

Ortobiológicos

conceito e atualização no emprego
de plasma rico em plaquetas e
lisados plaquetários no tratamento
de afecções articulares

MV. Me. Sarah Seidel

Sumário

Conceito e classificação
Processos de obtenção
Constituição produto final
Ação em tecido articular
Evidência científica
Perspectivas
Considerações finais

Conceitos

Ortobiológicos

Conjunto de produtos, autólogos ou não, formados por um concentrado de células ou fragmentos celulares

Hemocomponentes

Componentes lábeis do sangue submetidos a um processo **FÍSICO** que dá origem a um produto formado por parte do sangue total

Hemoderivados

Produtos obtidos a partir do plasma por meio de processos **FÍSICO-QUÍMICOS** ou **BIOTECNOLÓGICOS**

Conceitos

Plasma Rico em Plaquetas

Hemocomponente que concentra plaquetas acima dos níveis basais do sangue total, com ou sem enriquecimento leucocitário

DMOAD

Droga Modificadora da Doença Osteoartrósica

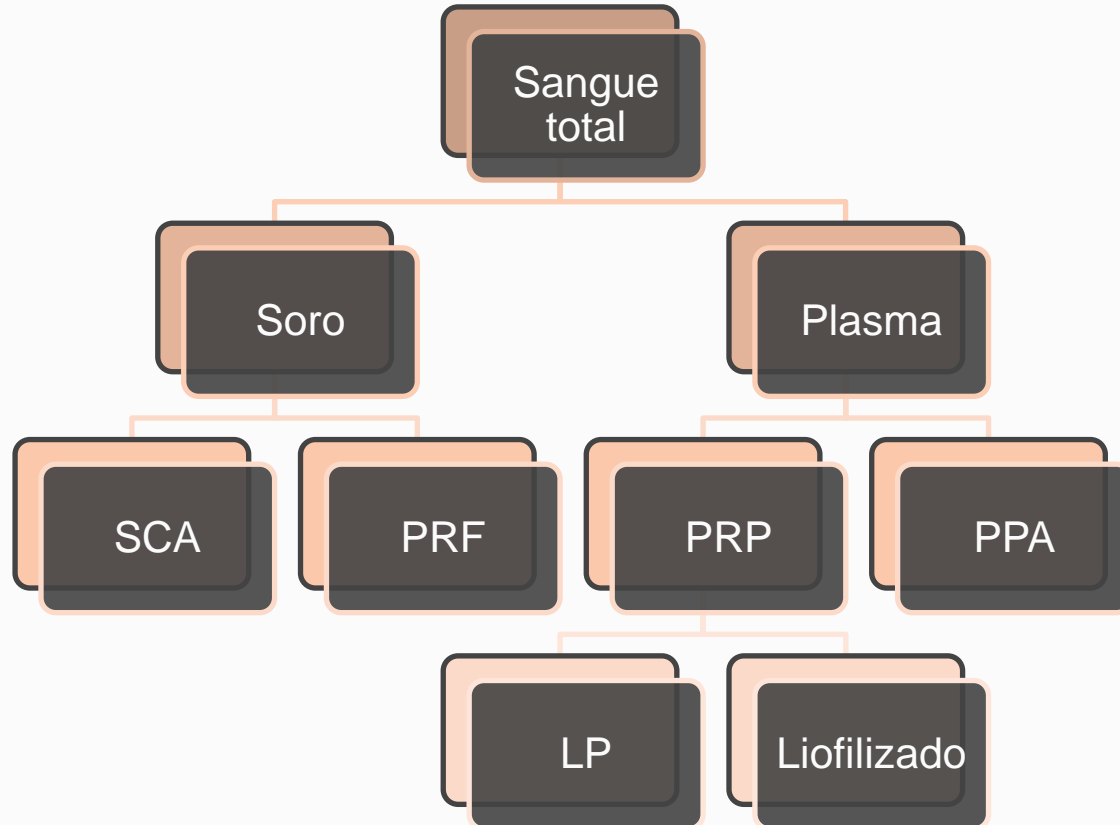
Métodos multimodais

Transplante

Estímulo celular

Arcabouço biodegradável

Hemocomponentes



Hemocomponentes

PRP

- Citrato de sódio
- Grande variabilidade
 - *Protocolo*
 - *Produto final*
- Tempo

PPA

- Heparina
- Incubação (24h)
- Filtração

PRF

- Sem anticoagulante
- Sólido

LP

- Ruptura membrana
- Liberação fatores
- Acelular

Liofilizado

- Congelamento
- Secagem
- Crioprotetores

Sistemas de classificação

AUTOR	CLASSIFICAÇÃO	METODOLOGIA
MISHRA et al. (2012)	Medicina esportiva	Concentração plaquetária Ativador exógeno Concentração leucocitária
EHRENFEST et al. (2014)	PRP PRF	Conteúdo celular Arquitetura de fibrina
DELONG et al. (2012)	PAW	Concentração plaquetária Ativador exógeno Concentração leucocitária
MAUTNER et al. (2015)	PLRA	Volume e frequência
MAGALON et al. (2016)	DEPA	Dose Eficiência Pureza Ativação

Métodos de obtenção: PRP



Centrifugação

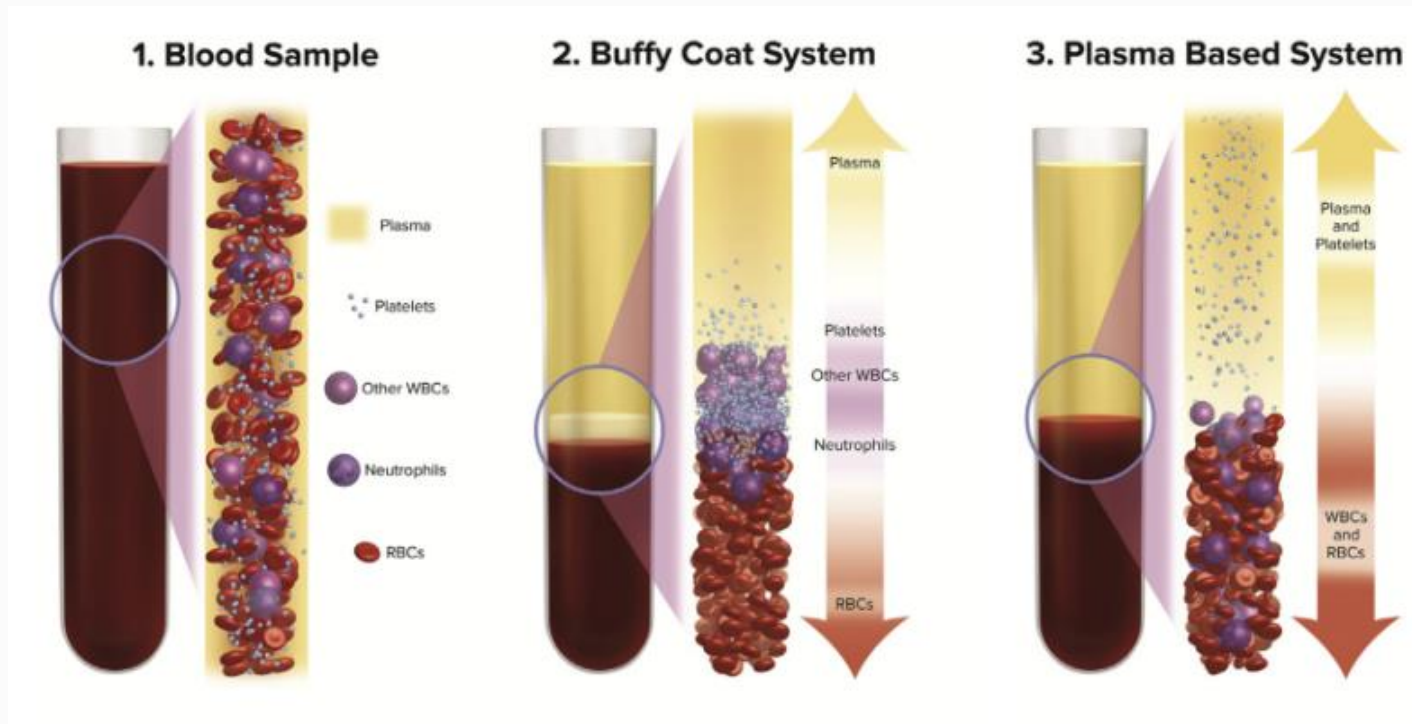


Plasmaferese



Filtração

Métodos de obtenção: PRP



Métodos de obtenção: PRP

Ativação?

Fracionamento

Homogeneização

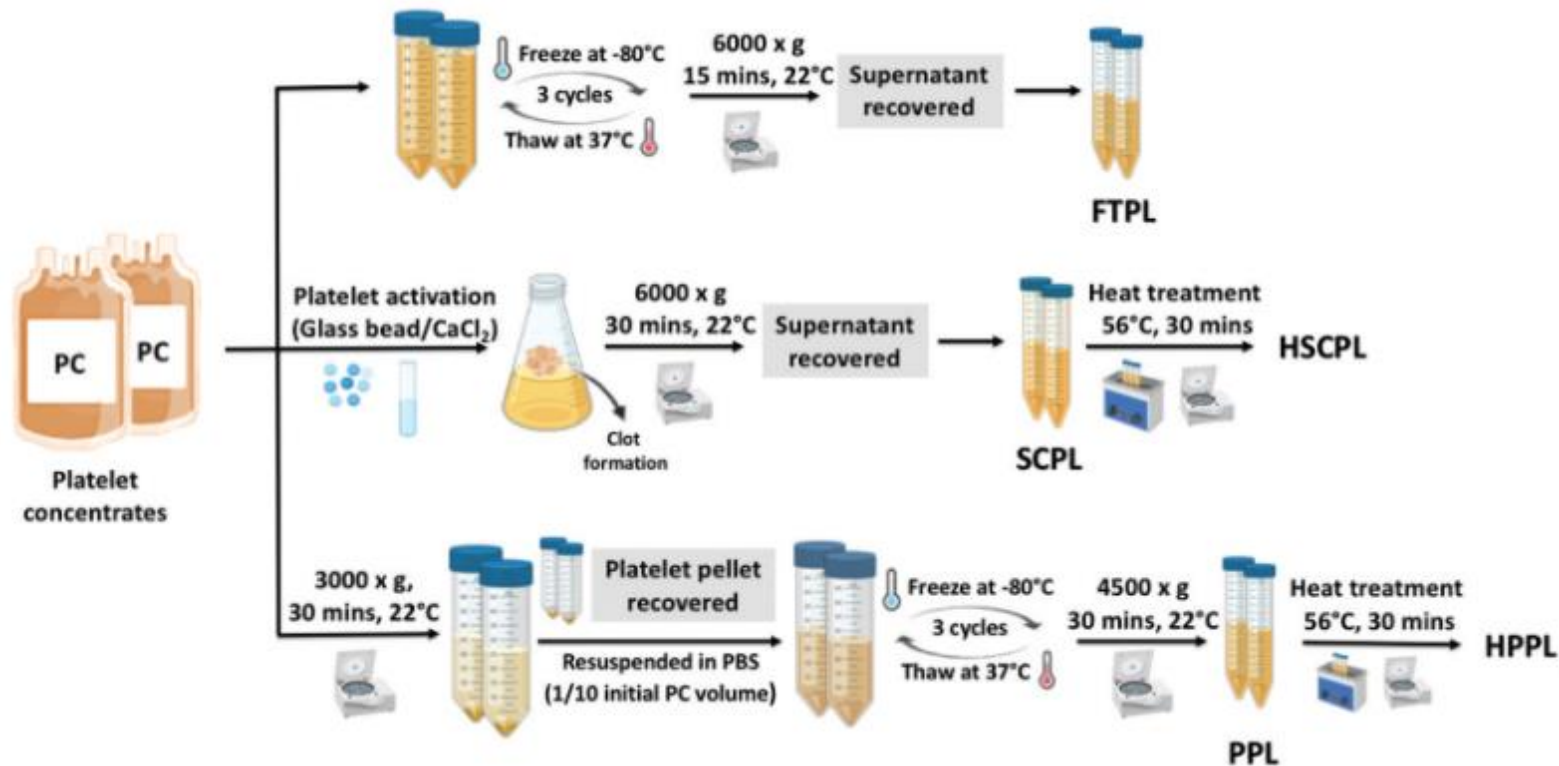
Proporção ST:AC

Anticoagulante: citrato

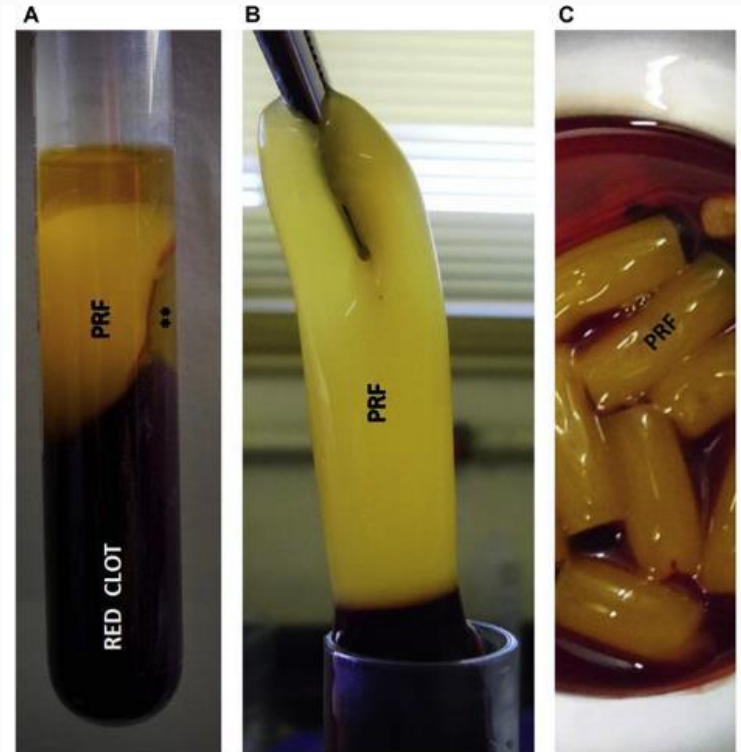
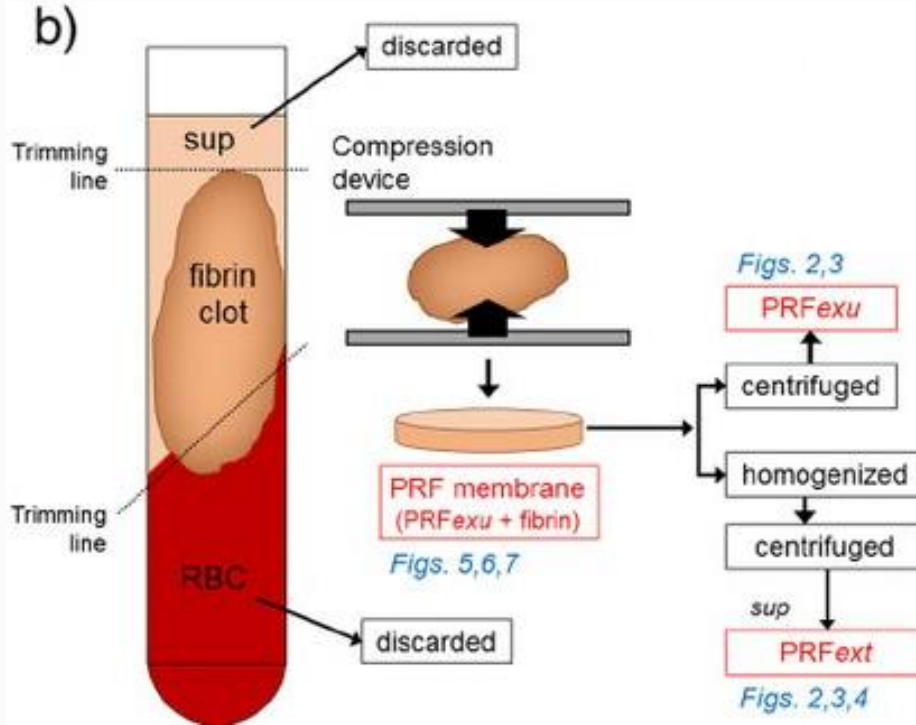
Calibre agulha

Antissepsia

Métodos de obtenção: Lisado Plaquetário



Métodos de obtenção: Plaqueta Rica em Fibrina



Jiménez-Aristazábal et al. Changes on the Structural Architecture and Growth Factor Release, and Degradation in Equine Platelet-Rich Fibrin Clots Cultured Over Time. 2019.

Qual protocolo escolher?



Article

Does Double Centrifugation Lead to Premature Platelet Aggregation and Decreased TGF- β 1 Concentrations in Equine Platelet-Rich Plasma?

