantar Fasciitis
- Osteoarthritis
- Neck Pain
- Tennis Elbow

Find Out if Regenerative Medicine is Right for You!

SAFE • ETHICAL • EFFECTIVE

Regenerative medicine is now available locally and can effectively reduce and even eliminate your pain without surgery or addictive medications. Regenerative medicine uses amniotic tissue cells to regenerate and repair tissues in your body that are damaged due to injury, age, disease, and defects. Stem cells have the power to go to these damaged areas, generate new cells and rebuild the area.

Colorado Springs

North Springs
Feb 28th
12:00 pm, 3:00 pm,
6:30 pm

Over 18 Seminars to Choose From


Karl Mecklenburg
Former Denver All-Star Linebacker
Motivational Speaker

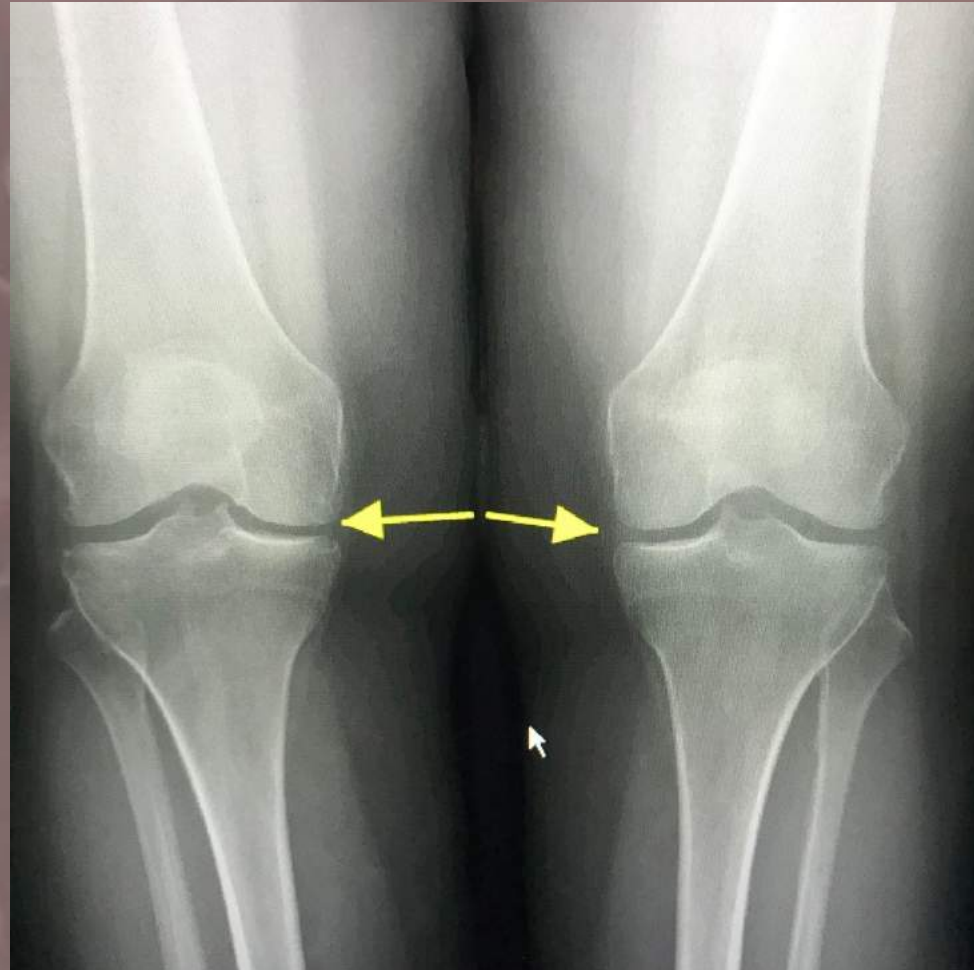

"I am truly amazed with this treatment! I had my knees treated and in just 3 1/2 weeks I am feeling so much better! I have heard so many stories of lives being changed for the better and now I am a believer too. Thanks for the improved quality of life!"

www.StemCellTherapyForPain.com

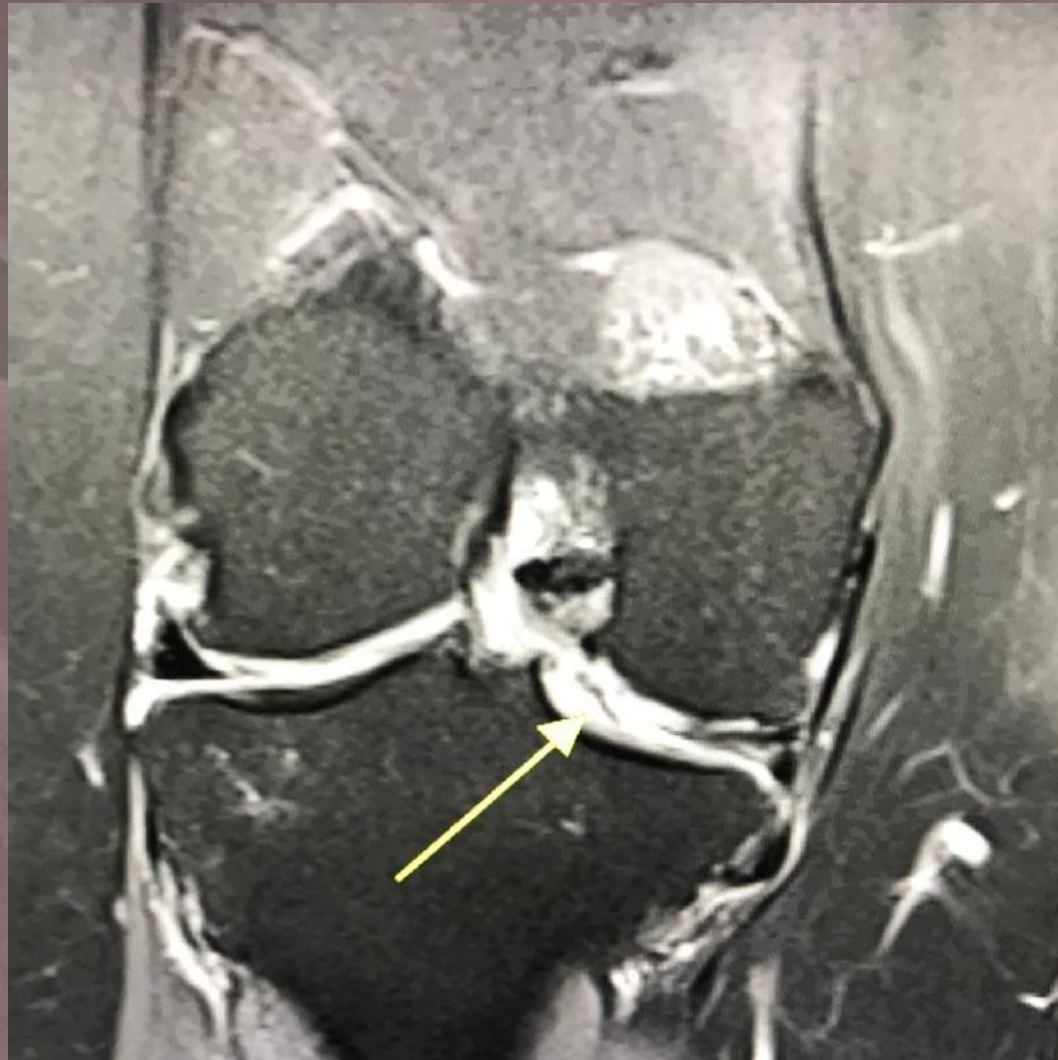
Reservations Required
CALL TODAY
877-756-2925

