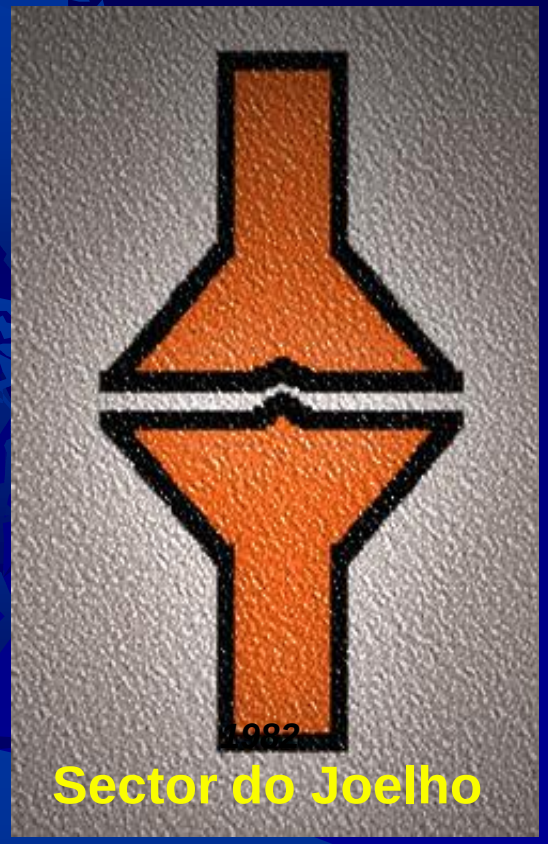
Faculdade de Medicina da Universidade de Coimbra
Hospitais da Universidade de Coimbra

Serviço de Ortopedia



Dir.: Prof. Doutor Abel Nascimento

Os factores de crescimento

Fundamentação e validação terapêutica

Fernando Fonseca

HUC
Serviço de Ortopedia

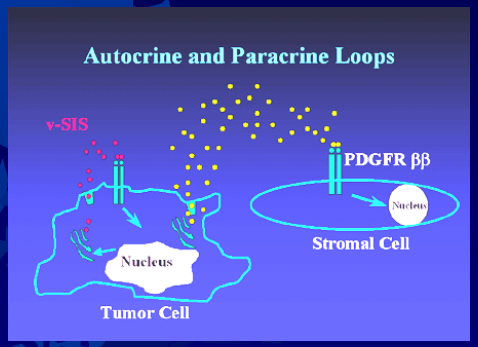
Factores de crescimento

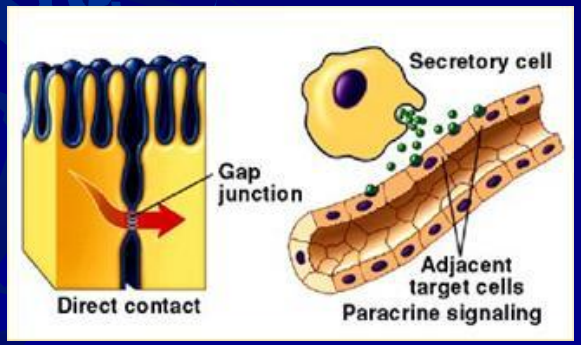
- Proteínas que:
  - Se ligam a receptores da superfície celular,
  - estimulando, de forma específica, a migração e proliferação de muitos tipos celulares e a síntese de novos tecidos.

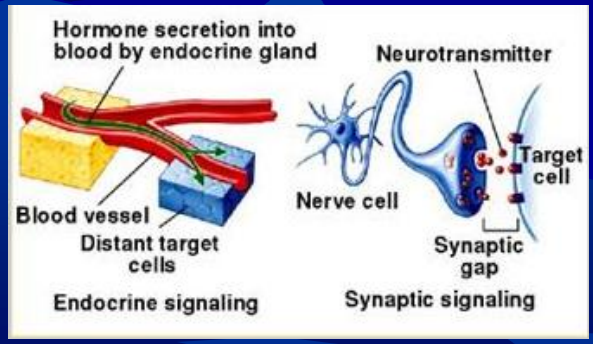
Lindberg K, Badylak SF. Porcine small intestinal submucosa (SIS): A bioscaffold supporting in vitro primary human epidermal cell differentiation and synthesis of basement membrane proteins. *Burns 2001;27:254-266.*

Regulação celular

- ✓ **Autócrina**– As células respondem a substâncias que elas próprias libertam
- ✓ ***Parácrina***– Moléculas libertadas por uma determinada célula para actuar sobre outra céllula localizada na vizinhança.
  - Tem uma semi-vida muito curta
  - `É actuação tipo dos factores de crescimento.
- ✓ **Endócrina** – Determinadas células lproduzem e libertam moléculas que são lançadas na corrente sanguínea atingindo células/orgão à distância
  - Hormonas (tiróide, suprarrenal, etc.).
- ✓ **Casos específicos**
  - **Contacto directo:** Moléculas localizadas na superfície de células adjacentes, têm conhecimento mútuo e podem servir como meio de sinalização entre as células.
    - O reconhecimento de certos marcadores celulares no processo de embriogénese.
  - **Sinapse** – Ocorre nas células do sistema nervoso, com a libertação na fenda sináptica de neurotransmissores..



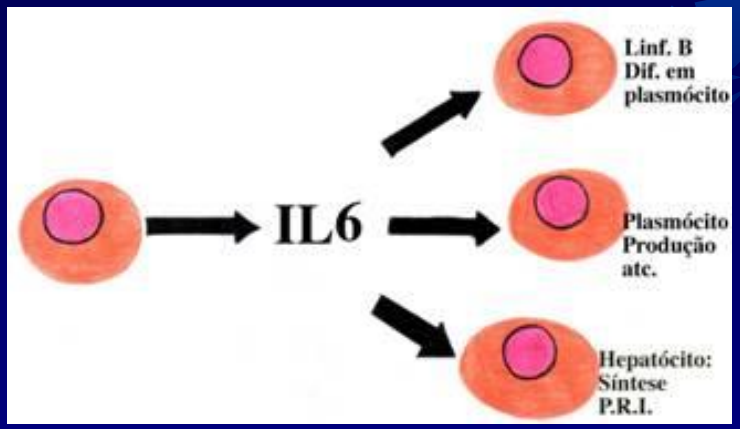


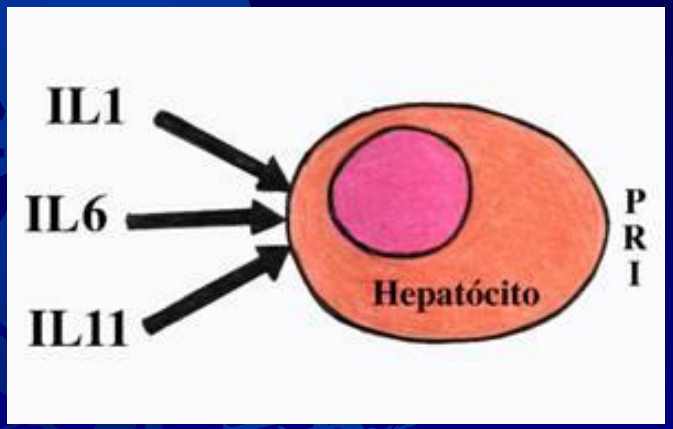


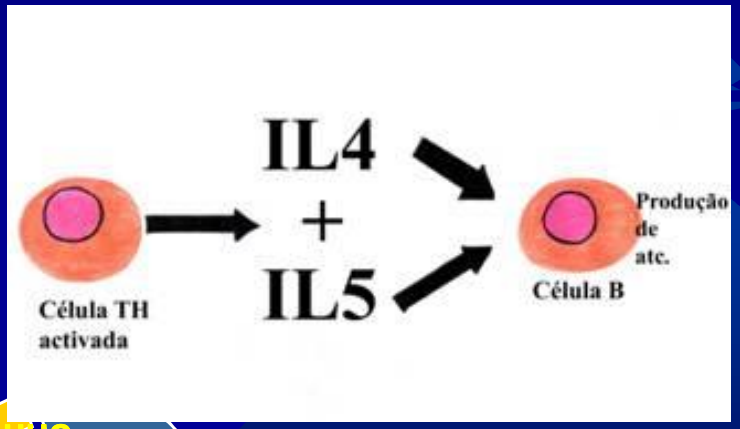
Citocinas

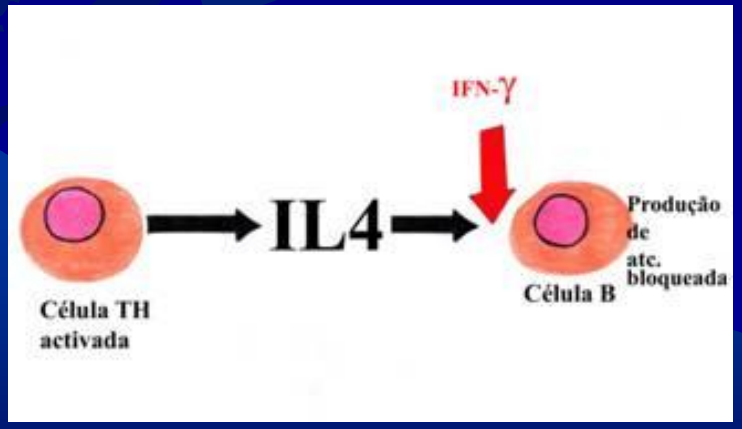
- ✓ Proteínas ou glicoproteínas:
  - com um peso molecular inferior a 30 Kd, e uma sequência de aminoácidos variável, mas estruturada de forma tridimensional numa hélice de tipo α.
  - As principais células produtoras são os linfócitos T helper e os macrófagos.
  - Actuam numa rede de células vizinhas, interagindo entre si, nomeadamente no desenvolvimento e estimulação da resposta humoral, inflamatória, regulação da hematopoese, controle da proliferação celular e indução da cicatrização.

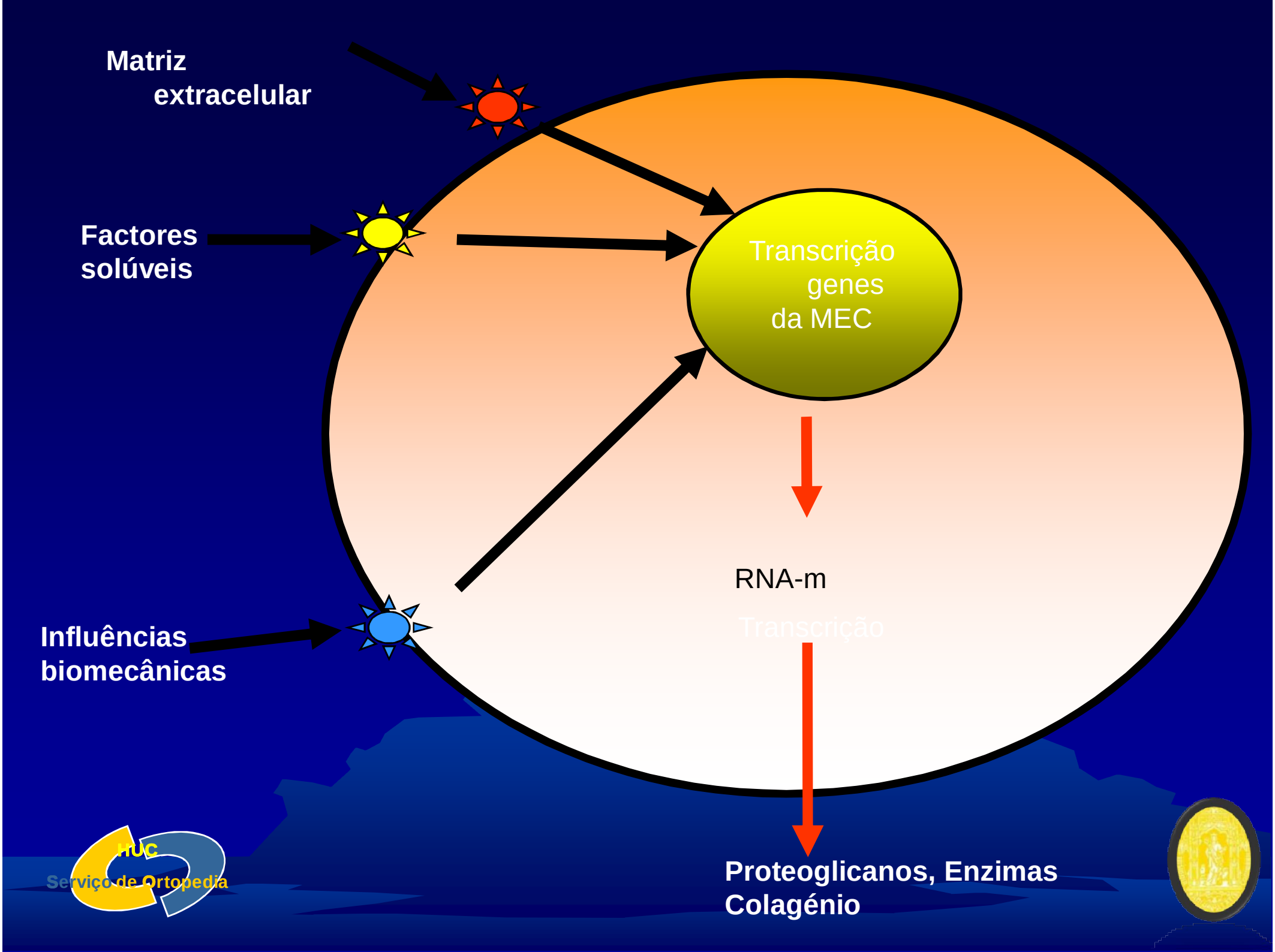
Características citocinas










Matriz
extracelular
Factores
solúveis
Transcrição
genes
da MEC
RNA-m
Transcrição
Influências
biomecânicas
Proteoglicanos, Enzimas
Colagénio
HUC
Serviço de Ortopedia

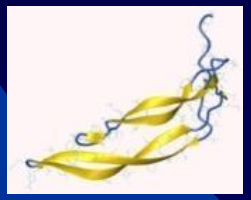
Factores de crescimento

Factor	Origem	Função essencial
PDGF (Platelet-Derived Growth Factor)	Plaquetas, célula endoteliais, placenta	Proliferação do tecido conjuntivo, células da clia e músculo liso
EGF (Epidermal Growth factor)	Glândula submandibular, glândula de Brunner-duodeno)	Proliferação de células mesenquimatosas, epiteliais e gliais
TGF-α (Transforming Growth factor)	Comum em células alvo e relacionado como EGF	Importante na cicatrização da pele
FGF (Transforming Growth factor)	Múltiplas linhas celulares. (pelo menos 19 famílias e 4 tipos de receptores)	Proliferação de diversas linhas celulares, inibição de stem-cells