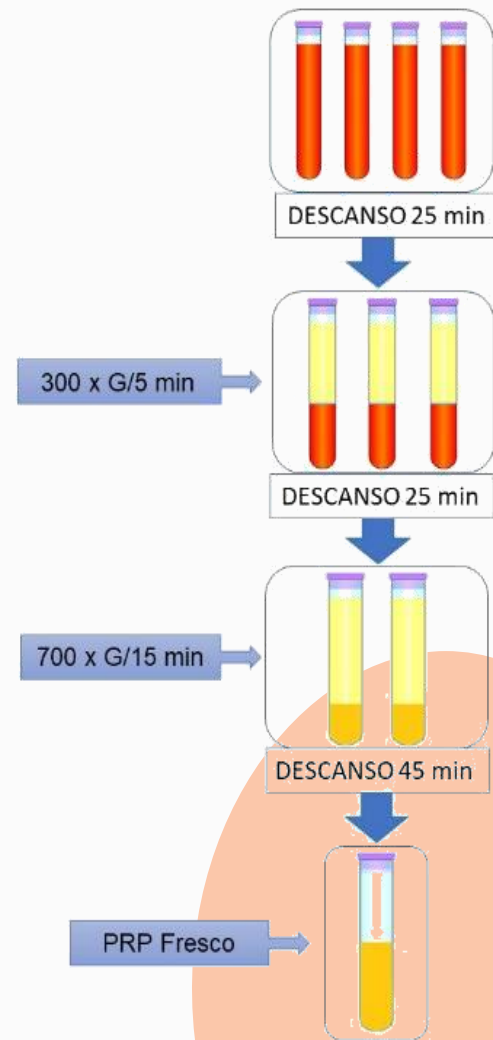
Sarah R. T. Seidel ^{1,*}, Cynthia P. Vendruscolo ¹, Juliana J. Moreira ¹, Joice Fülber ¹, Tatiana F. Ottaiano ², Maria L. V. Oliva ², Yara M. Michelacci ² and Raquel Y. A. Baccarin ^{1,*}

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Constituição produto final

VEGF
FC Endotelial Vascular
Aumenta angiogênese e permeabilidade vascular, mitogênico células endoteliais

HGF
FC de Hepatócito
Morfogênese, proliferação celular, anti-inflamatório, proteção, reparo e regeneração

EGF
FC Epidermal
Crescimento endotelial, angiogênese, regula colagenase, reparação pele

TGF- β
FC Transformante
Migração celular, neovascularização e angiogênese, síntese COL, inibe degradação MEC, ação mitogênica sobre FCs



KGF
FC Queratinócito
Crescimento e neoformação de queratinócitos

FGF
FC Fibroblástico
Reparo tecidual, crescimento e diferenciação de condrócitos e osteoblastos

IGF
FC Tipo Insulina
Formação MO, síntese FA e COL-1, proliferação e diferenciação de MSC

PDGF
FC Derivado de PLT
Reparo tecidual, crescimento e diferenciação de condrócitos e osteoblastos

CTGF
FC de Tecido Conjuntivo
Angiogênese, reparo cartilagem, fibrose e adesão PLT

Constituição produto final

VEGF
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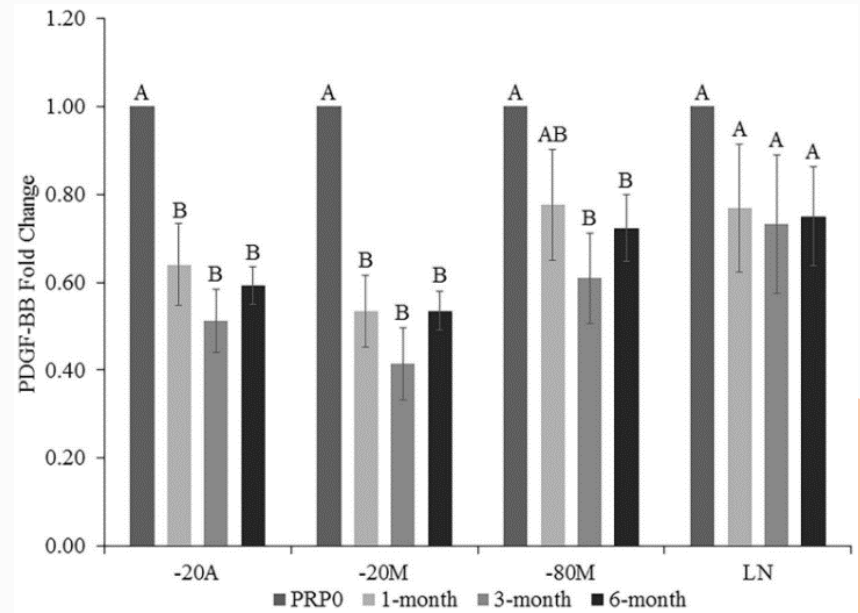
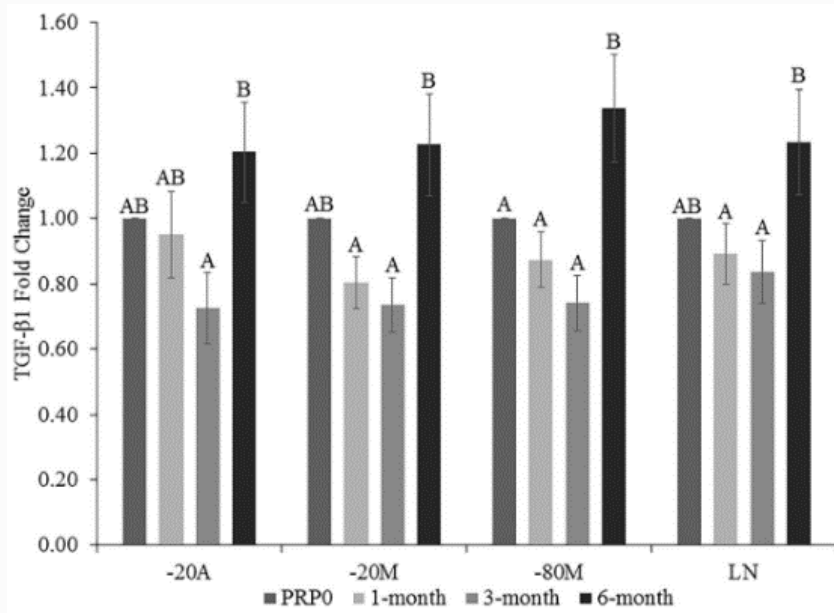
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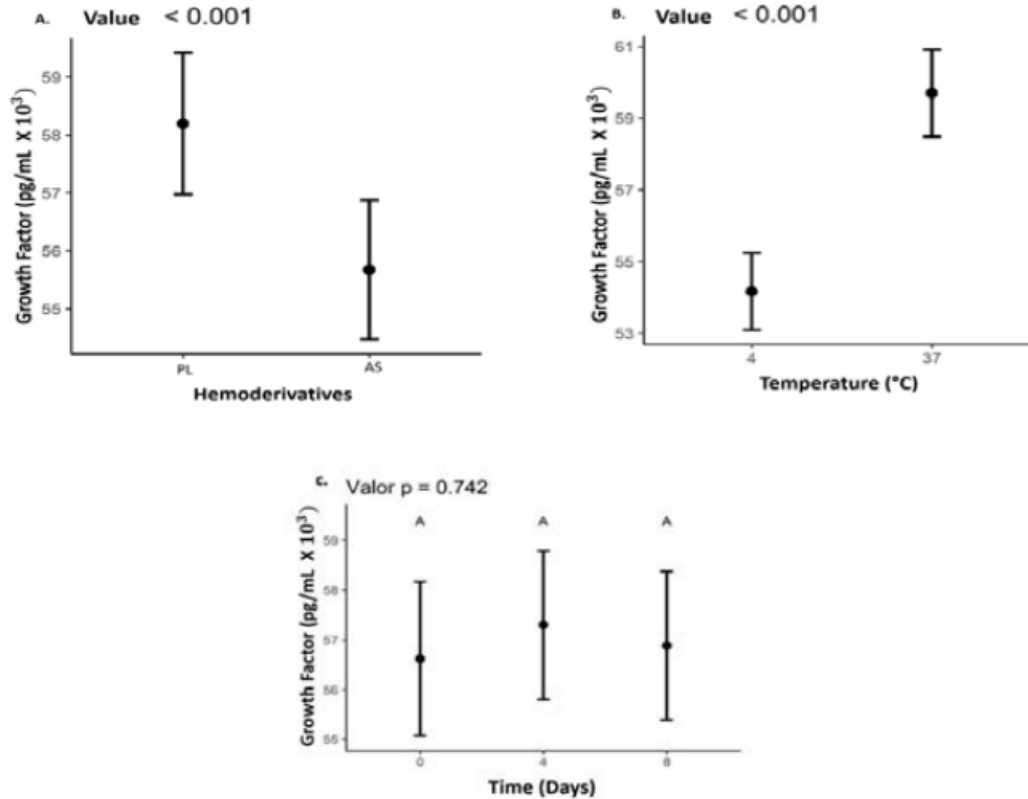
Constituição produto final

Plasma		Leukocytes	
Proteins	Albumin, globulins, fibrinogen, complement, and clotting factors	Neutrophils	
Electrolytes	Chloride, sodium, potassium, and calcium	Primary granules	Myeloperoxidase, acid hydrolases, defensins, and serine proteases
Hormones	IGF-1, estrogens, progesterone, androgens, ACTH, and HGH	Secondary granules	Collagenase, lactoferrin, cathelicidin, bactericidal phagocytins, and lysozyme
Biomarkers	COMP, CD11b, protein C, microRNA, osteocalcin, and osteonectin	Tertiary granules	Gelatinase and proteases
Platelets		Monocytes	Platelet-activating factor, TGF- β , VEGF, FGF, and EGF
Alpha granules	Adhesive proteins, clotting factors, and GFs PDGF, TGF- β , VEGF, FGF, EGF, and HGF	Erythrocytes	ATP, S-nitrosothiols, nitric oxide, hydrogen sulfide, hemoglobin, and free radicals
Dense bodies	Calcium and neurotransmitters		
Lysosomes	Lysosomal enzymes		

Estabilidade produto final: PRP

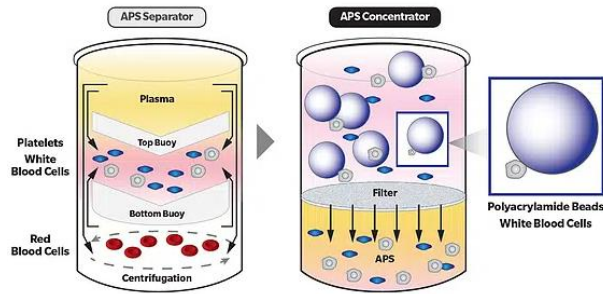


Estabilidade produto final: LP



Padronização

Pro-Stride Injection™



PRECISEPRP™
Equine 

PrecisePRP™ Equine
Leucoreduced allogeneic pooled freeze-dried platelet-rich plasma
VetStem, Inc.

PrecisePRP™ Equine
Leucoreduced allogeneic pooled freeze-dried platelet-rich plasma

For intra-articular injection in horses only

4.0×10^9 equine platelets / vial, freeze-dried

Single patient use vial for rehydration to 8 mL with sterile water

A freeze-dried species-specific source of concentrated platelets in plasma



Ação em tecido articular

Como o PRP pode influenciar o
ambiente articular?