Case Example

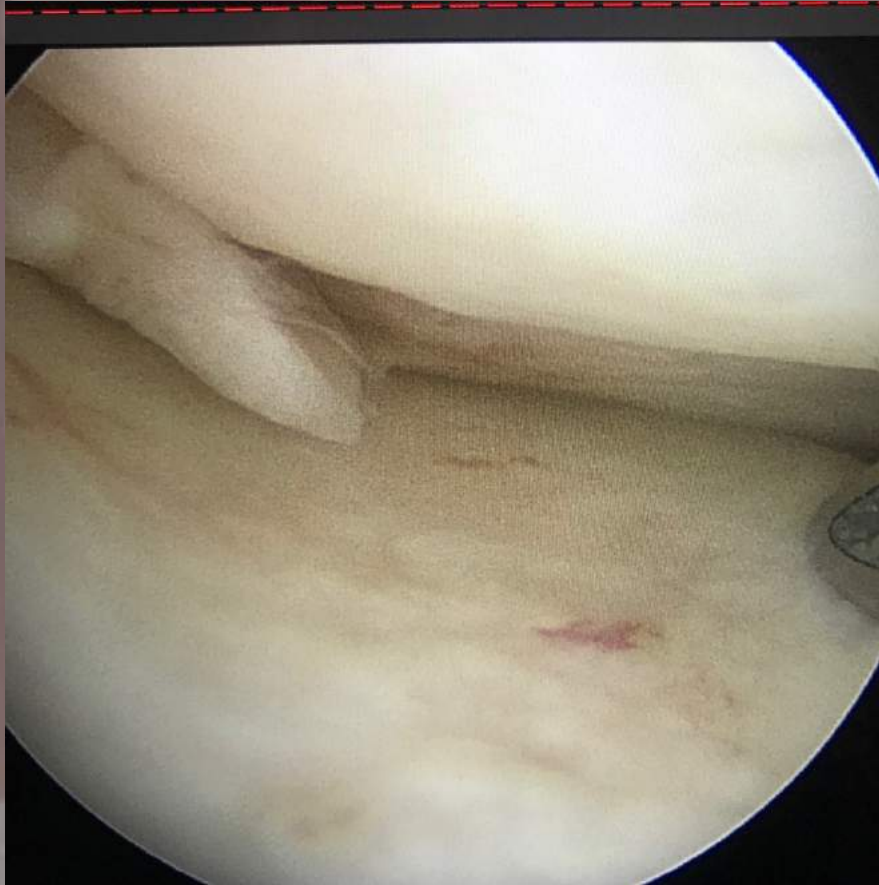
- 66 yo female with sharp and achy knee pain and occasional catching
- Exam reveals positive meniscal signs and swelling



Case Example



Case Example



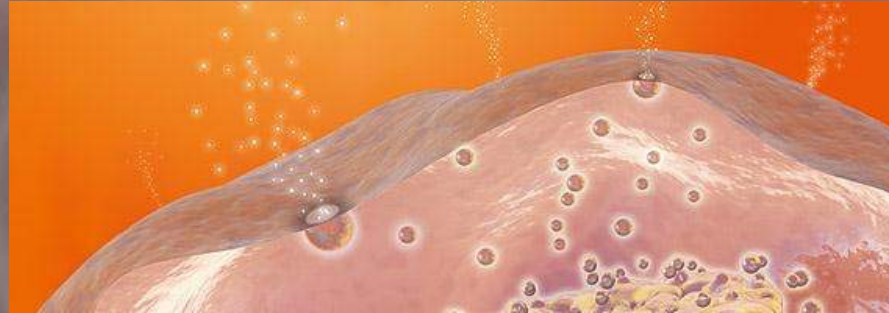
Case Example



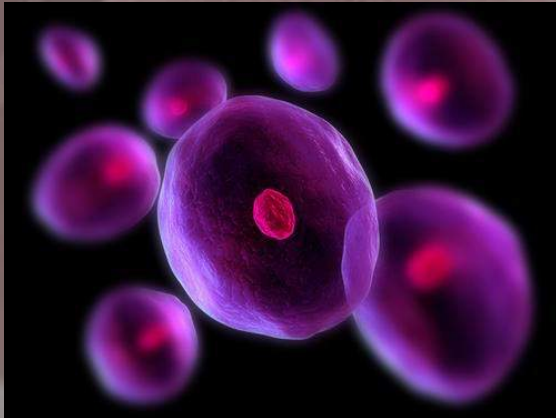
Bottom Line

- There are times that surgery can improve your result with biologic treatments
- We are not to the point where we are capable of reversing the damage caused by arthritis
- No-one is better suited to determine your best treatment plan than an orthopaedic surgeon
- Many Stem cell clinics are typically staffed by chiropractors

Signal
(Growth Factors, PRP)

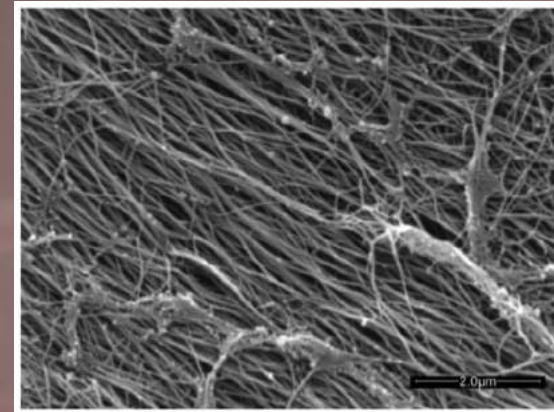


Cell
(Stem Cells, chondrocytes,
tenocytes, etc)

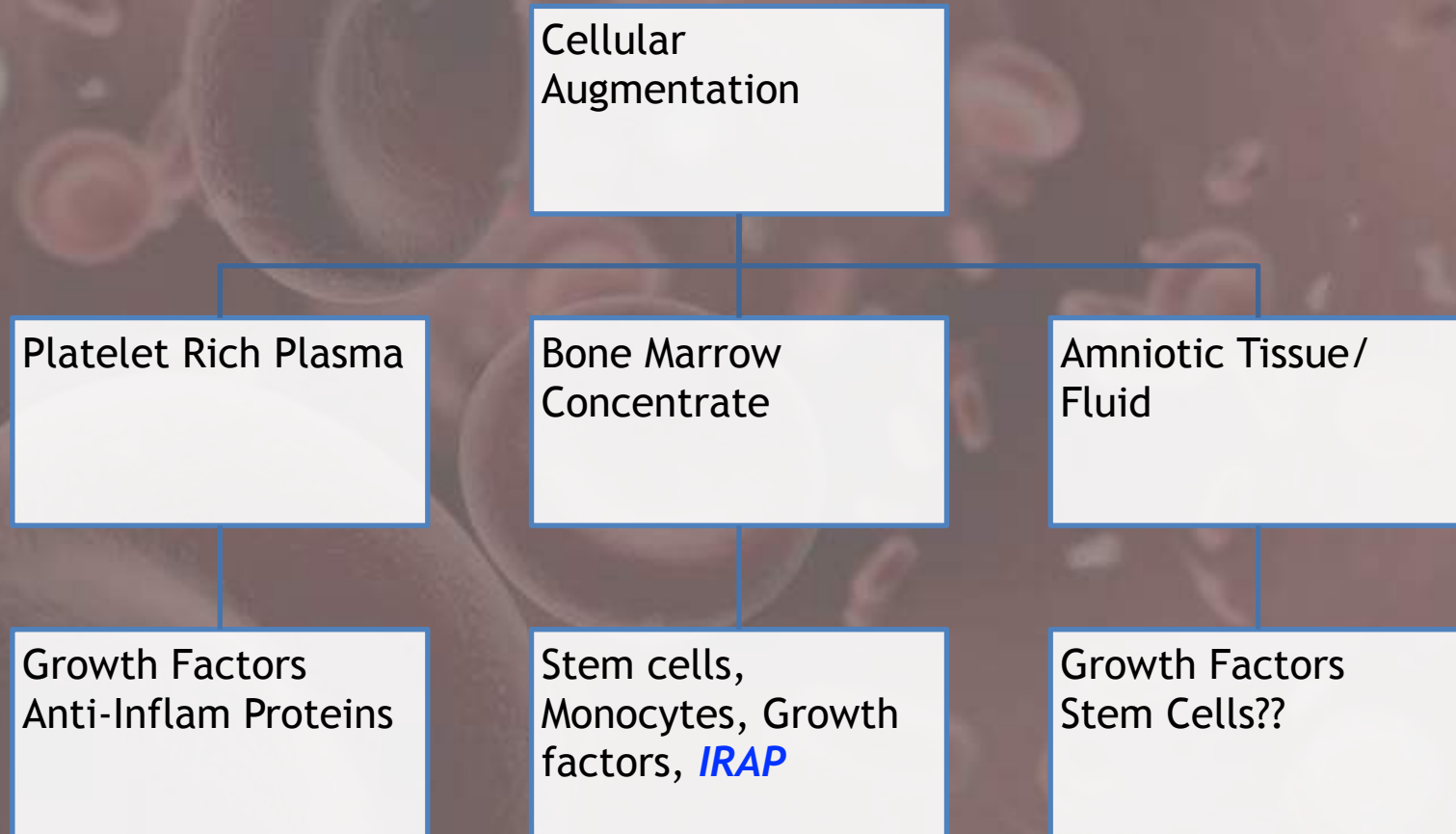


Healing
Trinity

Scaffold
(muscle, tendon, bone etc)



