

# PLASMA RICO EM PLAQUETAS

## PERSPECTIVAS DO USO EM ORTOPEDIA E MEDICINA REGENERATIVA

*Dr José Fabio Lana*



# O QUE É

**PRP** (PLASMA RICO EM PLAQUETAS) ?



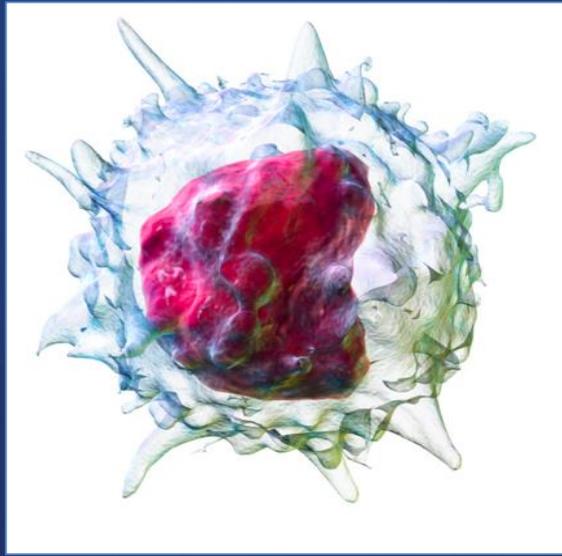
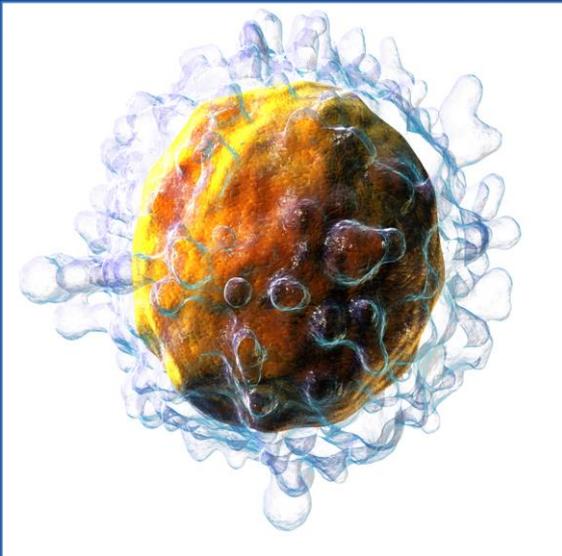
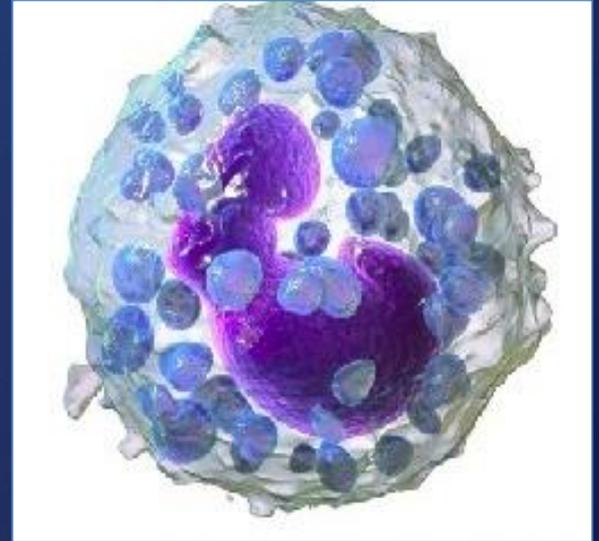
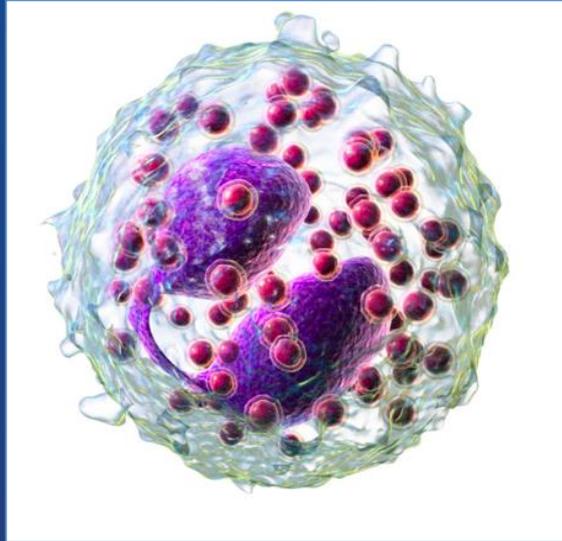
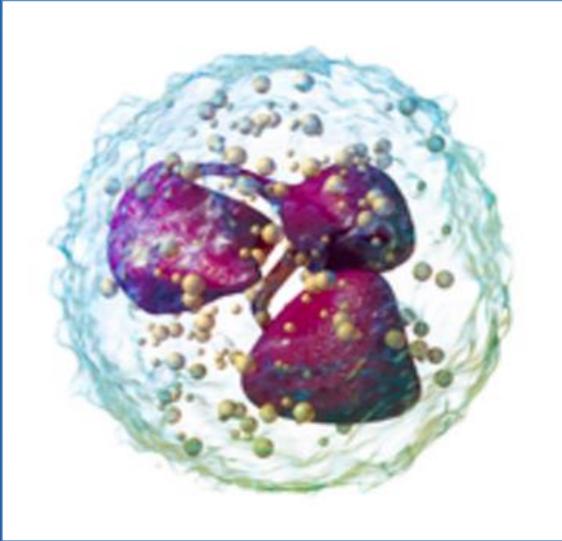
# O QUE É

## **PRP** (Platelet Rich Plasma) ?

**É o plasma com elevada concentração de plaquetas (3-5 x o valor basal), derivado da centrifugação do sangue autólogo**

# Cellular Components





# QUAIS SÃO OS PRINCIPAIS COMPONENTES E CÉLULAS ALVO DO PRP?

## Chemokines/cytokines

- IL-1 $\beta$
- PBP
- PF4

PRP

## Proteases/antiproteases

- $\alpha$ -2-macroglobulin
- ADAMTSs
- MMPs

## Small molecules

- Ca<sup>2+</sup>
- ADP
- Serotonin
- Epinephrine
- Histamine

## Growth factors

- CTGF
- HGF
- IGF
- PDGF
- VEGF
- TGF- $\beta$
- FGF-2

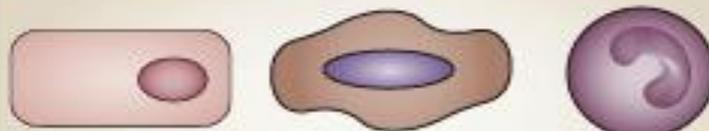
Connective Tissue Growth Factor  
Hepatocyte Growth Factor  
Insulin-like Growth Factor  
Platelet Derived Growth Factor  
Vascular Endothelial Growth Factor  
Transforming Growth Factor  $\beta$   
Fibroblastic Growth Factor

## Cartilage/bone



Chondrocyte Osteoblast

## Vascular

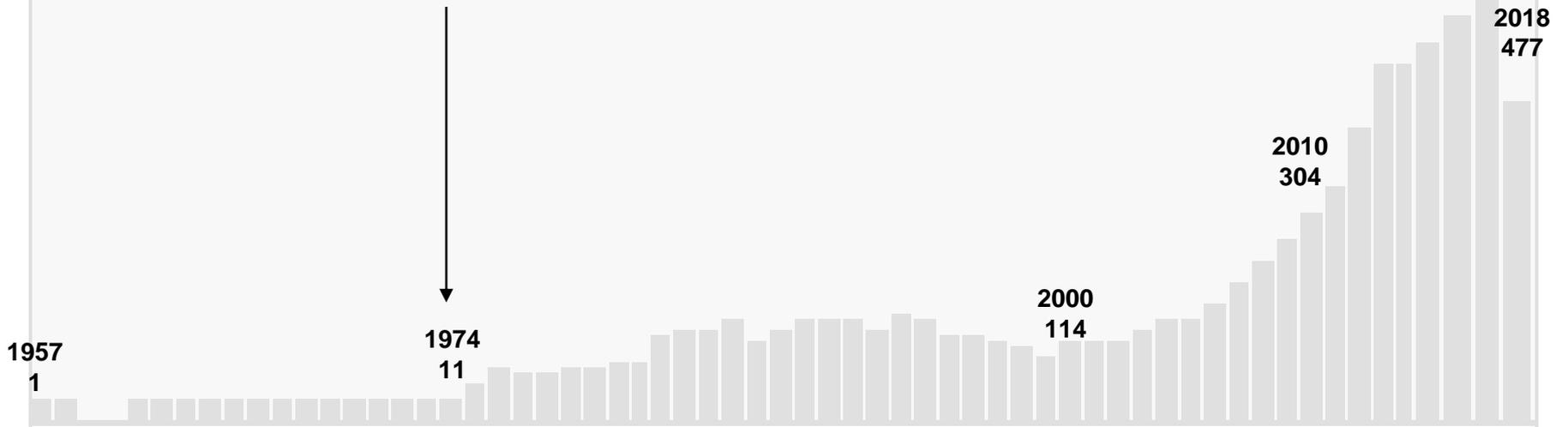


Endothelial cell  
Circulating mesenchymal cell  
Monocyte

## Synovium



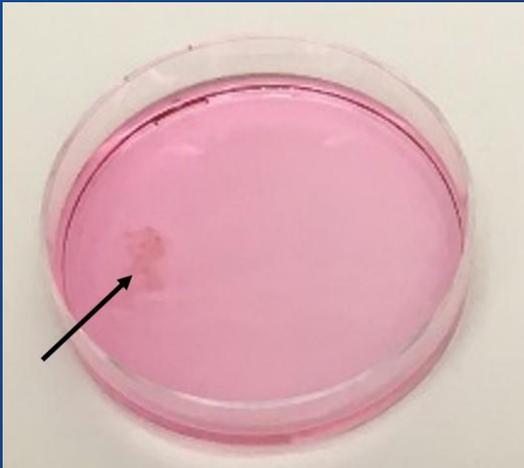
Macrophage Synoviocyte



# HISTÓRIA DA DESCOBERTA DO EFEITO DO PRP NA PROLIFERAÇÃO CELULAR

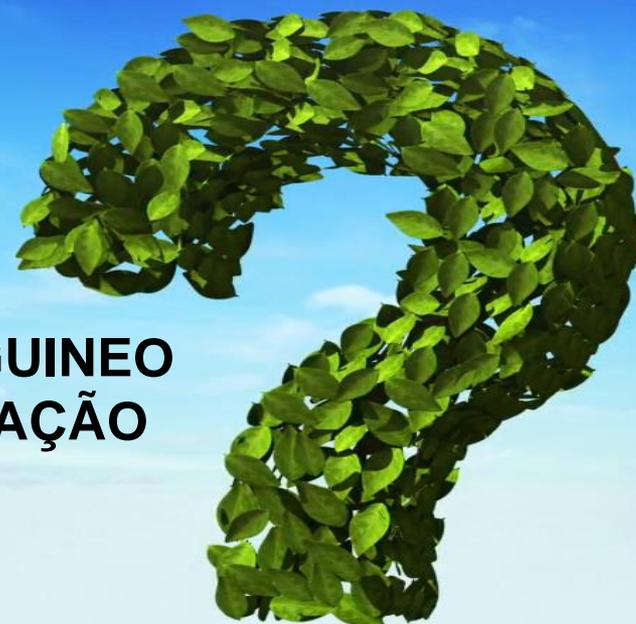
## Década de 70

Pesquisadores avaliaram a proliferação de células do músculo liso em cultura para investigar porque essas células se acumulam na aterosclerose