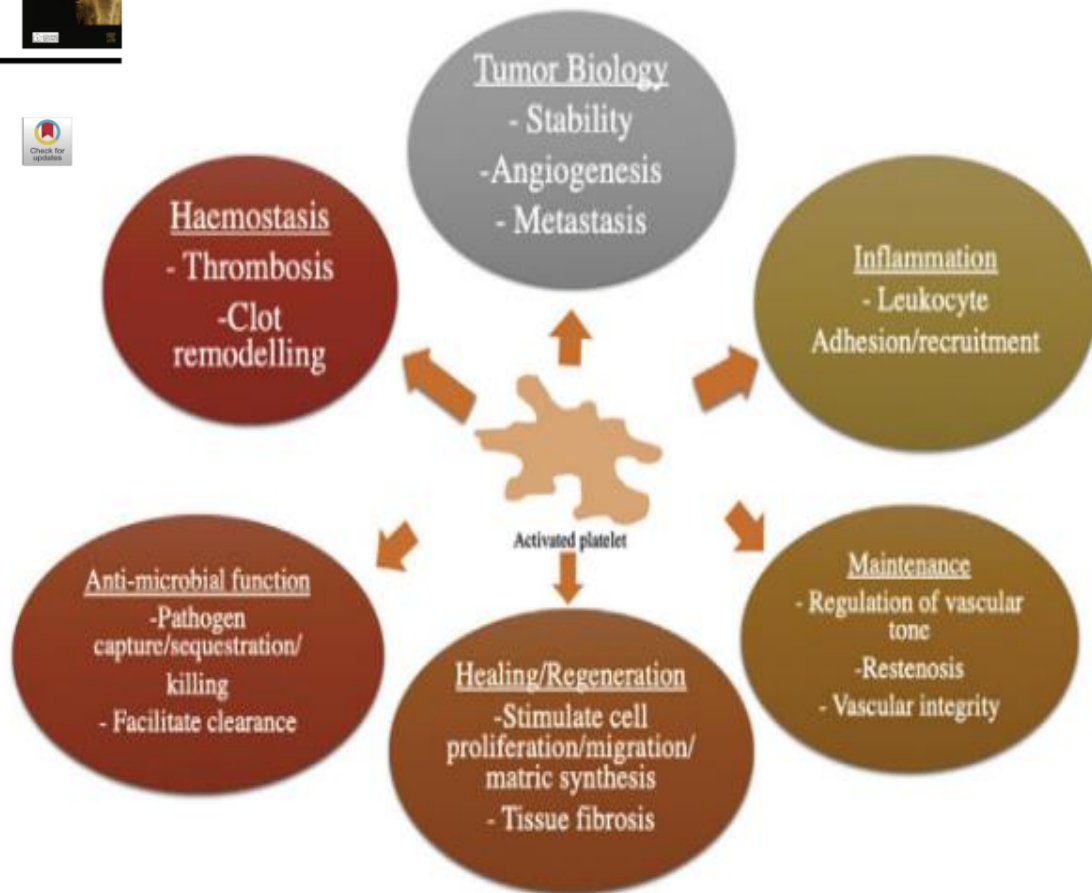
ELSEVIER



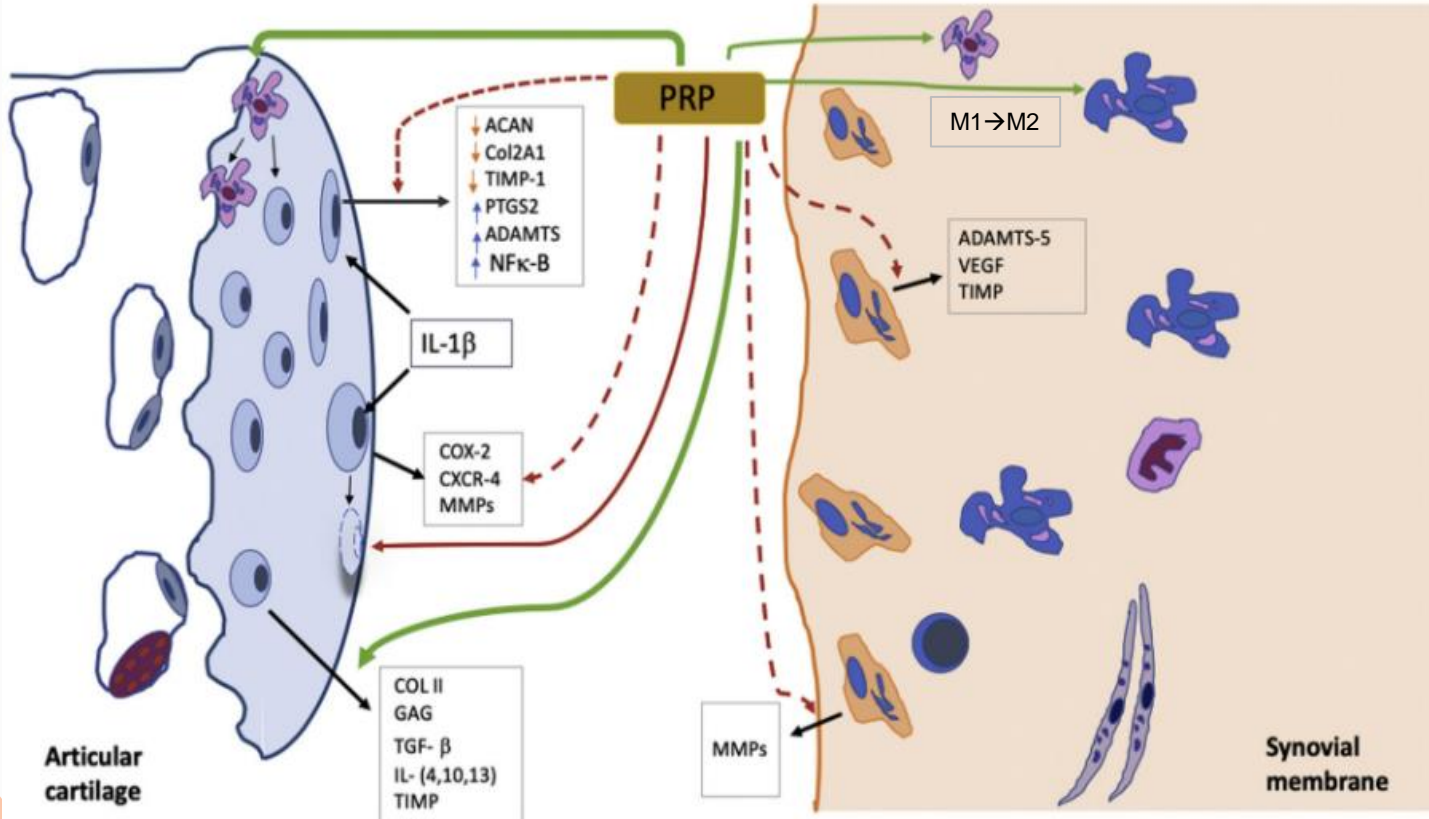
Review Article

Platelet-Rich Products and Their Application to Osteoarthritis

Livia Camargo Garbin ^{a,*}, Christine S. Olver ^b



Ação do PRP na OA



REVIEW

Biology of platelet-rich plasma and its clinical application in cartilage repair

Xuetao Xie^{1,2}, Changqing Zhang¹ and Rocky S Tuan^{2*}

Efeito anabólico

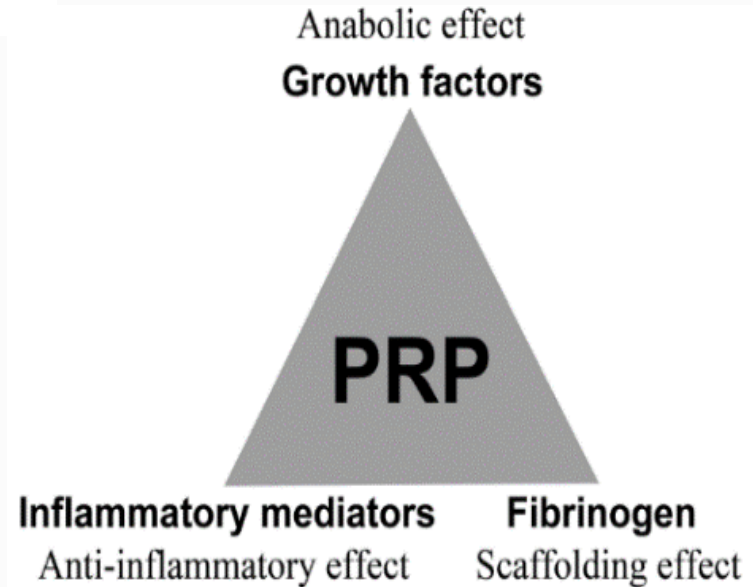
- Condrócitos, CTMs e sinoviócitos
- Acúmulo de MEC
- Produção de HA

Arcabouço bioativo

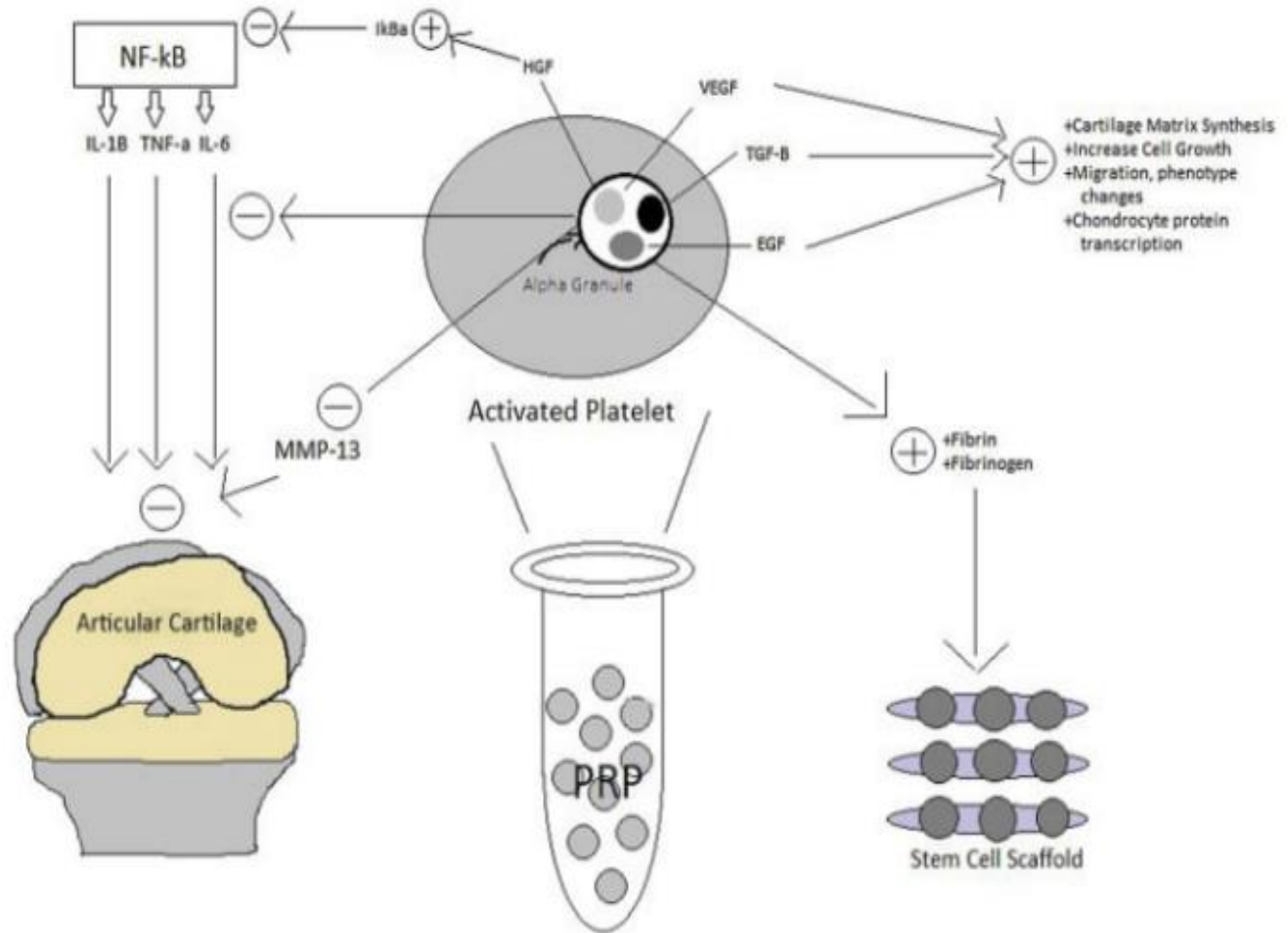
- Correção de defeitos
- Liberação gradativa

Mediadores inflamatórios

- Inibe inflamação
- Melhora sintomatologia OA



Inibição NF- κ B
 Via catabólica
 Transcrição de citocinas
 IL-1 β , TNF α , IL-6
 Diminui expressão MMP-13





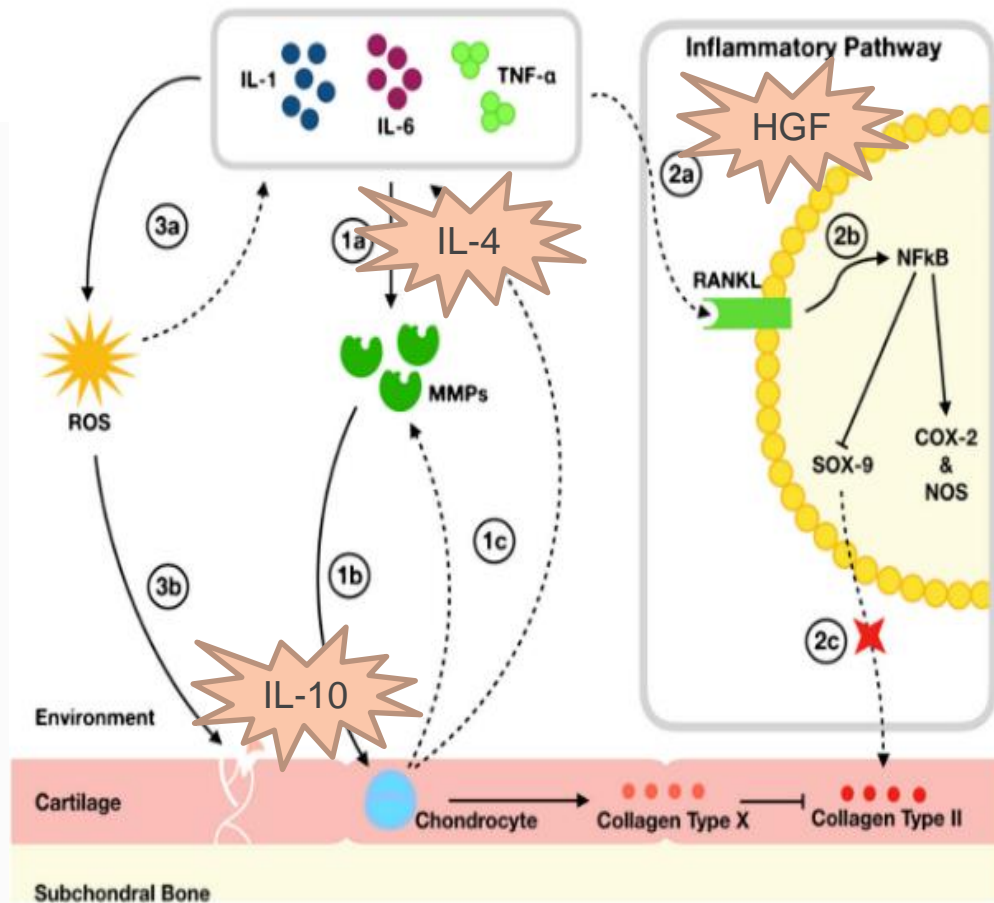
Platelet-Rich Plasma and Cartilage Repair

Mitchell I. Kennedy¹ • Kaitlyn Whitney¹ • Thos Evans² • Robert F. LaPrade^{1,2}

1
Síntese de MMPs,
Degradação COL
Produção de COL X,
Degradação cartilagem e condrócitos

2
RANKL ativa NFκB
Diminui SOX-9 e COL-II
Aumenta COX2 e NOS

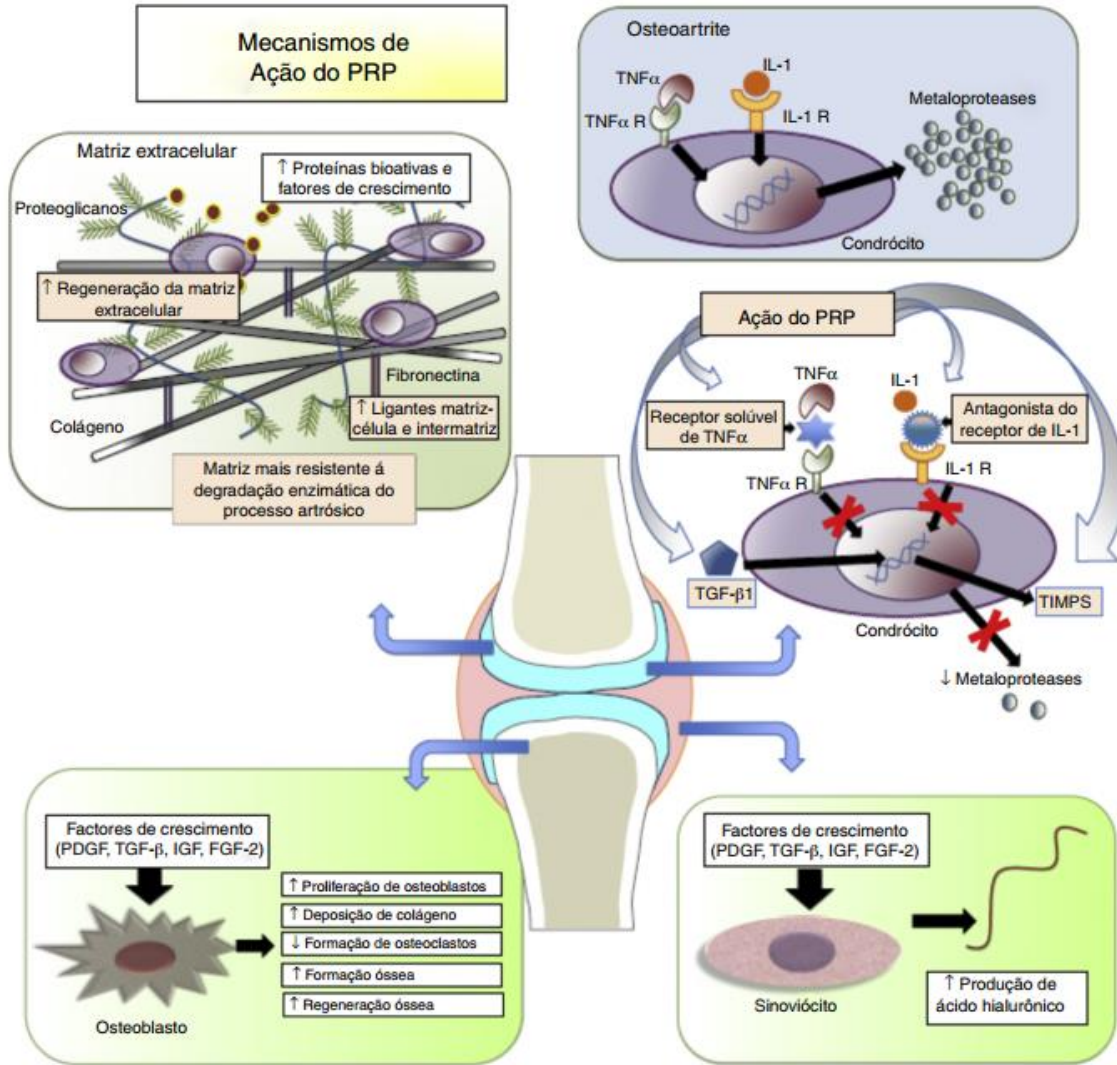
3
Estímulo ROS
Apoptose do condrócito
Fatores catabólicos e degenerativos



Artigo de revisão

Plasma rico em plaquetas no tratamento da osteoartrite

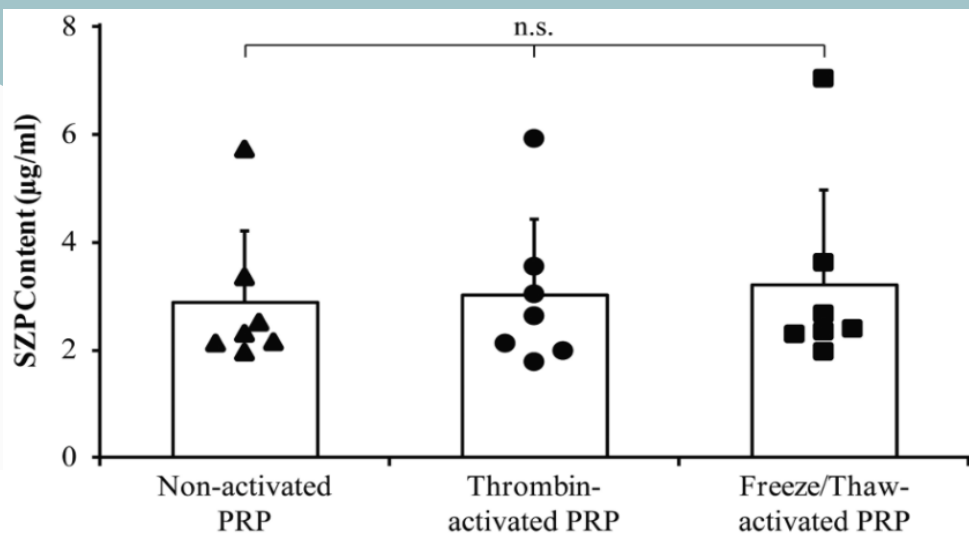
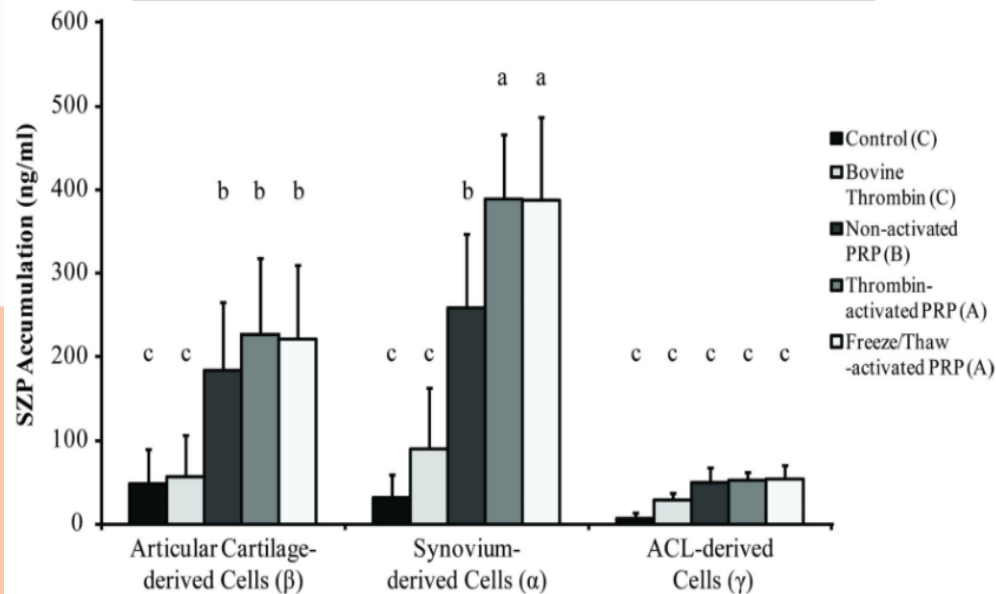
Eduardo Knop*, Luiz Eduardo de Paula e Ricardo Fuller