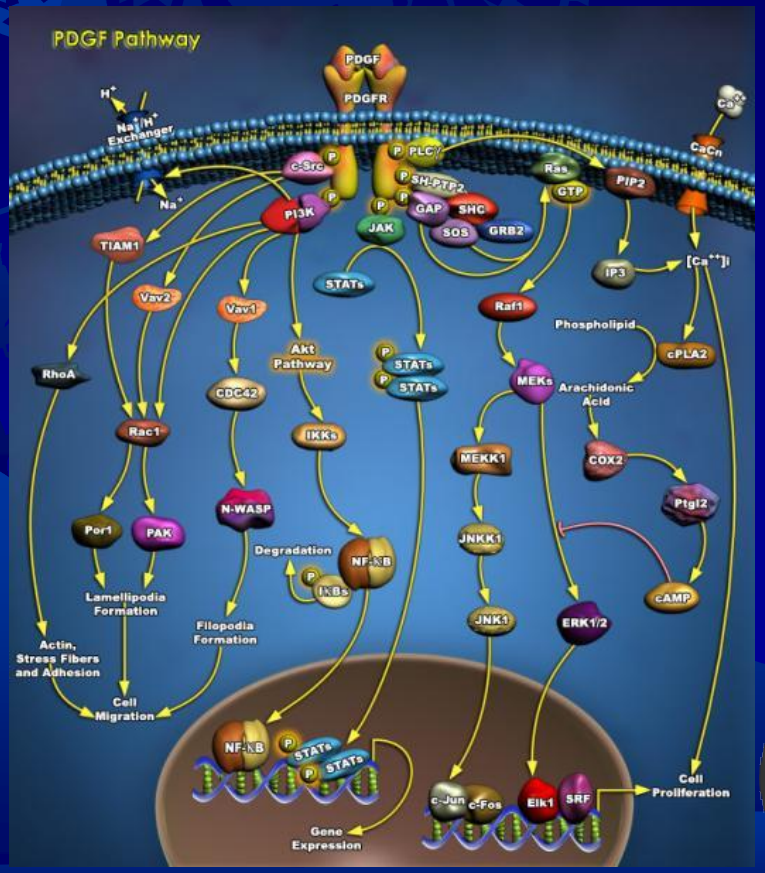
Factores de crescimento

Factor	Origem	Função essencial
Eritropoietina	Rim	Proliferação e diferenciação eritrócitos
TGF-β (Transforming Growth factor)	Células Th activadas e células natural killer (NK)	Acção anti-inflamatória (suppressão produção citocinas), promoção cicatrização cutânea, inibição da proliferação linfócitos e macrófagos
IGF-I (Transforming Growth factor)	Fígado	Proliferação de vários tipos celulares
IGF-II (Transforming Growth factor)	Vários tipos celulares	Proliferação de vários tipos celulares, principalmente de origem fetal

PDGFs



- ✓ Composto por duas cadeias distintas de polipeptídeos, A e B que podem formar homodímeros (AA; AB)ou heterodímeros (AB).
- ✓ Apenas o heterodímero interactua com o receptor PDGF.
- ✓ As acções dos PDGFs exercem-se em:
  - Células mesnquimatosas
  - Células tecido conjuntivo



PRGF

Platelet rich growth factor

- ✓ É um conjunto de proteínas plaquetárias e plasmáticas.
- ✓ Obtêm-se a partir do sangue periférico do próprio doente momentos antes da sua utilização.
- ✓ Aceleram a reparação e a regeneração dos diversos tecidos.

PRGF/PRP

Platelet-rich growth factor/platelet-rich plasma

- ✓ **Factores plaquetários**
  - **PDGF – Factor de crescimento derivado das plaquetas**
  - **VEGF – Factor de crescimento vascular endotelial**
  - **TGF β – Factor de crescimento transformado Beta**
  - **EGF - Factor de crescimento epidérmico**
  - **FGF β – Factor de crescimento fibroblástico**
- ✓ **Factores plasmáticos**
  - **IGF I - Factor de crescimento insulínico**
  - **HGF - Factor de crescimento hepatócito**

PRP contents & normal values where known ( )	Sanchez[27]	Eppley[8]	Anitua [25]	Marx[22]
Platelet Count (150-400 x10^9L^{-1})	634	1600	460	1086
α-granule factors				
EGF (129)[8] (pg/ml)	481.5	470	442.5	-
VEGF (155)[8] (pg/ml)	383	955	297.5	-
TGF-β1 (35)[8] (ng/ml)	74.99	120	37.83	170
PDGF (3.3)[8] (ng/ml)	35.62	17	13.33	133
bFGF	trace[9]	-	-	-
Plasmatic factors				
IGF-1 (ng/ml)	94.53	No ↑	115.71	No ↑
HGF(pg/ml)	593.87	-	435	-

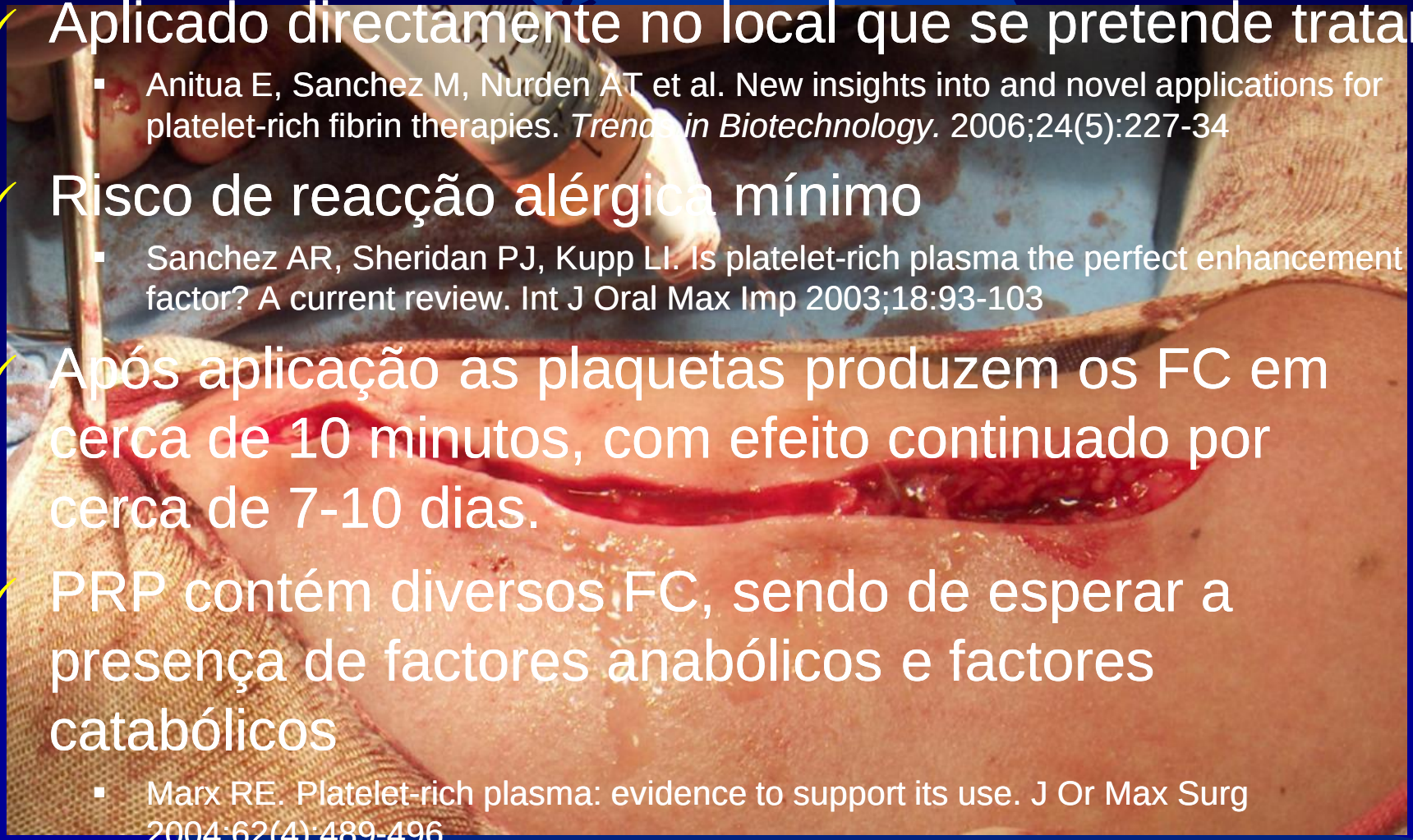
- **Eppley BL, Woodell JE, Higgins J.** Platelet quantification and Growth Factoranalysis from Platelet-Rich Plasma: implications for wound healing. *PlastvReconstr Surg 2004;114:1502-8*
- **Marx RE.** Platelet-rich plasma: evidence to support its use. *J Or Max Surg* 2004;62(4):489-496
- **Anitua E, Andia I, Sanchez M et al**. Autologous preparations rich in growth factors promote proliferation and induce VEGF and HGF production by human tendon cells in culture. *J Orth Res 2005;23:281-286*
- **Sanchez M, Anitua E, Azofra J et al.** Comparison of surgically repaired Achilles tendon tears using platelet-rich fibrin matrices. *Am J Sp Med* 2007;35(2):245-251<

- ✓ **Antoniades (1981)**
  - **1ª a purificar os PDGF a partir das plaquetas.**
  - **(*Proc Natl Acad Sci* USA; 1981, 78).**
- **Marx (2004)**
  - **Desenvolvimento da técnica preparação PRP.**
  - **(*J Or Max Surg*; 2004, 62).**

PRP/Factores de crescimento

- ✓ Utilização sangue autólogo
- ✓ Centrifugação (2 fases)
  - PPP- Plasma pobre em plaquetas
  - PRP- Plasma rico em plaquetas
- ✓ Activação das plaquetas e coágulo de fibrinogéneo
  - Agregação das plaquetas seguindo-se a libertação dos F C contidos nos grânulos a.
  - Activação lenta (5 a 10 minutos) – associa-se 50 microlitros de cloreto de cálcio por cada cm^3 de plasma rico em F C.
  - Activação rápida (1 a 2 minutos) – associam algumas gotas de trombina endógena.
- ✓ Utilizam-se os F C logo após a activação no caso da trombina ou alguns minutos após no caso do cloreto de cálcio.

PRP/Factores de crescimento



- ✓ Aplicado directamente no local que se pretende tratar
  - Anitua E, Sanchez M, Nurden AT et al. New insights into and novel applications for platelet-rich fibrin therapies. *Trends in Biotechnology.* 2006;24(5):227-34
- ✓ Risco de reacção alérgica mínimo
  - Sanchez AR, Sheridan PJ, Kupp LI. Is platelet-rich plasma the perfect enhancement factor? A current review. Int J Oral Max Imp 2003;18:93-103
- ✓ Após aplicação as plaquetas produzem os FC em cerca de 10 minutos, com efeito continuado por cerca de 7-10 dias.
- ✓ PRP contém diversos FC, sendo de esperar a presença de factores anabólicos e factores catabólicos
  - Marx RE. Platelet-rich plasma: evidence to support its use. J Or Max Surg 2004;62(4):489-496

Riscos e complicações

- ✓ Locais
  - Alterações degenerativas
  - Inflamação (primeiros dias)
  - Fibrose (inicia-se a partir da 2ª semana)
- ✓ Sistémicas
  - Infecção (risco mínimo com sistemas fechados)
  - Diminuição sistémica das citocinas

Growth Factor Delivery Methods in the Management of Sports Injuries:The State of Play

Leon Creaney and Bruce Hamilton

Br. J. Sports Med. published online 5 Nov 2007;
doi:10.1136/bjsm.2007.040071

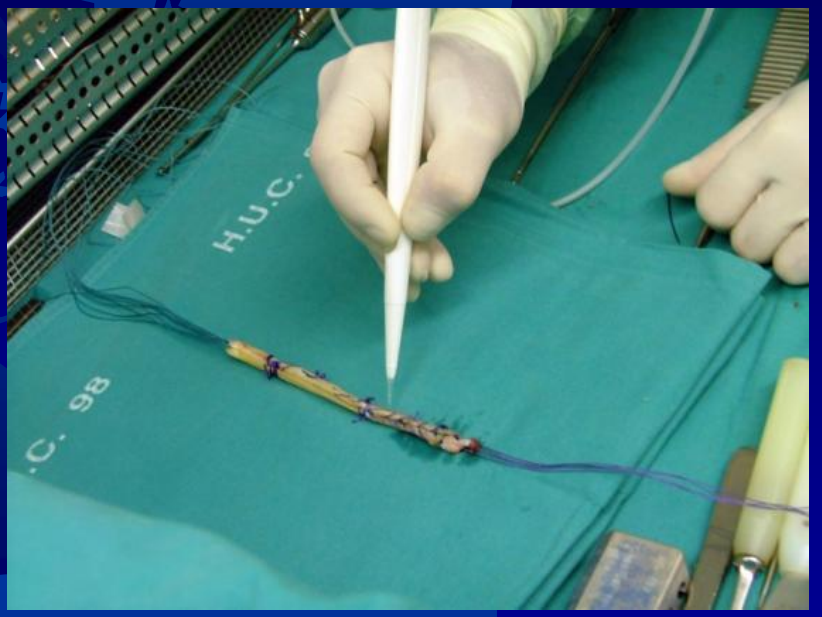

Alguns sistemas

“Artesanal”

HUC
Serviço de Ortopedia

Utiliza trombina bovina

Vivostar™



HUC
Serviço de Ortopedia

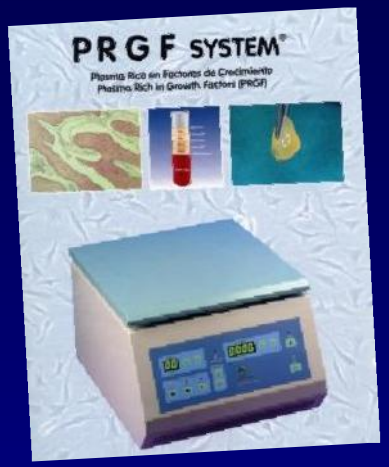
GPS™

HUC
Serviço de Ortopedia

Simphony™ PCS

HUC
Serviço de Ortopedia

PRGF™



HUC
Serviço de Ortopedia

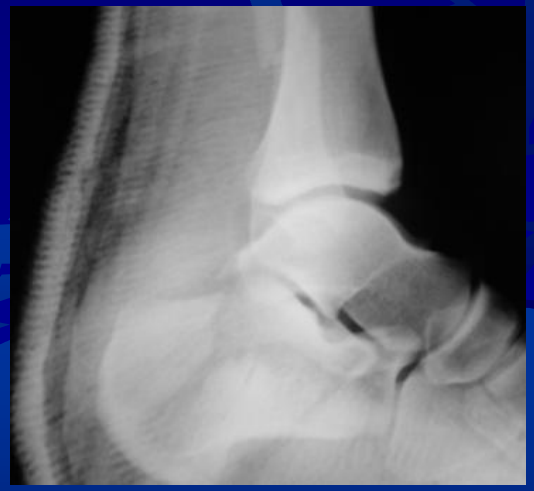
PRGF™


PPGF
0,5cc.
PGF
0,5cc.
PRGF
0,5cc.
FRACCION 1
FRACCION 2
FRACCION 3
Serie blanca
Serie roja