Regenerative Landscape

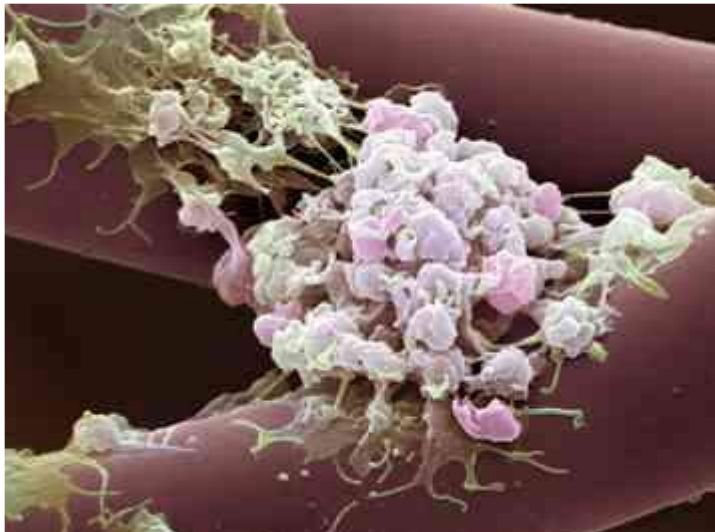


What is in your blood?

- Plasma: Nonliving Fluid Matrix
 - 55% of Whole Blood
 - 90% Water and 10% mix of Protein and Nutrients and Electrolytes
- Blood Cells: Living component
 - Red Blood Cells “Erythrocytes”
 - 44% of Whole Blood
 - White Blood Cells “Leukocytes”
 - 1% of Whole Blood
 - Platelets “Thrombocytes”
 - Very Small Volume

Role of Thrombocytes (PLATELETS)

- To help the blood clot
- They are the First Responders
- To aide in Tissue Healing through the release of cytokines
 - Cytokine- protein that creates a response

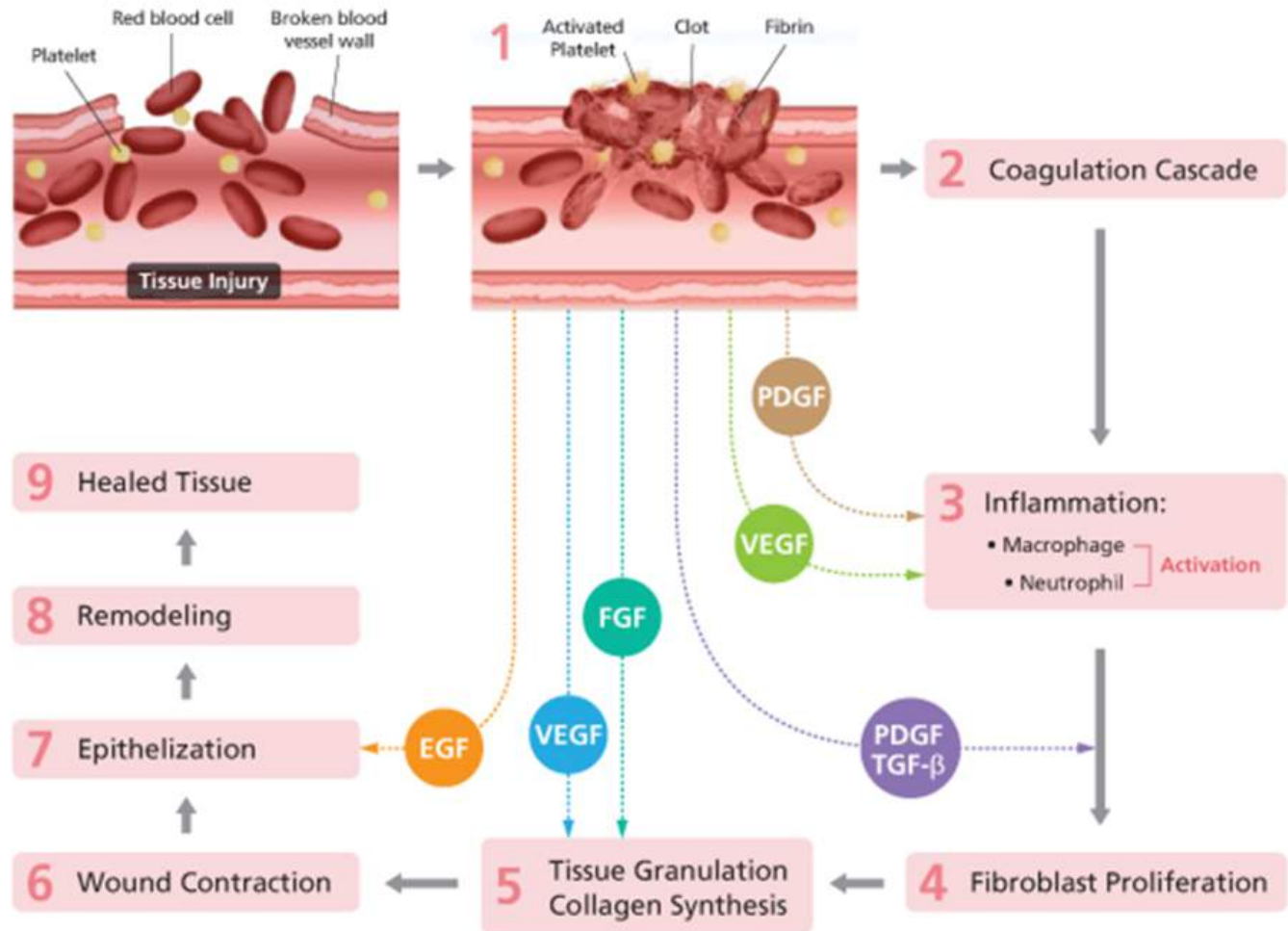



What's in a Platelet

- Dense Granules
 - ATP, ADP, Serotonin, Calcium
- α -granules Contain:
 - Clotting Elements
 - Growth Factors
 - Platelet Derived Growth Factor (PDGF)
 - Transforming Growth Factor Beta (TGF- β)
 - Fibroblast Growth Factor (FGF)
 - Vascular Endothelial Growth Factor (VEGF)
 - Epidermal Growth Factor (EGF)

How do Platelets Function?

