ACP – Autologous Conditioned Plasma

Erlend Aurmo

Dato: 20.10.2017

Agenda

01	Blod
02	Vevstilheling
03	Fremstilling
04	Bruk
05	Evidens

01 Blod

ACP behandling

- ACP®
  - (Autologous Conditioned Plasma)
  - Autologt-blodplasma, produsert ved seperasjon av blodkomponentene.
  - Arthrex PRP produkt

A Autologt → kroppens eget

C

Conditioned →

Separert og konsentrert

P

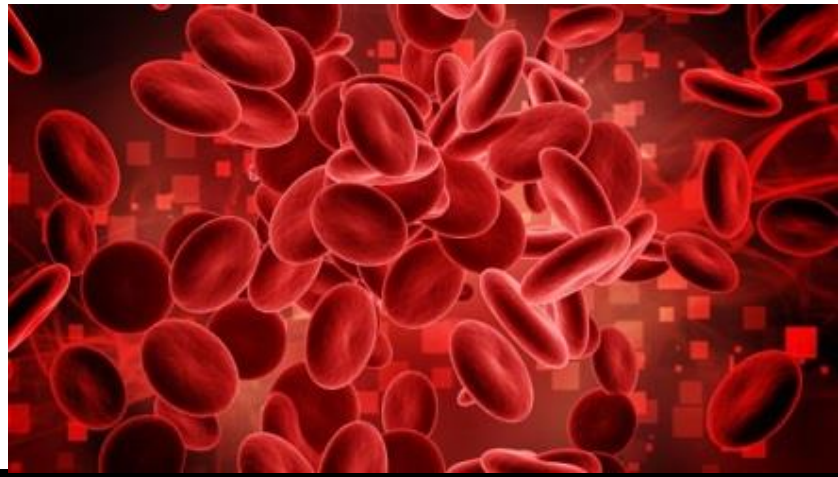
Plasma →

Blodplasma med dens bestanddeler

Blodets hovedkomponenter

- Fullblod - alt blod med dens bestanddeler jevnt blandet **innenfor** kroppen.
- Plasma
  - 55% av Fullblod
    - 90% vann og 10% fordelt på plasmaprotein (antistoffer), næringsstoffer, elektrolytter, avfallsstoffer og hormoner.

- Blodlegemer
  - Røde blodceller «Erytrocytter»
    - 44%av Fullblod
  - Hvite blodceller «Leukocytter»
    - 1% av Fullblod
  - Blodplater «Trombocytter»
    - Veldig lite volum

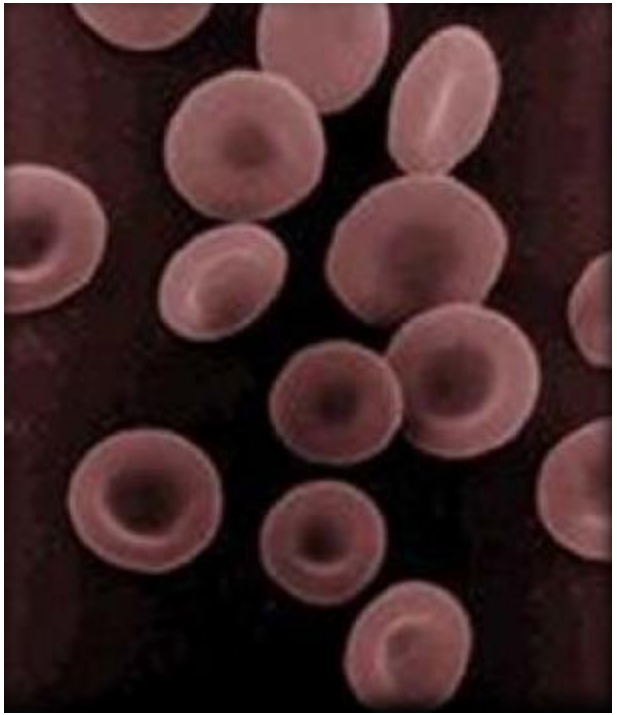


Erytrocytter (Røde blodceller)

- Frakter oksygen fra lungene til alle levende celler og frakter karbondioksid tilbake til lungene.

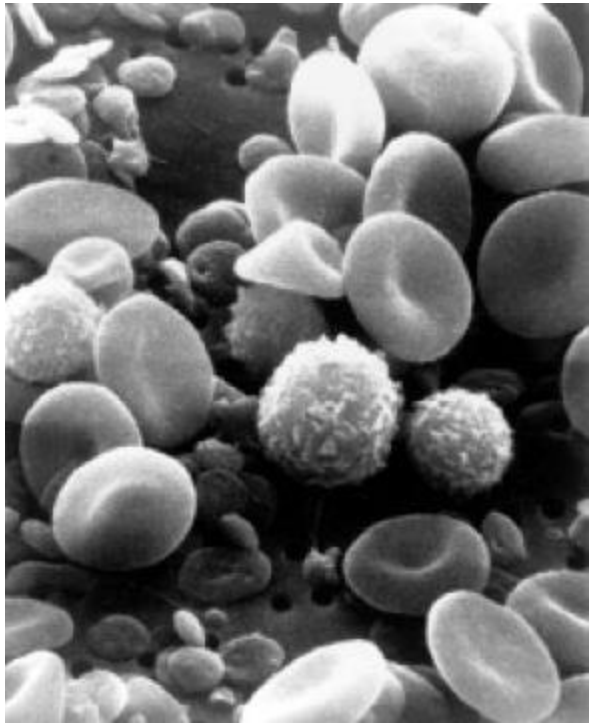
- Måles i hemoglobin
  - Heme: Jern
  - Globin: Protein til jern