Casos clínicos

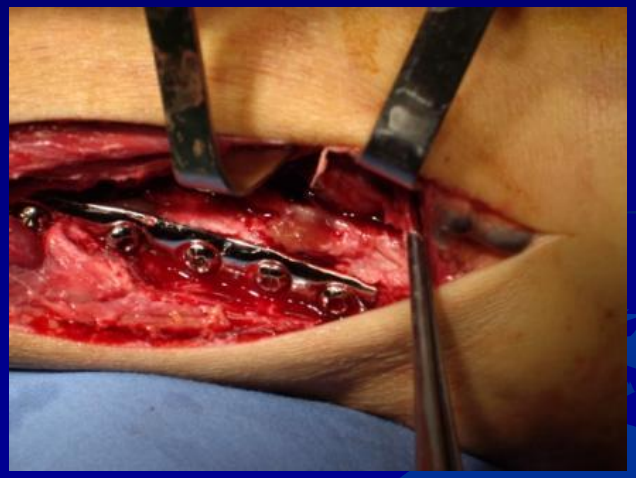
#1

- ✓ Fractura bi-maleolar tipo C
  - Abril de 2006
- ✓ Jogador profissional de futebol



HUC
Serviço de Ortopedia

- Operado em Abril de 2006.
  - Utilização de FC
  - Retorno competitivo em Julho de 2006

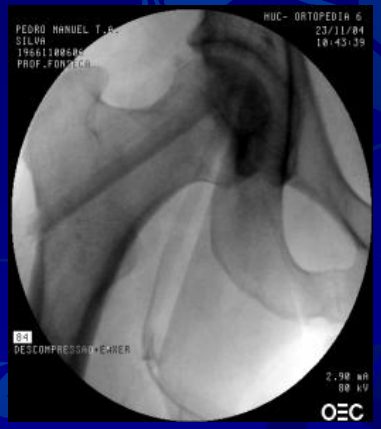


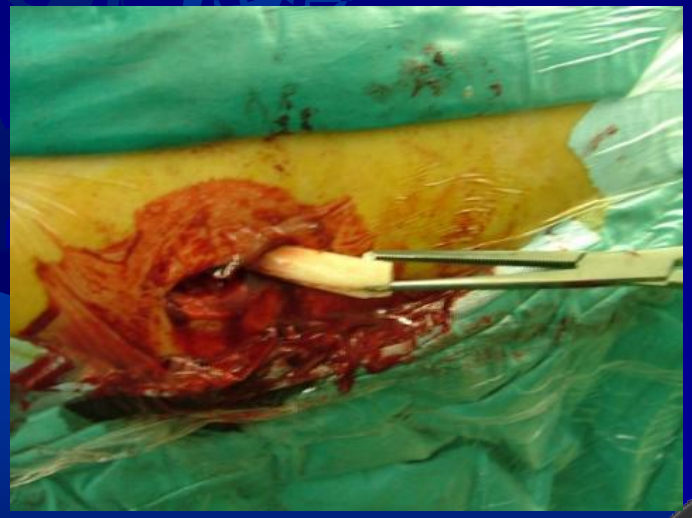
HUC
Serviço de Ortopedia

#2

- ✓ PAS, 37 anos
- ✓ Osteonecrose avascular cabeça femoral
  - Novembro de 2004

HUC
Serviço de Ortopedia

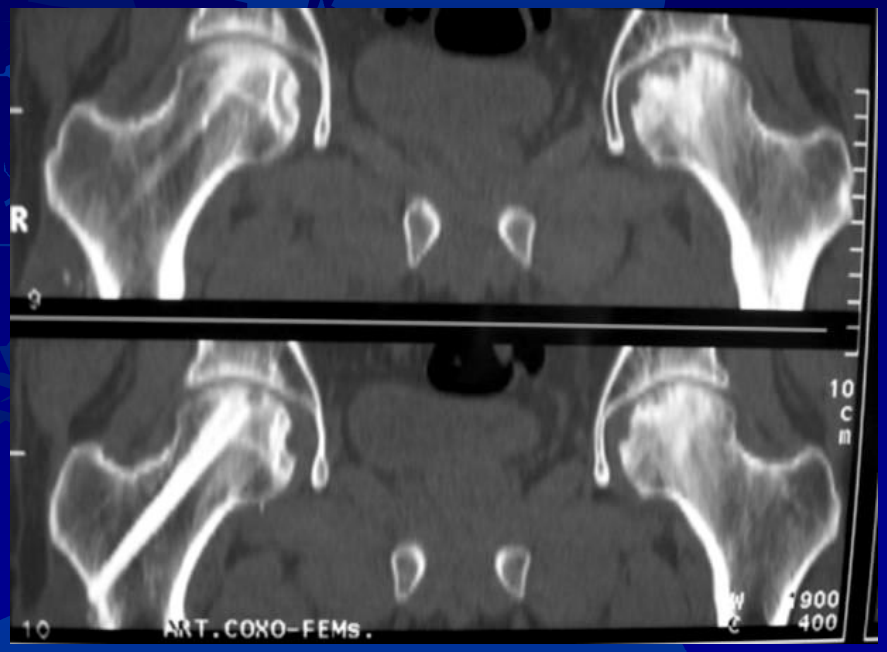




HUC

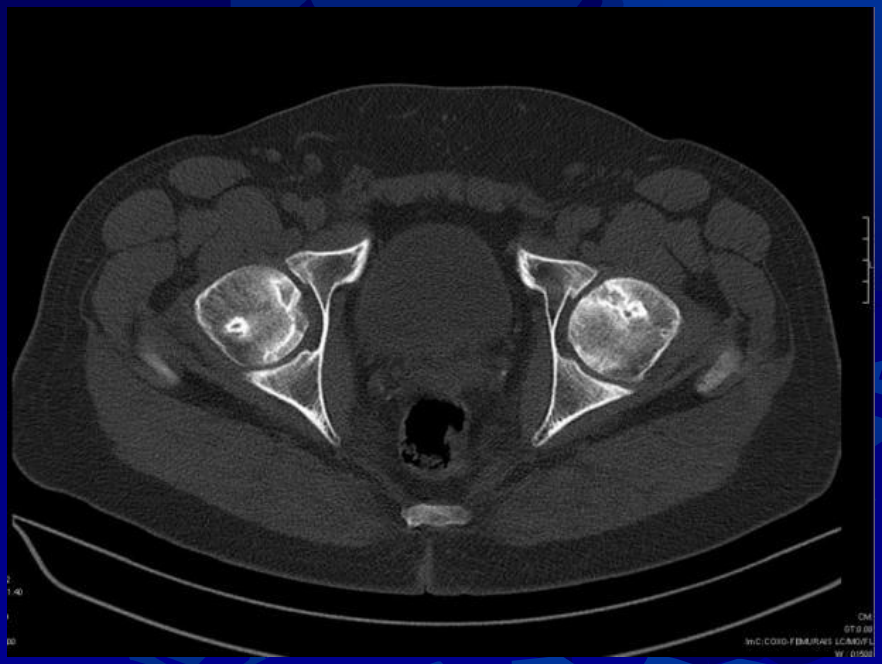
Serviço de Ortopedia

3 meses



HUC
Serviço de Ortopedia

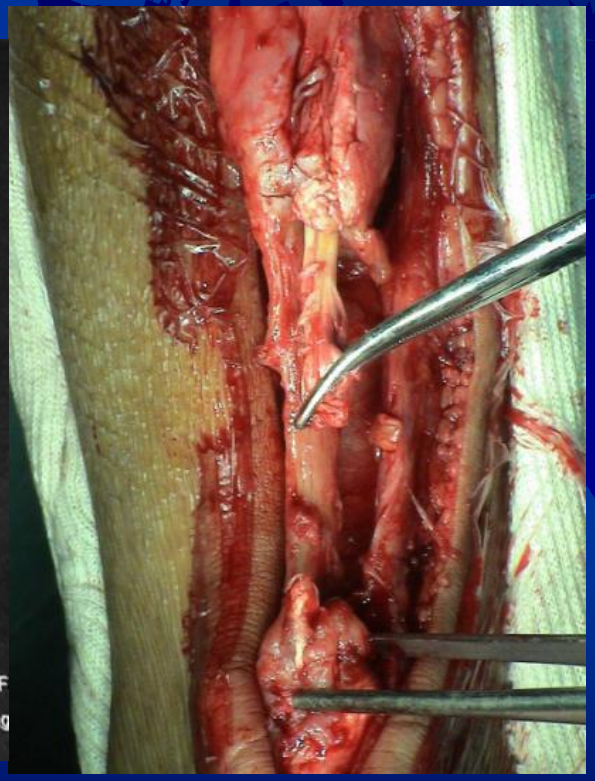
3 anos



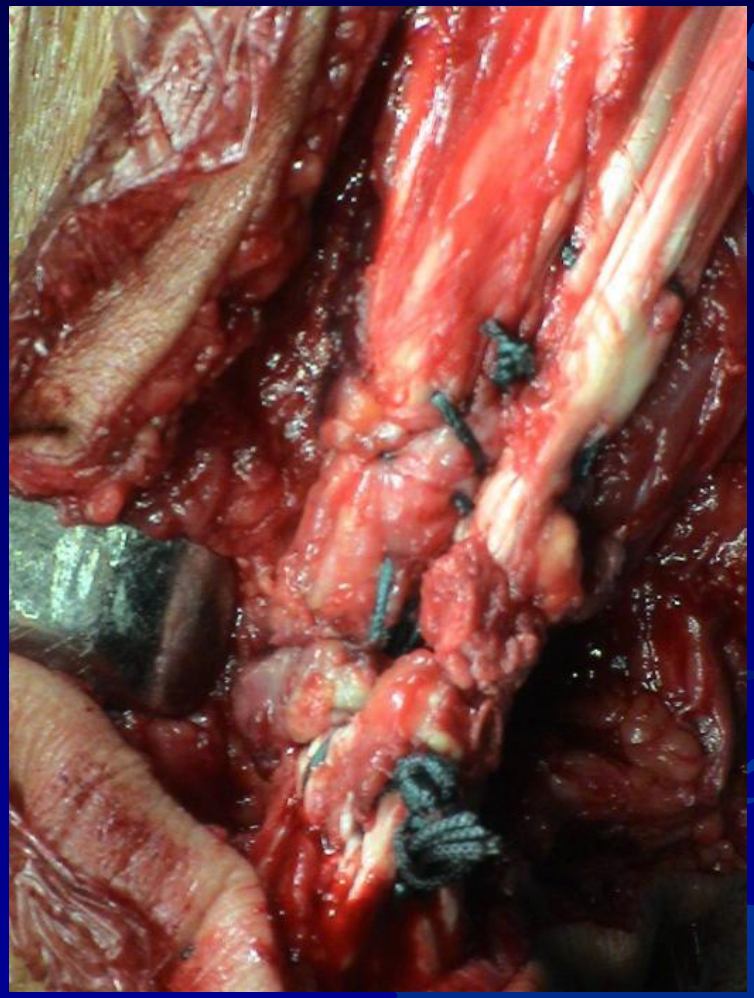
HUC
Serviço de Ortopedia

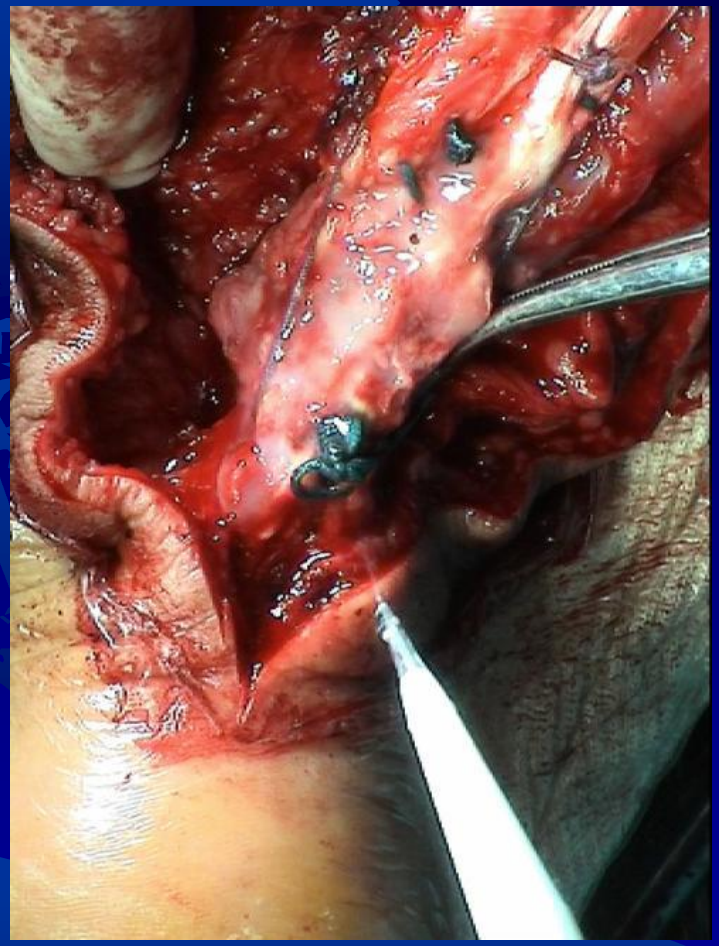
#3

- ✓ VMC, 37 anos
- ✓ Rotura crónica tendão de Aquiles



HUC
Serviço de Ortopedia





HUC
Serviço de Ortopedia

8 meses

HUC
Serviço de Ortopedia

#4

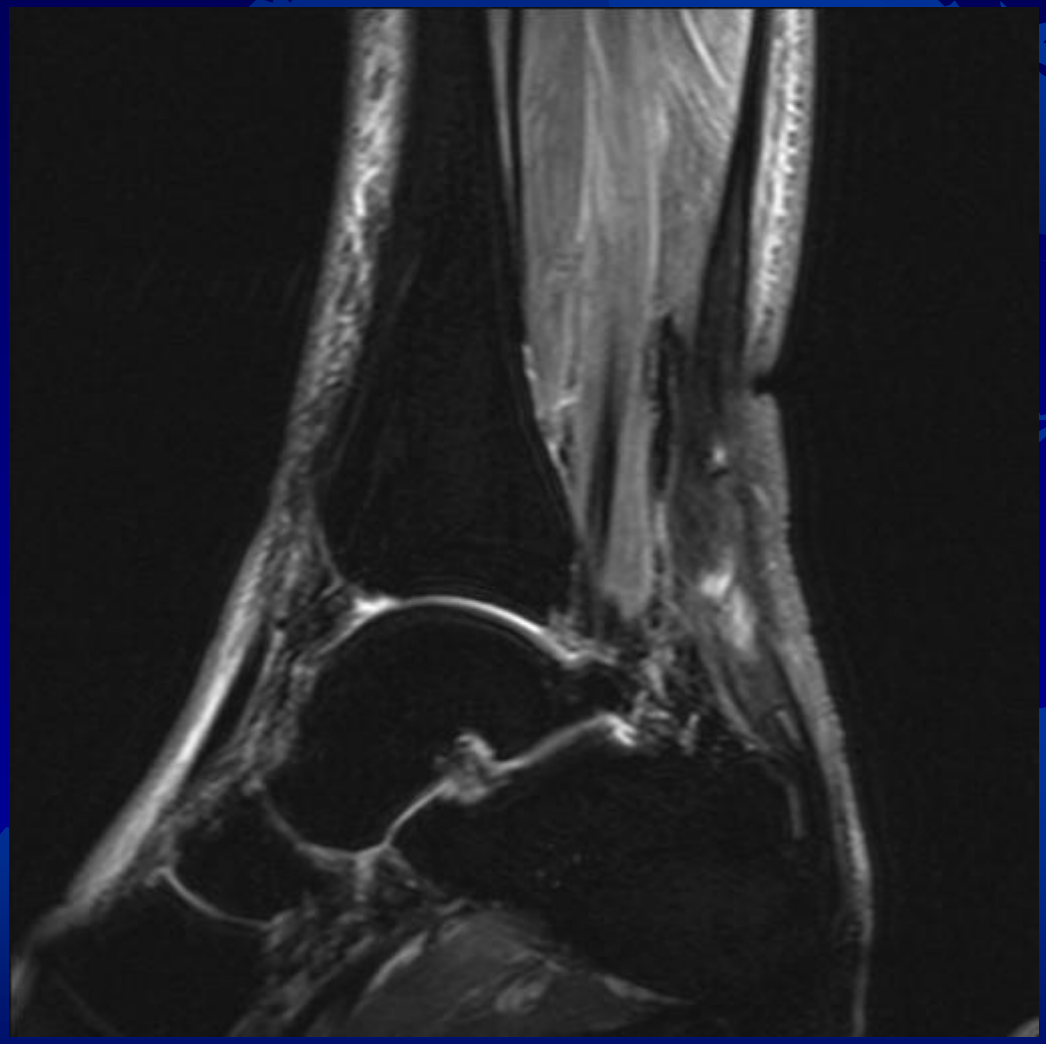
- ✓ AMMB, 49 anos
- ✓ Rotura aguda tendão aquiles