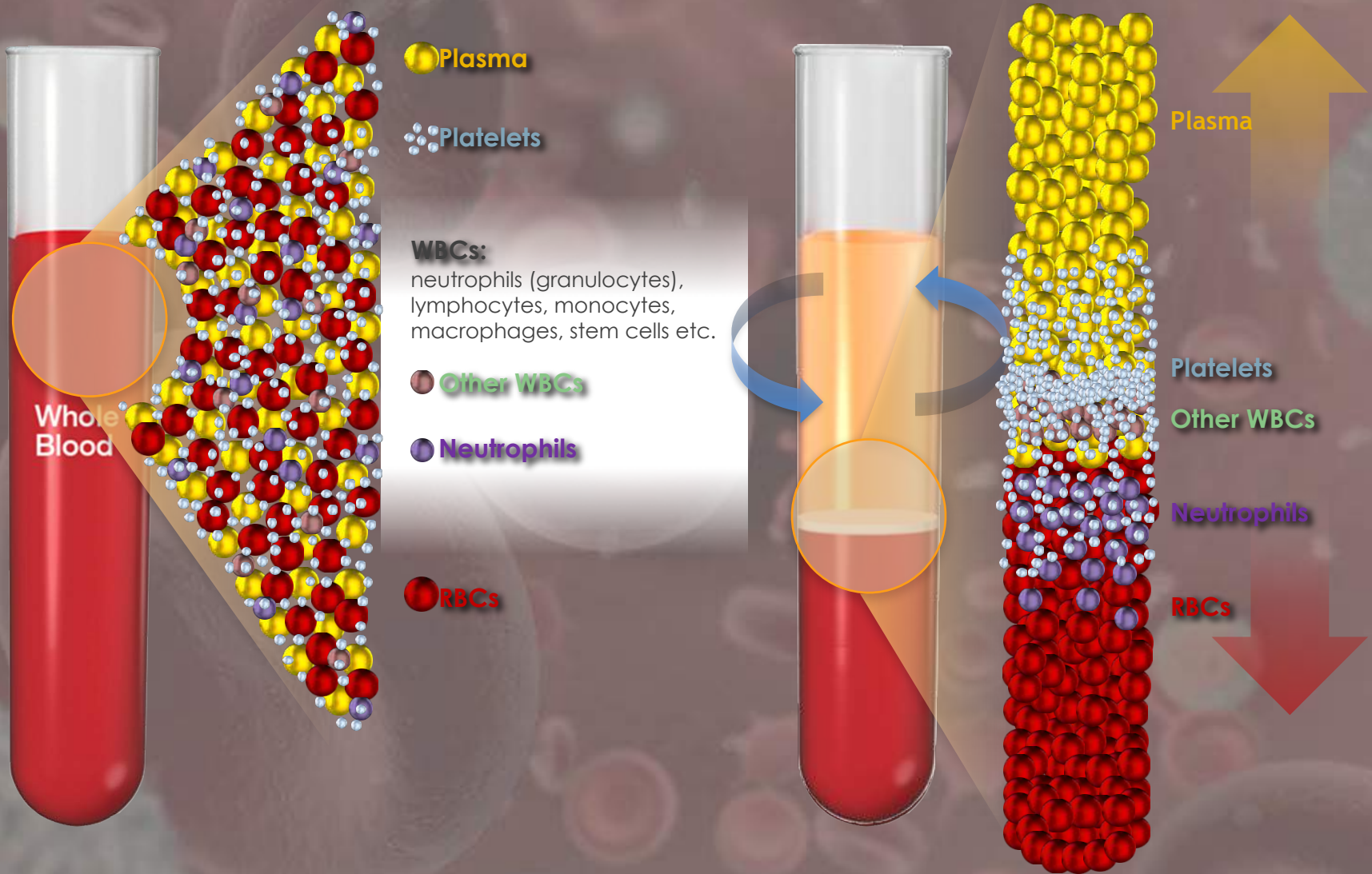
PRP Mechanism



A microscopic view of blood cells, including several large red blood cells and smaller white blood cells, set against a reddish-brown background. The text "Optimizing the Healing Cascade" is overlaid in white.

Optimizing the Healing Cascade

Separation by Centrifugation

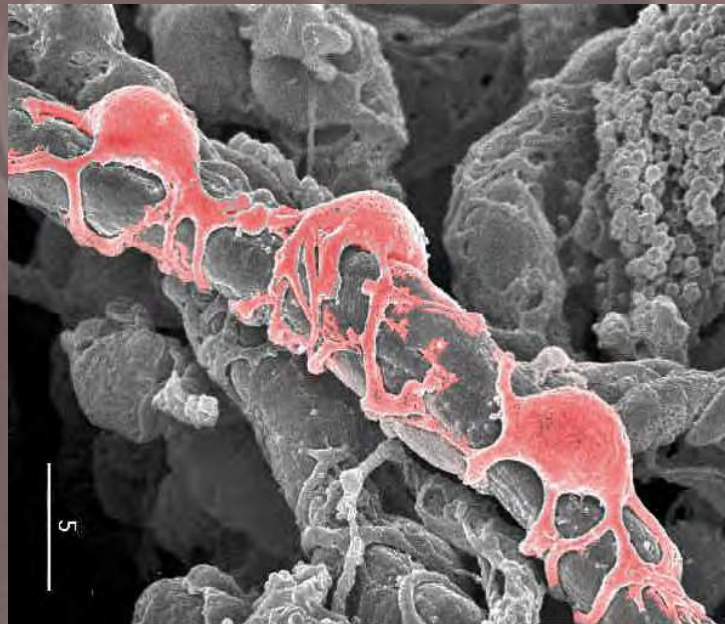


What's in Bone Marrow?

Healing Trinity - **Cell**, Signal(growth factors), Scaffold.

Hematopoietic Stem Cells

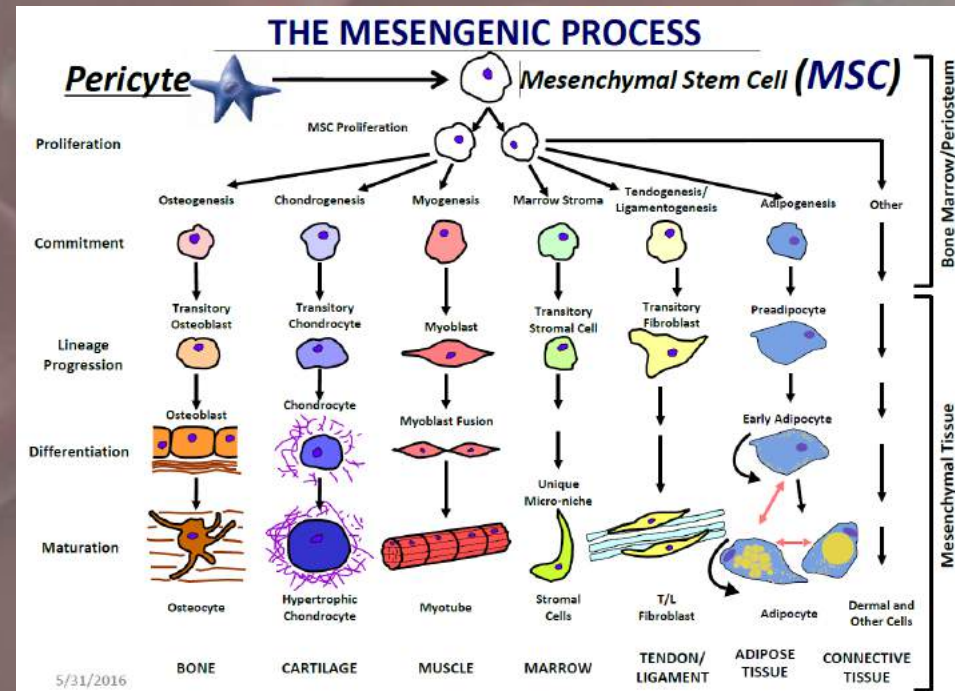
Mesenchymal Stem Cells



Al Caplan. Cell Stem Cell, 3:229-30, 2008.

Why BMA?

- Bone Marrow Aspirate is a source of progenitor cells
 - Hematopoietic Stem Cells (HSC) - blood forming cells, angiogenesis
 - Mesenchymal Stem Cell (MSC) - osteoblasts, chondrocytes, myocytes
- BMC contains PRP
- BMC also rich in **IRAP** (Interleukin Receptor antagonist Protein)



IRAP (Interleukin Receptor Antagonist Protein)

- IRAP is an anti-inflammatory protein that counteracts the destructive effects of inflammatory proteins such as Interleukin-1 that is produced within inflamed joints
- Also reduces affects of Matrix Metalloproteinases

What about Stem Cells?

- It's not just their ability to differentiate!
- They are the body's **Ship's Captain**
 - Anti-inflammatory (restores TH1 / TH2 balance)
 - Anti-apoptotic(prevent cell death)
 - Anti-microbial (LL-37)
 - Induce cell proliferation and angiogenesis, reduce scar formation



Biomet N-Stride

- I call this PRP+
- Proprietary system for prepping peripheral blood as PRP
- Contains high concentrations of **IRAP**
- No stem cells

J Orthop Res. 2014 Oct;32(10):1349-55. doi: 10.1002/jor.22671. Epub 2014 Jul 1.