- Er tyngst av blodlegemene



Leukocytter (hvite blodceller)

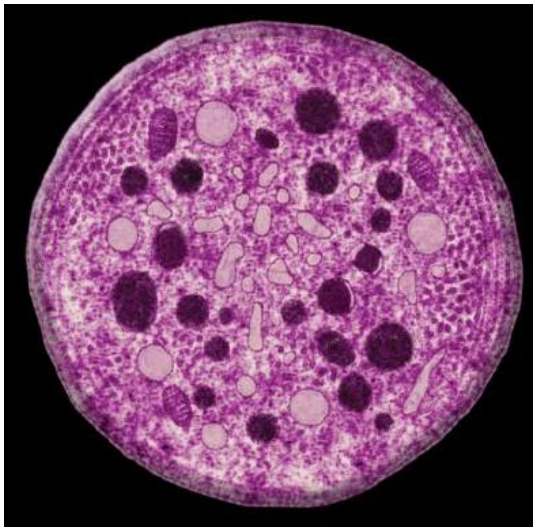
- Aktivt i immunforsvaret og ved bekjempelse av infeksjoner
- Granulocytter – inneholder granuler med cellenedbrytende stoff
  - Nøytrofile granulocytter
    - Angriper og innkapsler fremmede celler
  - Eosinifile granulocytter
    - Angriper og ødelegger fremmede proteiner
  - Basofile granulocytter
    - Reagerer på allergener og slipper ut histamin
- Agranulocytter – uten granuler
  - Monocytter
    - Aktivt angriper fremmedlegemer, omdannes til makrofager som fagocytere (spiser) debris
  - Lymfocytter
    - Angriper bestemte celler, regulerer immunresponsen
- Veier mindre enn erytrocytter



Trombocytter (plater)

- Initierer **primær hemostase** ved utskillelse av serotonin, og deltar i **sekundær hemostase** (koagulering)
- Bidrar til **vevstilheling** ved utskillelse av cytokiner (signalmolekyler)
- Høy konsentrasjon i fullblod og beinmarg
- Plateinnehold~4000 proteiner / 300 vekstfaktorer
  - α-granula : vekstfaktorer, koagulerendefaktorer
  - D-granula: serotonin, ADP

- Lettere enn leukocytter
- Mye lettere enn erytrocytter

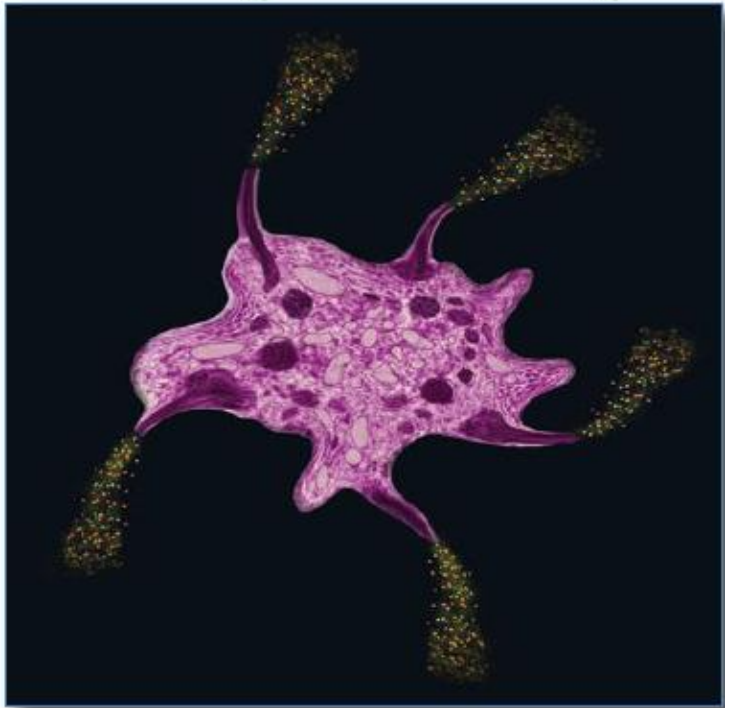


Vekstfaktorer i blodplater

Vekstfaktor	Navn	Lokalitet	Effekt
bFGF	Basic Fibroblast Growth Factor	Aktivert blodplate	Fremmer vekst og differensiering av kondrocytter og osteoblaster; mitogen for mesenchymale stamceller, kondrocytter og osteoblaster
EGF	Epidermal Growth Factor	Aktivert blodplate	Stimulerer endothelial kjemotakse/angiogenese som regulerer kollagen sekresjon og stimulerer epithelial/mesenchymal mitogenese
VEGF	Vascular Endothelial Growth Factor	Leukocytter, blodplater, endothelielle celler	Øker angiogenese og blodåre permeabilitet som stimulerer mitogenese for endothelialceller.
PDGF	Platelet Derived Growth Factor	Aktivert blodplate	Mitogen for mesenchymale stamceller og osteoblaster; stimulerer kjemotaksis og mitogenese i fibroblast/glia/glattmuskulatur celler. Regulerer kollagenskresjon og kollagensyntese. Stimulerer makrofag og nøytrofill kjemotaksis
TGF-β	Transforming Growth Factor	Aktivert blodplate	Stimulerer multipotente mesenchymal celleprolifiereing, regulerer endothelial, fibroblastisk og osteblastisk mitogenese. Regulerer kollagensyntese og kollagensekresjon.