Stimulation of the Superficial Zone Protein and Lubrication in the Articular Cartilage by Human Platelet-Rich Plasma

Ryosuke Sakata, MD, Sean M. McNary, PhD, Kazumasa Miyatake, MD, Cassandra A. Lee, MD, James M. Van den Bogaerde, MD, Richard A. Marder, MD, and A. Hari Reddi, PhD

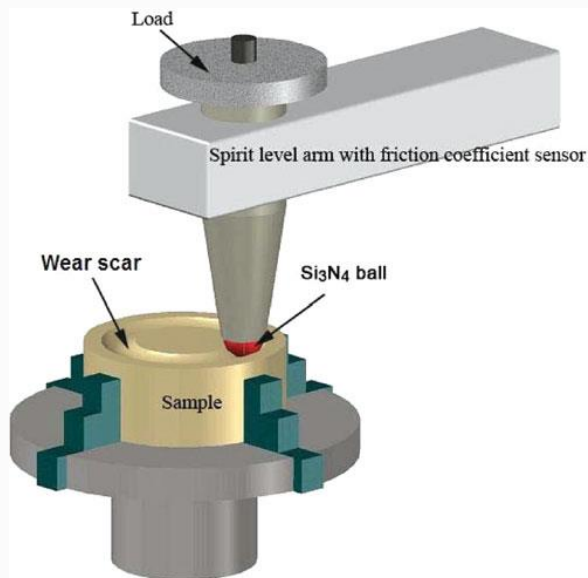
Concentração lubricina meios de cultivo



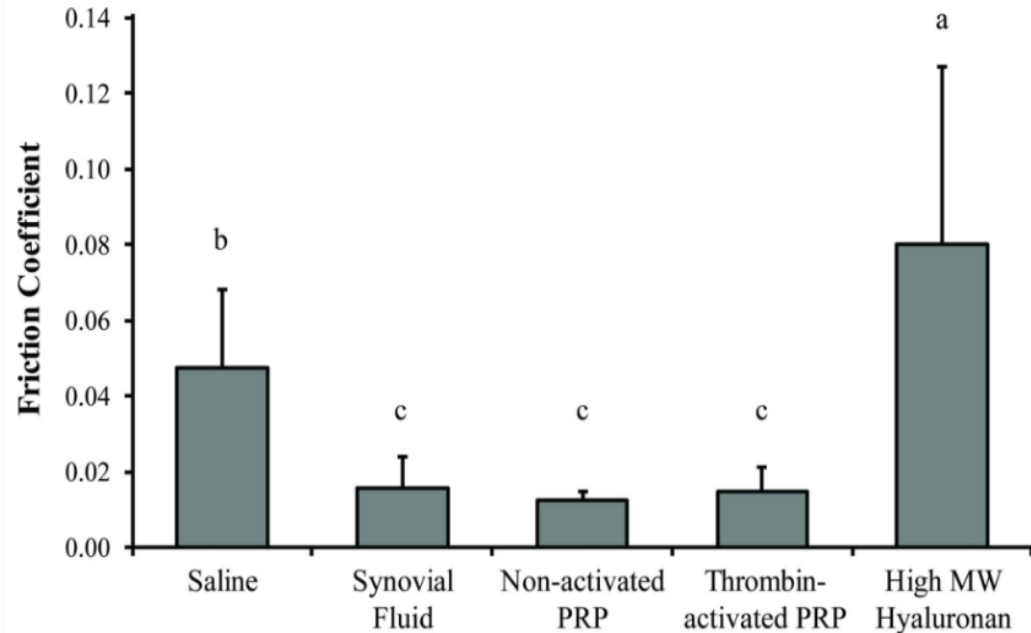
Concentração lubricina PRP

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Coeficiente de fricção cartilagem bovina



Onde os ortobiológicos irão agir?

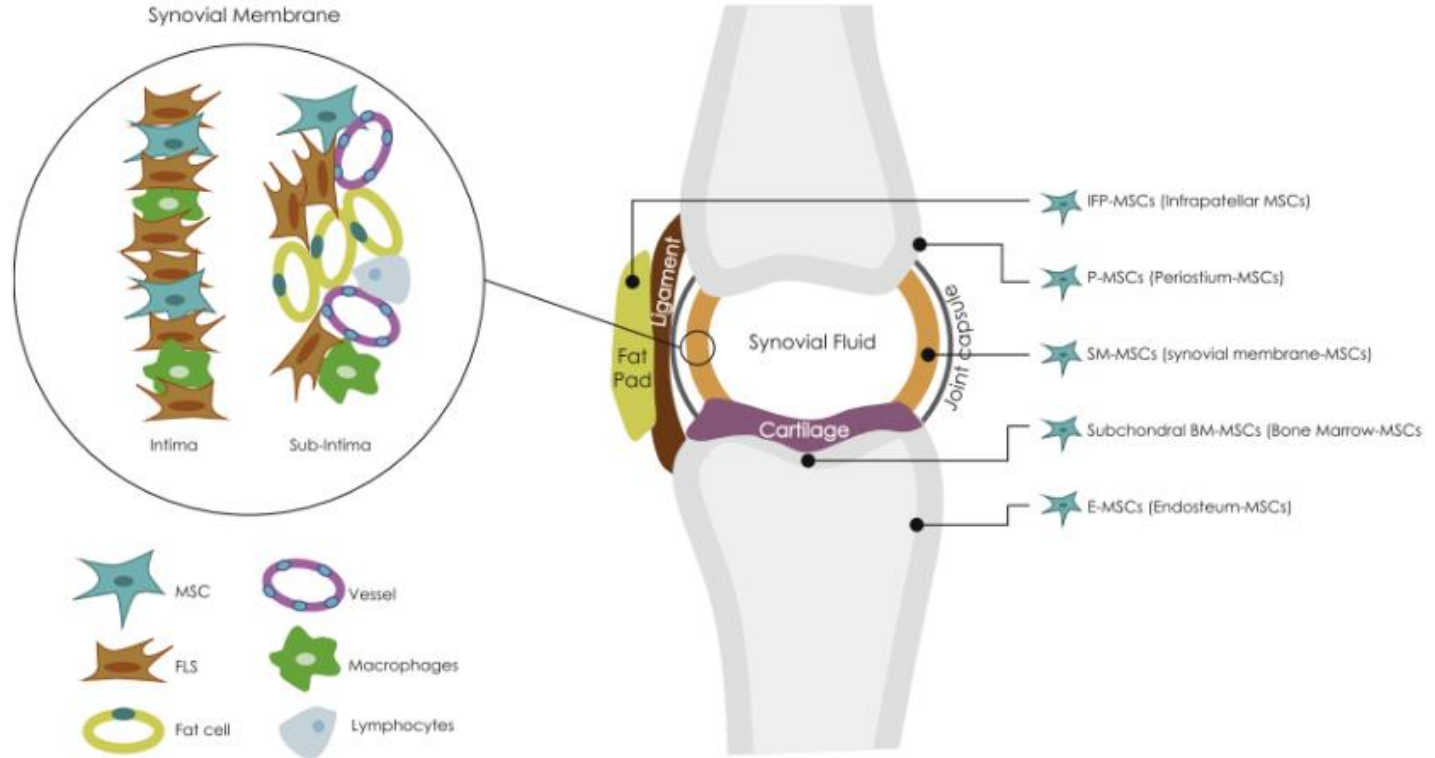
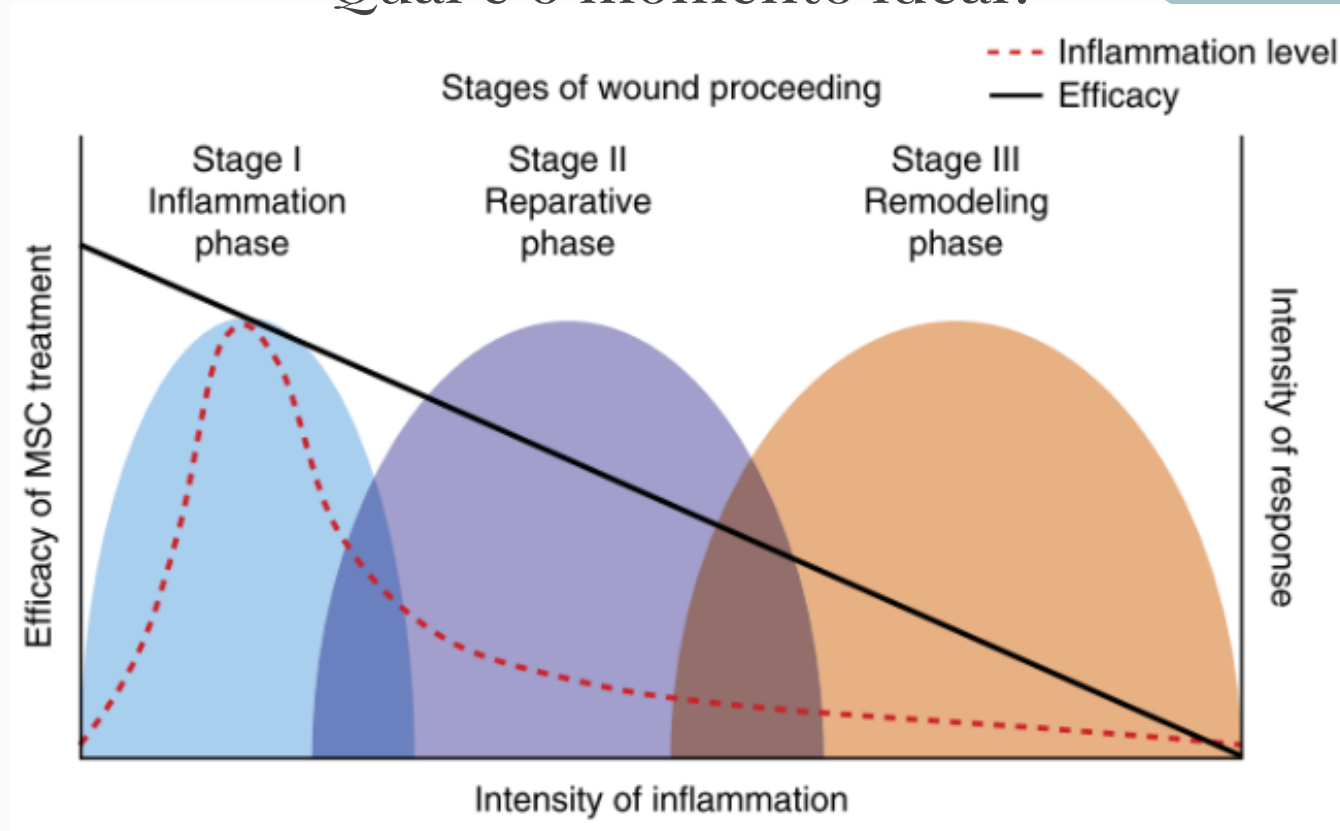


Fig. 1. Distribution of various cells in the synovium and joint tissues. FLS = fibroblast-like synoviocytes only represent *intima* fibroblasts. Joint location of different resident MSCs.

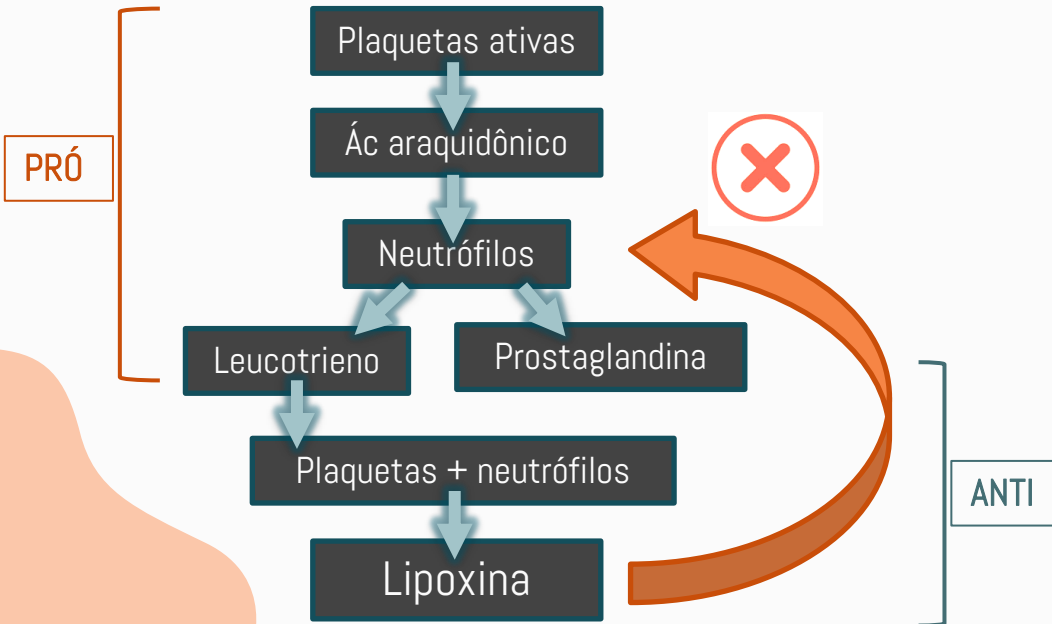
Qual é o momento ideal?





Leukocyte-rich PRP for knee osteoarthritis: Current concepts

José Fábio Lana ^a, Alex Macedo ^a, Icaro Lanzoni Gallo Ingrao ^a, Stephany Cares Huber ^b, Gabriel Silva Santos ^{a,*}, Maria Helena Andrade Santana ^b



Leucócitos

Fase inflamatória

Liberam moléculas pró e anti-inflamatórias
+ plaquetas ativas: maior potencial terapêutico

LR-PRP

Propriedade antimicrobiana

Maior produção de VEGF

Neutrófilos

Secreção de citocinas inflamatórias e MMPs

Lipoxina em OA

Manutenção do microambiente

Previne progressão

Inflamação prolongada e degeneração



Literatura vigente

O que podemos extrair dos artigos?