Autologous protein solution prepared from the blood of osteoarthritic patients contains an enhanced profile of anti-inflammatory cytokines and anabolic growth factors.

O'Shaughnessey K¹, Matuska A, Hoepfner J, Farr J, Klaassen M, Kaeding C, Lattermann C, King W, Woodell-May J.

Amniotic Fluid

- Fluid collected from healthy mothers undergoing a planned C-sections
- Contains abundance of anti-inflammatory proteins and growth factors
- Cryopreserved for storage
- **SOME contains live stem cells*****



Biological Components of FlōGraft® Freedom*

Secretomic Components

Growth Factor Symbol	Growth Factor Expanded Name	Functionality
Angiogenin	Angiogenin	Potent stimulator of angiogenesis (de novo blood vessel formation). Also interacts with endothelial and smooth muscle cells resulting in cell migration, invasion, proliferation and formation of tubular structures during wound healing
ANG-1	Angiopoietin	Potent stimulator of angiogenesis. Regulator of microvascular permeability, blood vessel maturation, adhesion, migration, survival. Promotes neo-vascularization in synergy with VEGF
FGF-6	Fibroblast growth factor 6	FGF family members possess broad mitogenic, proliferative and cell survival bioactivity, important in morphogenesis, tissue repair and embryonic development
FLRG	Follistatin-like protein 3	Involved in TGF- β mediated signalling, regulator of key developmental factors Activin A and BMP2
G-CSF	Granulocyte colony stimulating factor	Stimulator of hematopoiesis and neurogenesis
IGF-2	Insulin-like growth factor #2	Important fetal growth factor, regulatory and mitogenic properties.
IGFBP-2/3/4/6	Insulin-like growth factor binding proteins 2/3/4/6	Regulation of cell proliferation and IGF activity
MCP-1	Monocyte chemoattractant protein #1	Mobilization and recruitment of host-derived mesenchymal stem cells
MMP-1/7/9/10	Matrix metalloproteinase 1/7/9/10	Remodeling of extracellular matrix during development and wound healing
P-cadherin	P-cadherin	Marker of amniotic fluid derived stem, progenitor and epithelial cells
SDF-1 α	Stromal cell derived factor #1	Chemotactic factor for mesenchymal, endothelial and other host-derived stem cell populations
TIMP-1/2	Tissue inhibitor of metalloproteinases 1/2	Remodeling of extracellular matrix during development and wound healing
EGF	Epidermal growth factor	Potent stimulator of cellular growth, proliferation and differentiation
bFGF	Basic fibroblast growth factor	FGF family members possess broad mitogenic, proliferative and cell survival bioactivity, important in morphogenesis, tissue repair and embryonic development bFGF also linked to angiogenesis
EG-VEGF	Endocrine gland derived vascular endothelial growth factor	Similar to VEGF, pro-angiogenic and stimulator of cellular proliferation
HGF	Hepatocyte growth factor	Morphogenic factor important in organ development and wound healing
PDGF-AA	Platelet derived growth factor-AA	Potent cellular mitogen and regulator of angiogenesis
TGF- α	Transforming growth factor α	Mitogenic growth factor, member of EGF superfamily. Promotes cellular proliferation during wound healing and embryogenesis
TGF- β	Transforming growth factor β	Key signaling factor with broad bioactivity in cell proliferation, regulation of inflammation and fibrosis

Cellular Components

Amniotic fluid-derived stem and progenitor cells
Amniotic epithelial cells

*FlōGraft Freedom® is a cryopreserved, liquid injectable biologic augmentation, amniotic fluid-derived allograft. This human cells, tissues, and cellular/tissue-based product (HCT/P) is minimally manipulated amniotic fluid product and intended for homologous use only. FlōGraft® allograft is regulated by the FDA Center for Biologics Evaluation and Research (CBER) which regulates HCT/Ps under 21 CFR Parts 1270 and 21 CFR Part 1271 and Section 361 of the Public Services Act. This is a list of some, but not all, of the biological and molecular components found in amniotic tissue allograft products. Please refer to the product package inserts for additional product information and the Regulatory and Quality Assurance section of www.appliedbiologics.com for further regulatory, donor screening and processing information.

1. Rennie K and et al. (2012) Applications of Amniotic Membrane and Fluid in Stem Cell Biology and Regenerative Medicine. Stem Cells International, 2012:721538. doi:10.1155/2012/721538. 2. Underwood MA, Gilbert WM, and Sherman MP. (2005) Amniotic Fluid: Not Just Fetal Urine Anymore. Journal of Perinatology, 25:341-348. doi:10.1038/sj.jp.7211290. 3. Karacal N, Kozucu P, Cobanglu U and Kutlu N. (2005) Effect of human amniotic fluid on wound healing. Journal of Surgical Research, 129(2):283-7. 4. Nyman E, Huss F, Nyman L, Junker J and Kratz G. (2013) Hyaluronic acid, an important factor in the wound healing properties of amniotic fluid: in vitro studies of re-epithelialisation in human skin wounds. Journal of Plastic Surgery and Hand Surgery, 47(2):69-92. doi: 10.3109/2008565X.2012.733169 5. Ozgenel GY, Samli B and Ozcan M. (2001) Effects of human amniotic fluid on peritendinous adhesion formation and tendon healing after flexor tendon surgery in rabbits. Journal of Hand Surgery, 26(2):332-339.

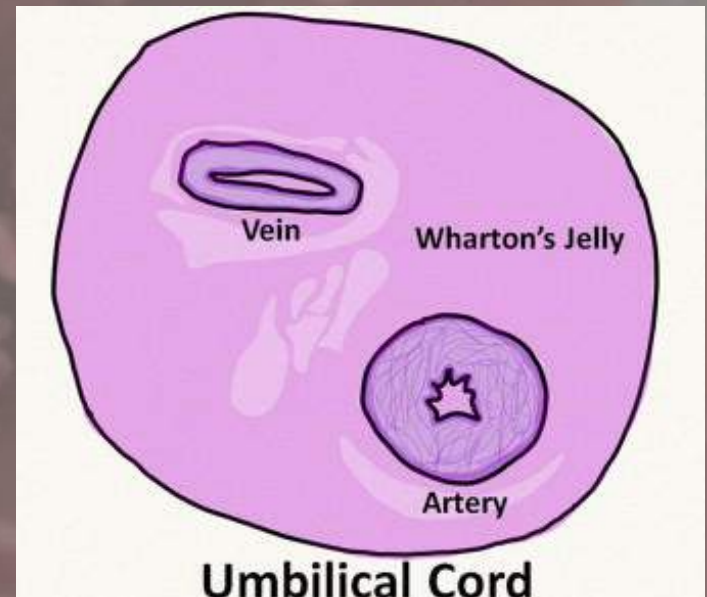
Umbilical Cord Matrix/Wharton's Jelly

- Also collected during live births from healthy mothers
- Contain high concentration of growth factors, cytokines, extracellular matrix and MSC's

CoreCyte™	
Key Cytokines Present in Structural Wharton's Jelly	
General Cytokines	pg/ml
Fetuin-A	345,099
Interleukin 37	357
Macrophage Colony	4,120
Serpin A4	6,573
Syndecan - 4	7.5
Growth Factor Cytokines	
Bone Morphogenic Protein - 7	
Complement Component 5a	
Fibroblast Growth Factor	
Platelet Derived Growth Factor	
Thrombospondin - 2	149
Scaffolding Cytokines	
Adhesion G Protein	650
Collagen 1,2,3	
Elastin	
Fibronectin	
Hyaluronic Acid	
Homeostatic Cytokines	
Cystatin - B	1,164
Galectin - 9	354
Granulysin	30
Lipocalin - 2	666
Syndecan - 4	7.5

Wharton's Jelly MSC's

- Easily obtained - 100% of samples
 - Cord Blood only 1:8
- MSC's are durable
- Ability to differentiate into multiple cell types
- Increased capacity for proliferation over BMC
- Immunogenically safe
- High concentration of cells