Observaram que as células só proliferavam na cultura na presença do soro sanguíneo

**QUAL COMPONENTE DO SORO SANGUINEO  
ERA RESPONSÁVEL PELA PROLIFERAÇÃO  
CELULAR EM CULTURA**



# DEMONSTRARAM QUE ERA UM COMPONENTE DAS PLAQUETAS.....

*Proc. Nat. Acad. Sci. USA*  
Vol. 71, No. 4, pp. 1207-1210, April 1974

## **A Platelet-Dependent Serum Factor That Stimulates the Proliferation of Arterial Smooth Muscle Cells *In Vitro***

**(primate/cell culture/atherosclerosis)**

RUSSELL ROSS\*, JOHN GLOMSET†, BEVERLY KARIYA\*, AND LAURENCE HARKER‡

\* University of Washington, School of Medicine, Department of Pathology, Seattle Wash. 98195; † University of Washington, School of Medicine, Department of Medicine, and Regional Primate Research Center, Seattle, Wash. 98195; and ‡ University of Washington, School of Medicine, Department of Medicine, Seattle, Wash. 98195

*Communicated by Sidney Udenfriend, November 21, 1973*

## 1978 - Propuseram o termo "Platelet derived growth factor" (PDGF)

Circ Res. 1978 Mar;42(3):402-9.

**Studies of the release from human platelets of the growth factor for cultured human arterial smooth muscle cells.**

Witte LD, Kaplan KL, Nossel HL, Lages BA, Weiss HJ, Goodman DS.

## 1979 - Demonstraram que os fatores de crescimento eram liberados a partir dos $\alpha$ -grânulos

Blood. 1979 Jun;53(6):1043-52.

**Platelet alpha granules contain a growth factor for fibroblasts.**

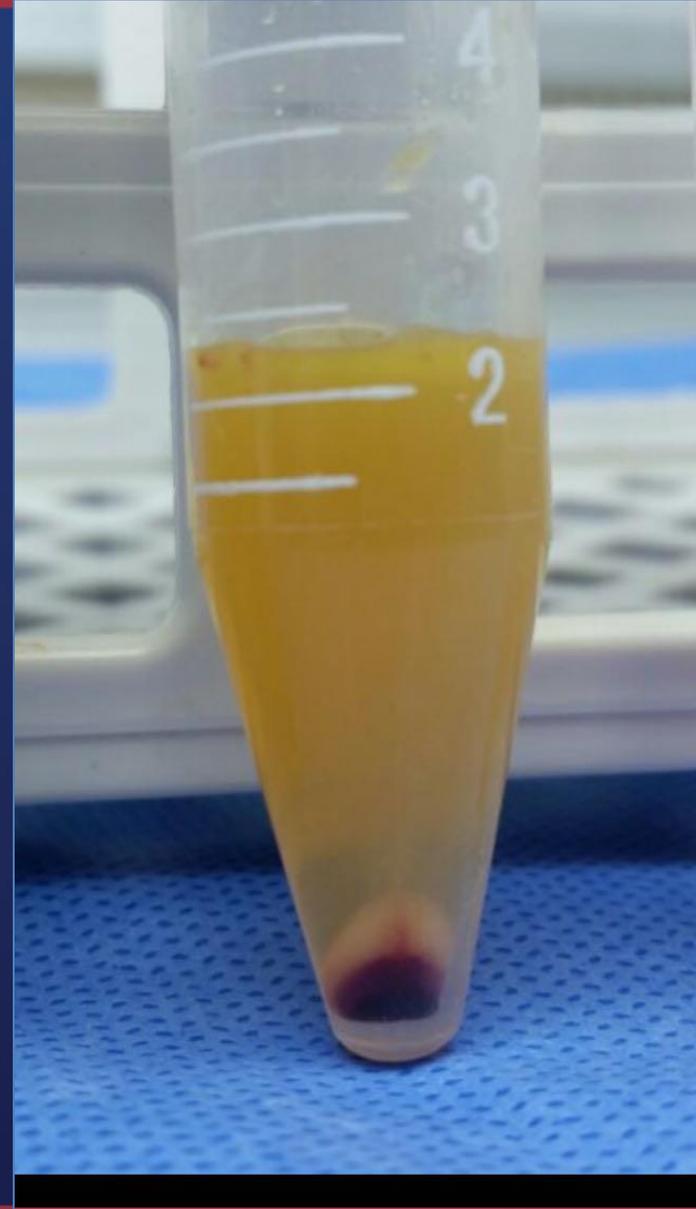
Kaplan DR, Chao FC, Stiles CD, Antoniades HN, Scher CD.



**Quais são as evidências científicas para o uso do PRP em Ortopedia e Medicina Regenerativa?**



**S  
C  
I  
E  
N  
T  
I  
F  
I  
C  
E  
V  
I  
D  
E  
N  
C  
E  
S**



# EVIDÊNCIAS DE ESTUDOS CLÍNICOS

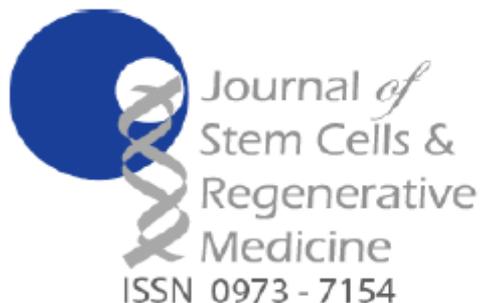


## PRP

## EM ESTUDOS CLÍNICOS – OSTEOARTRITE

REFERÊNCIA	Patologia/ Intervenção	Tipo de PRP	Desenho do estudo/ n / Avaliação	Resultados	Follow up/ Nível de evidência
Saegusa et al., 2011	OA joelho/ 3 injeções cada duas semanas	PRP 1,5 a 3x Ativado com CaCl <sub>2</sub> /ml	Série de casos n=261 WOMAC, EVA, SF – 36, Lequesne	<b>Melhora significativa em todos os escores</b>	6 meses/ IV
Sanchez et al., 2012	OA joelho 3 injeções semanalmente	PRP Endoret	Controlado, randomizado, multicêntrico N=187 WOMAC, Lequesne	<b>Resultados superiores ao do AH</b>	1, 2 e 6 meses/ I
Smith et al., 2016	OA joelho 3 injeções semanalmente	PRP Arthex	RCT, n=30 WOMAC	<b>Melhora 78% nos escores</b>	12 meses/ I
Cole et al 2016	OA joelho 3 injeções semanalmente	PRP Arthex	RCT, n=111 WOMAC, IKDC,EVA	<b>Melhora significativa nos escores</b>	52 semanas/ I
Lana et al, 2016	OA joelho 3 injeções cada duas semanas de PRP, AH ou PRP+AH	PRP 4 a 6 x	RCT, n=105 WOMAC, EVA	<b>Melhora significativa nos escores</b>	12 meses/ I
Gormeli et al 2017	OA joelho – 4 grupos 3 injeções de PRP 1 injeção de PRP, AH ou Salina	PRP 5x valor basal	RCT, n=182 IKDC, EVA	<b>Grupos tratados apresentaram melhores escores</b>	6 meses/ I

## PRP EM ESTUDOS CLÍNICOS - OSTEOARTRITE



RESEARCH ARTICLE

JSRM Code: 012030200002EPA050716

### Randomized controlled trial comparing hyaluronic acid, platelet-rich plasma and the combination of both in the treatment of mild and moderate osteoarthritis of the knee

Lana JFSD<sup>1,4</sup>, Weglein A<sup>3</sup>, Sampson S<sup>2</sup>, Vicente EF<sup>1</sup>, Huber SC<sup>1,7</sup>, Souza CV<sup>4</sup>, Ambach MA<sup>5</sup>, Vincent H<sup>6</sup>, Urban-Paffaro A<sup>7</sup>, Onodera CMK<sup>7</sup>, Annichino-Bizzacchi JM<sup>7</sup>, Santana MHA<sup>8</sup>, Belangero WD<sup>8</sup>

**Conclusões:** Resultados corroboram o uso do PRP autólogo como um tratamento efetivo para o tratamento de OA leve a moderada.

A combinação de AH+PRP apresentou melhores resultados do que o AH sozinho até 1 ano e PRP sozinho até 3M. AH+PRP – melhores escores funcionais nos primeiros 30 dias quando comparados ao AH ou PRP isolados.