Trombocytter

- Høy konsentrasjon av trombocytter i:
  - Fullblod
  - Beinmarg
- Blodplater ~4000 proteiner / 300 vekstfaktorer
  - α-granula : vekstfaktorer
  - D-granula: serotonin, ADP
- Trombocyttfunksjon
  - Akselerer vevstilhelingsprosessen (prolifering, kjemotaksis, angiogenese, kollagensyntese)
  - Fremmer differensiering av multi-potente mesenchymale stamceller, anti-inflammatorisk



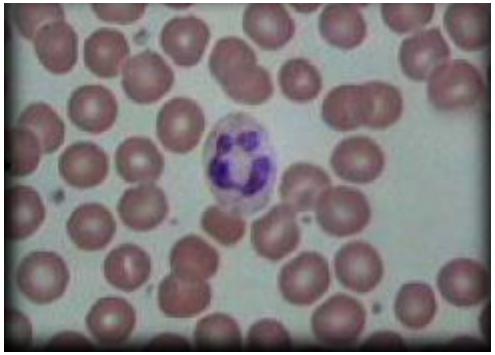
(1) Rubio-Azpeitia, Andia et al., Partnership between platelet-rich plasma and mesenchymal stem cells: in vitro experience; Muscles, Ligaments and Tendons Journal, 2014, Vol.4(1):52-62

Aktivering av vekstfaktorer

- Aktivering
  - Glatte fragmenter

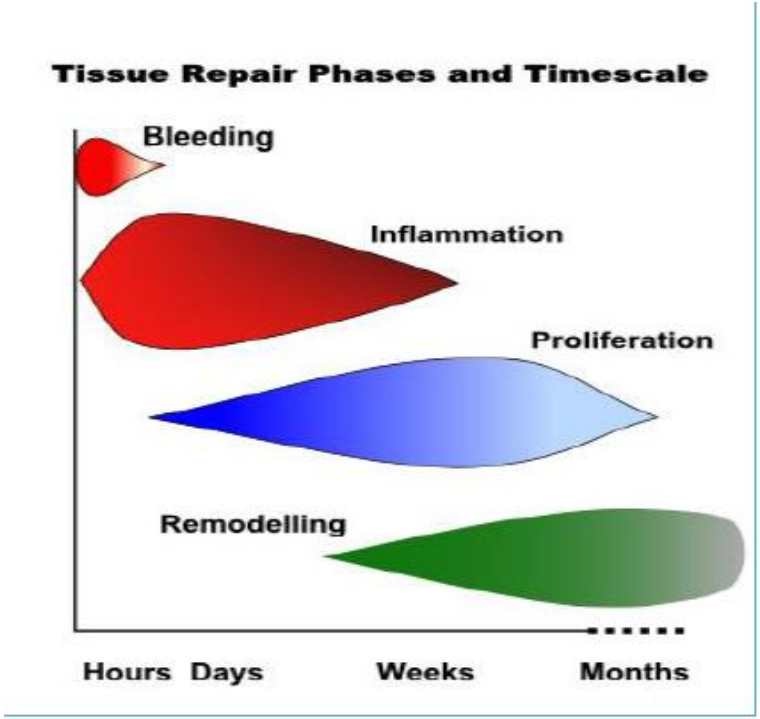
    ↓
  - Exogen: Thrombin, Calcium chloride, mekansik påvirkning
  - Endogen: kontakt med kollagen gradvis aktivering av plater