Pooled Platelet-Rich Plasma Lysate Therapy Increases Synoviocyte Proliferation and Hyaluronic Acid Production While Protecting Chondrocytes From Synoviocyte-Derived Inflammatory Mediators

Jessica M. Gilbertie^{1,2}, Julie M. Long¹, Alicia G. Schubert¹, Alix K. Berglund^{1,2}, Thomas P. Schaer³ and Lauren V. Schnabel^{1,2*}



Cultured Synoviocytes

Allowed to adhere and grow for 48hr

24hr stimulation with:

IL-1 β (10ng/mL)
LPS (100ng/mL)
Unstimulated control

Synoviocytes washed and treated for 48hr with:

25% PPP-L
25% PRP-L
No treatment control

Synoviocyte cell numbers assessed via density

Synoviocyte conditioned media collected

ELISAs:
HA
IL-1 β
IL-6
TNF- α

Cultured Chondrocytes



Allowed to adhere and grow for 48hr

Added (50%) to chondrocyte media for 48hr

qPCR:
COL1A1 PRG4
COL2A1 MMP-3
COL3A1 MMP-13
ACAN 18S

Obtenção do PRP

6 animais: machos e fêmeas

Repouso por 30 min e coleta do plasma total

250 G/5 min + 1.500 G/15 min

Sobrenadante (PPP) e pellet ressuspendido (PRP)

5 ciclos congelamento/descongelamento

Centrifugação 20.000 G/20 min

Amostras filtradas e congeladas

Caracterização do PRP

PPP

0.05×10^3 leucócitos/ μ L

9.38×10^3 plaquetas/ μ L

PRP

1.39 leucócitos/ μ L

1.226,38 plaquetas / μ L

Basal

5.60×10^3 leucócitos/ μ L

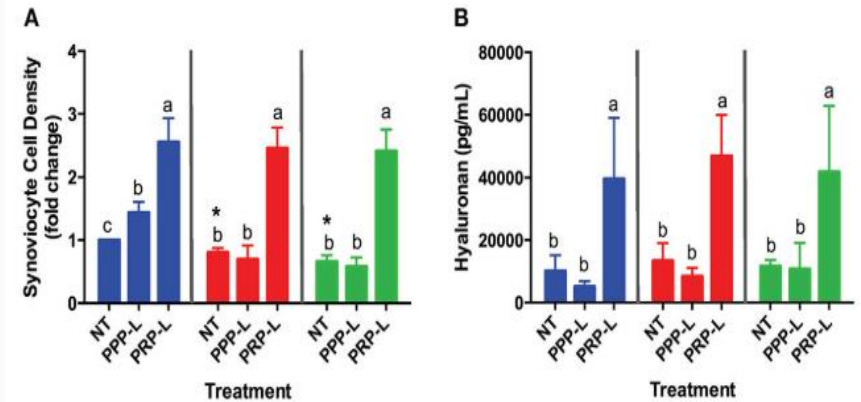
134.5×10^3 plaquetas/ μ L



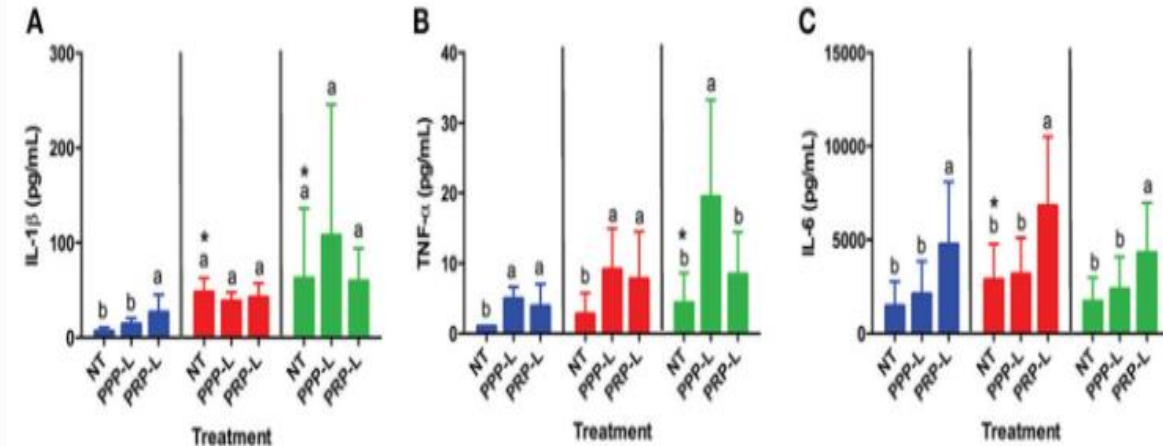
Pooled Platelet-Rich Plasma Lysate Therapy Increases Synoviocyte Proliferation and Hyaluronic Acid Production While Protecting Chondrocytes From Synoviocyte-Derived Inflammatory Mediators

Jessica M. Gilbertie^{1,2}, Julie M. Long¹, Alicia G. Schubert¹, Alix K. Berglund^{1,2}, Thomas P. Schaefer³ and Lauren V. Schnabel^{1,2*}

Crescimento de sinoviócitos e produção de HA



Mensuração de IL-1β, TNFα e IL-6



Meios da cultura de sinoviócitos

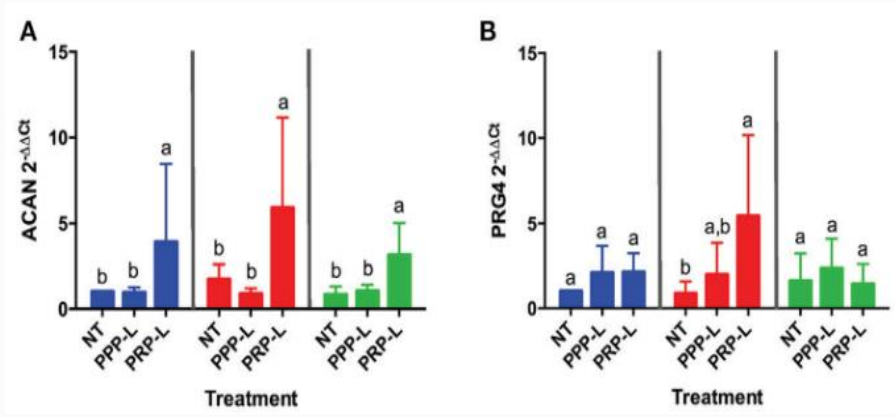
■ Unstimulated
■ IL-1β
■ LPS



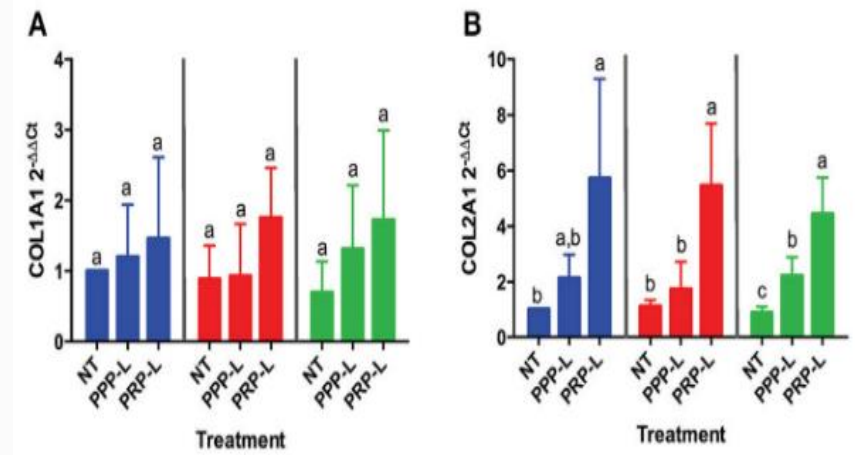
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Mensuração de agrecan e lubricina

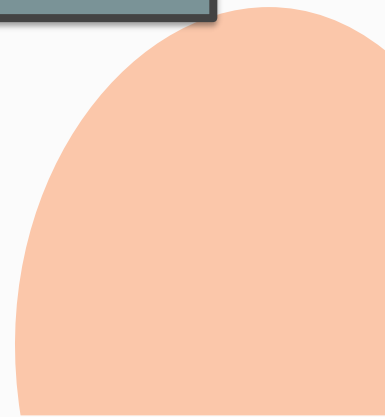


Mensuração de colágeno



Avaliação condrócitos

■ Unstimulated
■ IL-1β
■ LPS



Effects of blood-derived products and sodium hyaluronate on equine synovial fluid cells and on synovial fluid from osteochondrotic joints of horses after arthroscopy and administration of treatment

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Comparou efeito de 3 hemocomponentes e HA

PRP x IRAP x APP x HA

In vitro

Células de LS de articulação sadia

Hemocomponentes homólogos

In vivo

Animais com OCD tibiotársica

Hemocomponentes autólogos

2 ml IA

Preparo hemocomponentes

PRP

150 G/5 min + 800 G/10 min

Descarte 75% e homogeneiza 1h

APP

Tubos com heparina

Incuba a 37°C/24h

300 G/10 min + 900 G/10 min

Filtra

IRAP

Incuba a 37°C/24h

3200 G/20 min

Coleta soro e filtra

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IN VITRO

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Table 1—Median (interquartile [25th to 75th percentile] range) concentrations of PGE₂, IL-1β, TNF-α, IL-10, and IL-1ra in supernatant of equine synovial cell cultures (n = 8 samples) after challenge exposure with LPS for 3 hours and incubation with various treatments for 24 hours.

Treatment	PGE ₂ (pg/mL)	IL-1β (pg/mL)	TNF-α (pg/mL)	IL-10 (pg/mL)	IL-1ra (pg/mL)
Control	4,332.5 ^a (3,683.0–5,805.4)	0 (0–0)	0 (0–0)	0 (0–0.5)	0 ^a (0–7.3)
Phenylbutazone	153.1 ^b (90.2–917.3)	0 (0–0)	0 (0–0)	0 (0–28.2)	0 ^a (0–26.2)
PRP	7,481.1 ^c (6,390.5–9,249.2)	0 (0–0)	0 (0–0)	0 (0–2.3)	1,141.2 ^b (584.7–1,397.4)
IRAP	6,499.5 ^{a,c,d} (0–8,803.6)	135.2 (34.4–168.5)	0 (0–0)	19.2 (0–48.1)	9,603.1 ^c (6,364.7–10,163.4)
APP	4,476.5 ^{a,d} (0–7,100.9)	180.3 (31.4–239.1)	0 (0–0)	18.9 (7.7–52.9)	20,996.1 ^d (19,333.0–25,816.0)
Sodium hyaluronate	5,050.3 ^{a,c,d} (4,777.0–7,147.3)	0 (0–0)	0 (0–0)	0 (0–12.4)	0 ^a (0–18.8)

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Raquel Y. A. Baccarin D

AJVR • Vol 80 • No. 7 • July 2019

IN VIVO

Table 3—Median (interquartile [25th to 75th percentile] range) concentrations of PGE₂, IL-1 β , and IL-1ra and least squares mean (95% confidence interval) concentrations of TNF- α and IL-10 in synovial fluid of osteochondrotic tibiotarsal joints of horses (8 joints/treatment) before (time 0) and 48 hours after arthroscopy and injection of various treatments.

Treatment	PGE ₂ (pg/mL)		IL-1 β (pg/mL)		IL-1ra (pg/mL)		TNF- α (pg/mL)		IL-10 (pg/mL)	
	0 hours	48 hours	0 hours	48 hours	0 hours	48 hours	0 hours	48 hours	0 hours	48 hours
Control	33.9 ^a (23.9 to 52.1)	19.8* (15.5 to 29.9)	2.0 (1.5 to 2.2)	2.1 (1.6 to 2.5)	0 (0 to 0)	1,721* (536 to 3,266)	1.14 (0.34 to 1.94)	1.52 (0.33 to 2.70)	23.9 (-52.7 to 100.0)	33.2 (-54.4 to 120.0)
PRP	15.8 ^a (11.1 to 32.7)	30.3* (19.8 to 33.1)	3.1 (1.7 to 3.6)	2.1 (1.8 to 3.6)	0 (0 to 0)	3,730* (802 to 5,965)	1.59 (1.3 to 1.9)	1.67 (0.84 to 2.5)	47.7 (8.3 to 87.2)	52.4 (-53.4 to 158.0)
IRAP	70.9 ^b (39.8 to 77.5)	29.1* (21.3 to 37.7)	2.5 (1.9 to 2.5)	2.9 (2.6 to 3.2)	0 (0 to 0)	3,229* (1,779 to 5,126)	1.83 (1.13 to 2.53)	1.53 (0.84 to 2.48)	33.1 (-29.3 to 95.6)	30.6 (-17.4 to 78.3)
APP	13.8 ^a (12.5 to 19.0)	18.4 (16.4 to 43.1)	2.7 (2.2 to 4.1)	2.6 (2.4 to 3.5)	0 (0 to 0)	1,827* (292 to 4,487)	1.74 (0.44 to 3.04)	1.89 (1.46 to 2.33)	23.1 (-12.3 to 58.6)	77.1 (-119.0 to 273.0)
Sodium hyaluronate	32.4 ^{a,b} (21.2 to 37.7)	27.5 (16.4 to 38.6)	3.2 (2.5 to 4.1)	3.6 (1.7 to 5.9)	0 (0 to 0)	9,520* (247 to 12,627)	1.55 (0.78 to 2.31)	2.5 (-0.23 to 5.22)	17.4 (-23.5 to 58.4)	29.2 (-39.4 to 97.9)

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Effects of blood-derived products and sodium hyaluronate on equine synovial fluid cells and on synovial fluid from osteochondrotic joints of horses after arthroscopy and administration of treatment

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IN VIVO

Table 4—Median (interquartile [25th to 75th percentile] range) concentrations of chondroitin sulfate and hyaluronic acid and percentage of high-molecular-weight (HMW) hyaluronic acid in synovial fluid of osteochondrotic tibiotarsal joints of horses (8 joints/treatment) before and 48 hours after arthroscopy and injection of various treatments.

Treatment	Chondroitin sulfate ($\mu\text{g/mL}$)		Hyaluronic acid ($\mu\text{g/mL}$)		HMW hyaluronic acid (%)	
	0 hours	48 hours	0 hours	48 hours	0 hours	48 hours
Control	75.4 (40.6–136.7)	195.8* (88.6–356.4)	676.0 (419.0–744.9)	802.7 ^{a,b} (326.9–877.3)	74.0 (62.2–87.0)	45.5* (14.7–61.2)
PRP	38.0 (23.9–58.2)	68.9* (61.2–164.4)	377.6 (267.6–630.7)	390.4 ^a (241.8–583.9)	80.0 (75.0–89.0)	54.0* (35.0–82.0)
IRAP	40.5 (34.1–66.8)	109.4* (74.0–165.1)	288.2 (193.0–426.2)	206.5 ^c (174.5–247.9)	77.0 (63.0–81.0)	57.7 (39.5–63.0)
APP	65.5 (50.7–103.2)	181.0* (127.4–382.6)	541.6 (309.2–609.4)	406.2 ^{a,b} (239.9–605.4)	79.0 (38.5–90.3)	43* (29.3–60.3)
Sodium hyaluronate	47.3 (19.6–53.1)	159.9* (135.0–180.7)	492.2 (476.4–577.5)	584.1 ^b (526.7–664.5)	83.5 (62.7–91.5)	51.5* (24.7–71.5)

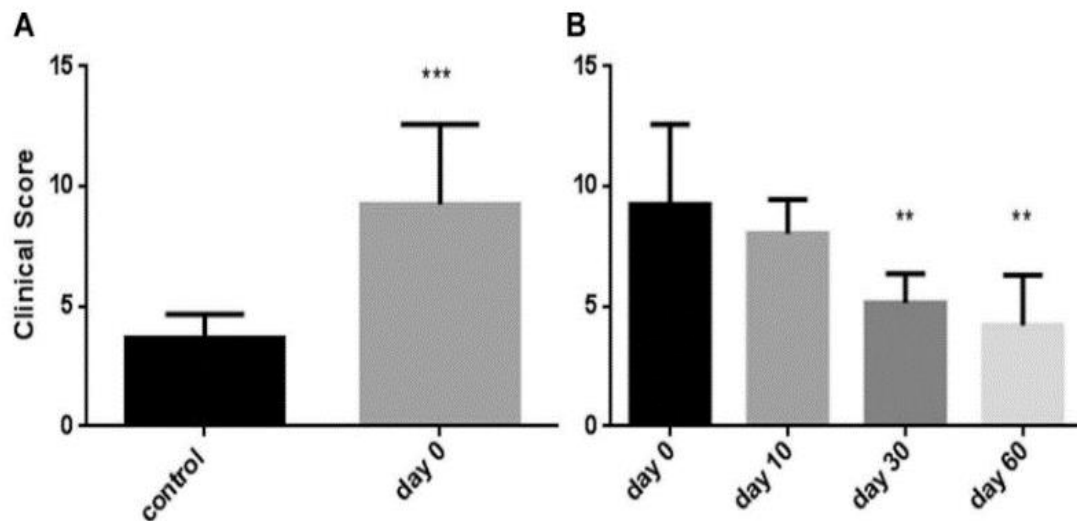


Original Research

Treatment With Platelet Lysate Inhibits Proteases of Synovial Fluid in Equines With Osteoarthritis

Gustavo Perrone^a, Yael Lastra^b, Camilo González^a, Nicolás Caggiano^b, Rubén Giménez^a, Román Pareja^b, Emilio De Simone^{b,*}

Escore clínico animais



A: controle x tratados, dia 0

B: tratados, dia 0 e pós tratamento

PL em OA

23 cavalos esporte (T) + 21 sadios (C)

PRP

1000 G/10 min + 1500 G/10 min

1 ml pellet

3 ciclos congelamento/descongelamento

Contagem plaquetária

400-700 × 10³ plaquetas/μL

1 ml IA → única

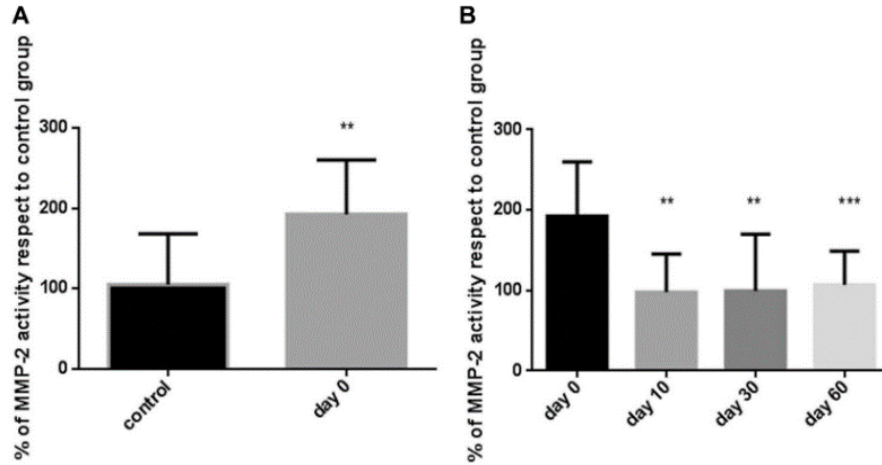


Original Research

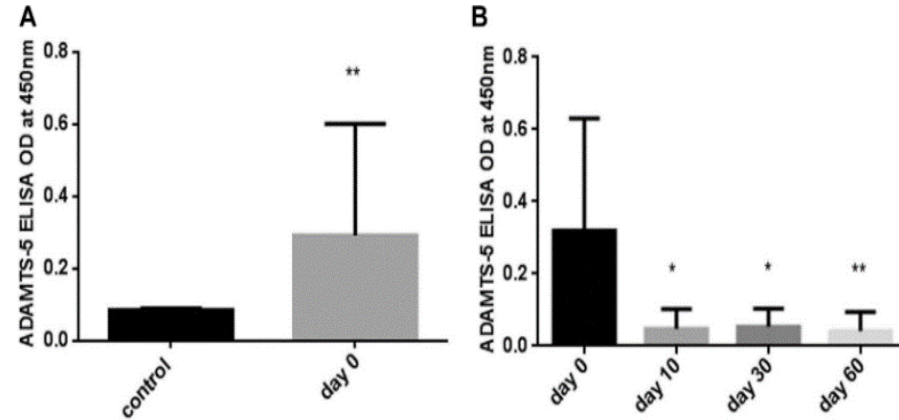
Treatment With Platelet Lysate Inhibits Proteases of Synovial Fluid in Equines With Osteoarthritis