# PRP EM ESTUDOS CLÍNICOS - OSTEOARTRITE

Shen et al. *Journal of Orthopaedic Surgery and Research* (2017) 12:16  
DOI 10.1186/s13018-017-0521-3

Journal of Orthopaedic  
Surgery and Research

RESEARCH ARTICLE

Open Access



## The temporal effect of platelet-rich plasma on pain and physical function in the treatment of knee osteoarthritis: systematic review and meta-analysis of randomized controlled trials

Longxiang Shen<sup>1†</sup>, Ting Yuan<sup>1†</sup>, Shengbao Chen<sup>2</sup>, Xuetao Xie<sup>1\*</sup> and Changqing Zhang<sup>1</sup>

**Conclusões:** Injeções intra-articulares de PRP são mais eficazes no tratamento da OA de joelho em termos de alívio da dor e auto-relato de melhora funcional em 3, 6 e 12 meses de seguimento, comparado com outras injeções, como salina, HA, ozônio e corticóides

## PRP EM ESTUDOS CLÍNICOS - TENDINOPATIA

# Nonsurgical Treatments of Patellar Tendinopathy: Multiple Injections of Platelet-Rich Plasma Are a Suitable Option

## A Systematic Review and Meta-analysis

Luca Andriolo,<sup>\*</sup> MD, Sante Alessandro Altamura,<sup>\*</sup> MD, Davide Reale,<sup>\*†</sup> MD, Christian Candrian,<sup>‡</sup> MD, Stefano Zaffagnini,<sup>\*</sup> MD, Prof., and Giuseppe Filardo,<sup>§</sup> MD, PhD  
*Investigation performed at Rizzoli Orthopaedic Institute, Bologna, Italy; and Ospedale Regionale di Lugano—EOC, Lugano, Switzerland*

The American Journal of Sports Medicine  
1–18  
DOI: 10.1177/0363546518759674  
© 2018 The Author(s)

**Conclusões** – Múltiplas injeções de PRP apresenta um bom resultado no tratamento da tendinopatia patelar

## PRP EM ESTUDOS CLÍNICOS - TENDINOPATIA

# The Efficacy of Platelet-Rich Plasma on Tendon and Ligament Healing



## A Systematic Review and Meta-analysis With Bias Assessment

Xiao Chen,\* BA, Ian A. Jones,\* BA, Caron Park,† PhD, and C. Thomas Vangsness Jr,\*‡ MD  
*Investigation performed at Keck School of Medicine of USC, Los Angeles, California, USA*

The American Journal of Sports Medicine  
2018;46(8):2020–2032  
DOI: 10.1177/0363546517743746  
© 2017 The Author(s)

**Conclusão** – PRP pode reduzir a dor associada a epicondilite e lesões do manguito rotador.

## PRP EM ESTUDOS CLÍNICOS – LOMBALGIA COM DEGENERAÇÃO DISCAL



CrossMark



PM R 8 (2016) 1-10

[www.pmrjournal.org](http://www.pmrjournal.org)

Original Research—CME

### Lumbar Intradiskal Platelet-Rich Plasma (PRP) Injections: A Prospective, Double-Blind, Randomized Controlled Study

Yetsa A. Tuakli-Wosornu, MD, MPH, Alon Terry, MD, Kwadwo Boachie-Adjei, BS, CPH,  
Julian R. Harrison, BS, Caitlin K. Gribbin, BA, Elizabeth E. LaSalle, BS,  
Joseph T. Nguyen, MPH, Jennifer L. Solomon, MD, Gregory E. Lutz, MD

**Conclusões** - Participantes que receberam o PRP intradiscal apresentaram uma melhora significativa na dor e função em comparação com o grupo controle (n total = 47 participantes)

# PRP EM ESTUDOS CLÍNICOS – LOMBALGIA COM DEGENERAÇÃO DISCAL

Review Article

*J Spine Surg* 2018;4(1):115-122

## Platelet-rich plasma injections: an emerging therapy for chronic discogenic low back pain

Suja Mohammed<sup>1</sup>, James Yu<sup>1,2</sup>

<sup>1</sup>Australian Medical Research Institute, New South Wales, Australia; <sup>2</sup>Sydney Spine and Pain, Hurstville, New South Wales, Australia

*Contributions:* (I) Conception and design: All authors; (II) Administrative support: S Mohammed; (III) Provision of study materials or patients: All authors; (IV) Collection and assembly of data: All authors; (V) Data analysis and interpretation: All authors; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

*Correspondence to:* James Yu, MD. Sydney Spine and Pain, Suite 706 Level 7, Waratah Private Hospital, 31 Dora St, Hurstville, NSW Australia.  
Email: drjamesyu@sydneyneuropain.com.au.

**Conclusões** – PRP é seguro e efetivo no tratamento da dor discogênica lombar

# PRP EM ESTUDOS CLÍNICOS – LOMBALGIA

ORIGINAL ARTICLE

OPEN ACCESS

## Effect of autologous platelet leukocyte rich plasma injections on atrophied lumbar multifidus muscle in low back pain patients with monosegmental degenerative disc disease

Mohamed Hussein<sup>1,\*</sup> and Tamer Hussein<sup>2</sup>

<sup>1</sup> Department of Orthopedics and Traumatology, Surgery New Hospital, Zagazig University Hospitals and Faculty of Medicine, Zagazig University, 44519 Zagazig City, Sharkiah, Egypt

<sup>2</sup> Department of Anesthesiology and ICU, Surgery New Hospital, Zagazig University Hospitals and Faculty of Medicine, Zagazig University, 44519 Zagazig City, Sharkiah, Egypt

Received 30 May 2015, Accepted 7 January 2016, Published online 22 March 2016

**Conclusão** – Injeção de PRP no músculo multifidus lombar foi efetiva e segura no alívio da dor lombar crônica e disfunção com uma taxa de sucesso de 71,2%.

# EVIDÊNCIAS DE ESTUDOS DE CIÊNCIAS BÁSICAS



**PRP EM CULTURA DE CONDRÓCITOS**

**APLICAÇÃO DO PRP EM ESTUDOS *IN VITRO***

Pettersson et al., 2009

Condrócitos humanos

Akeda et al., 2006

Condrócitos de porco

Spreafico et al., 2009

Condrócitos humanos

Park et al., 2012

Condrócitos de coelho

Saito et al 2009

Condrócitos de coelho

Gaissmaier et al 2005

Condrócitos humanos

Kaps et al 2002

Condrócitos bovino

**Promove a proliferação celular e a Síntese da matriz extracelular**

# APLICAÇÃO DO PRP EM ESTUDOS *IN VIVO*

## APLICAÇÃO INTRA-ARTICULAR DE PRP EM MODELOS ANIMAIS DE OSTEOARTRITE

Kwon et al., 2012

Estimula a proliferação celular

Mifune et al., 2012

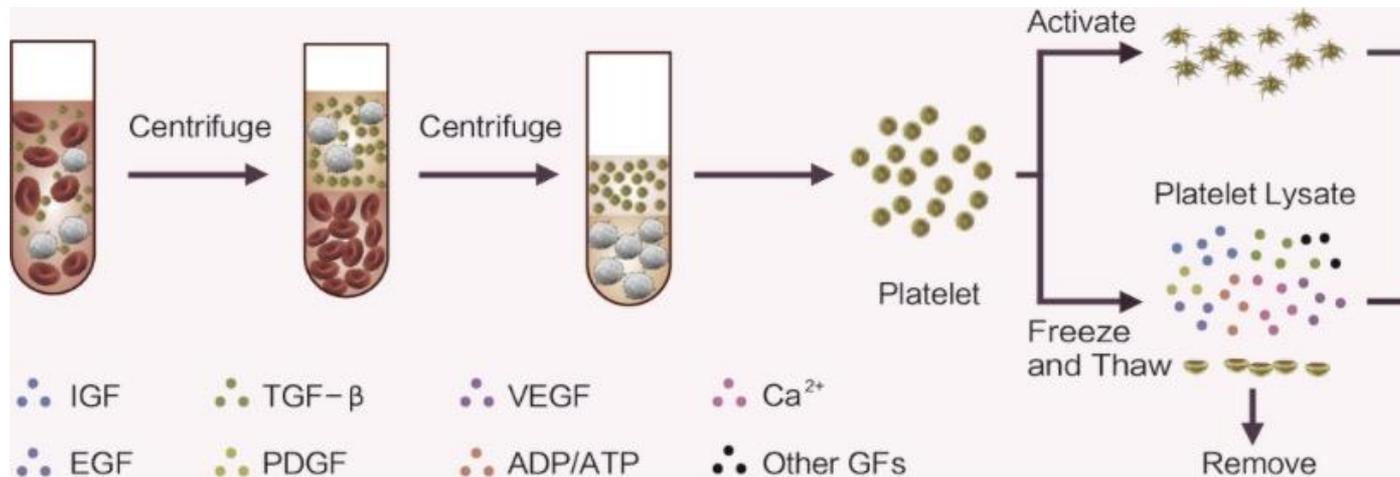
Aumenta o conteúdo de colágeno do tipo II

Saito et al., 2012

Suprime a progressão da osteoartrite

**O QUE SE CONHECE SOBRE SEU MECANISMO DE AÇÃO  
NA PROLIFERAÇÃO CELULAR E NA  
REPARAÇÃO DA CARTILAGEM?**

## PRP



# COMPONENTES DO PRP



**ADP**

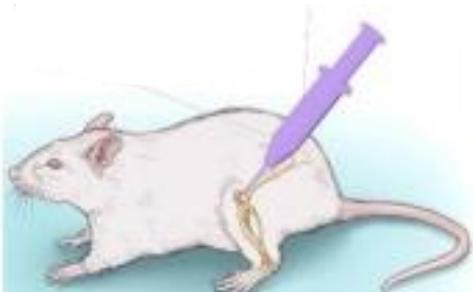
# Platelets promote cartilage repair and chondrocyte proliferation via ADP in a rodent model of osteoarthritis

Qi Zhou, Chunhua Xu, Xingyao Cheng, Yangyang Liu, Ming Yue, Mengjiao Hu, Dongjiao Luo, Yuxi Niu, Hongwei Ouyang, Jiansong Ji & Hu Hu

To cite this article: Qi Zhou, Chunhua Xu, Xingyao Cheng, Yangyang Liu, Ming Yue, Mengjiao Hu, Dongjiao Luo, Yuxi Niu, Hongwei Ouyang, Jiansong Ji & Hu Hu (2016) Platelets promote cartilage repair and chondrocyte proliferation via ADP in a rodent model of osteoarthritis, *Platelets*, 27:3, 212-222, DOI: [10.3109/09537104.2015.1075493](https://doi.org/10.3109/09537104.2015.1075493)