    ↓
  - Vokser haler – utskiller signalmolekyler



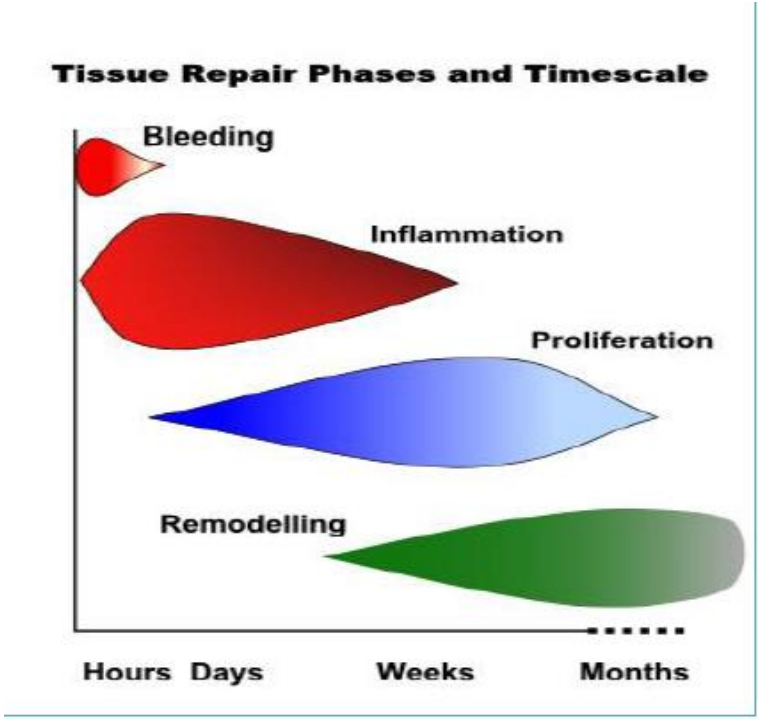
02 Vevstilheling

Vekstfaktorer - Virkningsmekanisme



- Hemostase
  - Tilstrømmer skadested – første sårlukkung
  - Aktivering - frigir intracellulært lager av cytokiner
- Inflammasjon
  - Utskiller store mengder cytokiner
  - Transport av leukocytter og monocytter
  - Nedbrytning vev/matrix – renser sårflate
- Proliferasjon
  - Utskiller store mengder vekstfaktorer – omformes til pro-helende mekanismer
- Remodelering
  - Oppbygging og nedbrytning av matrix

Vekstfaktorer - Virkningsmekanisme



- Vekstfaktorene er positive og aktive i alle fasene når vevet skal gjenopprettes og gro
  - Inflammatorisk
  - Fibroblast aktivtet
  - Vevsgranulasjon og kollagensyntese
  - Sårlukking
  - Epithelasering
  - Remodelering
  - Grodd vev
- For høye verdier av leukocytter kan føre til indirekte vevsdestruksjon
- Nyere forskning viser at endring fra pro-inflammatorisk til pro-helende mekanismer er avgjørende for effektiv vevsreparasjon

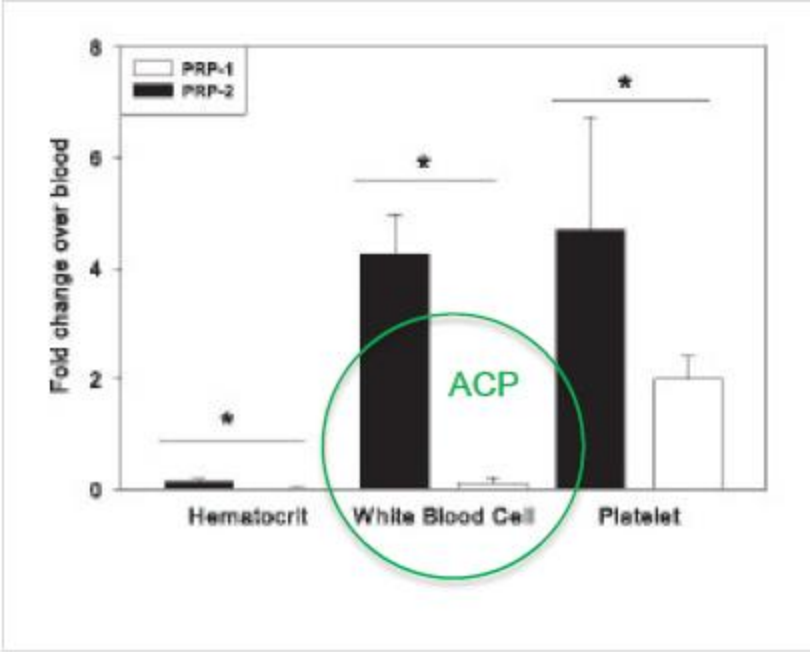
Review: Isabel Andia et al. 2012, „Molecular and Biological Aspects of Platelet-Rich Plasma Therapies“

Leukocytt påvirkning på vevstilheling

- Kan ha negativ effekt på vev som gror
  - Nøytrofile granulocytter
    - 70% av alle hvite blodceller
    - Hovedsakelig dreper av bakterier
      - Utskiller toksiske radikaler
      - MMP- matrix metalloproteinase

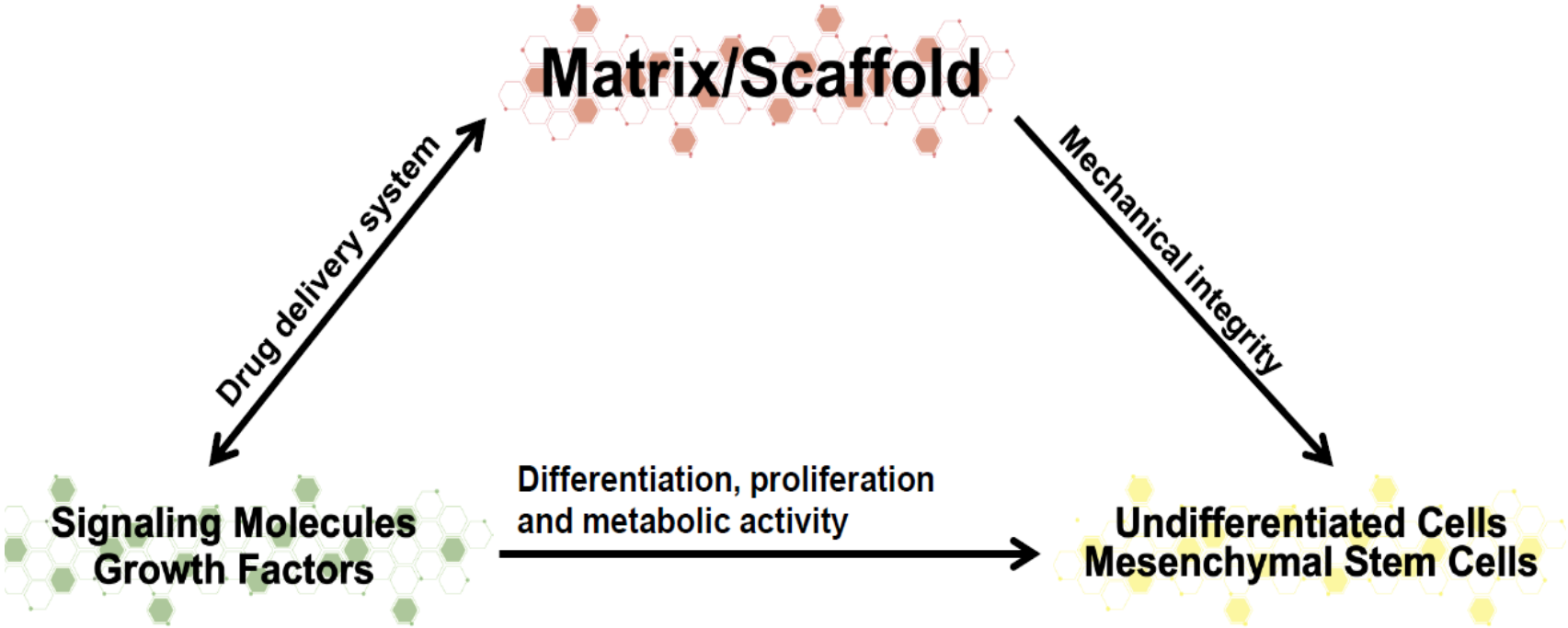
- For mange nøytrofiller demper sårtilhelingen