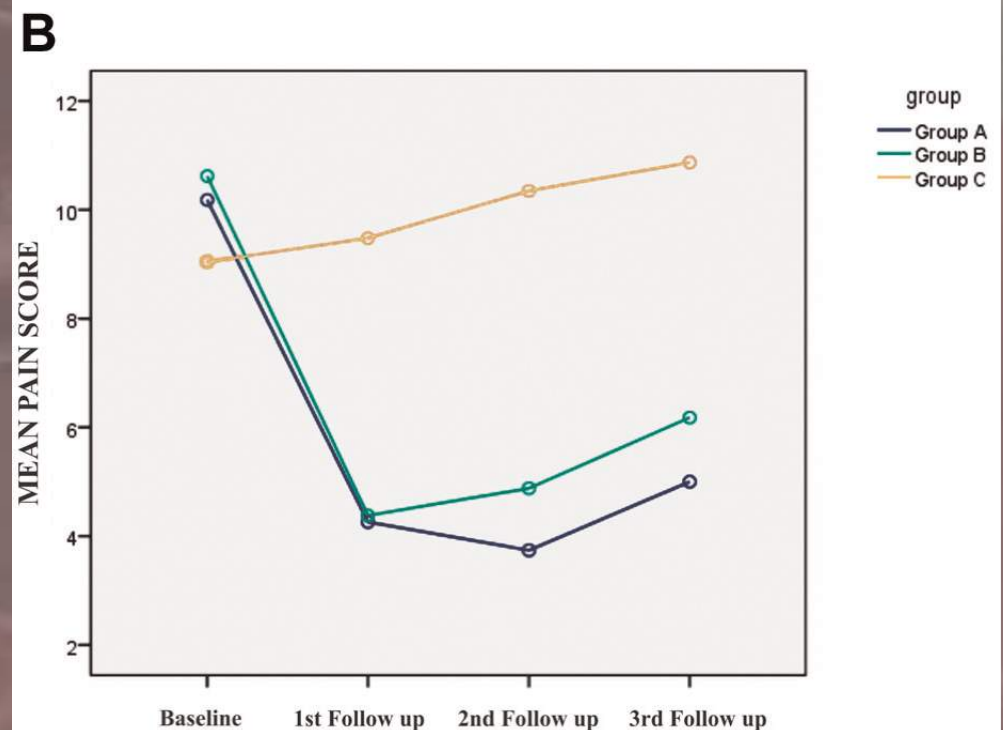


Literature Support

- LP-PRP has 10 Level 1 Peer reviewed articles supporting the efficacy in osteoarthritis

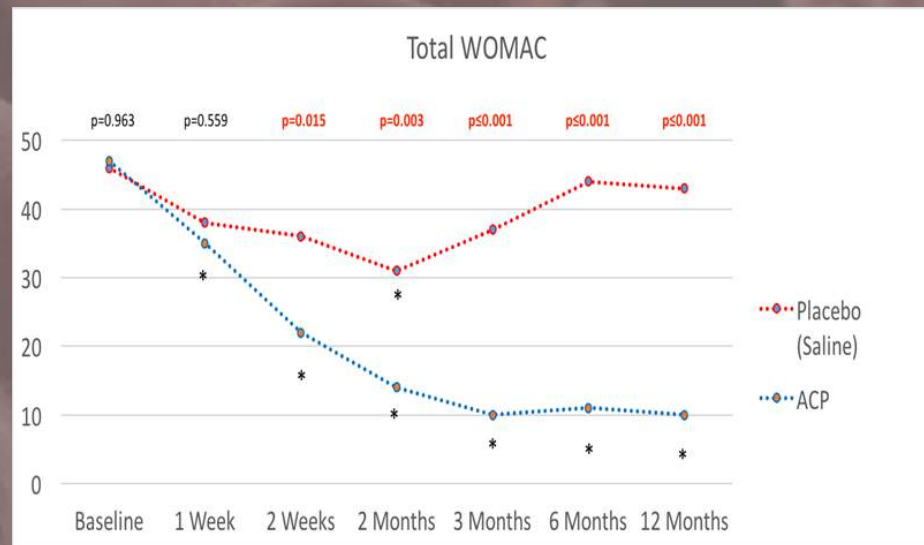
Comparison Between Hyaluronic Acid and Platelet-Rich Plasma, Intra-articular Infiltration in the Treatment of Gonarthrosis

Fabio Cerza,^{*,†} MD, Stefano Carni,[‡] MD, Alessandro Carcangiu,^{*,§} MD, Igino Di Vavo,^{*} MD, Valerio Schiavilla,^{*} MD, Andrea Pecora,^{*} MD, Giuseppe De Biasi,^{||} and Michele Ciuffreda^{||}
Investigation performed at the Paolo Colombo Hospital of Velletri, Rome, Italy



Literature Support

- LP-PRP has 10 Level 1 Peer reviewed articles supporting the efficacy in osteoarthritis



Intra-articular Autologous Conditioned Plasma Injections Provide Safe and Efficacious Treatment for Knee Osteoarthritis

An FDA-Sanctioned, Randomized, Double-blind, Placebo-controlled Clinical Trial

Patrick A. Smith,*¹ MD
Investigation performed at the Columbia Orthopaedic Group, Columbia, Missouri, USA

Leukocyte Poor Platelet Rich Plasma

- LP-PRP
 - PRP that has minimal WBC's
 - Depends on how PRP is prepared
 - Literature is clear on proper applications



Literature Support

PRP has evidence in soft tissue use as well

Hamstring Pain Reduction

Platelet-rich Plasma as an Effective Treatment for Proximal Hamstring Injuries

ROBERT J. WETZEL, MD; RONAK M. PATEL, MD; MICHAEL A. TERRY, MD

Table 2

PRP Group Pre- and Posttreatment VAS and NPRS Scores

Patient Age, y	VAS		NPRS	
	Pre	Post	Pre	Post
44	8	5	4	3
44	5	1	3	1
53	9	3	5	2
43	8	0	7	1
49	10	2	7	4
48	9	1	5	1
60	7	0	4	1
19	8	0	5	1
19	10	0	7	2
19	8	0	5	1
17	8	0	7	1
17	8	0	7	1
Mean	8.2	0.7	5.5	1.5

Abbreviations: NPRS, Nirschl Phase Rating Scale; Post, posttreatment; Pre, pretreatment; PRP, platelet-rich plasma; VAS, visual analog scale.

Table 3

TCT Group Pre- and Posttreatment VAS and NPRS Scores

Patient Age, y	VAS		NPRS	
	Pre	Post	Pre	Post
31	7	1	5	2
32	5	2	4	3
40	7	1	5	2
47	8	0	4	1
64	10	2	4	2
Mean	7.4	1.2	4.4	2

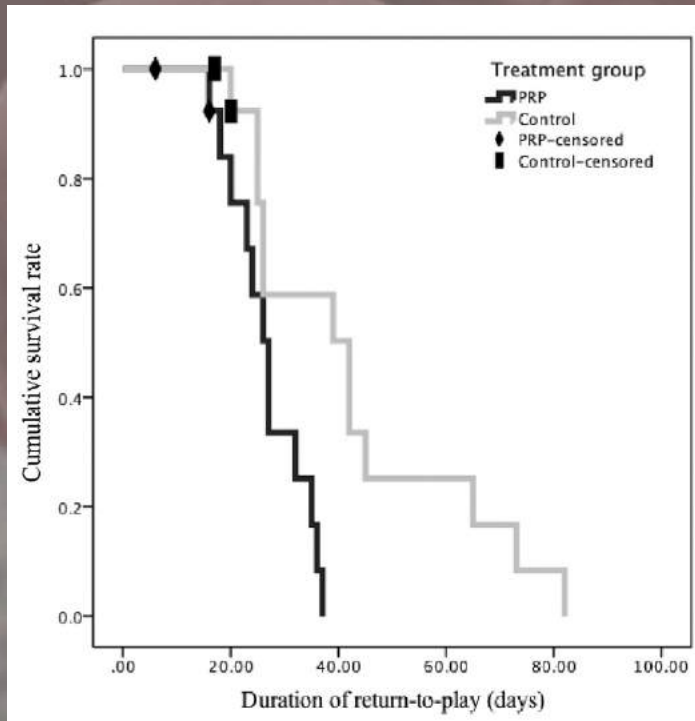
Abbreviations: NPRS, Nirschl Phase Rating Scale; Post, posttreatment; Pre, pretreatment; TCT, traditional conservative treatment; VAS, visual analog scale.