HUC
Serviço de Ortopedia

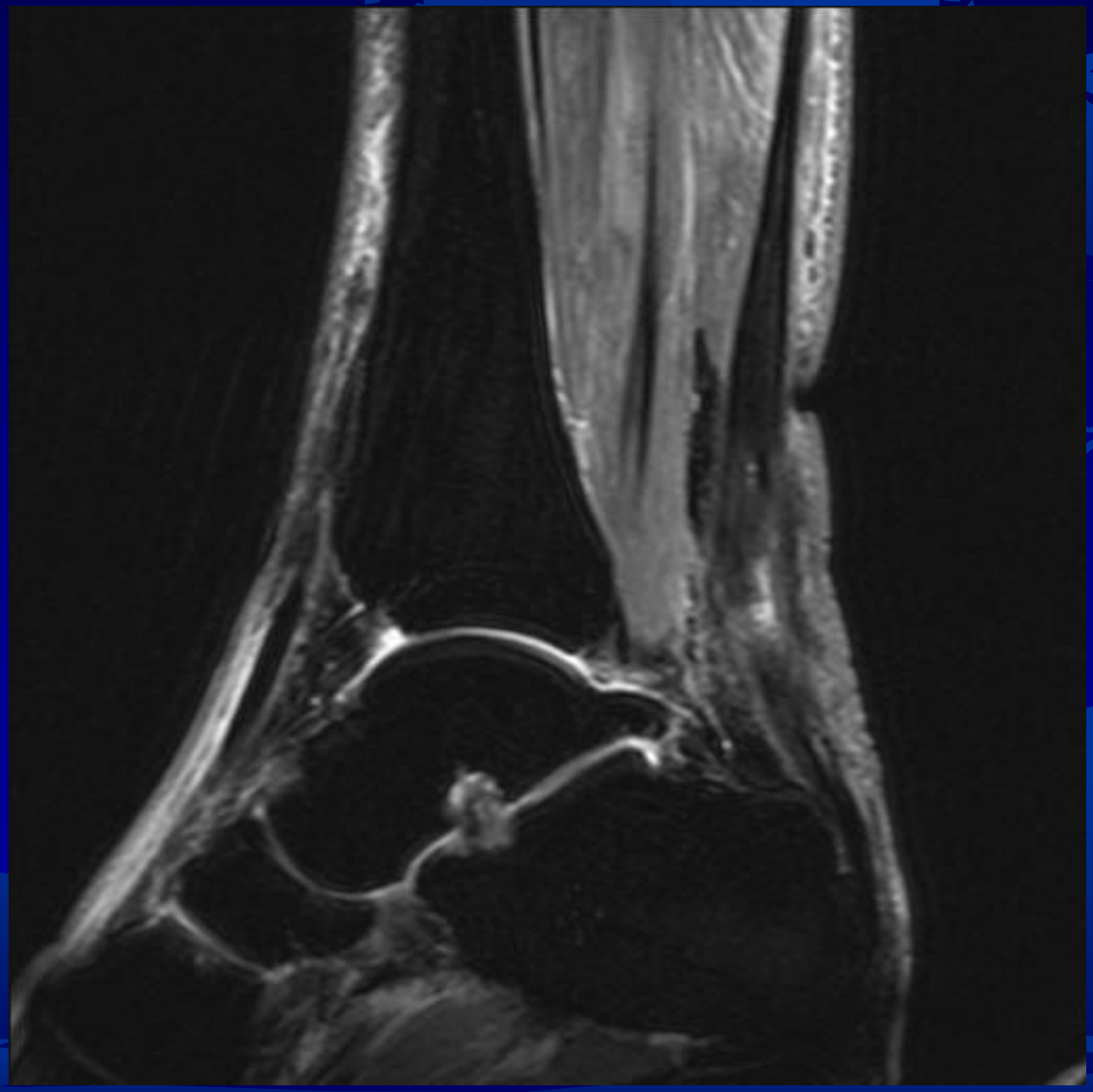
Sutura percutânea

HUC
Serviço de Ortopedia

1 mês



5 meses



HUC
Serviço de Ortopedia

5

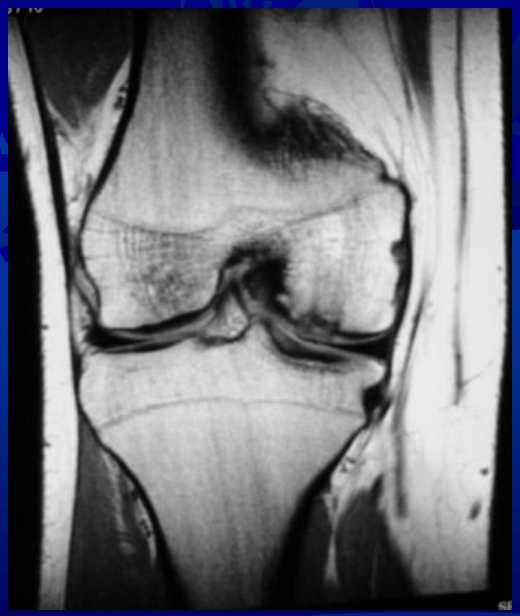
- ✓ AAMC, 19 anos
- ✓ OCD grau III

HUC
Serviço de Ortopedia

Cirurgia

HUC
Serviço de Ortopedia

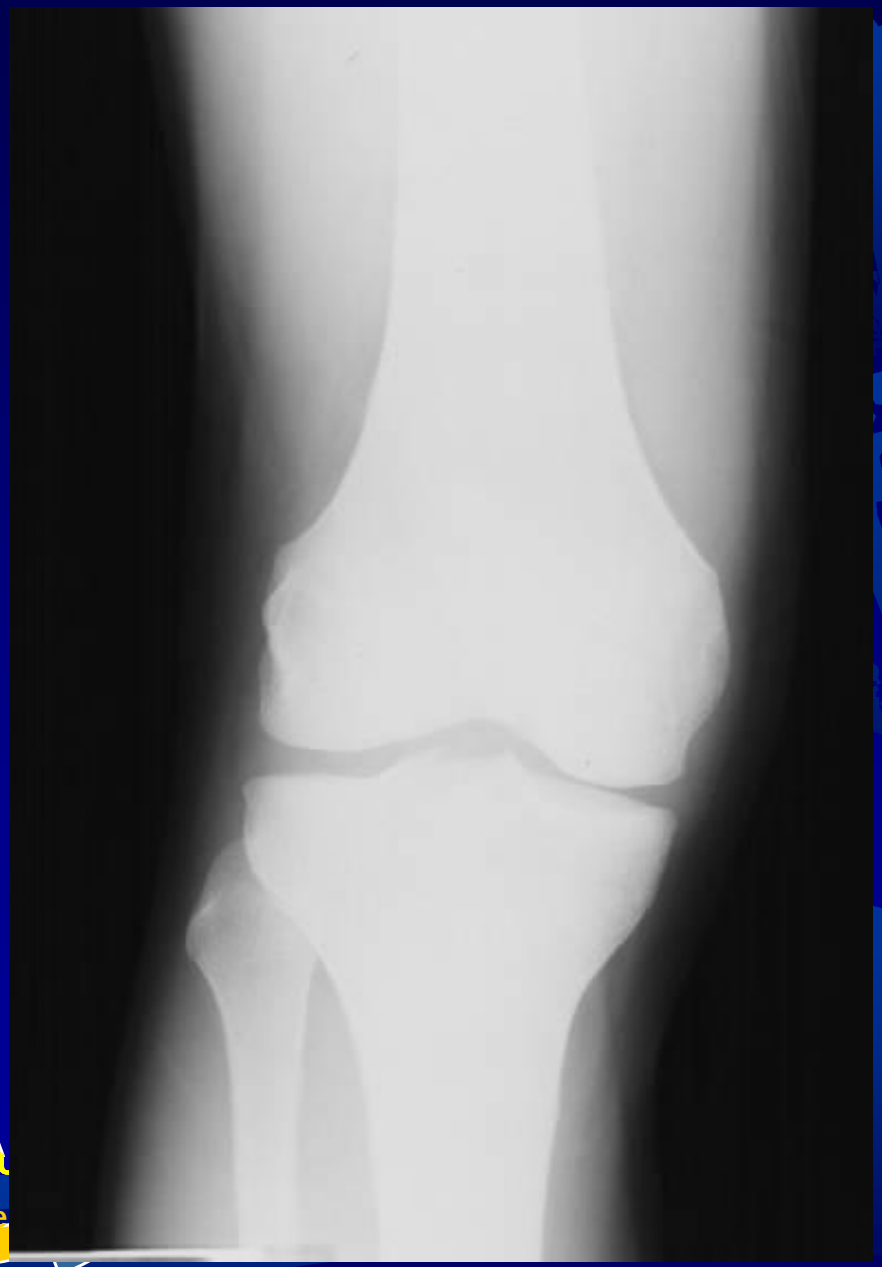
3 meses

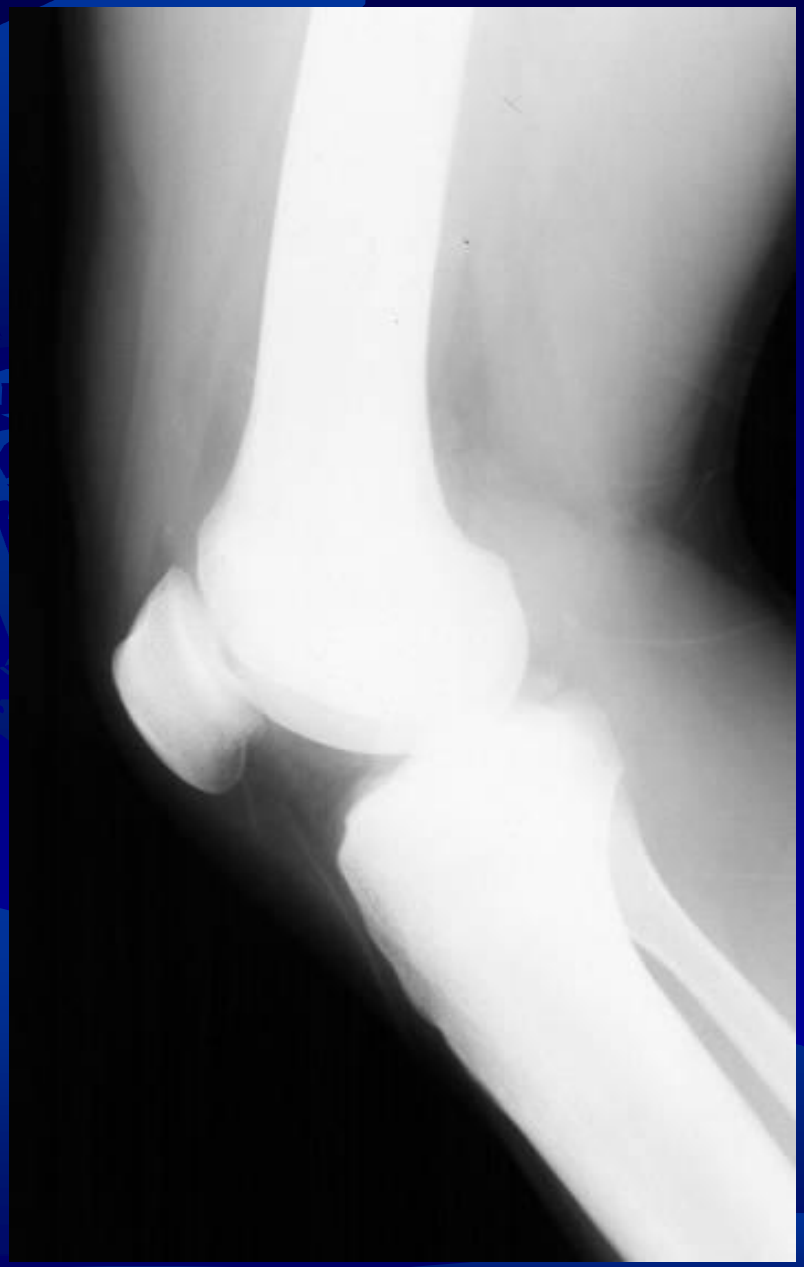


#6

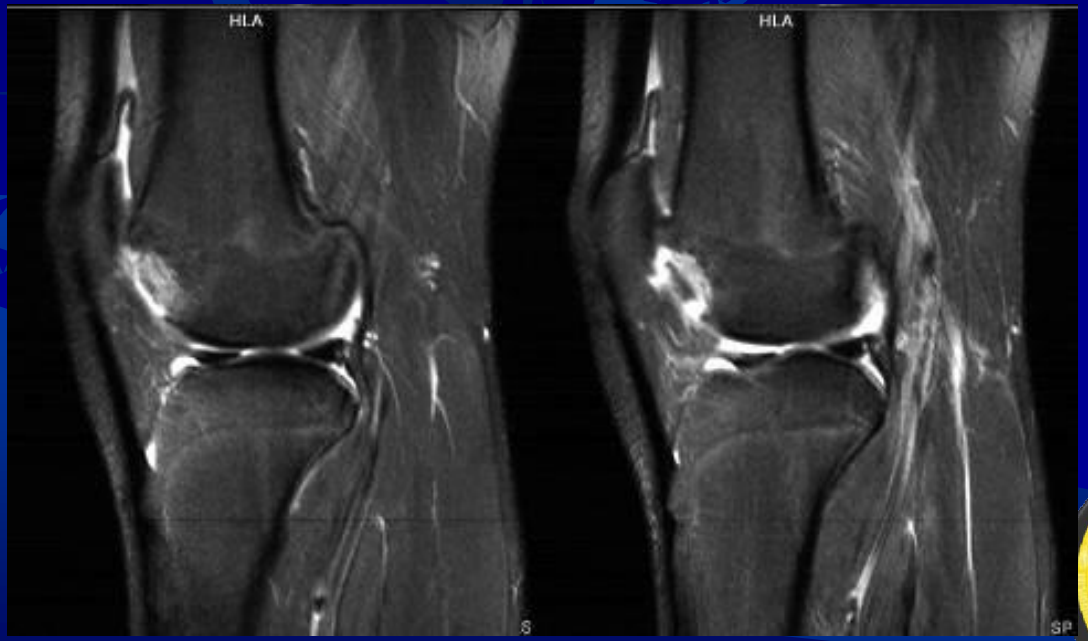
- AJMC, PU 19860200404
  - Sexo masculino, 18 anos
  - Síndrome osteocartilagíneo femoro-patelar à dtª
  - Sem antecedentes de traumatismo prévio.
  - Diversos episódios de hidrartrose
  - Mobilidade 135-0-0.
  - Sem instabilidade cápsulo-ligamentar
  - Sinais rotulianos positivos (+++/+++)
    - Rabot
    - Zohlen
  - ICRS – D
  - Lysholm - 60