- Effekt å dempe inflammert vev, ikke drepe bakterier



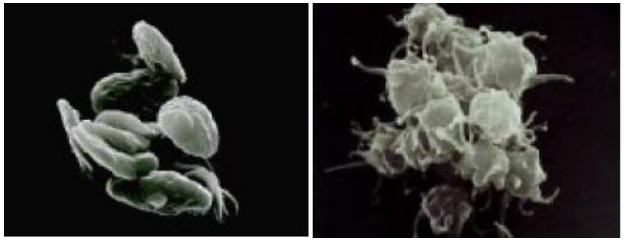
Tissue Regeneration

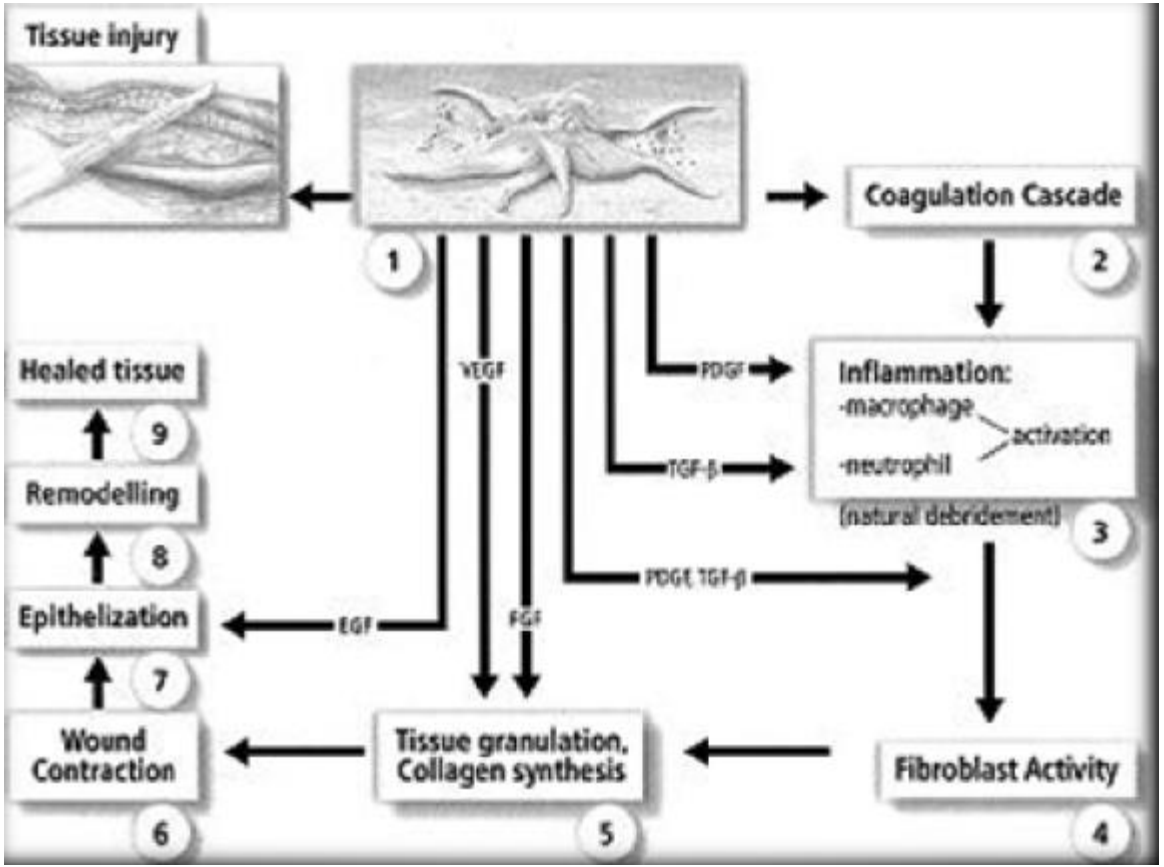
Healing Triad



Smith et al., The current state of scaffolds for musculoskeletal regenerative applications; Nature Reviews Rheumatology, 2015, Vol.11(4): 213-222