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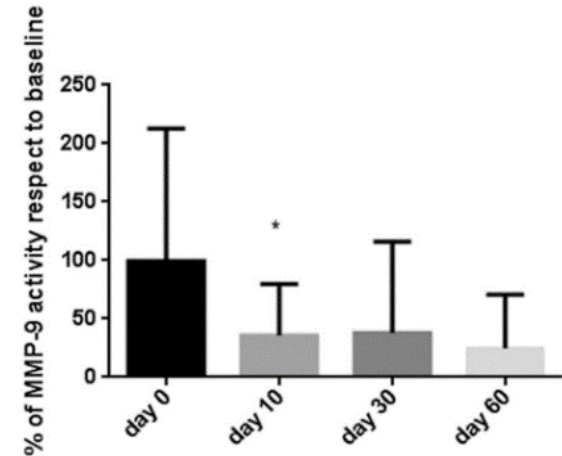
Atividade de MMP-2



Mensuração ADAMTS



Atividade de MMP-9



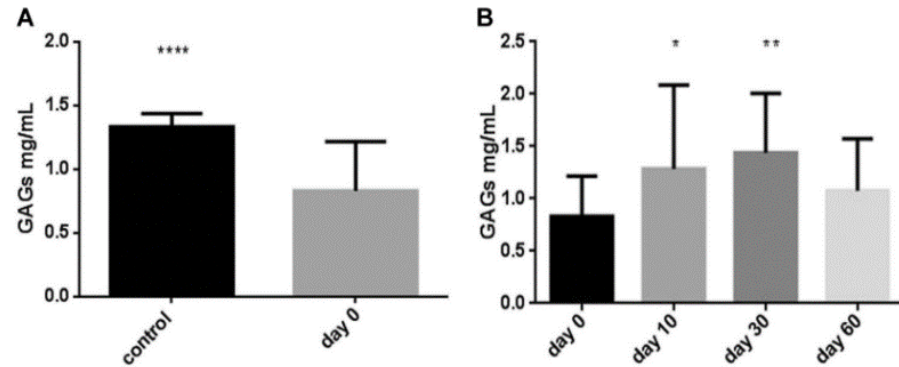
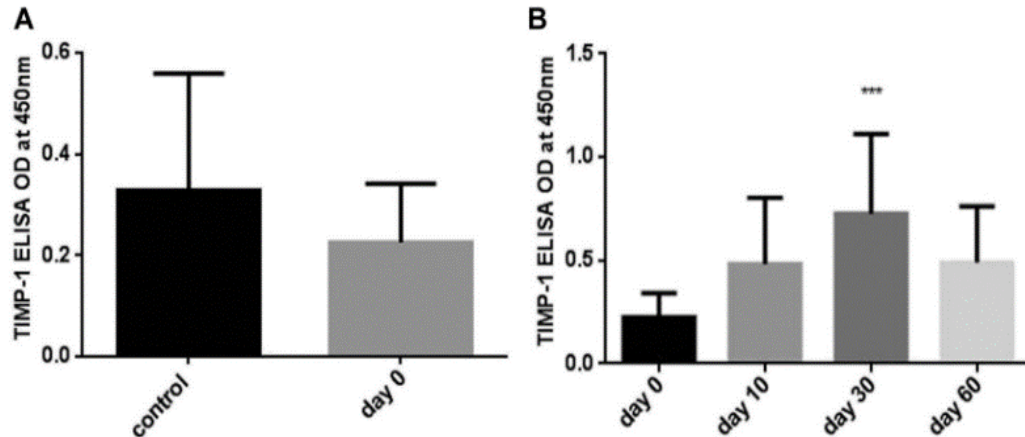


Original Research

Treatment With Platelet Lysate Inhibits Proteases of Synovial Fluid in Equines With Osteoarthritis

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Mensuração TIMP-1



Mensuração GAGs

Considerações dos autores

PL alivia dor e sinais clínicos em OA

Sem reações adversas

↓ MMP-9

Inibição de recrutamento de leucócitos,

Ação de TGF-B1 e IGF

↑ TIMP

TGF-B1

↑ GAGs

Deterioração articular

Clinical findings, synovial fluid cytology and growth factor concentrations after intra-articular use of a platelet-rich product in horses with osteoarthritis



PRP IA: sadio e OA

5 sadios x 5 OA

PRP

Sistema de filtração

Concentração

Plaquetária 4.7x

Leucocitária 2.1x

Avaliação clínica

Group	Control	OA
OA scale (0–3)	0 ± 0	1.80 ± 0.83
Synovial effusion score (0–3)		
Day 0	0.00 ± 0.00**	1.00 ± 1.22**
Day 1	1.00 ± 0.00*	1.40 ± 0.89
Day 2	1.00 ± 0.00*	1.60 ± 0.54
Day 5	0.60 ± 0.54	0.80 ± 0.83
Day 21	0.60 ± 0.54	1.00 ± 0.70
Day 56	0.00 ± 0.00	0.40 ± 0.89
Flexion score (0–3)		
Day 0	0.00 ± 0.00	0.20 ± 0.44
Day 1	0.40 ± 0.54	0.40 ± 0.54
Day 2	0.00 ± 0.00	0.20 ± 0.44
Day 5	0.00 ± 0.00	0.20 ± 0.44
Day 21	0.00 ± 0.00	0.00 ± 0.00
Day 56	0.00 ± 0.00	0.00 ± 0.00
Periarticular signs (yes/no)		
Day 0	0/5	1/4
Day 1	5/0	3/2
Day 2	5/0	5/0
Day 5	3/2	2/3
Day 21	3/2	2/3
Day 56	0/5	0/5

Clinical findings, synovial fluid cytology and growth factor concentrations after intra-articular use of a platelet-rich product in horses with osteoarthritis



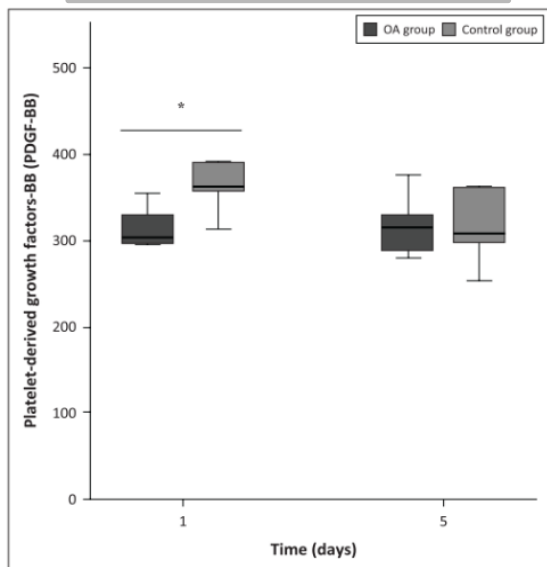
Análise do líquido sinovial

Day	NCC (cells/ μ L)	Neutrophils (%)	TP (g/L)	SAA (mg/L)	PDGF-BB (pg/mL)	TGF- β 1 (pg/mL)
Day 0						
Control	111.60 \pm 39.89	1.60 \pm 2.45	15.48 \pm 6.31	0.00 \pm 0.00	-	-
OA	87.40 \pm 53.64	5.40 \pm 8.50	14.22 \pm 2.56	0.00 \pm 0.00	-	-
Day 1						
Control	22940.00 \pm 11103.28 ^{*,****}	83.40 \pm 2.70 ^{*,****}	46.64 \pm 11.11 [*]	0.00 \pm 0.00	390.47 \pm 82.15 ^{**,***}	4021.27 \pm 783.00 ^{**,***,****}
OA	20464.00 \pm 12055.93 ^{*,****}	71.20 \pm 5.40 ^{*,****}	39.06 \pm 7.10 [*]	0.00 \pm 0.00	302.27 \pm 47.44 ^{**}	2792.48 \pm 615.46 ^{**,***,****}
Day 2						
Control	13212.00 \pm 3413.46 [*]	64.00 \pm 4.00 ^{**,**}	30.18 \pm 11.55 [*]	0.00 \pm 0.00	-	-
OA	7372.00 \pm 6122.10	38.80 \pm 14.32 ^{**,**}	22.46 \pm 5.90 [*]	0.00 \pm 0.00	-	-
Day 5						
Control	3654.00 \pm 2037.59 ^{***}	14.80 \pm 11.86 ^{****}	20.56 \pm 8.02	0.95 \pm 2.14	316.42 \pm 45.69 ^{***}	851.73 \pm 351.82 ^{***,****}
OA	1660.40 \pm 1250.72 ^{***}	8.20 \pm 15.54 ^{****}	16.54 \pm 6.09	0.00 \pm 0.00	318.06 \pm 37.82	678.35 \pm 289.58 ^{***,****}
Day 21						
Control	207.60 \pm 49.90	2.60 \pm 1.67	17.14 \pm 6.61	0.00 \pm 0.00	-	-
OA	213.00 \pm 123.80	5.20 \pm 6.97	12.18 \pm 3.18	0.00 \pm 0.00	-	-
Day 56						
Control	224.80 \pm 71.94	10.80 \pm 11.16	14.62 \pm 4.51	0.00 \pm 0.00	-	-
OA	95.60 \pm 71.40	4.20 \pm 6.79	13.78 \pm 3.26	0.00 \pm 0.00	-	-

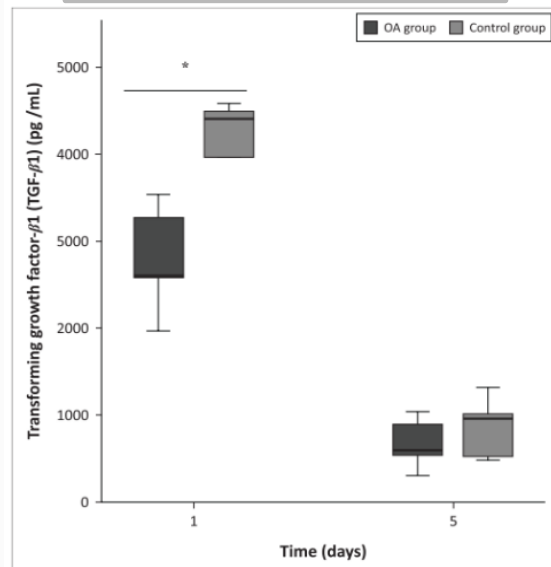
Clinical findings, synovial fluid cytology and growth factor concentrations after intra-articular use of a platelet-rich product in horses with osteoarthritis



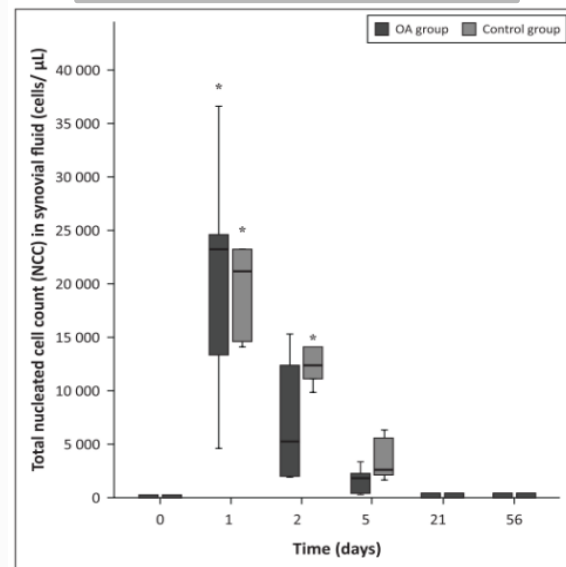
Mensuração PDGF-BB



Mensuração TGF-β1



Mensuração NCC



RESEARCH

Open Access



A safety evaluation of allogeneic freeze-dried platelet-rich plasma or conditioned serum compared to autologous frozen products equivalents in equine healthy joints

Livia Camargo Garbin^{1,2}, Erin K. Contino³, Christine S. Olver⁴ and David D. Frisbie^{3*}

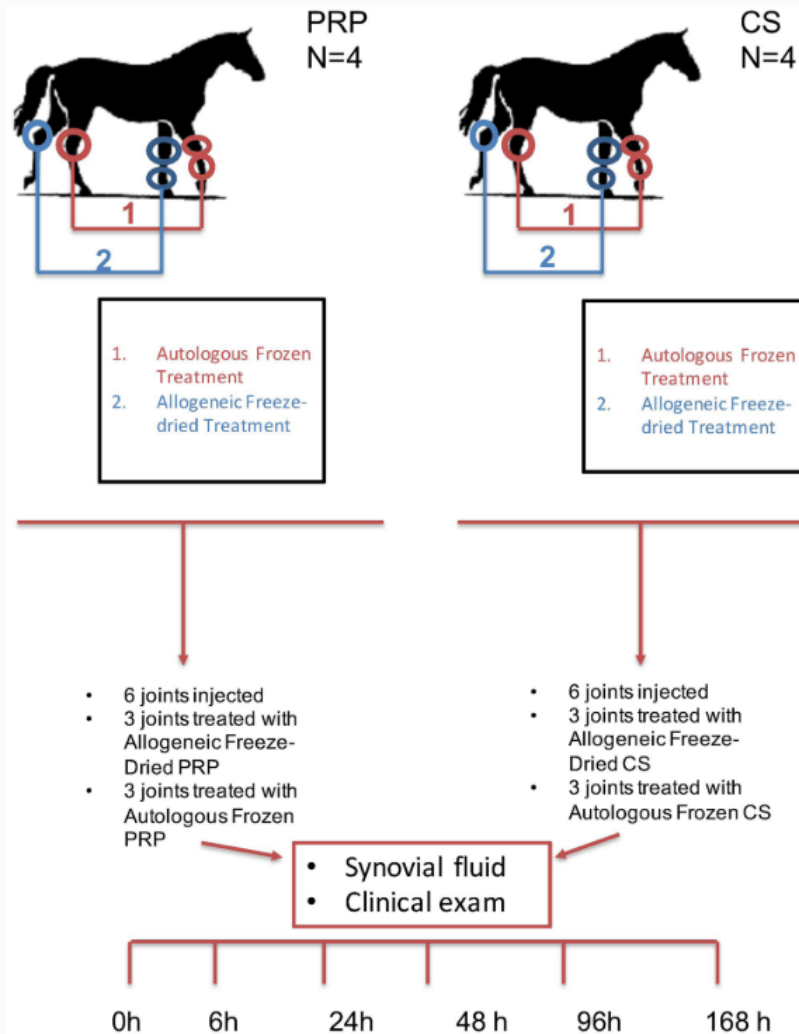
Segurança hemocomponentes liofilizados PRP/SCA