Radiologia

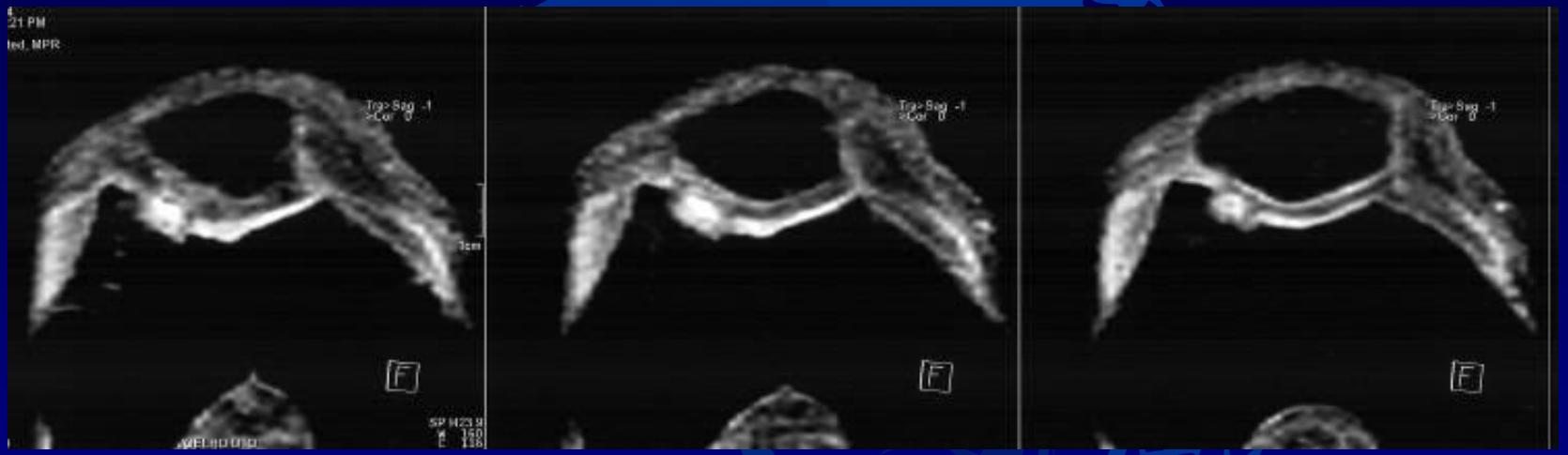


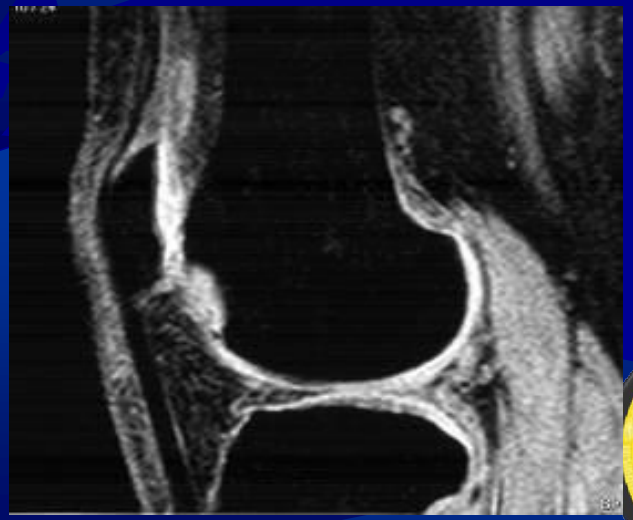


RMN



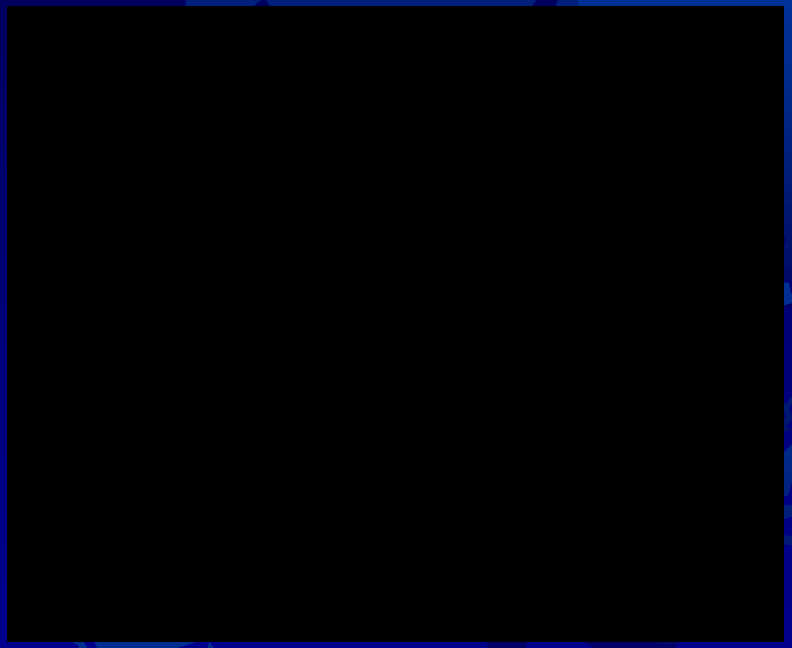
RMN





HUC
Serviço de Ortopedia

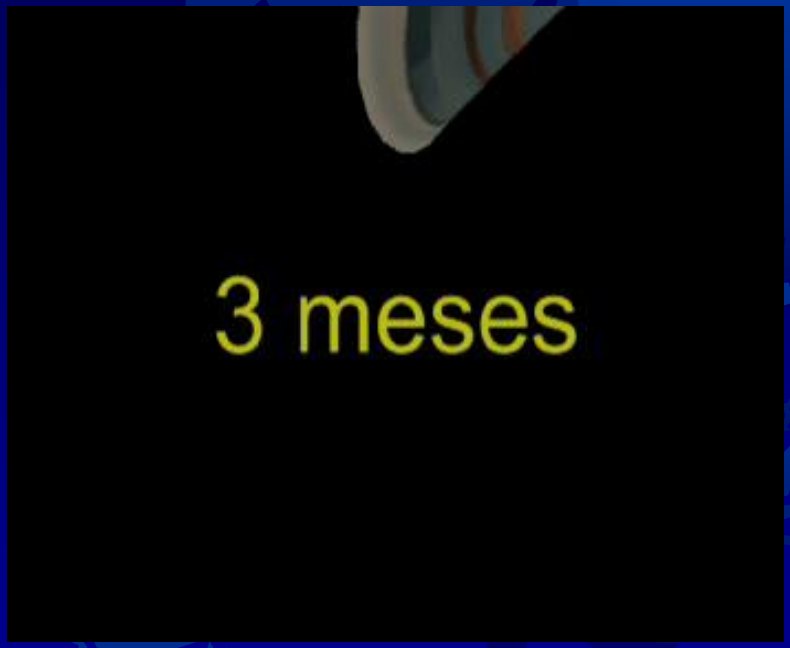
3 de Junho de 2004



HUC
Serviço de Ortopedia

Controlo em Agosto 2004

- Marcha sem limitações
- Atrofia músculo quadricipital
- Mobilidade 135-0-0.
- Sem hidrartrose
- Sinais rotulianos negativos
- ICRS – Grupo A
- Lysholm - 92


3 meses

3 meses


5 IMA 8 / 16
H
RP
5cm
SP A90.8


RP
5cm
SP A83.6


4 IMA 6 / 20
H
AR
5cm
SP R89.1

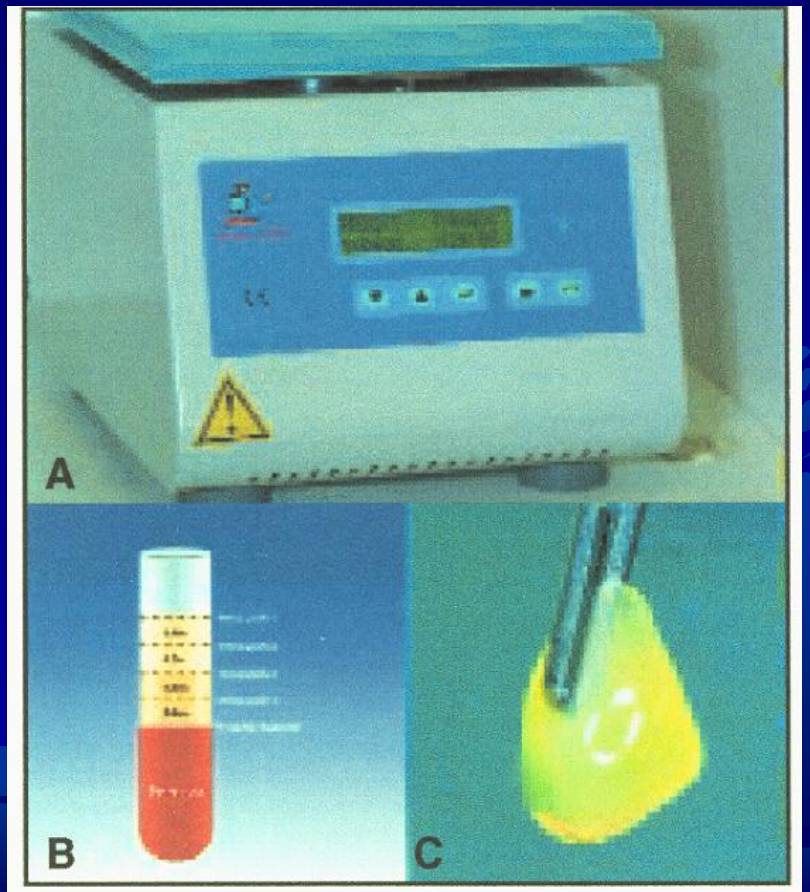

7 IMA 28 / 60
H
AR
5cm
SP R70.9

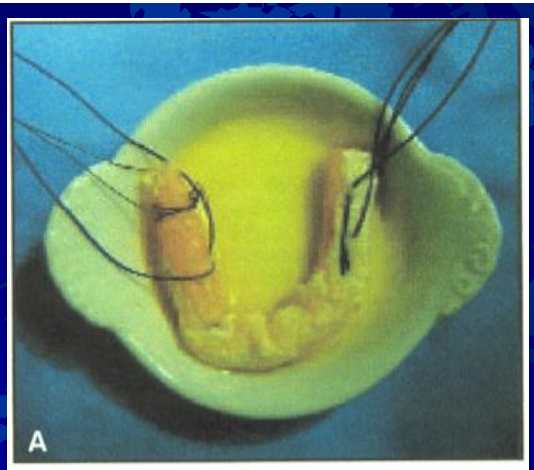
Questão

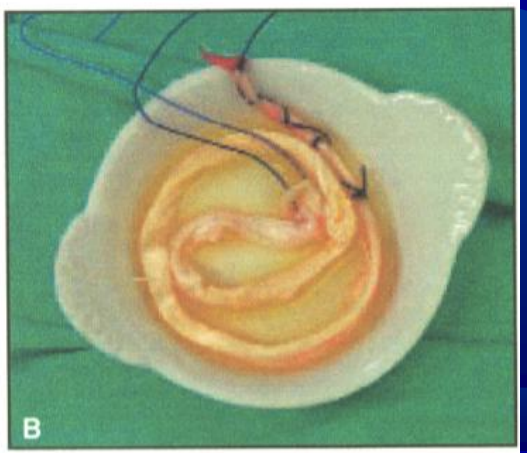
Será assim tão grande o sucesso?