# MODELO DE INDUÇÃO DE OSTEOARTRITE EM RATOS PELA ADMINISTRAÇÃO INTRA-ARTICULAR DE MONOSÓDIO IODO ACETATO

**Monosodio iodo acetato (MIA)**



2 semanas

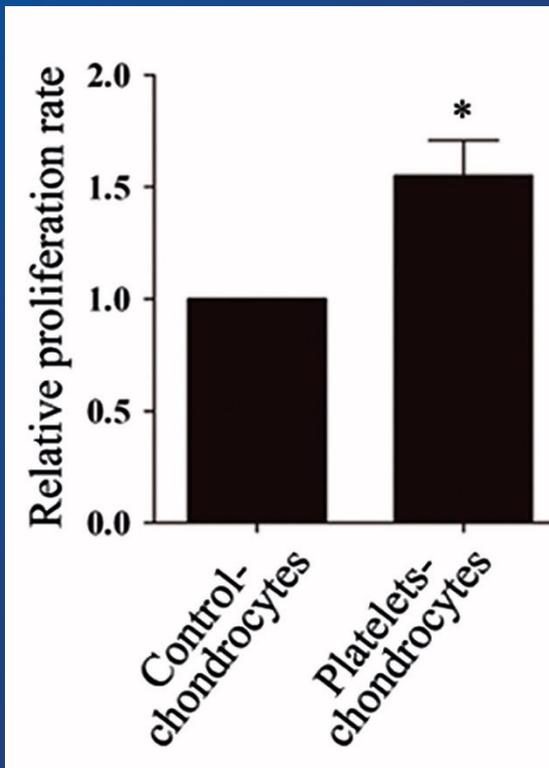


**Transplante de condrócitos  
tratados com plaquetas**

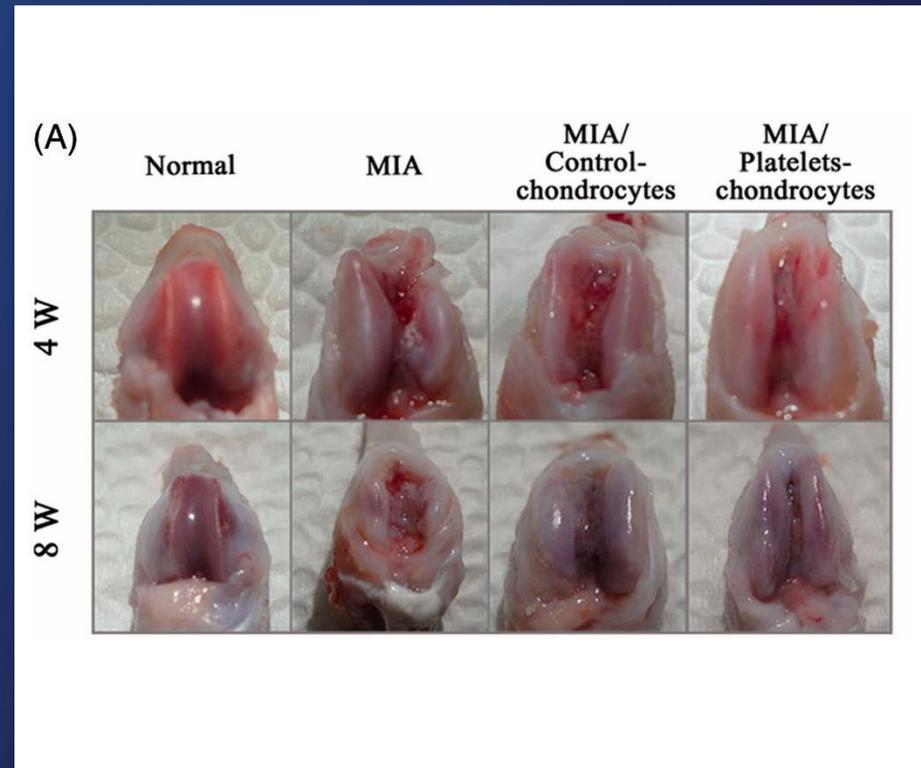


## TRANSPLANTE DE CONDRÓCITOS TRATADOS COM PLAQUETAS PROMOVEU O REPARO DA CARTILAGEM EM MODELO DE OSTEOARTRITE EM RATOS

PLAQUETAS AUMENTARAM A PROLIFERAÇÃO DE CONDRÓCITOS

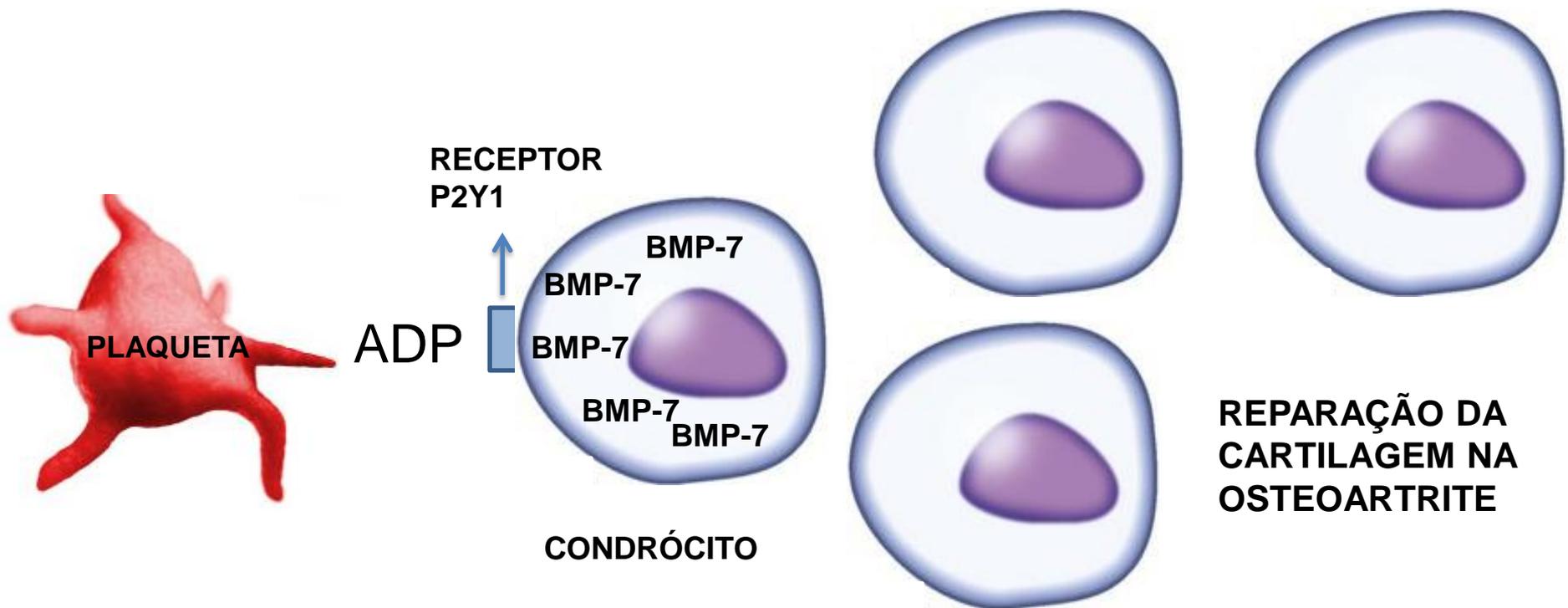


AVALIAÇÃO MACROSCÓPICA DA CARTILAGEM ARTICULAR



## CONCLUSÃO

O ADP DERIVADO DAS PLAQUETAS, VIA RECEPTORES P2Y1, PROMOVE A PRODUÇÃO DE BMP7 NOS CONDRÓCITOS RESULTANDO NA PROLIFERAÇÃO DOS MESMOS E NA REPARAÇÃO DA CARILAGEM EM MODELO DE OA EM RATOS



# AINDA SOBRE O PAPEL DO PRP NA PROLIFERAÇÃO CELULAR.....

## TENÓCITOS



Histochem Cell Biol (2011) 135:453–460

DOI 10.1007/s00418-011-0808-0

ORIGINAL PAPER

## **Platelet-released growth factors can accelerate tenocyte proliferation and activate the anti-oxidant response element**

**M. Tohidnezhad · D. Varoga · C. J. Wruck ·  
L. O. Brandenburg · A. Seekamp · M. Shakibaei ·  
T. T. Sönmez · Thomas Pufe · S. Lippross**



# HGF Mediates the Anti-inflammatory Effects of PRP on Injured Tendons

Jiaying Zhang<sup>1</sup>, Kellie K. Middleton<sup>1</sup>, Freddie H. Fu<sup>1</sup>, Hee-Jeong Im<sup>2</sup>, James H-C. Wang<sup>1\*</sup>

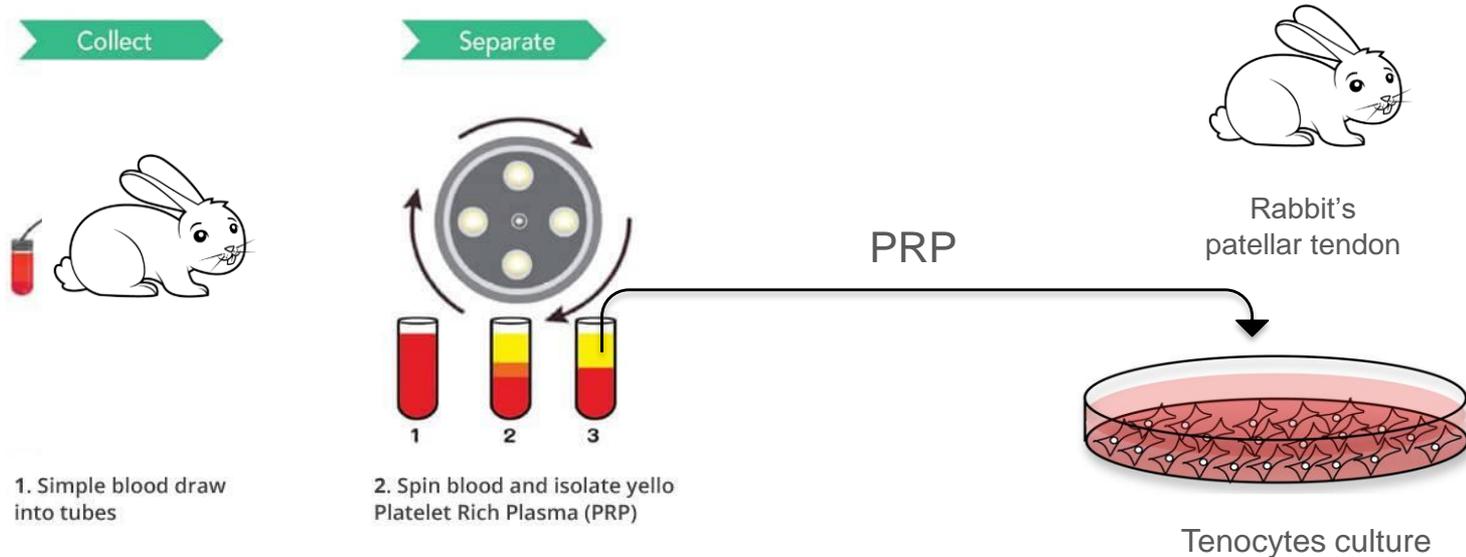
<sup>1</sup> MechanoBiology Laboratory, Departments of Orthopaedic Surgery, Bioengineering, and Mechanical Engineering and Materials Science, University of Pittsburgh, Pittsburgh, Pennsylvania, United States of America, <sup>2</sup> Departments of Biochemistry and Internal Medicine Rush University Medical Center, Chicago, Illinois, United States of America