Autólogo: congelamento

Alógeno: secagem de fração dos autólogos

Aplicação: 4 doadores/fração + RL

Animal: próprio controle



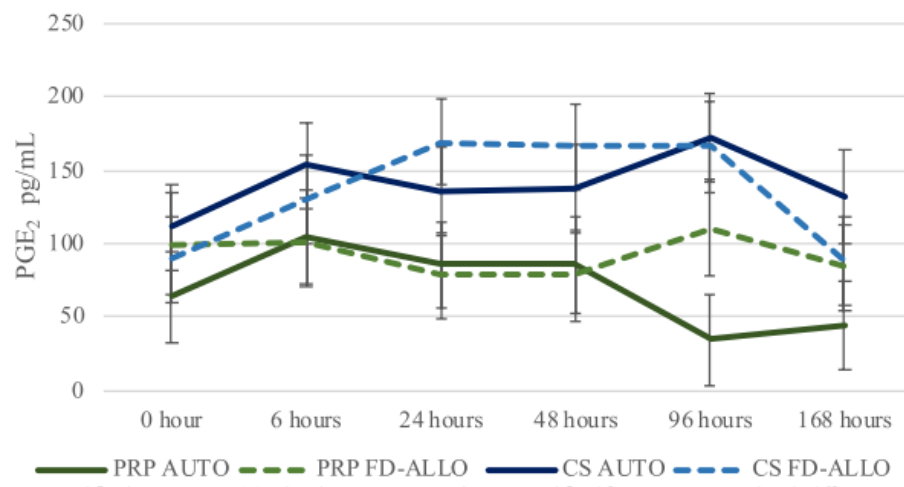
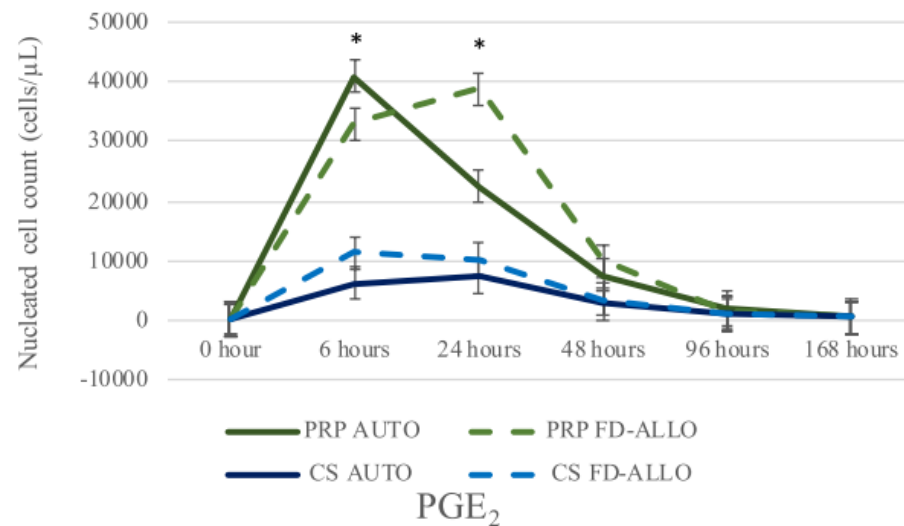
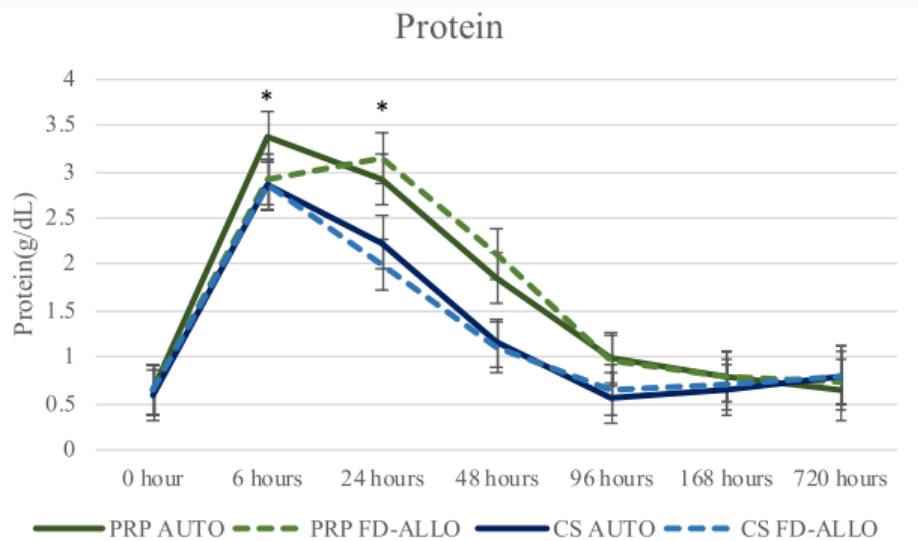
RESEARCH

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A safety evaluation of allogeneic freeze-dried platelet-rich plasma or conditioned serum compared to autologous frozen products equivalents in equine healthy joints

Livia Camargo Garbin^{1,2}, Erin K. Contino³, Christine S. Olver⁴ and David D. Frisbie^{3*}



A Platelet-Rich Plasma-Derived Biologic Clears *Staphylococcus aureus* Biofilms While Mitigating Cartilage Degeneration and Joint Inflammation in a Clinically Relevant Large Animal Infectious Arthritis Model

Jessica M. Gilbertie^{1,2}, Thomas P. Schaefer^{3†}, Julie B. Engiles^{3,4}, Gabriela S. Seiler⁵, Bennett L. Deddens⁵, Alicia G. Schubert¹, Megan E. Jacob^{2,6}, Darko Stefanovski³, Gordon Ruthel⁴, Noreen J. Hickok⁷, Devorah M. Stowe⁶, Alexa Frink¹ and Lauren V. Schnabel^{1,2†}

Indução:

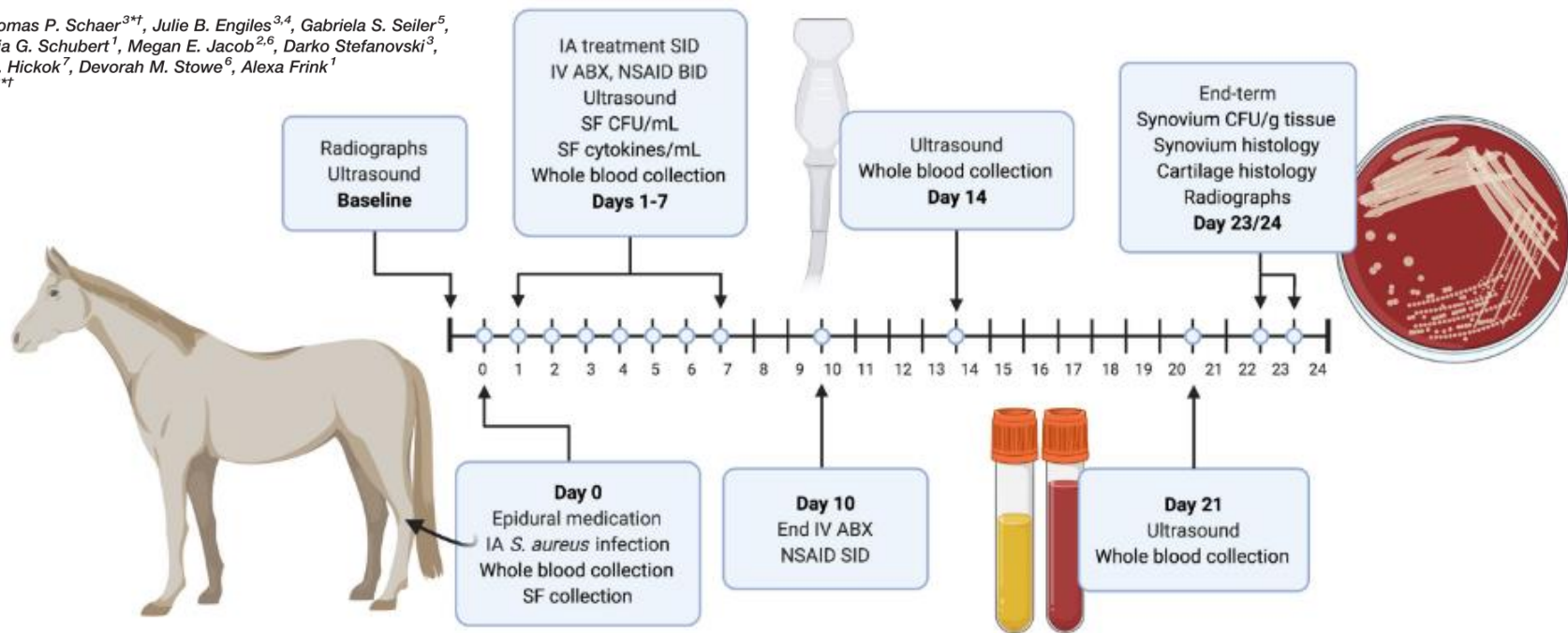
Staphylococcus aureus 1x10⁶ CFU

Tratamento:

24h pós-indução

500mg amicacina + 5mL salina

500mg amicacina + 5mL BIO-PLY

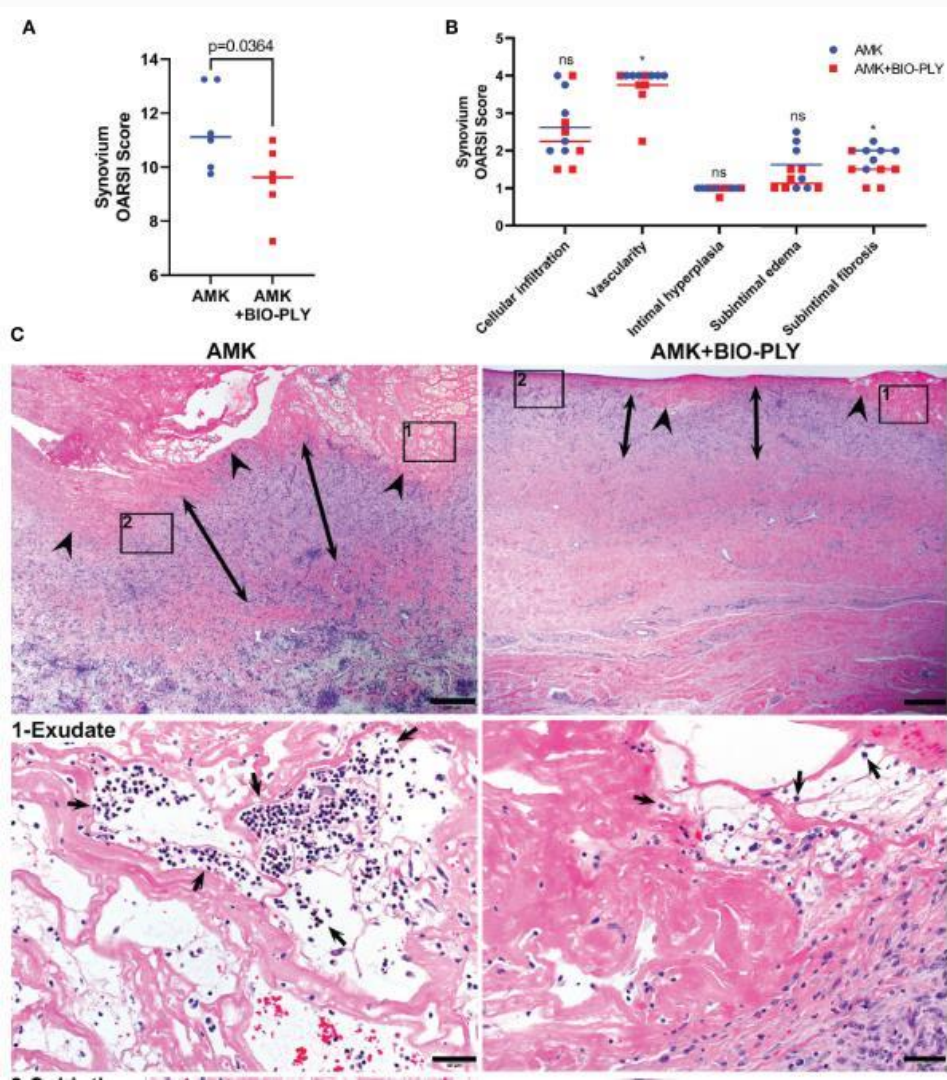


A Platelet-Rich Plasma-Derived Biologic Clears *Staphylococcus aureus* Biofilms While Mitigating Cartilage Degeneration and Joint Inflammation in a Clinically Relevant Large Animal Infectious Arthritis Model

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Bio-PLY + ampicilina

Reduziu perda de proteoglicano cartilágineo associado à infecção





The effect of platelet rich plasma combined with microfractures on the treatment of chondral defects: an experimental study in a sheep model

G. Milano †, E. Sanna Passino †, L. Deriu †, G. Careddu †, L. Manunta †, A. Manunta †, M.F. Saccomanno †, C. Fabbriciani †

PRP + microfraturas

15 ovelhas

Lesão condral 8 mm

Tratamento 12 m pós indução

4 perfurações (MF)

1.5 mm x 5 mm

Eutanásia 6 m pós tto

Grupos

G1: microfraturas (MF)

G2: MF + PRP gel + cola

G3: MF + PRP líquido

PRP

2.400 rpm/3 min

3.000 rpm/12 min

Gel

6 ml PRP

2 ml gluconato de Cálcio 10%

2 ml cola de fibrina

Concentração

$4 \times 1.415 \times 10^3$ plaquetas/ μ L

Avaliação macro

A (G1)

Tecido de reparação delgado

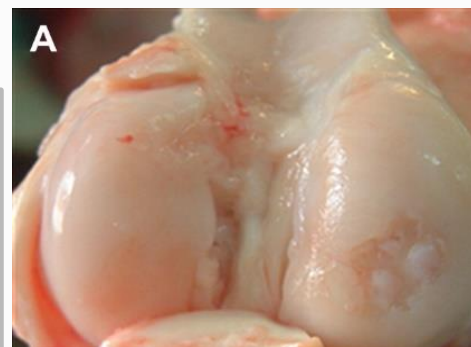
B (G2)

Similar à cartilagem sadia

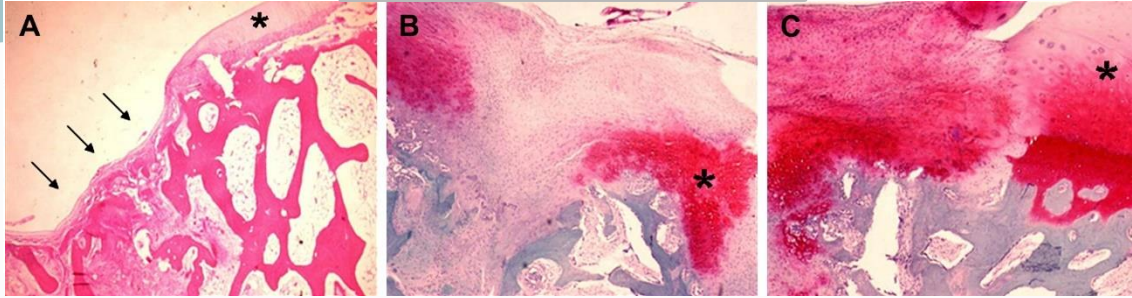
C (G3)

Cobre o defeito

Delgado e irregular

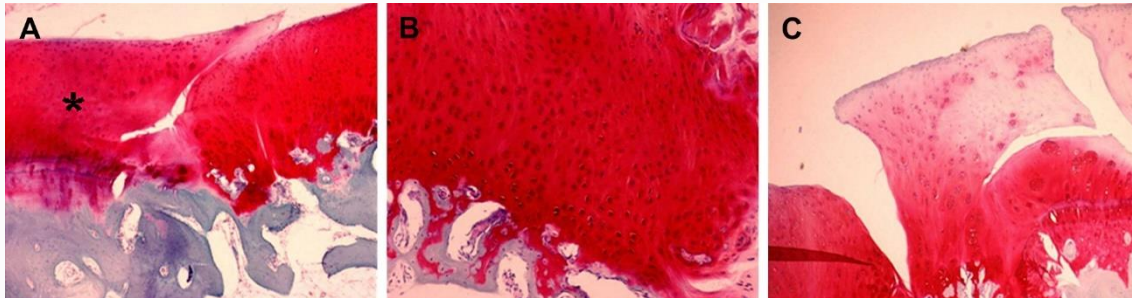


Avaliação histológica



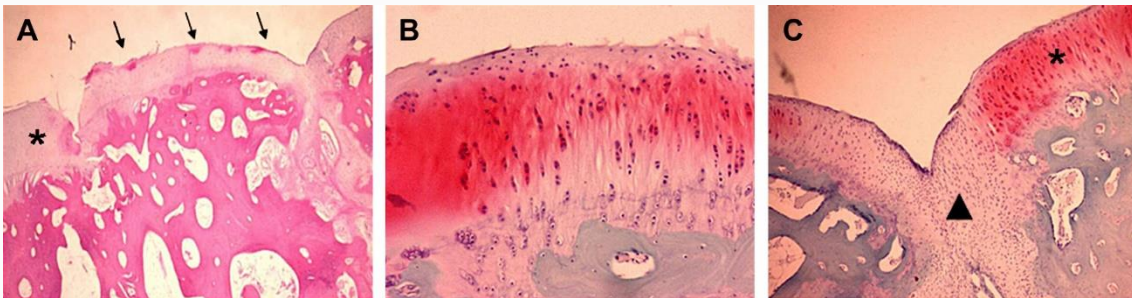
G1

A: tecido de reparo delgado
 B: MF com células arredondadas, MEC fibrosa e mal organizada
 C: tecido de reparo parcialmente integrado ao sadio



G2

A: espessura semelhante à sadio (*), zona de transição
 B: poucas células arredondadas, intensa coloração Safranina
 C: aglomerados de células tipo condrócitos em zona de transição



G3

A: fina camada, cobre o defeito
 B: células tipo condrócitos organizadas em colunas
 C: tecido fibrocartilaginoso (seta), cartilagem normal com intensa proliferação celular (*)



The effect of platelet rich plasma combined with microfractures on the treatment of chondral defects: an experimental study in a sheep model

G. Milano †✉, E. Sanna Passino †, L. Deriu †, G. Careddu †, L. Manunta †, A. Manunta †, M.F. Saccomanno †, C. Fabbriciani †

Considerações dos autores

Potencial eficácia no reparo de defeito condral

TGF-β1, BMP-2, FGF

Sem inflamação ou reação imune

Não houve formação de tecido hialino

Pouca Safranina

Atividade celular limitada

MEC de baixa qualidade

PRP

Gel + cola de fibrina

Melhores resultados

Não comparou efeitos isolados

Propriedades histológicas,
macroscópicas e mecânicas:

MF < PRP líquido < PRP gel

Treatment of canine osteoarthritis with allogeneic platelet-rich plasma: review of five cases

José Catarino,¹ Pedro Carvalho,^{2,3} Sara Santos,¹ Ângela Martins,^{1,4} and João Requicha^{1,5,*}

Animal	Breed	Age (years)	Joint
1	Mixed breed	12	Knee
2	Labrador Retriever	10	Tibiotarsal
3	Labrador Retriever	13	Knee
4	German Shepherd	14	Elbow
5	German Pointer	6	Carpal

OA

Diagnóstico imagem

Refratários a tratamentos

Medicamentosos

Fisioterápicos

6 meses sem tratamento prévio

PRP

Alogênico

Dupla centrifugação

Sem detalhes do protocolo

1×10^6 plaquetas/ μL

Treatment of canine osteoarthritis with allogeneic platelet-rich plasma: review of five cases

José Catarino,¹ Pedro Carvalho,^{2,3} Sara Santos,¹ Ângela Martins,^{1,4} and João Requicha^{1,5,*}

Grau de claudicação

Animal	Day 0	Day 30	Day 60	Day 90
1	Grade III	Grade II	Grade II	Grade I
2	Grade II	Grade II	Grade I	No lameness
3	Grade IV	Grade III	Grade II	Grade II
4	Grade III	Grade III	Grade II	Grade II
5	Grade II	Grade II	Grade I	No lameness

Escore de dor

Animal	Day 0	Day 30	Day 60	Day 90
1	Intense	Moderate	Mild	Painless
2	Moderate	Mild	Mild	Painless
3	Intense	Moderate	Mild	Painless
4	Severe	Intense	Mild	Mild
5	Moderate	Mild	Mild	Mild

Animal	Breed	Age (years)	Joint
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3	Labrador Retriever	13	Knee
4	German Shepherd	14	Elbow
5	German Pointer	6	Carpal

The background features abstract, organic shapes in shades of orange and teal. A large orange shape is in the top left, and a teal shape is in the bottom right. A white space separates them, containing the text. A small orange oval is positioned at the bottom center, overlapping the teal shape.