Aplicación de plasma autólogo rico en factores de crecimiento en cirugía artroscópica

M. Sánchez[(1)], J. Azofra[(1)], B. Aizpurúa[(1)],
R. Elorriaga[(1)], E. Anitua[(2)], I. Andía[(3)]







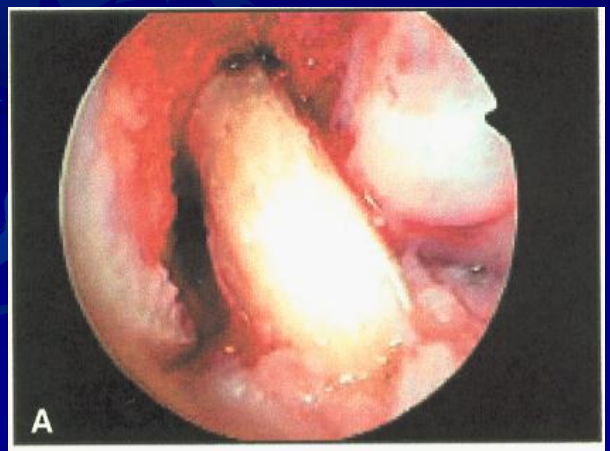


Tabla I

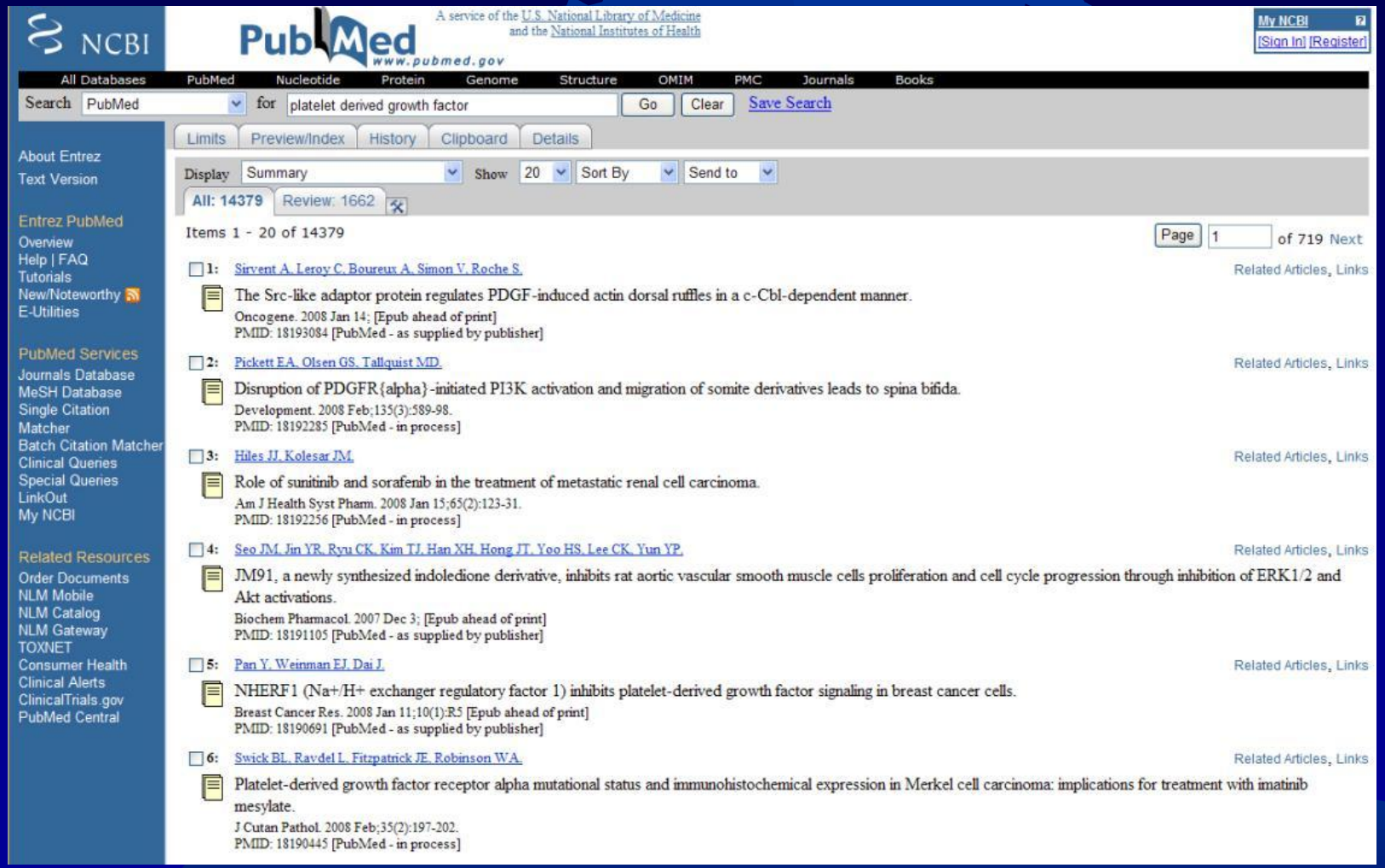
RESULTADOS OBTENIDOS

Evolución clínica	Grupo A 50 pacientes (sin PRGF)	Grupo A 50 pacientes (conn PRGF)
Presencia de grandes hematomas postoperatorios que cursan con dolor, edema pretibial y febrícula.	18% (9 pacientes)	6% (3 pacientes)
Presencia de hematomas menores	30% (15 pacientes)	16% (8 pacientes)
Artritis infecciosa (se resolvieron con sinovectomía, lavado artroscópico y tramiento antibiótico, 6 semanas)	2% (1 paciente)	2% (1 paciente)
Derrames postoperatorios que al menos requirieron de una artrocentesis evacuadora	26% (13 pacientes)	24% (12 pacientes)
El síndrome del "Cíclope" ha obligado a realizar una artrolisis	6% (3 pacientes)	2% (1 paciente)
Manipulaciones forzadas	4% (2 pacientes)	0
Rodillas perfectamente estables	70% (35 pacientes)	82% (41 pacientes)
Rodillas que presentan una maniobra de Lachman con un tope anterior, con test dinámico (pívot-shift) negativo ó insinuación del mismo.	30% (15 pacientes)	18% (9 pacientes)
Movilidad completa	62% (31 pacientes)	62% (31 pacientes)
La limitación de la flexión por debajo de los 120º	4% (2 pacientes)	4% (2 pacientes)
Falta de extensión, sin contar los casos de cíclopes: "flexo" menor ó igual a 5º y tolerable.	8% (4 pacientes)	18% (9 pacientes)

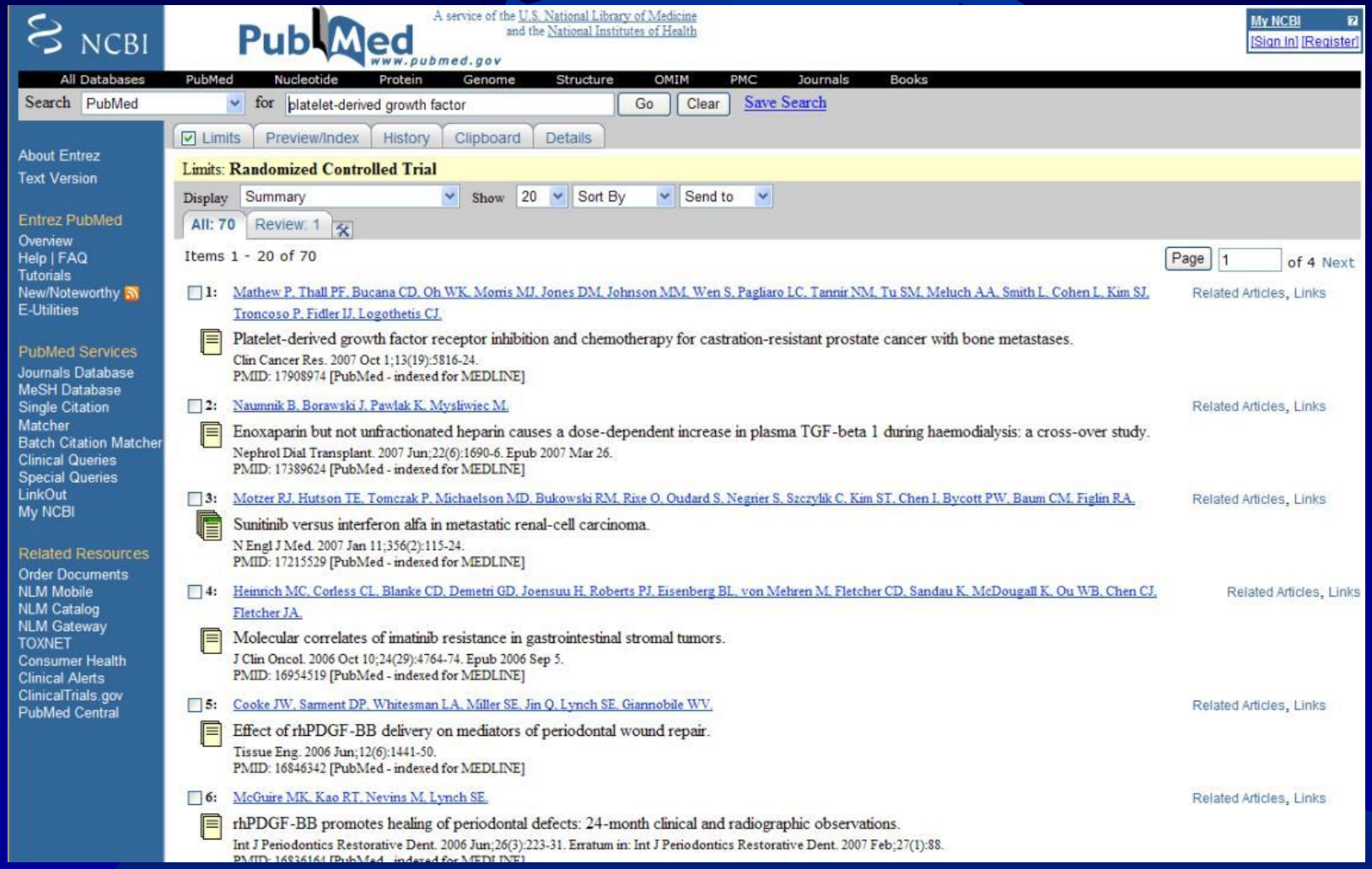
Pesquisa bibliográfica

- ✓ PubMed
- ✓ Cochrane
  - Evidence based medicine

PubMed


NCBI
PubMed
www.pubmed.gov
A service of the U.S. National Library of Medicine and the National Institutes of Health
My NCBI
[Sign In] [Register]
All Databases PubMed Nucleotide Protein Genome Structure OMIM PMC Journals Books
Search PubMed for platelet derived growth factor Go Clear Save Search
Limits Preview/Index History Clipboard Details
About Entrez
Text Version
Entrez PubMed
Overview
Help | FAQ
Tutorials
New/Noteworthy
E-Utilities
PubMed Services
Journals Database
MeSH Database
Single Citation Matcher
Batch Citation Matcher
Clinical Queries
Special Queries
LinkOut
My NCBI
Related Resources
Order Documents
NLM Mobile
NLM Catalog
NLM Gateway
TOXNET
Consumer Health
Clinical Alerts
ClinicalTrials.gov
PubMed Central
Display Summary Show 20 Sort By Send to
All: 14379 Review: 1662
Items 1 - 20 of 14379
Page 1 of 719 Next
1: Sirvent A, Leroy C, Boureux A, Simon V, Roche S.
The Src-like adaptor protein regulates PDGF-induced actin dorsal ruffles in a c-Cbl-dependent manner.
Oncogene. 2008 Jan 14; [Epub ahead of print]
PMID: 18193084 [PubMed - as supplied by publisher]
Related Articles, Links
2: Pickett EA, Olsen GS, Tallquist MD.
Disruption of PDGFR{alpha}-initiated PI3K activation and migration of somite derivatives leads to spina bifida.
Development. 2008 Feb;135(3):589-98.
PMID: 18192285 [PubMed - in process]
Related Articles, Links
3: Hiles JJ, Kolesar JM.
Role of sunitinib and sorafenib in the treatment of metastatic renal cell carcinoma.
Am J Health Syst Pharm. 2008 Jan 15;65(2):123-31.
PMID: 18192256 [PubMed - in process]
Related Articles, Links
4: Seo JM, Jin YR, Ryu CK, Kim TJ, Han XH, Hong JT, Yoo HS, Lee CK, Yun YP.
JM91, a newly synthesized indoledione derivative, inhibits rat aortic vascular smooth muscle cells proliferation and cell cycle progression through inhibition of ERK1/2 and Akt activations.
Biochem Pharmacol. 2007 Dec 3; [Epub ahead of print]
PMID: 18191105 [PubMed - as supplied by publisher]
Related Articles, Links
5: Pan Y, Weinman EJ, Dai J.
NHERF1 (Na+/H+ exchanger regulatory factor 1) inhibits platelet-derived growth factor signaling in breast cancer cells.
Breast Cancer Res. 2008 Jan 11;10(1):R5 [Epub ahead of print]
PMID: 18190691 [PubMed - as supplied by publisher]
Related Articles, Links
6: Swick BL, Ravdel L, Fitzpatrick JE, Robinson WA.
Platelet-derived growth factor receptor alpha mutational status and immunohistochemical expression in Merkel cell carcinoma: implications for treatment with imatinib mesylate.
J Cutan Pathol. 2008 Feb;35(2):197-202.
PMID: 18190445 [PubMed - in process]
Related Articles, Links

Estudos RCT



NCBI

PubMed www.pubmed.gov

A service of the U.S. National Library of Medicine and the National Institutes of Health

My NCBI [Sign In] [Register]

All Databases | PubMed | Nucleotide | Protein | Genome | Structure | OMIM | PMC | Journals | Books

Search PubMed for platelet-derived growth factor Go Clear Save Search

Limits | Preview/Index | History | Clipboard | Details

About Entrez
Text Version

Entrez PubMed
Overview
Help | FAQ
Tutorials
New/Noteworthy
E-Utilities

PubMed Services
Journals Database
MeSH Database
Single Citation Matcher
Batch Citation Matcher
Clinical Queries
Special Queries
LinkOut
My NCBI

Related Resources
Order Documents
NLM Mobile
NLM Catalog
NLM Gateway
TOXNET
Consumer Health
Clinical Alerts
ClinicalTrials.gov
PubMed Central

Limits: **Randomized Controlled Trial**

Display Summary Show 20 Sort By Send to

All: 70 Review: 1

Items 1 - 20 of 70 Page 1 of 4 Next

1: Mathew P, Thall PF, Bucana CD, Oh WK, Morris MJ, Jones DM, Johnson MM, Wen S, Pagliaro LC, Tannir NM, Tu SM, Meluch AA, Smith L, Cohen L, Kim SJ, Troncoso P, Fidler IJ, Logothetis CJ. Related Articles, Links

Platelet-derived growth factor receptor inhibition and chemotherapy for castration-resistant prostate cancer with bone metastases.
Clin Cancer Res. 2007 Oct 1;13(19):5816-24.
PMID: 17908974 [PubMed - indexed for MEDLINE]

2: Naumnik B, Borawski J, Pawlak K, Mysliwiec M. Related Articles, Links

Enoxaparin but not unfractionated heparin causes a dose-dependent increase in plasma TGF-beta 1 during haemodialysis: a cross-over study.
Nephrol Dial Transplant. 2007 Jun;22(6):1690-6. Epub 2007 Mar 26.
PMID: 17389624 [PubMed - indexed for MEDLINE]

3: Motzer RJ, Hutson TE, Tomczak P, Michaelson MD, Bukowski RM, Rixe O, Oudard S, Negrier S, Szczylik C, Kim ST, Chen I, Bycott PW, Baum CM, Figlin RA. Related Articles, Links

Sunitinib versus interferon alfa in metastatic renal-cell carcinoma.
N Engl J Med. 2007 Jan 11;356(2):115-24.
PMID: 17215529 [PubMed - indexed for MEDLINE]

4: Heinrich MC, Corless CL, Blanke CD, Demetri GD, Joensuu H, Roberts PJ, Eisenberg BL, von Mehren M, Fletcher CD, Sandau K, McDougall K, Ou WB, Chen CJ, Fletcher JA. Related Articles, Links

Molecular correlates of imatinib resistance in gastrointestinal stromal tumors.
J Clin Oncol. 2006 Oct 10;24(29):4764-74. Epub 2006 Sep 5.
PMID: 16954519 [PubMed - indexed for MEDLINE]