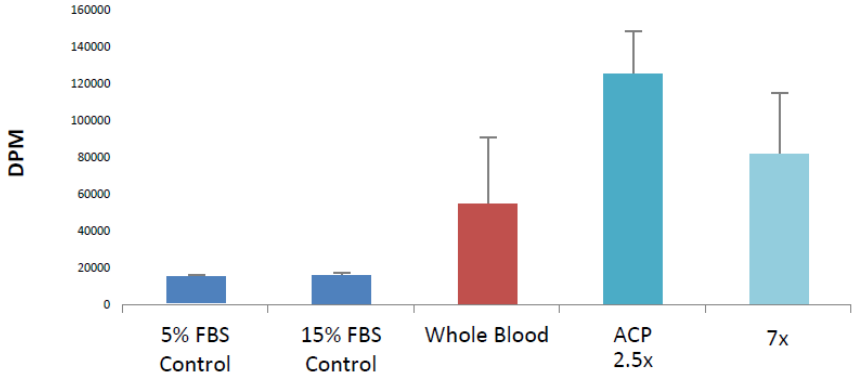
- Positiv effekt av vekstfaktorer i vevstilheling



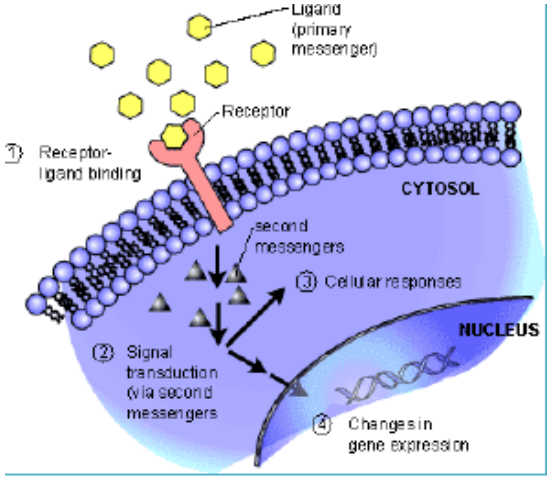


Signalmolekyler og cellereseptorer

Osteoblast Proliferation (Tenocytes, Myocytes)