Experimentos *in vitro* com células de tendão de coelho

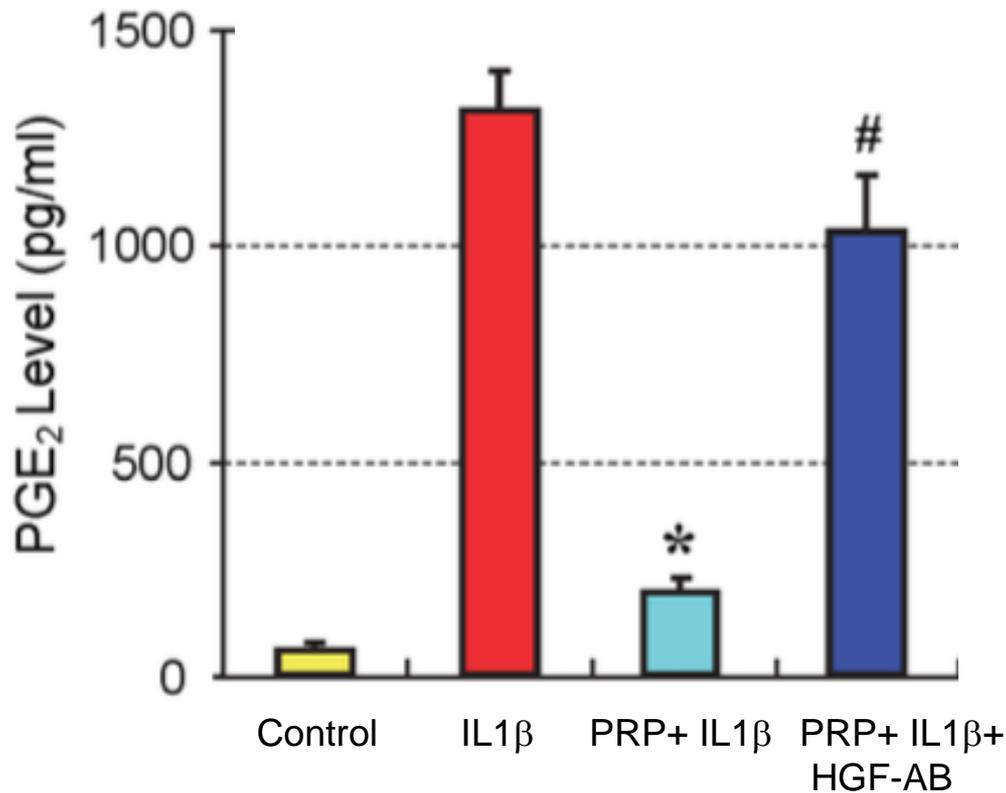
Experimentos *in vivo* em modelo de lesão de tendão de aquiles de camundongo

# HGF Mediates the Anti-inflammatory Effects of PRP on Injured Tendons

## EXPERIMENTOS *IN VITRO*



**PRP REDUZIU A PRODUÇÃO DE  $PGE_2$  NAS CÉLULAS DA CULTURA DO TENDÃO VIA FATOR DE CRESCIMENTO DOS HEPATÓCITOS**



# HGF Mediates the Anti-inflammatory Effects of PRP on Injured Tendons

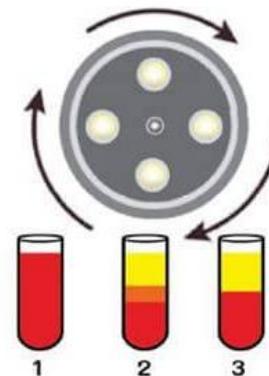
## IN VIVO EXPERIMENTS

Collect



1. Simple blood draw into tubes

Separate



2. Spin blood and isolate yellow Platelet Rich Plasma (PRP)

# HGF Mediates the Anti-inflammatory Effects of PRP on Injured Tendons

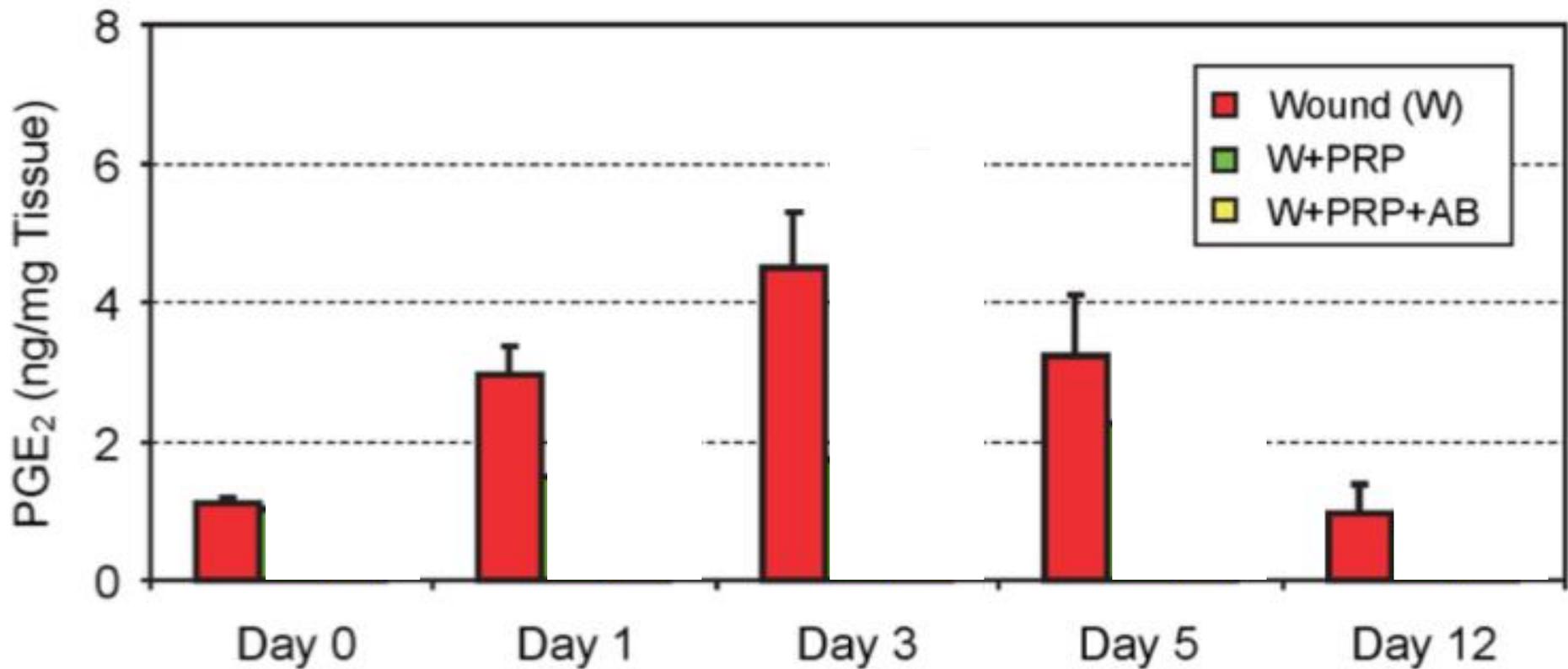
## EXPERIMENTOS *IN VIVO*

Indução da lesão no tendão de aquiles (1mm diâmetro) de camundongos



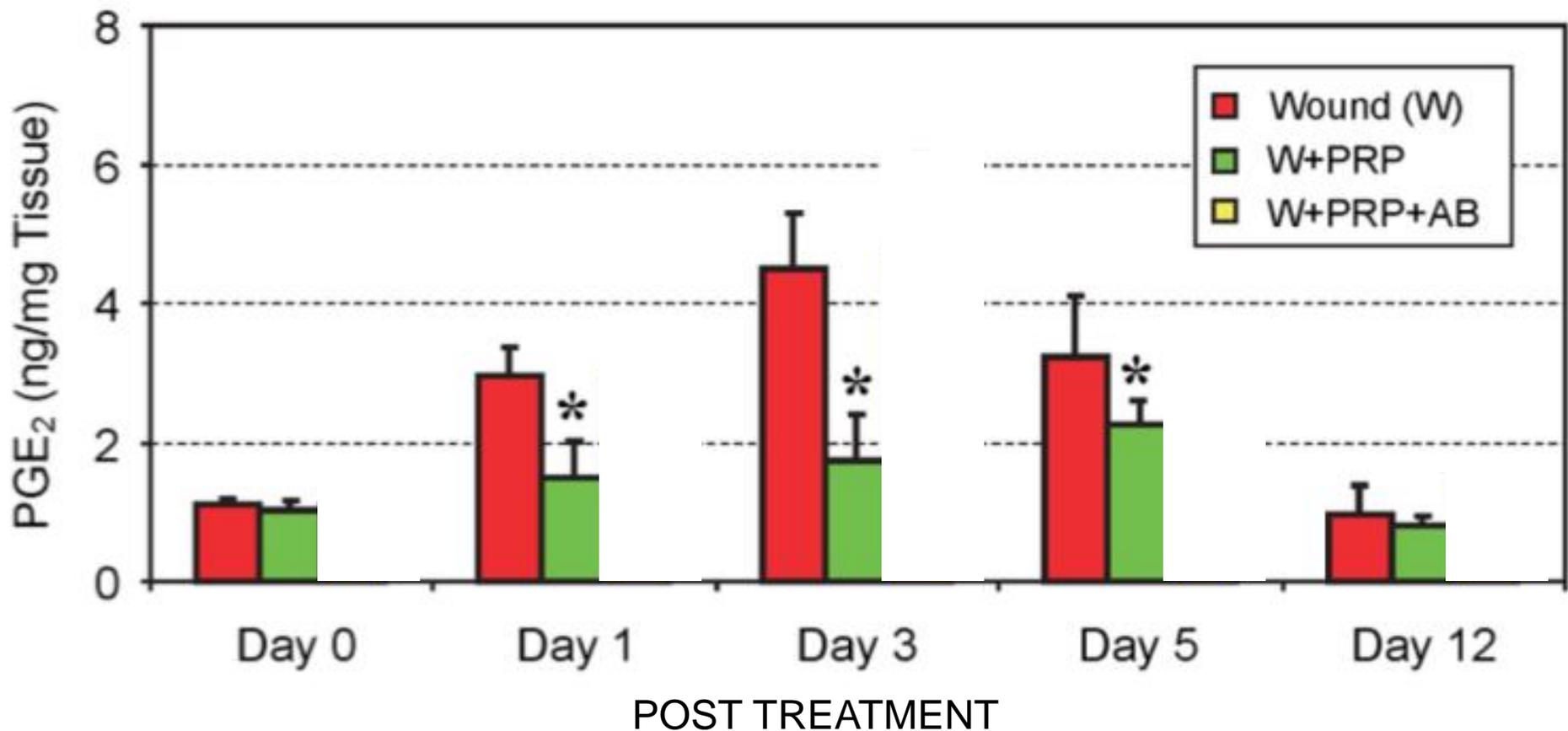
Tratamentos foram realizados imediatamente após