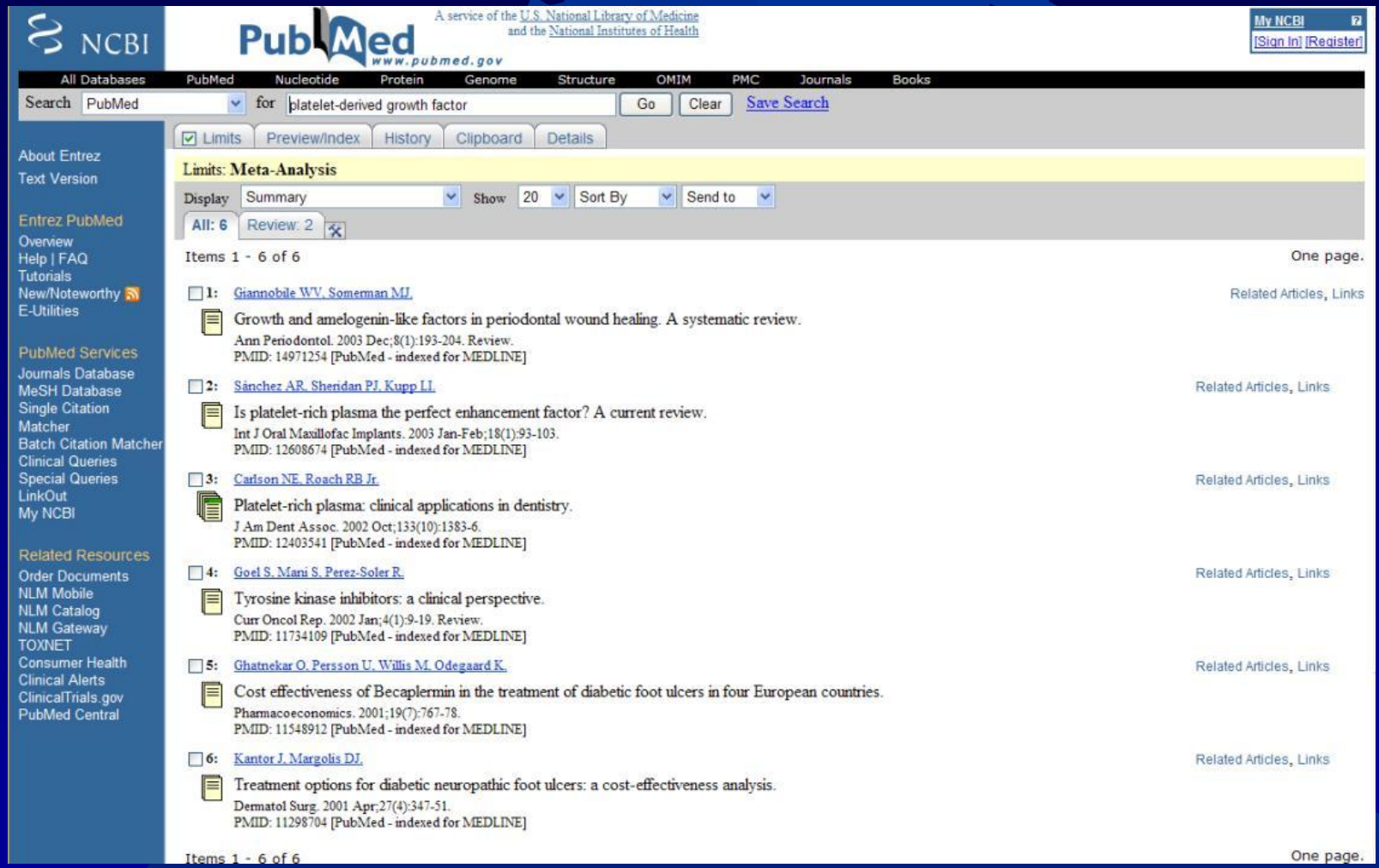
5: Cooke JW, Sarment DP, Whitesman LA, Miller SE, Jin Q, Lynch SE, Giannobile WV. Related Articles, Links

Effect of rhPDGF-BB delivery on mediators of periodontal wound repair.
Tissue Eng. 2006 Jun;12(6):1441-50.
PMID: 16846342 [PubMed - indexed for MEDLINE]

6: McGuire MK, Kao RT, Nevins M, Lynch SE. Related Articles, Links

rhPDGF-BB promotes healing of periodontal defects: 24-month clinical and radiographic observations.
Int J Periodontics Restorative Dent. 2006 Jun;26(3):223-31. Erratum in: Int J Periodontics Restorative Dent. 2007 Feb;27(1):88.
PMID: 16836164 [PubMed - indexed for MEDLINE]

Meta-análise



NCBI

PubMed www.pubmed.gov

A service of the U.S. National Library of Medicine and the National Institutes of Health

My NCBI [Sign In] [Register]

All Databases | PubMed | Nucleotide | Protein | Genome | Structure | OMIM | PMC | Journals | Books

Search PubMed for platelet-derived growth factor Go Clear Save Search

Limits | Preview/Index | History | Clipboard | Details

About Entrez
Text Version

Entrez PubMed
Overview
Help | FAQ
Tutorials
New/Noteworthy
E-Utilities

PubMed Services
Journals Database
MeSH Database
Single Citation Matcher
Batch Citation Matcher
Clinical Queries
Special Queries
LinkOut
My NCBI

Related Resources
Order Documents
NLM Mobile
NLM Catalog
NLM Gateway
TOXNET
Consumer Health
Clinical Alerts
ClinicalTrials.gov
PubMed Central

Limits: **Meta-Analysis**

Display Summary Show 20 Sort By Send to

All: 6 Review: 2

Items 1 - 6 of 6 One page.

1: Giannobile WV, Somerman MJ. Related Articles, Links
Growth and amelogenin-like factors in periodontal wound healing. A systematic review.
Ann Periodontol. 2003 Dec;8(1):193-204. Review.
PMID: 14971254 [PubMed - indexed for MEDLINE]

2: Sánchez AR, Sheridan PJ, Kupp LI. Related Articles, Links
Is platelet-rich plasma the perfect enhancement factor? A current review.
Int J Oral Maxillofac Implants. 2003 Jan-Feb;18(1):93-103.
PMID: 12608674 [PubMed - indexed for MEDLINE]

3: Carlson NE, Roach RB Jr. Related Articles, Links
Platelet-rich plasma: clinical applications in dentistry.
J Am Dent Assoc. 2002 Oct;133(10):1383-6.
PMID: 12403541 [PubMed - indexed for MEDLINE]

4: Goel S, Mani S, Perez-Soler R. Related Articles, Links
Tyrosine kinase inhibitors: a clinical perspective.
Curr Oncol Rep. 2002 Jan;4(1):9-19. Review.
PMID: 11734109 [PubMed - indexed for MEDLINE]

5: Ghatnekar O, Persson U, Willis M, Odegaard K. Related Articles, Links
Cost effectiveness of Becaplermin in the treatment of diabetic foot ulcers in four European countries.
Pharmacoeconomics. 2001;19(7):767-78.
PMID: 11548912 [PubMed - indexed for MEDLINE]

6: Kantor J, Margolis DJ. Related Articles, Links
Treatment options for diabetic neuropathic foot ulcers: a cost-effectiveness analysis.
Dermatol Surg. 2001 Apr;27(4):347-51.
PMID: 11298704 [PubMed - indexed for MEDLINE]

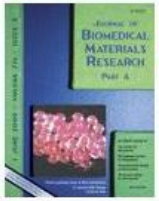
Items 1 - 6 of 6 One page.

EBM


www.cochrane.org > search results
Cochrane.org search
THE COCHRANE COLLABORATION
Powered by Google
Searched for platelet-rich factors
Results 1 - 7 of about 7
Sort by: Date / Relevance
» Cochrane reviews
» The Cochrane Library
» News
» Events
» Training resources
» For healthcare users
» About us
[MS WORD] Tsunami notes
... set as triggers varied, as did other factors. However, the reviewers concluded that, 'In ... Platelet-rich plasmapheresis (PRP) is another technique that ...
www.cochrane.org/evidenceaid/injuriesandwounds/transfusion/bloodtransfusion.doc - 2005-11-30
Cochrane Reviews - by topic 'Wounds'
... Staphylococcus aureus colonization Autologous platelet rich-plasma for treating chronic ... New Granulocyte-colony stimulating factors as adjunctive therapy ...
www.cochrane.org/reviews/en/topics/96.html - 40k
Cochrane Reviews - Alphabetically: [P]
... Acute Coronary Syndromes Platelet-rich-plasmapheresis for minimising ... of labour Prophylactic platelet transfusion for haemorrhage ... with risk factors for neonatal ...
www.cochrane.org/reviews/en/index_list_p_reviews.html - 95k
Cochrane Reviews - Alphabetically: [P]
... Coronary Syndromes Platelet-rich plasma (PRP) with bone/bone substitutes versus bone/bone substitutes for treatment of periodontal intrabony defects (title ...
www.cochrane.org/reviews/en/index_list_p.html - 101k
Cochrane Reviews - Alphabetically: Full list
... with D-cycloserine for anxiety disorders (title stage) Autologous platelet rich-plasma for treating chronic wounds (title stage) Autologous serum eye drops for ...
www.cochrane.org/reviews/en/index_list_all_titles.html - 101k
Cochrane Reviews - Alphabetically: Full list
The Cochrane Collaboration Cochrane Reviews, ... Alphabetically: Full list. View stages (what is this?): all, Titles, Protocols, Reviews. ...
www.cochrane.org/reviews/en/index_list_all_reviews.html - 101k
Cochrane Reviews - Alphabetically: Full list
The Cochrane Collaboration Cochrane Reviews, ... Alphabetically: Full list. View stages (what is this?): all, Titles, Protocols, Reviews. ...
www.cochrane.org/reviews/en/index_list_all.html - 101k
Search
platelet-rich factors
whole site
Search
Advanced Search
Search Tips
Resources
Cochrane A-Z
Global contacts
General help
Medical terms
Browse summaries of Cochrane Reviews
General Cochrane help
top of page | contact us | disclaimer | The Cochrane Library | The Cochrane Collaboration

- ✓ Muitos estudos
  - “in vitro”
  - Modelos animais
- ✓ Estudos no ser humano (poucos)
  - Feridas pele e tecido celular subcutâneo
  - Lesões tendinosas e ligamentares
  - Lesões musculares
  - Regeneração óssea

Regeneração óssea



Journal of Biomedical Materials Research Part A

e-mail print

What is RSS?

Early View (Articles online in advance of print)

Published Online: 7 Jan 2008

Save Title to My Profile Set E-Mail Alert

Go to the homepage for this journal to access trials, sample copies, editorial and author information, news, and more.

Save Article to My Profile Download Citation

< Previous Abstract | Next Abstract >

Abstract | References | Full Text: HTML | Related Articles | Citation Tracking

Controlled delivery of platelet-rich plasma-derived growth factors for bone formation

Helen H. Lu [1,2]*, Jennifer M. Vo [1], Hsin Sheila Chin [1], Jeffrey Lin [1,2], Matthew Cozin [2], Rick Tsay [2], Sidney Eisig [2], Regina Landesberg [2]

[1]Biomaterials and Interface Tissue Engineering Laboratory, Department of Biomedical Engineering, Columbia University, New York, New York 10027

[2]Division of Oral and Maxillofacial Surgery, College of Dental Medicine, Columbia University, New York, New York 10032

email: Helen H. Lu (hl2052@columbia.edu)

*Correspondence to Helen H. Lu, Biomaterials and Interface Tissue Engineering Laboratory, Department of Biomedical Engineering, Columbia University, New York, New York 10027

Funded by:

- Whitaker Foundation
- Wallace H. Coulter Foundation
- College of Dental Medicine at Columbia University

KEYWORDS

platelet-rich plasma • alginate • growth factor delivery • bone regeneration

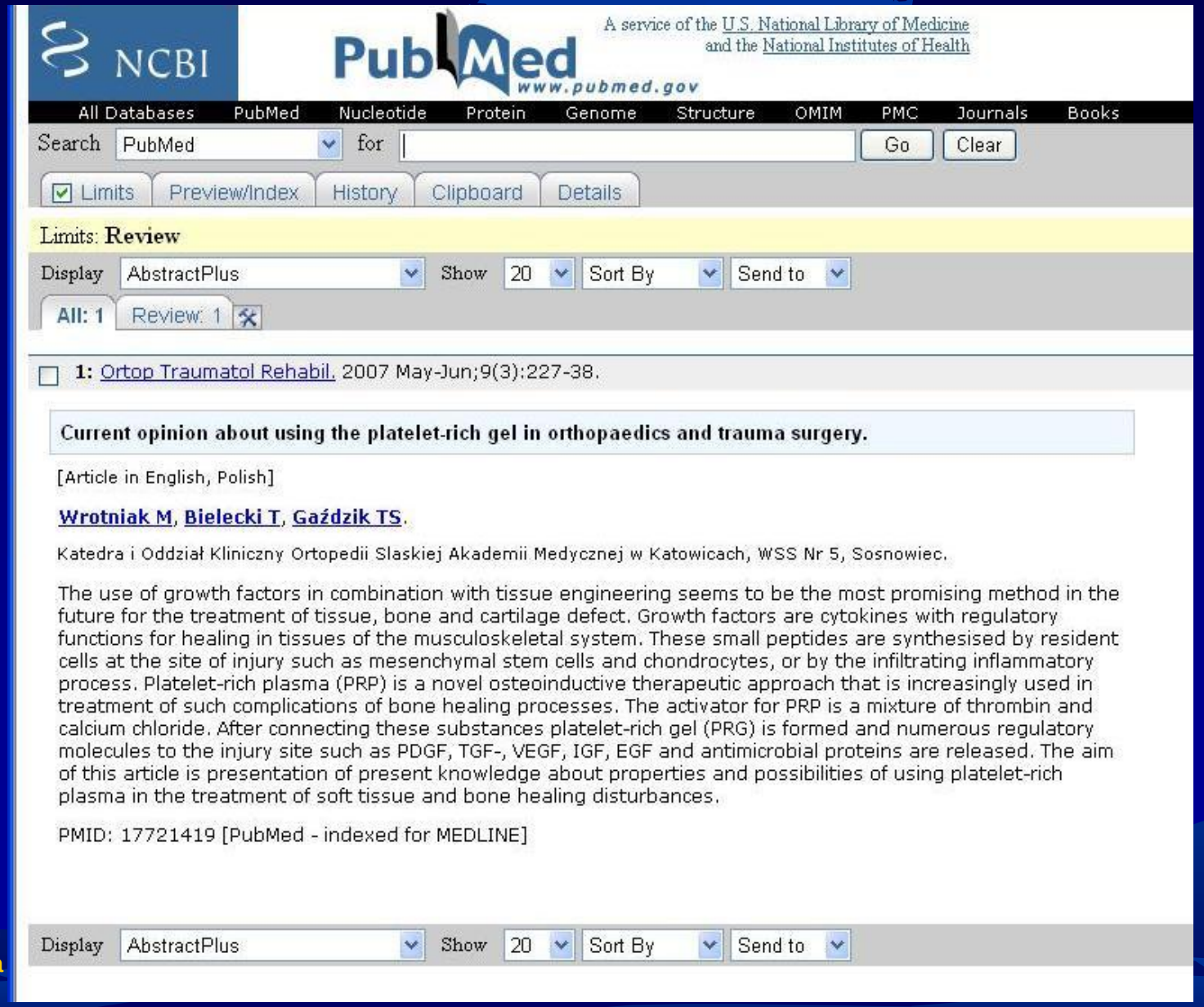
ABSTRACT

Platelet-rich plasma (PRP) represents an autologous source of growth factors essential for bone regeneration. The clinical efficacy of PRP is, however, unpredictable, and this is likely due to the inefficient and inconsistent delivery of PRP-derived growth factors. Previous investigations have shown that current methods of PRP preparation result in a premature release of the relevant bone stimulatory factors. As successful bone regeneration requires multiple factors presented in a physiologic temporal and spatial cascade, the objective of this study is to control the bioavailability of PRP-derived growth factors using a hydrogel carrier system. Specifically, the release of platelet-derived growth factor, transforming growth factor beta-1, and insulin-like growth factor from two types of alginate carriers was compared over time. The effects of the released factors on the growth and alkaline phosphatase (ALP) activity of human osteoblast-like cells were also evaluated. It was found that factor release profiles varied as function of carrier type, and binding of growth factors to the alginate matrix also modulated their release. The bioactivity of released factors was maintained *in vitro* and they promoted cell proliferation and ALP activity. These results demonstrate the potential of this autologous multifactor delivery system for controlling the bioavailability of PRP-derived factors. Future studies will focus on optimizing this system to increase the clinical efficacy of PRP by matching the distribution and temporal sequencing of PRP-derived factors to the bone healing cascade. © 2008 Wiley Periodicals, Inc. J Biomed Mater Res 2008