Evidências
científicas

The Role of Platelet-Rich Plasma in Cartilage Pathology: An Updated Systematic Review of the Basic Science Evidence

Michael P. Fice, B.A., J. Chance Miller, B.A., Robert Christian, M.D., Charles P. Hannon, M.D., Niall Smyth, M.D., Christopher D. Murawski, B.S., Brian J. Cole, M.D., M.B.A., and John G. Kennedy, M.D., F.R.C.S.



Critérios de inclusão

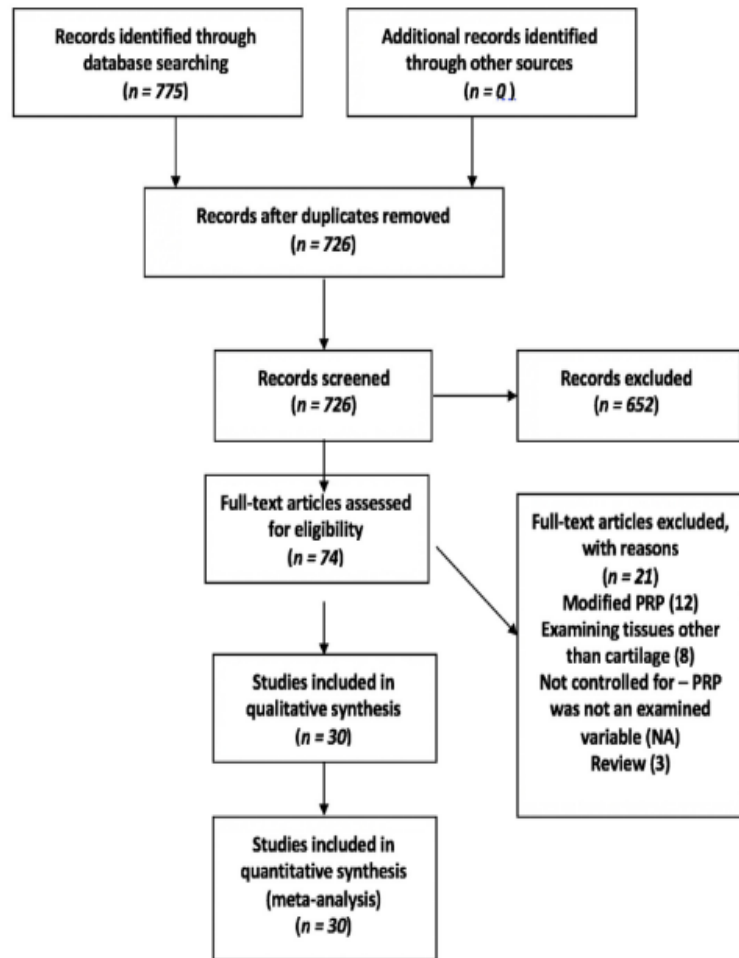
PRP em condrócitos e cartilagem
Excetuou discos intervertebrais e meniscos
PRP sozinho, sem reagente ou material
Revisão por pares e em inglês
Grupo controle

Identification

Screening

Eligibility

Included



The Role of Platelet-Rich Plasma in Cartilage Pathology: An Updated Systematic Review of the Basic Science Evidence

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Diminuição inflamação *in vitro*
 Melhora histologia *in vivo*
 Melhora produção de MEC
 Proliferação de condrócitos
 Reduz MMP-3 e 13

Ação em processo inflamatório pouco elucidada
 Metodologia
 Parâmetros avaliados
 Padronização de técnica
 Caracterização do PRP



Table 3. Platelet-Rich Plasma Cytology Reporting in Basic Science Studies on Cartilage Repair Published Since 2011

Component	Reported Studies, n (%)	Studies Not Reporting, n (%)
Platelet count	21 (70.0)	9 (30.0)
WBC count	9 (30.0)	21 (70.0)
RBC count	2 (6.7)	28 (93.3)
Platelet + WBC + RBC count	2 (6.7)	28 (93.3)
Platelet + WBC count	9 (30.0)	21 (70.0)
Platelet count without WBCs or RBCs	12 (40.0)	18 (60.0)
No reference to Platelet, WBC or RBC count	9 (30.0)	21 (70.0)

RBC, red blood cell; WBC, white blood cell.

Platelet-rich plasma versus hyaluronic acid in the treatment of knee osteoarthritis

A meta-analysis

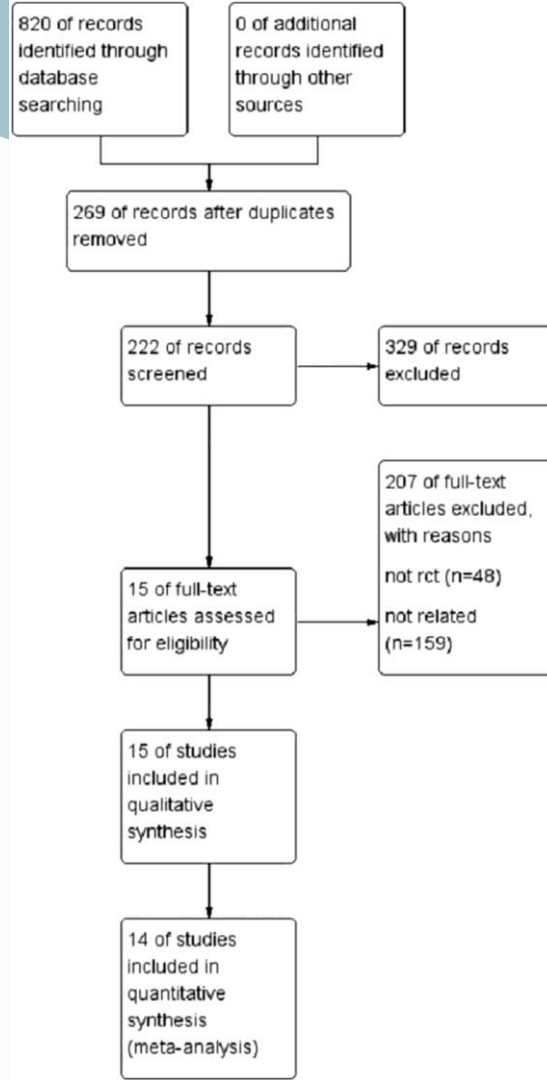
Zehan Chen, BS^a, Chang Wang, MD^a, Di You, MD^b, Shishun Zhao, PhD^a, Zhe Zhu, PhD^c, Meng Xu, MD^{d,*}

Critérios de inclusão

- OA de joelho,
- PRP (GT) HA (GC),
- RCTs,
- Citar estudos envolvendo indicadores VAS, IKDC, WOMAC, KOOS
- Citar efeitos adversos

Critérios de exclusão

- Uso de animal ou cadáver,
- Impossibilidade de extrair ou converter dados válidos,
- Estudos retrospectivos, revisões ou papers de conferência



OPEN

Platelet-rich plasma versus hyaluronic acid in the treatment of knee osteoarthritis

A meta-analysis

Zehan Chen, BS^a, Chang Wang, MD^a, Di You, MD^b, Shishun Zhao, PhD^a, Zhe Zhu, PhD^c, Meng Xu, MD^{d,*}

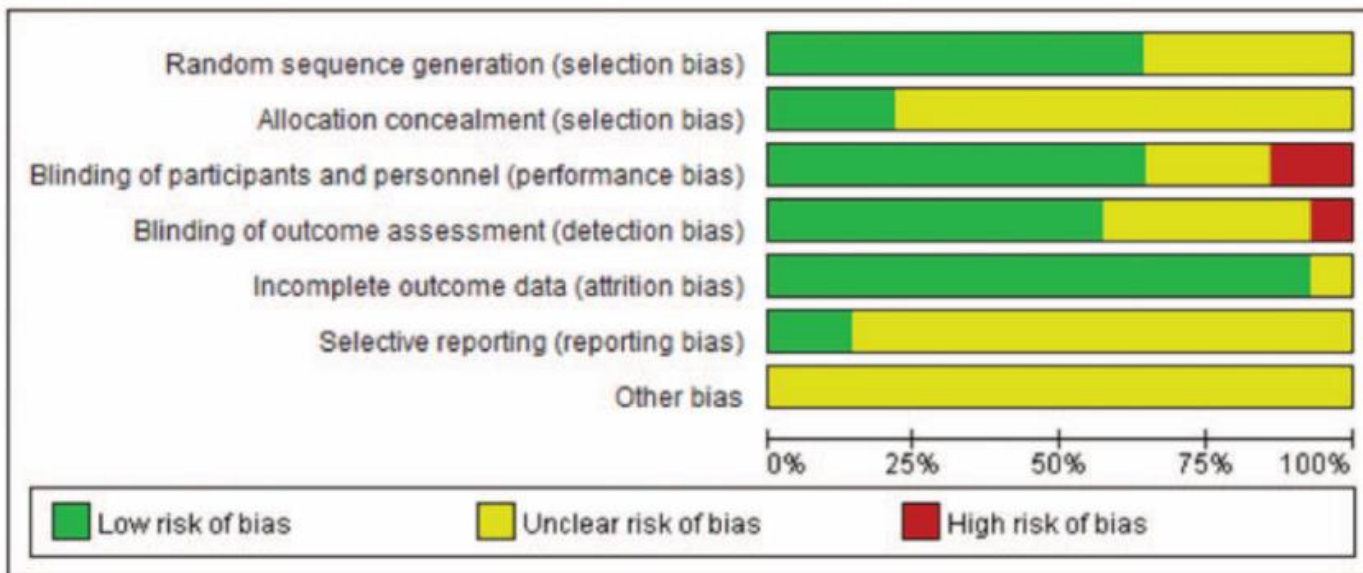
Conclusão

PRP > AH

Redução da dor

Melhora da função articular

Tratamento conservativo da OA



RESEARCH ARTICLE

Open Access

Platelet-rich plasma in orthopedic therapy: a comparative systematic review of clinical and experimental data in equine and human musculoskeletal lesions

Patrícia M Brossi, Juliana J Moreira, Thaís SL Machado and Raquel YA Baccharin*

Preparation method		In vivo models or clinical studies	
Commercial	System used	Injection	Location (intra-articular, intra-lesional, peri-lesional, etc.)
	Detail any modifications to manufacturer protocol		Volume injected
	Detail any manufacturer options (if any) and option selected (i.e. final volume of PRP)		Ultrasound guidance (yes or no)
Manual	Volume of blood collected		Timing of injection relative to injury or surgery
	Type and final concentration of anticoagulant		Re-dosing interval
	Centrifugation speed in gravitational (<i>g</i>) force; (rpm are not appropriate—results in variable <i>g</i> force depending on centrifuge radius)		Post-injection rehabilitation
	Centrifugation time		Prior or concurrent treatments
	Number of spin cycles	Complications	Describe major and minor
	Final volume of PRP		Detail number affected
			Duration post-treatment
	Outcome measures	As appropriate to tissue/injury of study	
Characterization of PRP			
Hematology	Platelet, leukocyte, and red blood cell concentration in blood and PRP		
	Consider reporting fibrinogen concentration		
Growth factors	Consider reporting, particularly for new protocols that have not been validated to increase growth factor concentration		
Storage	Fresh or frozen-thawed		
Activation			
Yes	Agent (i.e. calcium chloride, autologous thrombin, bovine thrombin, etc.)		
	Agent concentration		
	Time to clot		
	Releasate only or entire clot used		
No			

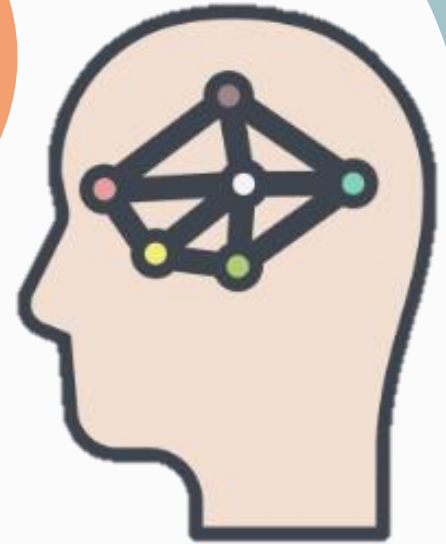
Perspectivas futuras

Explorar possibilidades hemocomponentes

- Vesículas extracelulares
- Terapias acelulares

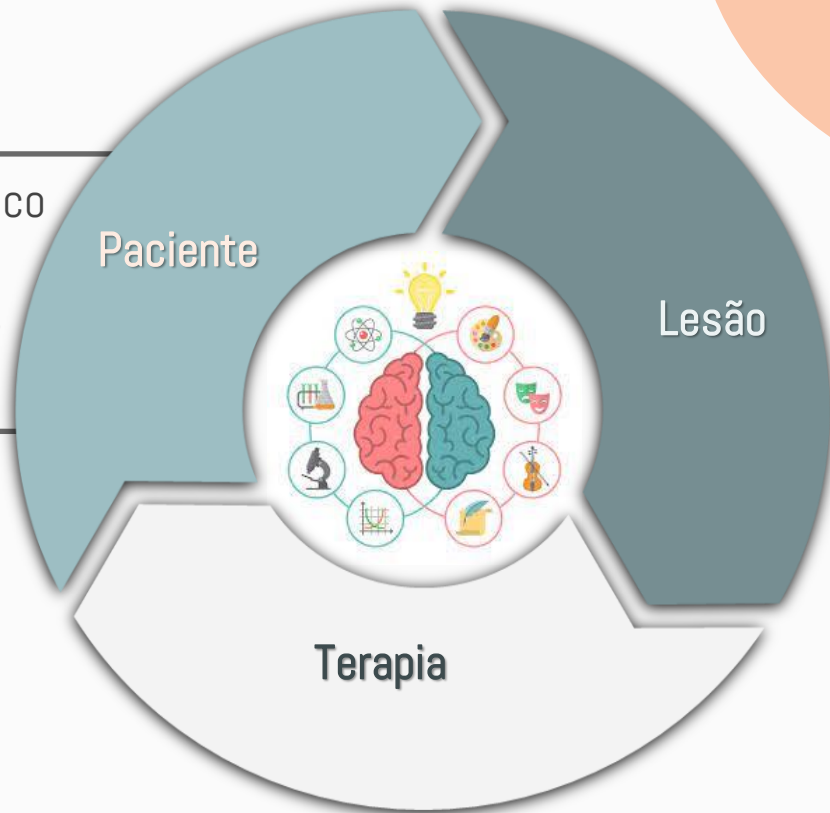
Associação de terapias regenerativas

Otimizar efeitos



Considerações finais

Compreender potencial terapêutico
Considerar individualidade
Medicina baseada em evidências
Consistência



Obrigada!

Grupo de Pesquisa Aplicada em Medicina Equina

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