## PRP REDUZIU A PRODUÇÃO DE $PGE_2$ NO TENDÃO DE AQUILES LESIONADO VIA FATOR DE CRESCIMENTO DOS HEPATÓCIOTS



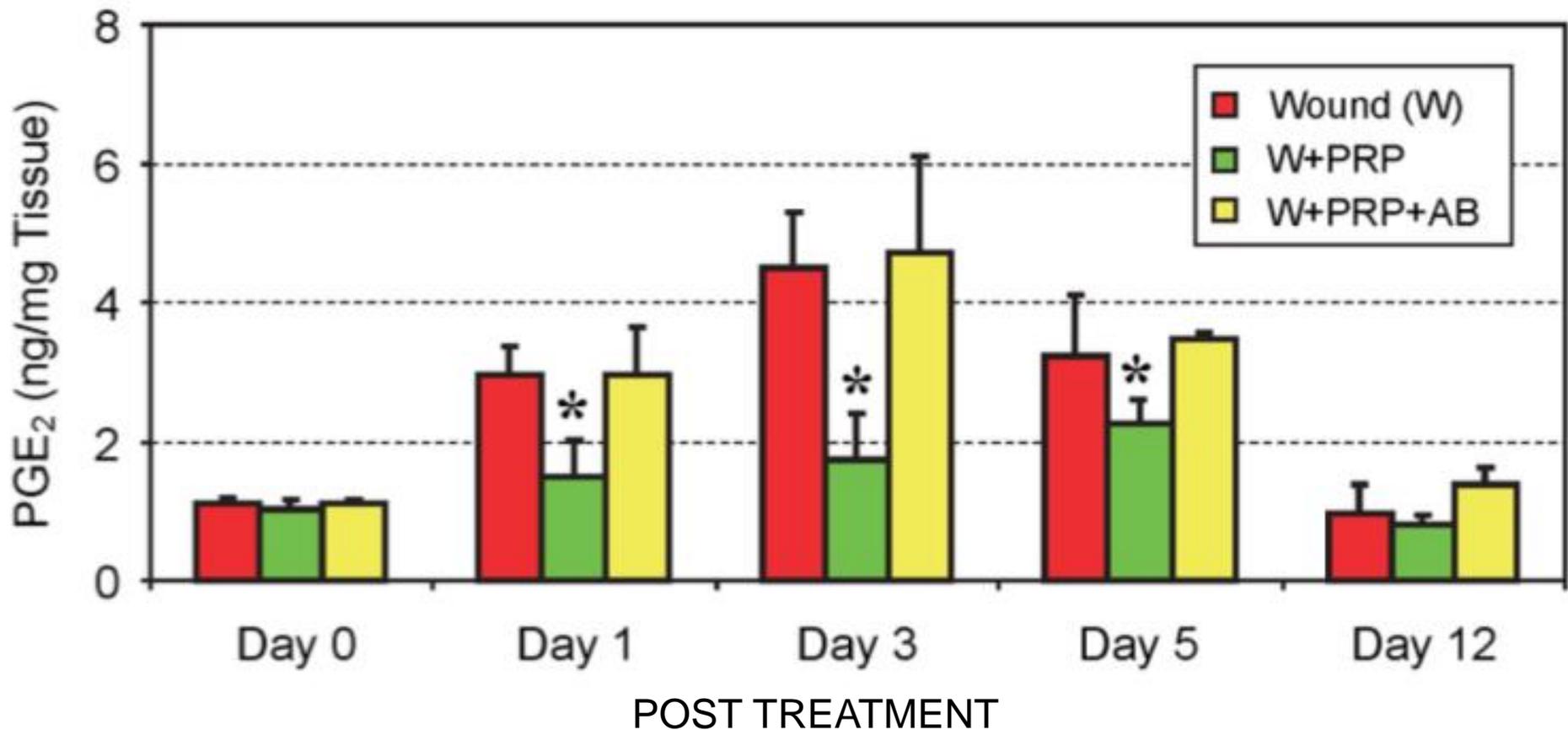
AB = ANTICORPO CONTRA O HGF

## PRP REDUZIU A PRODUÇÃO DE $PGE_2$ NO TENDÃO DE AQUILES LESIONADO VIA FATOR DE CRESCIMENTO DOS HEPATÓCIOTS



AB = ANTICORPO CONTRA O HGF

## PRP REDUZIU A PRODUÇÃO DE $PGE_2$ NO TENDÃO DE AQUILES LESIONADO VIA FATOR DE CRESCIMENTO DOS HEPATÓCITOS



AB = ANTICORPO CONTRA O HGF

## UM ASPECTO QUE CHAMA A ATENÇÃO NOS ESTUDOS COM O PRP.....



**FALTA DE PADRONIZAÇÃO DO PRP**

## Publicações

BioResearch Open Access  
Volume 2, Number 4, August 2013  
© Mary Ann Liebert, Inc.  
DOI: 10.1089/biores.2013.0015

### Prediction and Modulation of Platelet Recovery by Discontinuous Centrifugation of Whole Blood for the Preparation of Pure Platelet-Rich Plasma

Amanda G.M. Perez,<sup>1</sup> Rafael Lichy,<sup>1</sup> José Fábio S.D. Lana,<sup>1-3</sup> Ana Amélia Rodrigues,<sup>3</sup>  
Ângela Cristina M. Luzo,<sup>4</sup> William D. Belangero,<sup>3</sup> and Maria Helena A. Santana<sup>1</sup>

## Publicações

Hindawi Publishing Corporation  
ISRN Hematology  
Volume 2014, Article ID 176060, 8 pages  
<http://dx.doi.org/10.1155/2014/176060>



*Research Article*

### **Relevant Aspects of Centrifugation Step in the Preparation of Platelet-Rich Plasma**

**Amanda G. M. Perez,<sup>1</sup> José Fábio S. D. Lana,<sup>2</sup> Ana Amélia Rodrigues,<sup>3</sup>  
Angela Cristina M. Luzo,<sup>4</sup> William D. Belangero,<sup>3</sup> and Maria Helena A. Santana<sup>1</sup>**

- Aceleração centrífuga (xg), volume do sangue processado, prevenção da agregação e gradiente plaquetário – relevantes para o preparo do PRP
- A observação destes fatores garante a qualidade do PRP (variáveis resultam da natureza autóloga do produto)
- É um ponto de início da padronização do preparo do PRP

## Publicações

### **DISTRIBUTION, RECOVERY AND CONCENTRATION OF PLATELETS AND LEUKOCYTES IN L-PRP PREPARED BY CENTRIFUGATION**

Bruna Alice Gomes de Melo<sup>1</sup>, Andréa Arruda Martins Shimojo<sup>1</sup>, Amanda Gomes Marcelino Perez<sup>1</sup>, José Fabio Santos Duarte Lana<sup>2</sup>, Maria Helena Andrade Santana<sup>1\*</sup>

**In press 2018**

- A composição do L-PRP pode ser alterada pelas condições de centrifugação
- O perfil de concentração gera um raio de: Plaquetas / leucócitos, Linfócitos / granulócitos – Garantindo a preparação correta do L-PRP com diferentes equilíbrios entre anabólicos / catabólicos

## Publicações

### **Simulation and Validation of the Effects of Anticoagulants and Whole Blood Volume on Centrifugation Performance for the Preparation of Platelet –Rich Plasma**

Sofia E. M. Galdames<sup>1</sup>, Edson R. Onaga<sup>1</sup>, Mariana B.e Souza<sup>1</sup>, Andrea A.M. Shimojo<sup>1</sup>, José Fábio Lana<sup>3</sup>, Angela C. M. Luzo<sup>2</sup> and Maria H. A. Santana<sup>1</sup>

**In press 2018**

- The anticoagulant influences erythrocyte sedimentation, PRP volume and composition

## Publicações



RESEARCH ARTICLE

JSRM Code: 012010300002

*In vitro* study of the role of thrombin in platelet rich plasma (PRP) preparation: utility for gel formation and impact in growth factors release