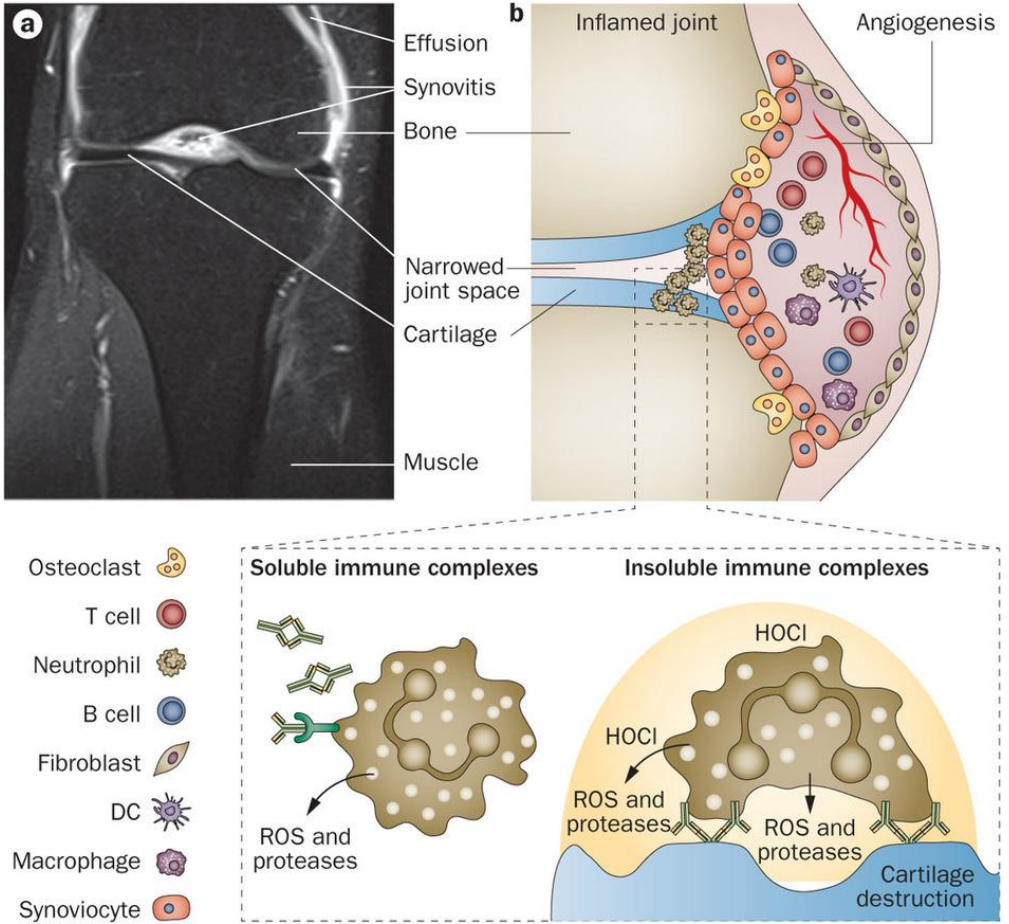


Mazzocca et al., ESSKA 2010

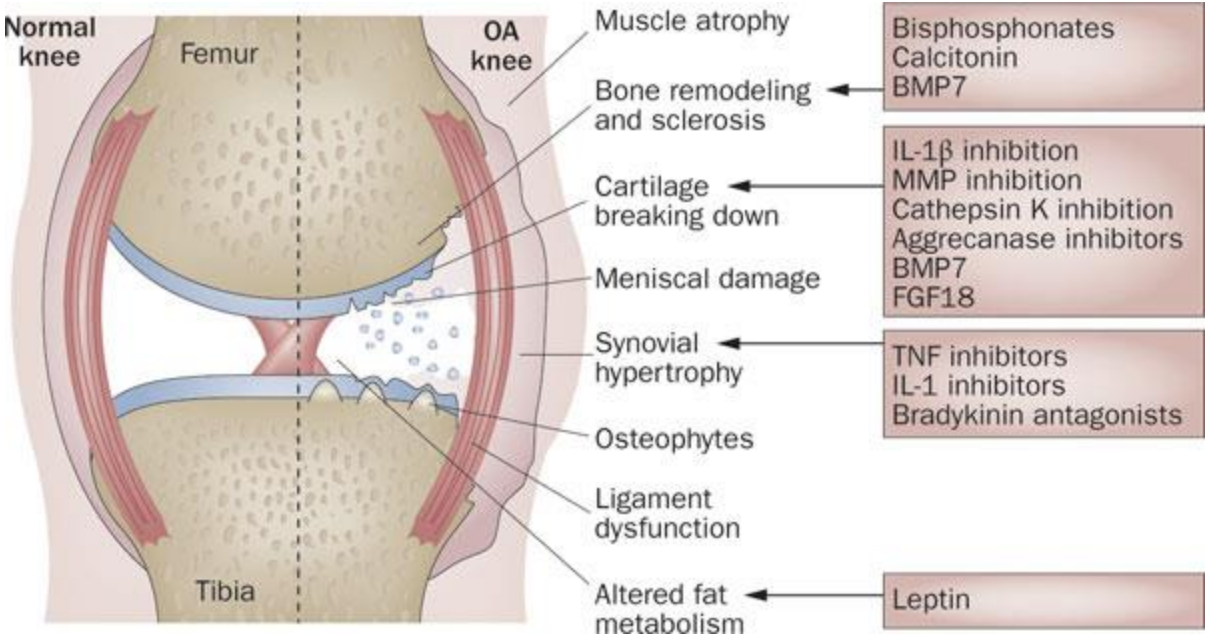


Degenerative lidelser

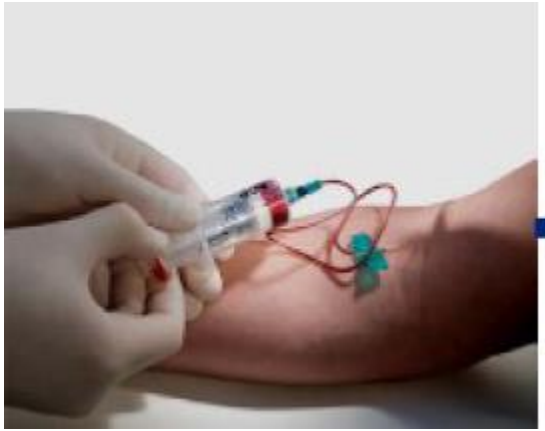
- Ubalanse mellom anabolske og katabolske mekanismer, forsterket ved pro-inflammatoriske cytokiner, matrix komponenter og mekanisk stress



Artrosekne


Normal knee
Femur
OA knee
Tibia
Muscle atrophy
Bone remodeling and sclerosis
Cartilage breaking down
Meniscal damage
Synovial hypertrophy
Osteophytes
Ligament dysfunction
Altered fat metabolism
Bisphosphonates
Calcitonin
BMP7
IL-1β inhibition
MMP inhibition
Cathepsin K inhibition
Aggrecanase inhibitors
BMP7
FGF18
TNF inhibitors
IL-1 inhibitors
Bradykinin antagonists
Leptin