Literature Support

PRP has evidence in soft tissue use as well

Hamstring

Return To Sport



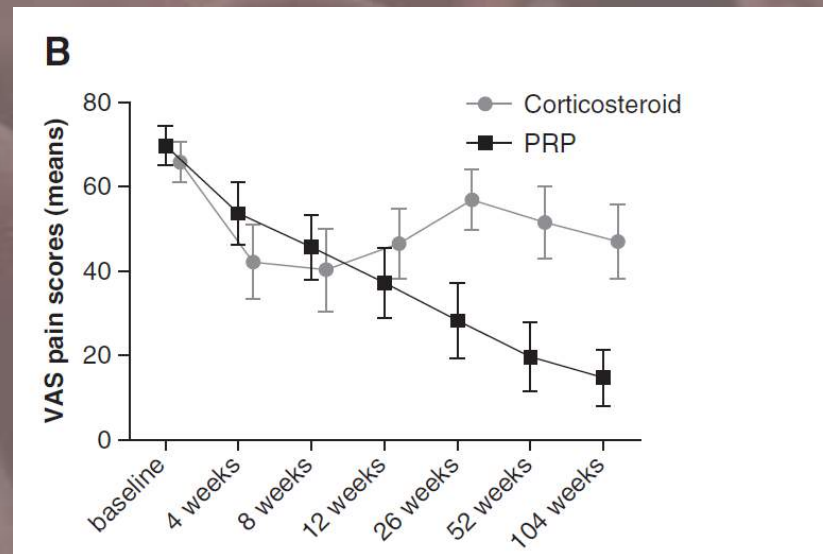
Platelet-Rich Plasma Injections for the Treatment of Hamstring Injuries

A Randomized Controlled Trial

Mohamad Shariff A Hamid,^{*1} MBBS, M Sports Med,
Mohamed Razif Mohamed Ali,[‡] MBCh BAO, FRCS(Edin), MSc, M Sports Med,
Ashril Yusof,[§] BMS, MSES, PhD, John George,^{||} MBBS, DMDS, FRCR,
and Leena Poh Chen Lee,[¶] MMedSc, BSc App Rehab
*Investigation performed at the Sports Medicine Clinic, University of Malaya Medical Centre,
Kuala Lumpur, Malaysia*

Literature Support

PRP has evidence in soft tissue use as well
Lateral Epicondylitis



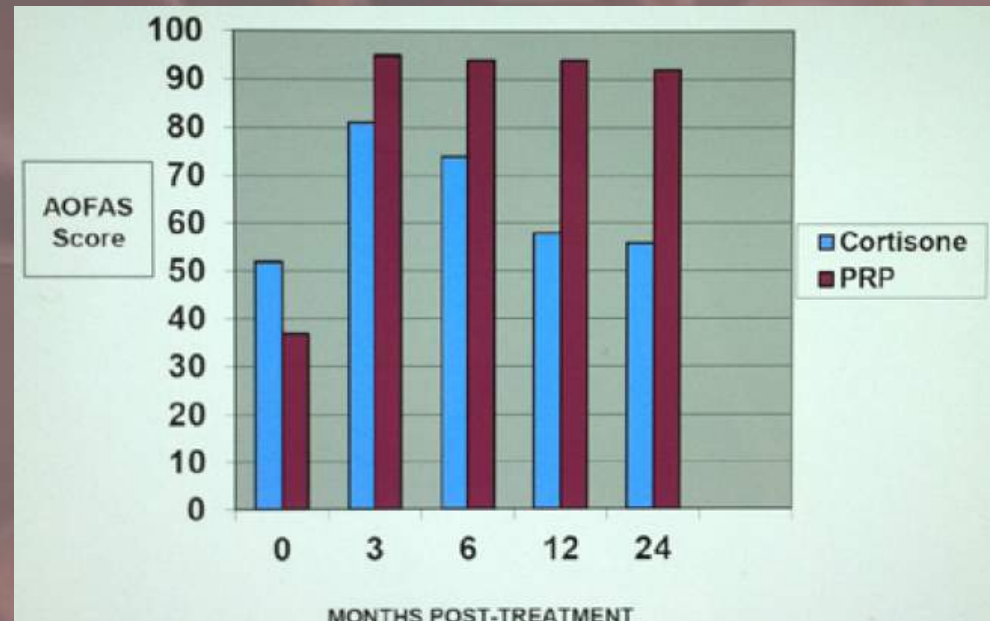
Ongoing Positive Effect of Platelet-Rich Plasma Versus Corticosteroid Injection in Lateral Epicondylitis

A Double-Blind Randomized Controlled Trial With 2-year Follow-up

Taco Gosens,¹ MD, PhD, Joost C. Peerboom,¹ MD, Wilbert van Laar,¹ and Brenda L. den Ouden,¹ PhD
Investigation performed at St Elisabeth Hospital, Tilburg, the Netherlands, and Haga Hospital, The Hague, the Netherlands

Literature Support

PRP has evidence in soft tissue use as well
Plantar Fasciitis



Literature Support BMC per Arthritis Grade

Success is proportional to severity of
Arthritis

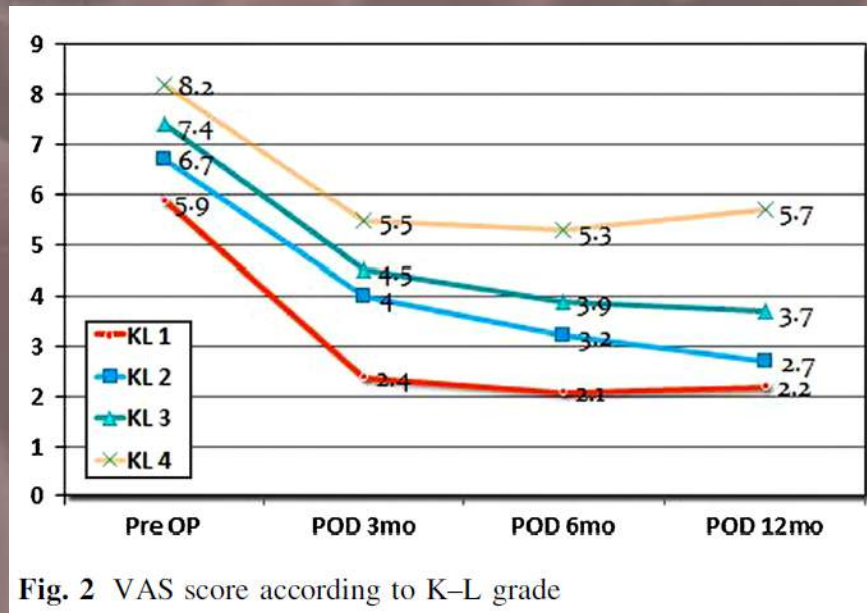


Fig. 2 VAS score according to K-L grade

**Clinical outcome of autologous bone marrow aspirates
concentrate (BMAC) injection in degenerative arthritis
of the knee**

Jae-Do Kim · Gun Woo Lee · Gu Hee Jung ·
Cheung Kue Kim · Taehun Kim · Jin Hyung Park ·
Seong Sook Cha · Young-Bin You

Literature Support

BMC Improves Quality of Life Scores

Clinical Outcome of Bone Marrow Concentrate in Knee Osteoarthritis

Kristin S. Oliver, MD, Matthew Buge, MD, David Crane, MD, Chakrapani Pothukonda

Table 1. The blue line indicates the mean reported KOOS score for Function in Sports and Recreation at time 0, 90 days and 180 days. The standard deviation at each data point is represented by the vertical black lines.

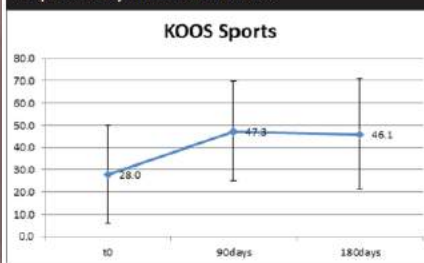


Table 2. The blue line indicates the mean reported KOOS score for Pain at time 0, 90 days and 180 days. The standard deviation at each data point is represented by the vertical black lines.