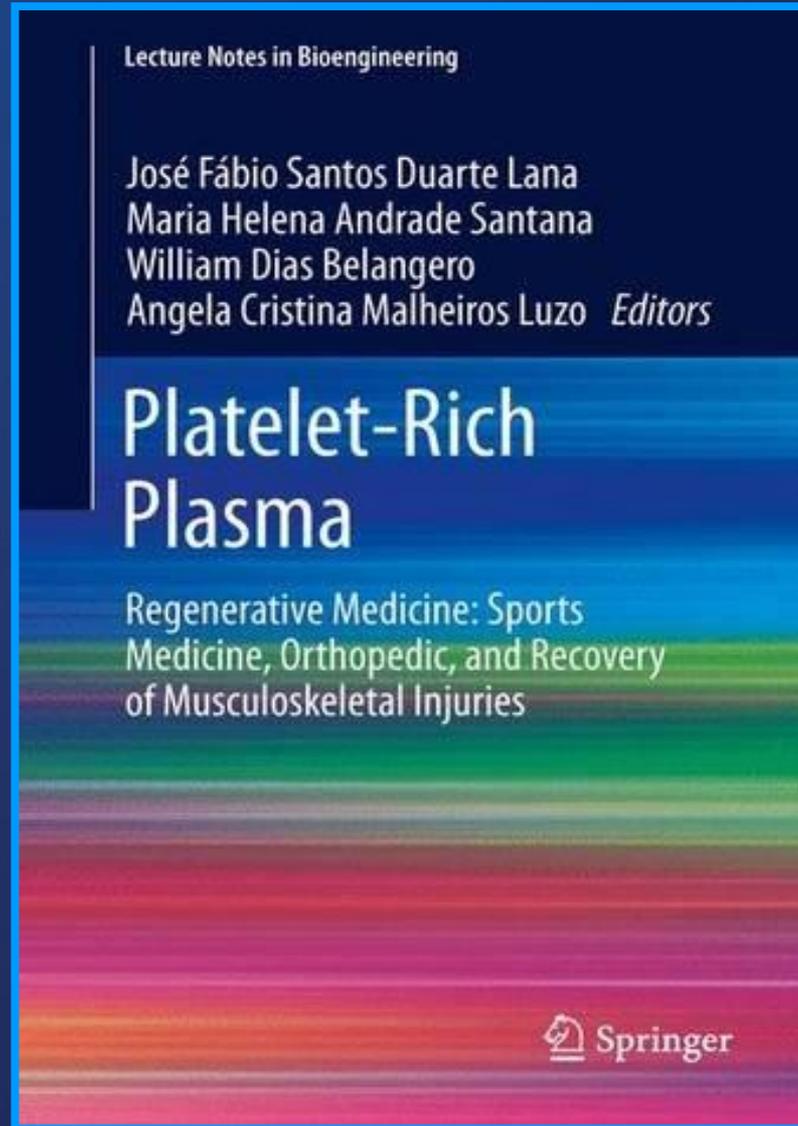
Huber SC<sup>1</sup>, Cunha JL<sup>1</sup>, Montalvão SAL<sup>1</sup>, da Silva LQ<sup>1</sup>, Paffaro AU<sup>1</sup>, da Silva FAR<sup>1</sup>, Rodrigues BL<sup>1</sup>, Lana JFSD<sup>1</sup>, Annichino-Bizzacchi JM<sup>1</sup>

- A técnica de utilizar soro como fonte de trombina mostrou-se eficiente e reprodutível para promover a formação do gel de PRP, com a vantagem de ser simples e rápido para obtenção
- A ativação do PRP usando diferentes concentrações de trombina não produziu uma maior liberação dos FC, não sendo necessário sua utilização quando o PRP é utilizado como suspensão

## OUR SCIENTIFIC CONTRIBUTION



Lana et al  
LAS VEGAS 2014



## Publicações



- Princípios básicos do metabolismo celular bioquímico que aumenta a eficácia do PRP – Preparing the soil
- Padronização do preparo do PRP para uso clínico – desafio. Nesse contexto, uma estratégia confiável para estudar o preparo do PRP é ilustrada, com o objetivo de garantir a qualidade do PRP para estudos clínicos
- Usos específicos do PRP são descritos com ilustrações detalhadas de experiências pessoais em lesões ortopédicas, ligamentos e tendões, doenças degenerativas, medicina esportiva, cicatrização crônica de feridas, bem como aspectos de reabilitação em tendinopatias

## Chapter 2 – Lana et al



## Chapter 2 1 Platelet-Rich Plasma in Pain 2 Medicine 3

**José Fábio Santos Duarte Lana, Eduardo Fonseca Vicente, Adam Weglein, William Dias Belangero, Fabrício Dias Assis, and André Marques Mansano** 4  
5  
6

**Summary** 7

For the past 20 years, autologous Platelet-Rich Plasma (PRP) 8  
has been safely employed and its use has been documented in 9  
many areas, including orthopedics, sports medicine, dentistry, 10

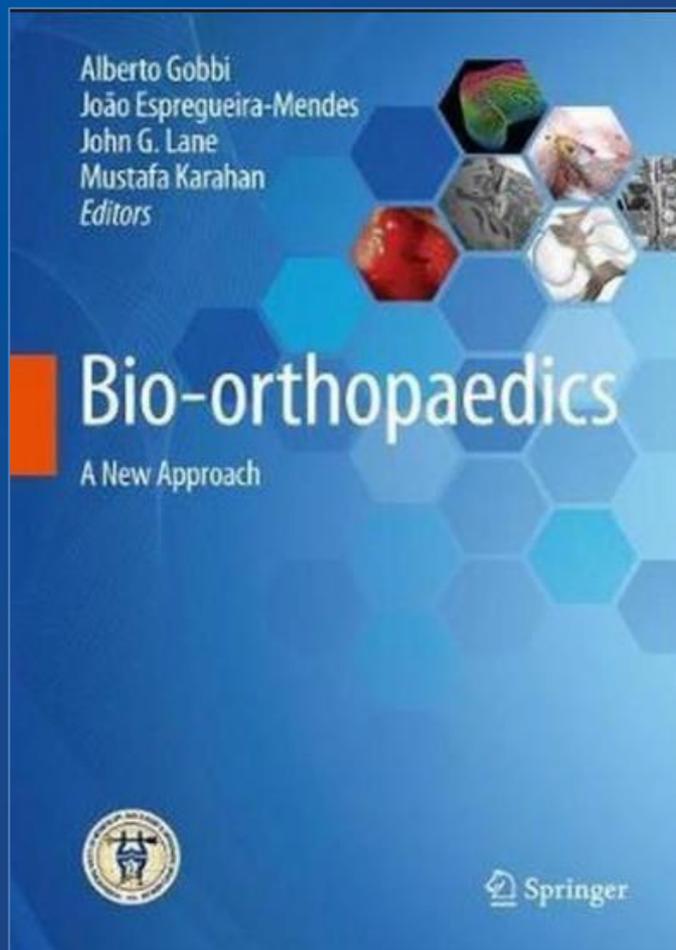
J.F.S.D. Lana (✉) • E.F. Vicente  
Research Institute of Sports Medicine – iMOR,  
Av. Santos Dumont 2946, Uberaba, MG CEP 38050-400, Brazil  
e-mail: [josefabiolana@gmail.com](mailto:josefabiolana@gmail.com)

A. Weglein, DO, DABMA  
University of Texas Houston Medical School, Houston, TX, USA  
University of North Texas Health Science Center,  
Ft Worth Texas 6800 West Loop South Ste 500, Bellaire,  
TX 77401, USA

W.D. Belangero  
Department of Orthopedics and Traumatology – Faculty of Medical  
Sciences, University of Campinas,  
Tessália Vieira de Camargo 126, Campinas, SP CEP 13083-852,  
Brazil

F.D. Assis • A.M. Mansano  
Interventional Pain Practice-WIP – Singular – Pain-Control Center,  
R. Maria Monteiro 968, Campinas, SP CEP 13025-151, Brazil

N. Maffulli (ed.), *Platelet Rich Plasma in Musculoskeletal  
Practice*, DOI 10.1007/978-1-4471-7271-0\_2,  
© Springer-Verlag London 2016



## The Role of Biological Treatments in Spine Disorders

48

José Fábio Santos Duarte Lana,  
Edilson Silva Machado, Renato Bender Castro,  
João Lopo Madureira Junior,  
Paulo David Fortis Gusmão,  
Nivaldo Evangelista Teles,  
Luiz Felipe Chaves Carvalho,  
João Paulo Bezerra Leite, Bruno Tavares Rabello,  
and Ozório de Almeida Lira Neto

### Contents

48.1	<b>Introduction</b> .....	599
48.1.1	Chronic Pain and Spine.....	599
48.1.2	Disc Degeneration and Discogenic Pain.....	600
48.1.3	The Intervertebral Disc.....	601
48.1.4	Degenerative Process.....	601
48.1.5	Therapeutic Perspectives.....	602
48.1.6	Biological Therapy.....	602
48.1.7	Cell Therapy.....	603
48.1.8	Facet Syndrome.....	604
48.1.9	Lumbar Spinal Stenosis.....	605
48.1.10	Spinal Scapular Humeral Pain.....	606
48.1.11	Spino-pelvic Pain.....	608
48.1.12	PRP, BMAC, and BIOFAT Production.....	611
	<b>Conclusions</b> .....	614
	<b>References</b> .....	614

### 48.1 Introduction

This chapter addresses several aspects of spine disorders and their implications for pain, functional impairment, and their problems and treatments.

There will be discussions on different causes, such as chronic pain, disc degeneration and discogenic pain, facet syndrome, lumbar spinal stenosis, spinal scapular humeral pain, and spino-pelvic pain. It will be presented the different types of treatments, but with emphasis on the biological approach and its particularities.

#### 48.1.1 Chronic Pain and Spine

## Randomized Controlled Trial Hyaluronic Acid + PRP 2016 Publication – Lana et al.

JSRM Code: 012020300011

### Randomized controlled trial comparing hyaluronic acid, platelet-rich plasma and the combination of both in the treatment of mild and moderate osteoarthritis of the knee

Lana JFSD<sup>1,4</sup>, Weglein A<sup>3</sup>, Sampson S<sup>2</sup>, Vicente EF<sup>1</sup>, Huber SC<sup>1,7</sup>, Souza CV<sup>4</sup>, Ambach MA<sup>5</sup>, Vincent H<sup>6</sup>, Urban-Paffaro A<sup>7</sup>, Onodera CMK<sup>7</sup>, Annichino-Bizzacchi JM<sup>7</sup>, Santana MHA<sup>8</sup>, Belangero WD<sup>8</sup>

**Objective:** This study aims at evaluating the clinical effects of Platelet Rich Plasma (PRP) and Hyaluronic Acid (HA) as individual treatments for mild to moderate Osteoarthritis (OA) and it also examines the potential synergistic effects of PRP in combination with HA. Research continues to emerge examining the potential therapeutic efficacy of HA and PRP as autologous injectable treatments for joint arthritis. However, there is a paucity of research investigating the effects of combining HA and PRP on pain and functional status in patients with OA.

**Design:** In this multi-center, randomized, controlled, double blind, prospective trial, 105 patients with mild to moderate knee osteoarthritis, who met the study criteria, were randomly allocated to one of three interventions: HA (n=36), PRP (n=36), or HA+PRP (n=33). Each patient received 3 intra-articular knee injections of their assigned substance, with 2 week intervals between each injection. Clinical outcomes were evaluated using the Western Ontario and McMaster Universities Arthritis Index (WOMAC) and Visual Analogue Scale (VAS) questionnaire at baseline and after 1,3,6 and 12 months.