Received: 20 February 2007; Revised: 14 August 2007; Accepted: 28 August 2007

DIGITAL OBJECT IDENTIFIER (DOI)

2007



NCBI

PubMed www.pubmed.gov

A service of the U.S. National Library of Medicine and the National Institutes of Health

All Databases PubMed Nucleotide Protein Genome Structure OMIM PMC Journals Books

Search PubMed for Go Clear

Limits Preview/Index History Clipboard Details

Limits: **Review**

Display AbstractPlus Show 20 Sort By Send to

All: 1 Review: 1

1: Ortop Traumatol Rehabil. 2007 May-Jun;9(3):227-38.

Current opinion about using the platelet-rich gel in orthopaedics and trauma surgery.

[Article in English, Polish]

Wrotniak M, **Bielecki T**, **Gaździk TS**.

Katedra i Oddział Kliniczny Ortopedii Slaskiej Akademii Medycznej w Katowicach, WSS Nr 5, Sosnowiec.

The use of growth factors in combination with tissue engineering seems to be the most promising method in the future for the treatment of tissue, bone and cartilage defect. Growth factors are cytokines with regulatory functions for healing in tissues of the musculoskeletal system. These small peptides are synthesised by resident cells at the site of injury such as mesenchymal stem cells and chondrocytes, or by the infiltrating inflammatory process. Platelet-rich plasma (PRP) is a novel osteoinductive therapeutic approach that is increasingly used in treatment of such complications of bone healing processes. The activator for PRP is a mixture of thrombin and calcium chloride. After connecting these substances platelet-rich gel (PRG) is formed and numerous regulatory molecules to the injury site such as PDGF, TGF-, VEGF, IGF, EGF and antimicrobial proteins are released. The aim of this article is presentation of present knowledge about properties and possibilities of using platelet-rich plasma in the treatment of soft tissue and bone healing disturbances.

PMID: 17721419 [PubMed - indexed for MEDLINE]

Display AbstractPlus Show 20 Sort By Send to

Roturas ligamentares 2003

1: Sports Med. 2003;33(5):381-94.

The roles of growth factors in tendon and ligament healing.

Molloy T, Wang Y, Murrell G.

Orthopaedic Research Institute, St George Hospital Campus, University of New South Wales, Sydney, Australia.

Tendon healing is a complex and highly-regulated process that is initiated, sustained and eventually terminated by a large number and variety of molecules. Growth factors represent one of the most important of the molecular families involved in healing, and a considerable number of studies have been undertaken in an effort to elucidate their many functions. This review covers some of the recent investigations into the roles of five growth factors whose activities have been best characterised during tendon healing: insulin-like growth factor-I (IGF-I), transforming growth factor beta (TGFbeta), vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF), and basic fibroblast growth factor (bFGF). All five are markedly up-regulated following tendon injury and are active at multiple stages of the healing process. IGF-I has been shown to be highly expressed during the early inflammatory phase in a number of animal tendon healing models, and appears to aid in the proliferation and migration of fibroblasts and to subsequently increase collagen production. TGFbeta is also active during inflammation, and has a variety of effects including the regulation of cellular migration and proliferation, and fibronectin binding interactions. VEGF is produced at its highest levels only after the inflammatory phase, at which time it is a powerful stimulator of angiogenesis. PDGF is produced shortly after tendon damage and helps to stimulate the production of other growth factors, including IGF-I, and has roles in tissue remodelling.In vitro and in vivo studies have shown that bFGF is both a powerful stimulator of angiogenesis and a regulator of cellular migration and proliferation. This review also covers some of the most recent studies into the use of these molecules as therapeutic agents to increase the efficacy and efficiency of tendon and ligament healing. Studies into the effects of the exogenous application of TGFbeta, IGF-I, PDGF and bFGF into the wound site singly and in combination have shown promise, significantly decreasing a number of parameters used to define the functional deficit of a healing tendon. Application of IGF-I has been shown to increase in the Achilles Functional Index and the breaking energy of injured rat tendon. TGFbeta and PDGF have been shown separately to increase the breaking energy of healing tendon. Finally, application of bFGF has been shown to promote cellular proliferation and collagen synthesis in vivo.

PMID: 12696985 [PubMed - indexed for MEDLINE]

AJSM, 2004

The Influence of Locally Applied Platelet-Derived Growth Factor–BB on Free Tendon Graft Remodeling After Anterior Cruciate Ligament Reconstruction

Andreas Weiler,*† Cornelius Förster,‡ Patrick Hunt,† Roman Falk,† Tobias Jung,† Frank N. Unterhauser,† Volker Bergmann,§ Gerhard Schmidmaier,† and Norbert P. Haas†

From †Sports Traumatology & Arthroscopy Service, Trauma & Reconstructive Surgery, Charité, Humboldt-University of Berlin, Germany, the ‡Department of Trauma & Reconstructive Surgery, University of Rostock, Germany, and the §Institute of Veterinary Pathology, Free University of Berlin, Germany

Background: Ligaments and tendons do not gain mechanical properties of the native tissue after injury or grafting.

Purpose: To determine the influence of platelet-derived growth factor on tendon graft remodeling.

Study Design: Laboratory animal study.

Methods: Forty-eight sheep underwent anterior cruciate ligament reconstruction and were sacrificed after 3, 6, 12, and 24 weeks. In 6 animals at each time point, platelet-derived growth factor was locally delivered via coated sutures. After mechanical testing, tissue samples were taken for histologic, immunohistochemical, and electron microscopy evaluations.

Results: With platelet-derived growth factor treatment, cross-sectional area was significantly lower at 3 and 12 weeks. Load to failure was significantly higher at 6 weeks. Tensile stress was significantly higher at 3 and 12 weeks. Crimp length was significantly higher at 3 and 6 weeks. Vascular density was significantly higher at 6 weeks. Electron microscopy showed a significantly higher collagen fibril amount at 12 weeks. Differences in these parameters at other time points were not significant.

Conclusions: There were alterations in several but not all time points. The local application of platelet-derived growth factor alters the tissue's mechanical properties during free tendon graft remodeling after anterior cruciate ligament reconstruction. Growth factors present a promising tool toward the complete mechanical restitution of a healing ligament substitute.

Keywords: anterior cruciate ligament (ACL); tendon graft; remodeling; growth factors; animal model

AJSM, 2007

Comparison of Surgically Repaired Achilles Tendon Tears Using Platelet-Rich Fibrin Matrices

Mikel Sánchez,* MD, Eduardo Anitua,† MD, DDS, Juan Azofra,* MD, Isabel Andía,† PhD, Sabino Padilla,‡ MD, PhD, and Iñigo Mujika,‡§ PhD
*From the *Arthroscopic Surgery Unit, USP–La Esperanza Clinic, Vitoria-Gasteiz, Basque Country, Spain, the †BTI Biotechnology Institute, Vitoria-Gasteiz, Basque Country, Spain, and the ‡Department of Research and Development, Medical Services, Athletic Club Bilbao, Basque Country, Spain*

Background: Platelet-rich fibrin matrices release a natural mixture of growth factors that play central roles in the complex processes of tendon healing.

Hypothesis: Application of autologous platelet-rich matrices during Achilles tendon surgery may promote healing and functional recovery.

Study Design: Case-control study and descriptive laboratory study; Level of evidence, 3.

Methods: Twelve athletes underwent open suture repair after complete Achilles tendon tear. Open suture repair in conjunction with a preparation rich in growth factors (PRGF) was performed in 6 athletes and retrospectively compared with a matched group that followed conventional surgical procedure. The outcomes were evaluated on the basis of range of motion, functional recovery, and complications. Achilles tendons were examined by ultrasound at 50 ± 11 months in retrospective controls and 32 ± 10 months in the PRGF group. In the laboratory portion of the study, PRGF treatment was characterized by the number of platelets and concentration of insulin (IGF-I), transformed (TGF-β1), platelet-derived (PDGF-AB), vascular endothelial (VEGF), hepatocyte (HGF), and epidermal (EGF) growth factors in patients affected by musculoskeletal traumatic injuries.

Results: Athletes receiving PRGF recovered their range of motion earlier (7 ± 2 weeks vs 11 ± 3 weeks, $P = .025$), showed no wound complication, and took less time to take up gentle running (11 ± 1 weeks vs 18 ± 3 weeks, $P = .042$) and to resume training activities (14 ± 0.8 weeks vs 21 ± 3 weeks, $P = .004$). The cross-sectional area of the PRGF-treated tendons increased less ($t = 3.44$, $P = .009$). TGF-β1 (74.99 ± 32.84 ng/mL), PDGF-AB (35.62 ± 14.57 ng/mL), VEGF (383.9 ± 374.9 pg/mL), EGF (481.5 ± 187.5 pg/mL), and HGF (593.87 ± 155.76 pg/mL) significantly correlated with the number of platelets (677 ± 217 platelets/μL, $P < .05$).

Conclusion: The operative management of tendons combined with the application of autologous PRGF may present new possibilities for enhanced healing and functional recovery. This needs to be evaluated in a randomized clinical trial.

Keywords: sports; platelets; growth factors; surgical repair; Achilles tendon

Br J Sports Med 2007

1: Br J Sports Med. 2007 Nov 5 [Epub ahead of print]

Growth Factor Delivery Methods in the Management of Sports Injuries:The State of Play.

Creaney L, Hamilton B.

Queen Mary University of London, United Kingdom.

In recent years there have been rapid developments in the use of growth factors for accelerated healing of injury. Growth factors have been used in Maxillo-facial and Plastic Surgery with success and the technology is now being developed for Orthopaedics and Sports Medicine applications. Growth factors mediate the biological processes necessary for repair of soft tissues such has muscle, tendon and ligament following acute traumatic, or overuse injury, and animal studies have demonstrated clear benefits in terms of accelerated healing. There are various ways of delivering higher doses of growth factors to injured tissue, but each has in common, a reliance on release of growth factors from blood platelets. Platelets contain growth factors in their á-granules (IGF-1, bFGF, PDGF, EGF, VEGF, TGF-â1) and these are released upon injection at the site of an injury. Three commonly utilised techniques are known as Platelet-rich plasma, autologous blood injections, and autologous conditioned serum. Each of these techniques have been studied clinically in humans to a very limited degree so far, but results are promising in terms of earlier return to play following muscle and particularly tendon injury. The use of growth factors in Sports Medicine is restricted under the terms of the WADA anti-doping code, particularly because of concerns regarding the IGF-1 content of such preparations, and the potential for abuse as performance-enhancing agents. We review the basic science and clinical trials related to the technology, and discuss the use of such agents in relation to the WADA code.

PMID: 17984193 [PubMed - as supplied by publisher]

Estudos tipo RCT

Technique	Species	Tissue-type	Study Details	Results	Type
Autologous Blood Injections (ABI)	Animal	Tendon Ligament	Taylor 2002[37] – Rabbit – normal Patella Tendon	No harmful effects	Crossover
	Human	**Tendon Ligament**	**1)Edwards 2003[31] – Lateral Epicondylitis 2) Connell 2006[30] – Medial Epicondylitis 3)Connell 2006[30] – Lateral Epicondylitis**	1)79% patients complete pain relief 2&3) No pain at 6 months	**Cohort**
Autologous Conditioned Serum (ACS)	Animal	Muscle	Wright-Carpenter 2004[28] – Mice Gastrocnemius	Increased satellite cells & myofibres	Controlled Trial
	Human	**Muscle**	**Wright-Carpenter 2004[29] – Human Skeletal Muscle**	Improved recovery 22.3 v 16.6 days	**Controlled Trial**
Platelet-Rich Plasma (PRP)	Animal	Tendon Ligament	Aspenberg 2004[33] – Rat Achilles tendon rupture	30% improved strength at 1 week	Cohort
		Muscle	Carda 2005[32] – Skeletal Muscle tears	Improved healing at 6 days	Cohort
	Human	**Tendon Ligament**	**1)Mishra 2006[7] – Elbow tendinopathy 2)Sanchez 2005[35] – Achilles tendon rupture 3)Sanchez 2007[27] – Achilles tendon rupture**	**1) 60% ↓VAS at 8/52 v 16%↓ control 2&3) full recovery 14 weeks v 21**	**1)Controlled Trial 2)Case Report 3)non-randomised Trial**
		Muscle	**Sanchez 2005[36]**	**Full recovery in ½ time v controls**	**Case series**
Suramin	Animal	Muscle	Chan 2005[43] – Mice Gastrocnemius	↓scar tissue ↑tetanic strength	Controlled Trial
Relaxin	Animal	Muscle	Negishi 2006[45] – Mice Skeletal Muscle	↓fibrosis ↑myofibre regeneration	Crossover

ABI
(Autologous blood injection)

HUC
Serviço de Ortopedia

Conclusão

- Factos
  - Os FC dinamizam a reparação tecidular após traumatismo
  - Têm potencial para acelerar a reparação de tecidos moles
  - Existem várias técnicas para aumentar a concentração de FC nos tecidos traumatizados
    - Ministração de sangue total autólogo
    - Plasma rico em plaquetas
  - Faltam estudos consistentes das sua eficácia no ser humano
    - A maior parte apontam para a sua eficácia nas roturas tendinosas e musculares
  - A maioria dos estudos ainda são em modelos laboratoriais e animais
  - A sua utilização é considerada como “doping” em certos países
  - Atenção à utilização directa de sangue autólogo (ABI)


Muito obrigado
www.fernandomfonseca.net