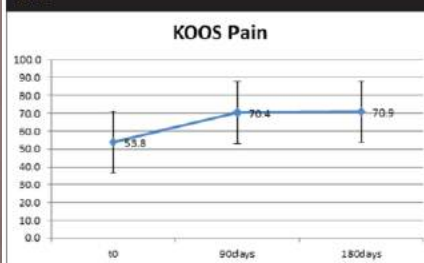


Table 3. The blue line indicates the mean reported KOOS score for Symptoms at time 0, 90 days and 180 days. The standard deviation at each data point is represented by the

Table 4. The blue line indicates the mean reported KOOS score for Function in Activities of Daily Living at time 0, 90 days and 180 days. The standard deviation at each data point is represented by the vertical black lines.

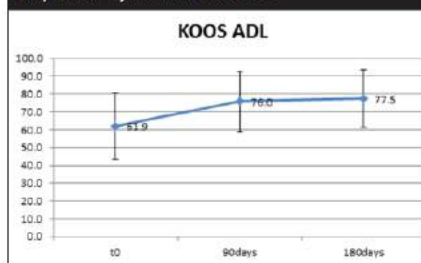


Table 5. The blue line indicates the mean reported KOOS score for Knee Related Quality of Life at time 0, 90 days and 180 days. The standard deviation at each data point is represented by the vertical black lines.

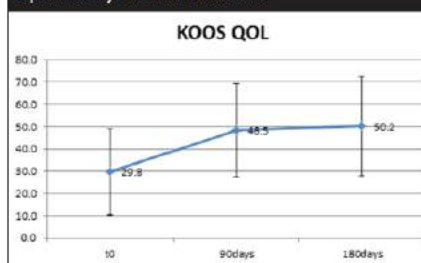


Table 6. KOOS increases between pre-treatment and 180 days post-treatment based on Kellgren-Lawrence Staging of knee osteoarthritis

Literature Support

Surgical application of BMC is well documented and has very promising results associated



Fig. 2

Anteroposterior radiographs of a twenty-five-year-old patient who had sustained a type-I open fracture. The radiographs were made at the time of fracture (a); at the time of nonunion, before injection of autologous bone marrow (b); at one month after bone marrow injection, at which time the patient was allowed to begin partial weight-bearing (c); at two months after bone marrow injection (d); and at three months after bone marrow injection, at which time the external fixation was removed (e).

PERCUTANEOUS AUTOLOGOUS BONE-MARROW GRAFTING FOR NONUNIONS

INFLUENCE OF THE NUMBER AND CONCENTRATION OF PROGENITOR CELLS

By PH. HERNIGOU, MD, A. POIGNARD, MD, F. BEAUJEAN, MD, AND H. ROUARD, MD

Investigation performed at the Service de Chirurgie Orthopédique, Hôpital Henri Mondes, Cochin, France

Literature Support

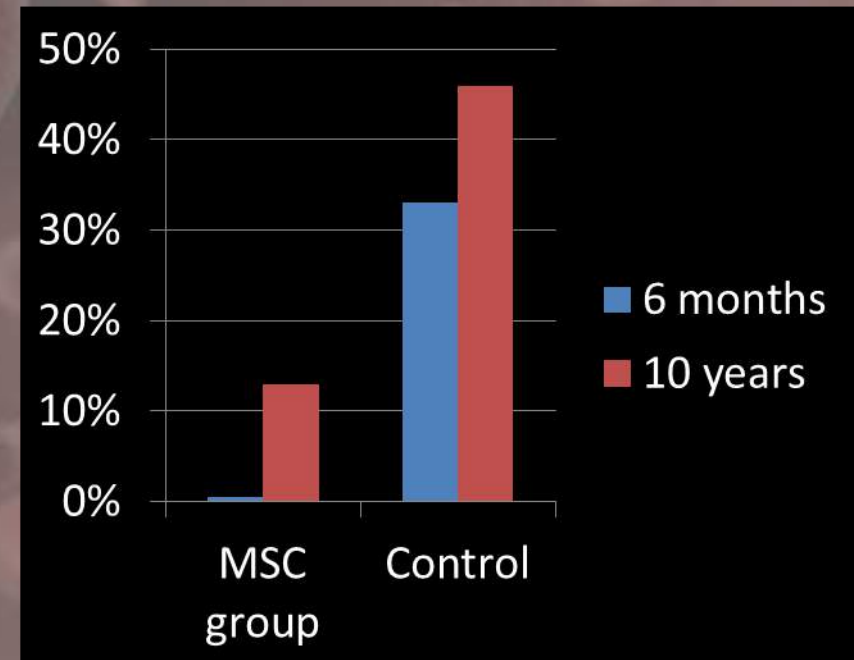
Surgical application is well documented and has very promising results associated

Rotator Cuff Repair

Biologic augmentation of rotator cuff repair with mesenchymal stem cells during arthroscopy improves healing and prevents further tears: a case-controlled study

Philippe Hernigou • Charles Henri Flouzat Lachaniette •
Jerome Delambre • Sebastien Zilber • Pascal Duffiet •
Nathalie Chevallier • Helene Rouard

Failure Rate



Literature Support

Surgical application is well documented and has very promising results associated

Meniscus

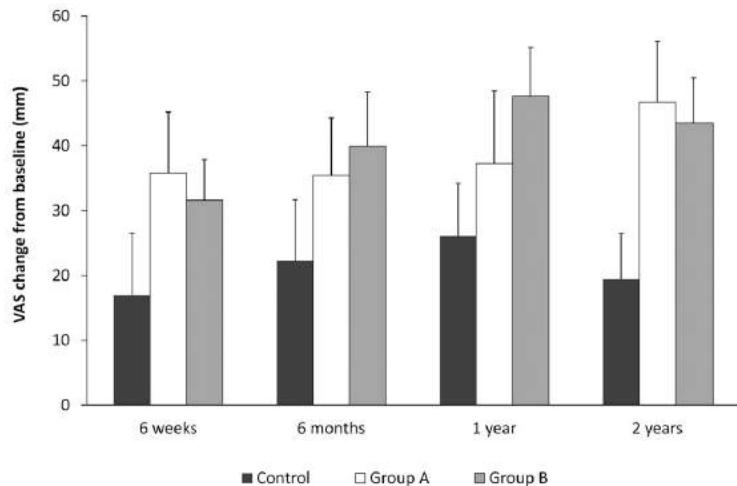


Fig. 2
Improvement in VAS pain scores through two years post meniscectomy surgery in patients with evidence of cartilage degeneration on MRI. The time points at which strong trends or significant differences from the control were observed were at two years for Group A ($p = 0.05$), and at one year ($p = 0.08$) and two years ($p = 0.04$) for Group B. Control = sodium hyaluronate, Group A = 50×10^6 hMSCs, and Group B = 150×10^6 hMSCs. The bars represent 95% confidence intervals.

Adult Human Mesenchymal Stem Cells Delivered via Intra-Articular Injection to the Knee Following Partial Medial Meniscectomy

A Randomized, Double-Blind, Controlled Study

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Literature Support

- Chondrogenic differentiation of umbilical cord-derived stem cells in type 1 collagen-hydrogel for cartilage engineering. Injury, 2013 April
 - UC-derived MSC's undergo chondrogenesis
 - Most cells remain viable
 - Hydrogel was shown to be a viable 3D scaffold for growing cartilage

Literature Support

- Evaluation of the Curative Effect of UC MCS Therapy for Knee Arthritis in Dogs Using Imaging Technology. Stem Cell International, 2018
 - Treated animals demonstrated improvement in cartilage appearance on MRI
 - No change in X-Ray

Take Home Points

- We still do not have the “Fountain of Youth”
 - But... we are getting closer
- Have a thorough evaluation by a physician with an in depth understanding of orthopaedic problems and their treatments
- Ask a lot of questions
 - Goals of treatment?
 - Detailed information of products being used?
 - Training of the provider?

Thank you!



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