**Results:** The study showed that the PRP group have significant reduction in VAS scores at 1 (p= 0.003), 3 (p= 0.0001), 6 (p= 0.0001) and 12 (p= 0.000) months when compared to HA. In addition, the PRP group illustrated greater improvement in WOMAC physical activity scale at 12 months (p= 0.008) when compared to the HA group. Combining HA and PRP resulted in a significant decreases in pain (p=0.0001) and functional limitation (p=0.0001) when compared to HA alone at 1 year post treatment; and significantly increased physical function at 1 (p=0.0004) and 3 (p=.011) months when compared to PRP alone.

**Conclusion:** The findings of the study support the use of autologous PRP as an effective treatment of mild to moderate knee osteoarthritis. It also shows that the combination of HA and PRP resulted to better outcomes than HA alone up to 1 year and PRP alone up to 3 months. Furthermore, the results suggest that combination of PRP and HA could potentially provide better functional outcomes in the first 30 days after treatment with both PRP and HA alone.

**Key Words:** Hyaluronic acid, Joint pathology, Knee, Osteoarthritis, Platelet-rich plasma

# PRP plays a key role in healing

COPYRIGHT © 2017 BY THE JOURNAL OF BONE AND JOINT SURGERY, INCORPORATED

## A Call for Standardization in Platelet-Rich Plasma Preparation Protocols and Composition Reporting

A Systematic Review of the Clinical Orthopaedic Literature

Jorge Chahla, MD, PhD, Mark E. Cinque, MS, Nicolas S. Piuze, MD, Sandeep Mannava, MD, PhD, Andrew G. Geeslin, MD, Iain R. Murray, MD, PhD, Grant J. Dornan, MSc, George F. Muschler, MD, and Robert F. LaPrade, MD, PhD

*Investigation performed at the Steadman Philippon Research Institute, Vail, Colorado, and The Cleveland Clinic Foundation, Cleveland, Ohio*



**Standardization is fundamental**



## FOR PLATELET RICH PLASMA Quality Control



Contributions for classification of platelet rich plasma – proposal of a new classification: MARSPILL

Lana et al

Platelet-rich plasma (PRP) has emerged as a significant therapy used in medical conditions with the aim to try to standardize PRP contents for studying cellular components for PRP. The main focus is the distribution of platelets, monocytes, and neutrophils. In this study, we incorporated in the classification a number of spiral-shaped cells. The other focus is the distribution of platelets, monocytes (in the form of platelet-rich plasma) and neutrophils (in the form of platelet-rich plasma) property for

## PLATELET RICH PLASMA CLASSIFICATION MARSPILL 2017

Jose Fabio Santos Duarte Lana<sup>\*1</sup>, Joseph Purita<sup>2</sup>, Christian Paulus<sup>2</sup>, Stephany Cares Huber<sup>3</sup>, Bruno Lima Rodrigues<sup>2</sup>, Ana Amélia Rodrigues<sup>4</sup>, Maria Helena Santana<sup>5</sup>, João Lopo Madureira Jr<sup>6</sup>, Ângela Cristina Malheiros Luzo<sup>7</sup>, William Dias Belangero<sup>4</sup> & Joyce Maria Annichino-Bizzacchi<sup>8</sup>

<sup>1</sup>Institute of Bone & Cartilage, Indaiatuba-SP, Brazil

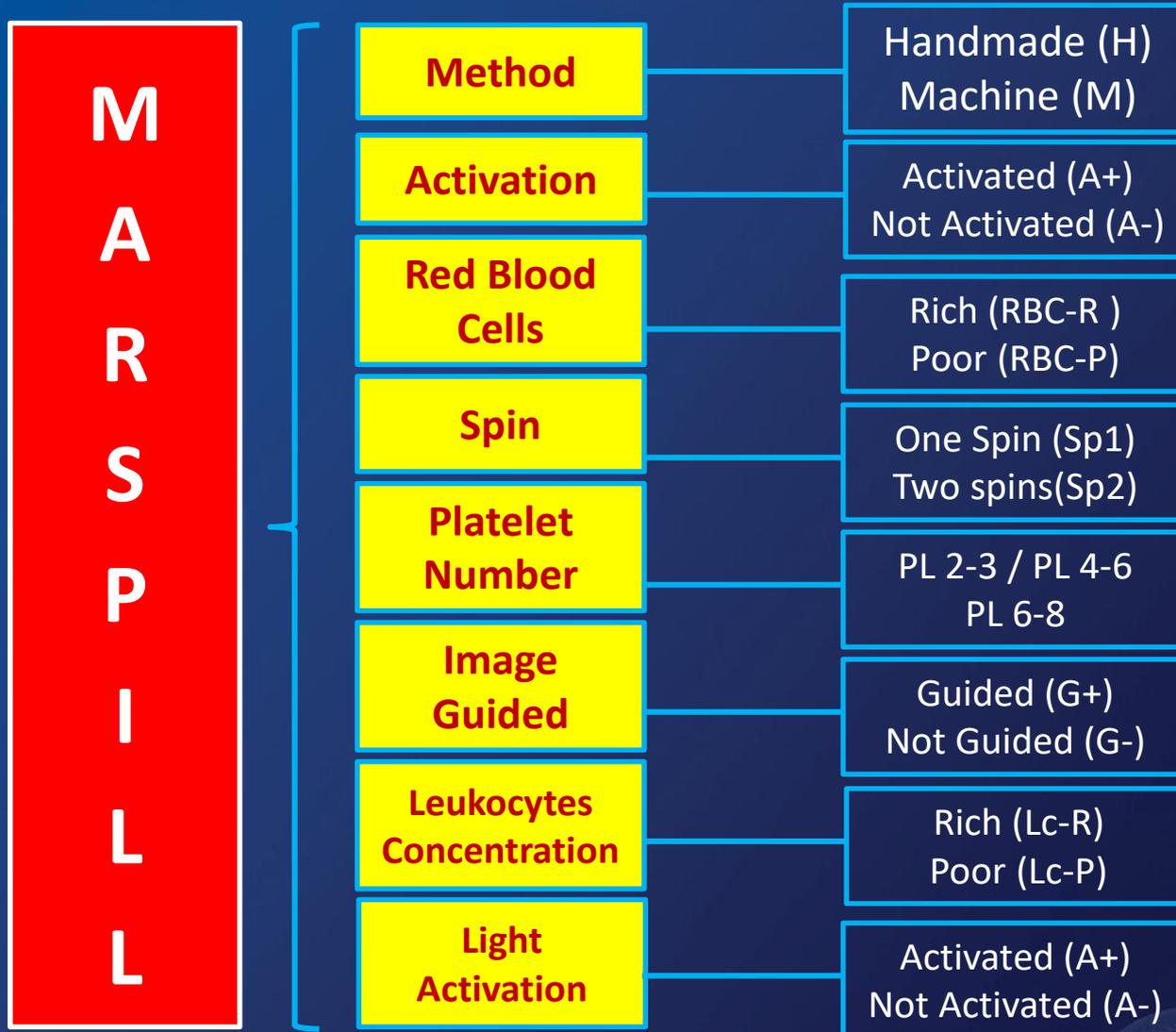
<sup>2</sup>Institute of Regenerative Medicine, Boca Raton, FL, USA

<sup>3</sup>Hematology & Hemotherapy Center, University of Campinas, Campinas-SP, Brazil

<sup>4</sup>Orthopaedic Biomaterials Laboratory, School of Medical Sciences, University of Campinas, Campinas-SP, Brazil

First draft submitted: 22 March 2017; Accepted for publication: 31 May 2017; Published online: 31 July 2017

**Keywords:** growth factors • leukocytes • mononuclear cells • platelet-rich plasma • regenerative medicine



# MARSPILL Classification

- The biological focus on **Buffy Coat (WHITE BLOOD CELLS LAYER)** collection as carrier of **Mononuclear Cells (Lymphocytes and Monocytes)** for tissue regeneration.

- There are three types of granulocyte named according to their staining characteristics in blood films. They are **neutrophils, eosinophils** and **basophils**.
- Mononuclear cells are divided into **lymphocytes** and **monocytes**.

**Platelet Rich Plasma RICH in  
Mononuclear Cells  
(PRP- RMC)**

**Platelet Rich Plasma POOR in  
Mononuclear Cells  
(PRP- PMC)**

# MARSPILL Classification

- Example of a PRP production of clinical study through MARSPILL classification:

**Standardized PRP according the New Classification**  
PRP-RMC (Platelet Rich Plasma, Rich in Mononuclear Cells)

**M** (H), **A** (A-), **R** (RBC-P), **S** (Sp<sup>2</sup>), **P** (PL[4-6]), **I** (G+), **L** (Lc-R[2-3]), **L** (L-)

**M A R S P I L L**





[www.orthoregen.com.br](http://www.orthoregen.com.br)

# ORTHOREGEN 2018

## International Course

**CURSO PRÁTICO E TEÓRICO EM MEDICINA  
REGENERATIVA DO APARELHO LOCOMOTOR**

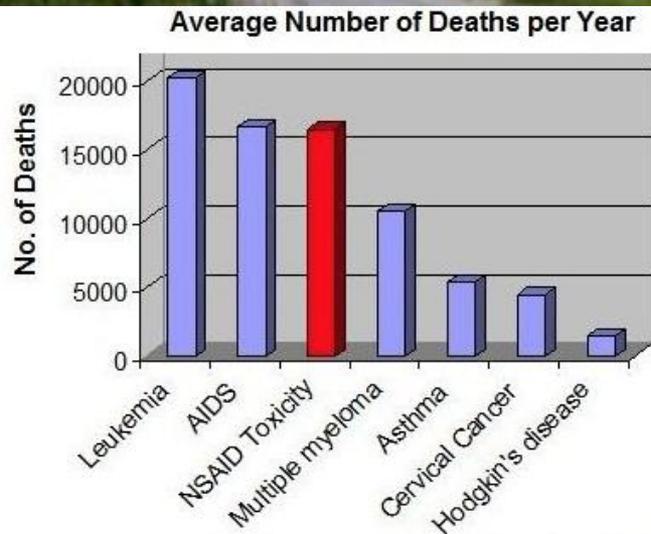


# TRATAMENTOS ORTOPÉDICOS

**ANALGÉSICOS  
ANTI-INFLAMATÓRIOS**

**PLASMA RICO EM PLAQUETAS**

**CIRURGIAS**





*Obrigado!*