03 Fremstilling

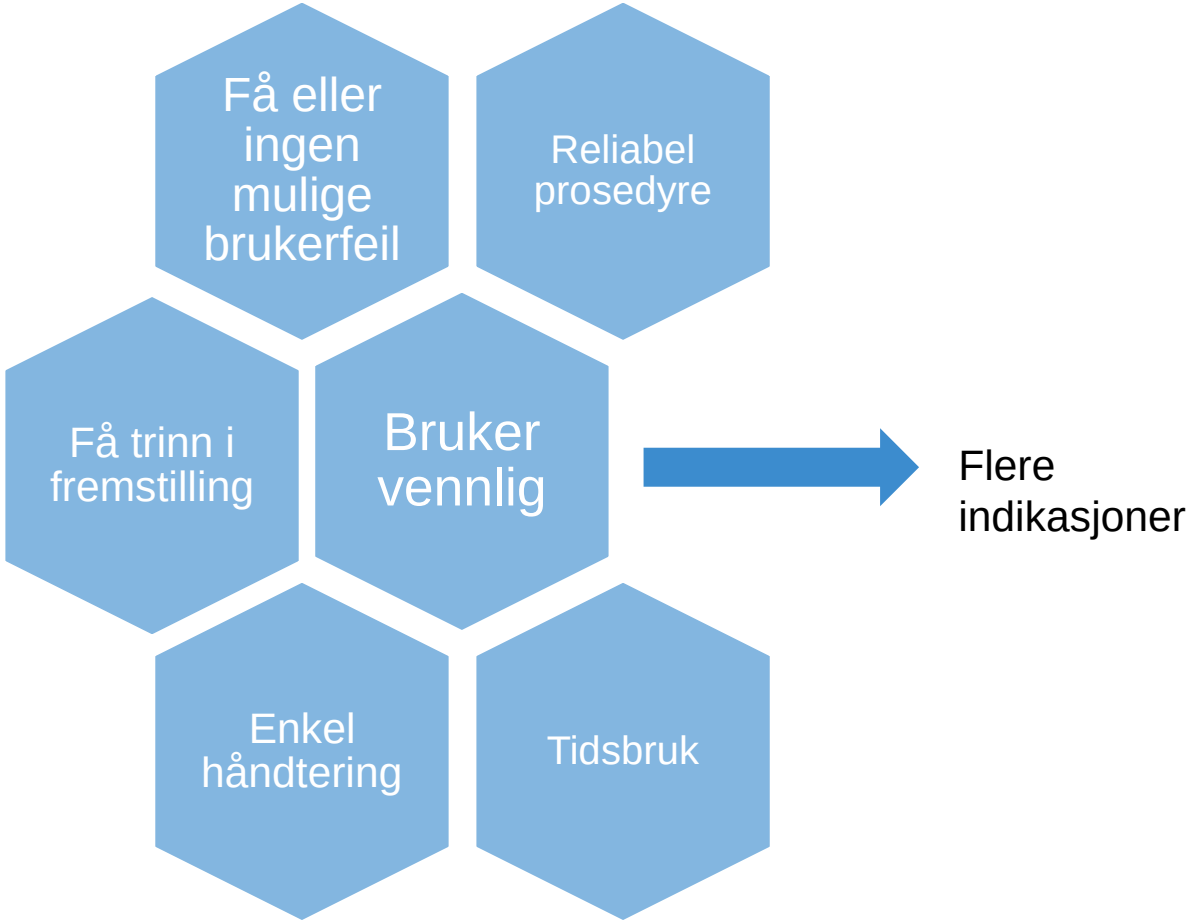


Ekstraher ca 15ml venøst blod. Sett på rød kork.

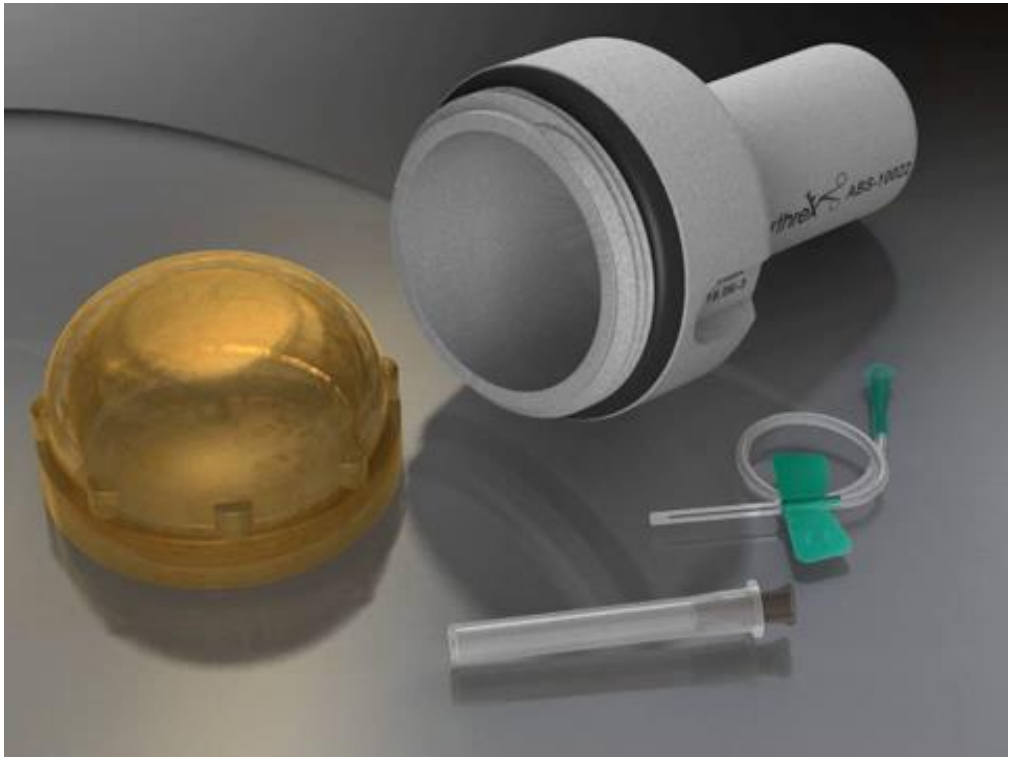
Plasser sprøyten i sentrifugen og sett inn motvekt på motsatt side. Sentrifuger blodet i 5min ved 1500rpm

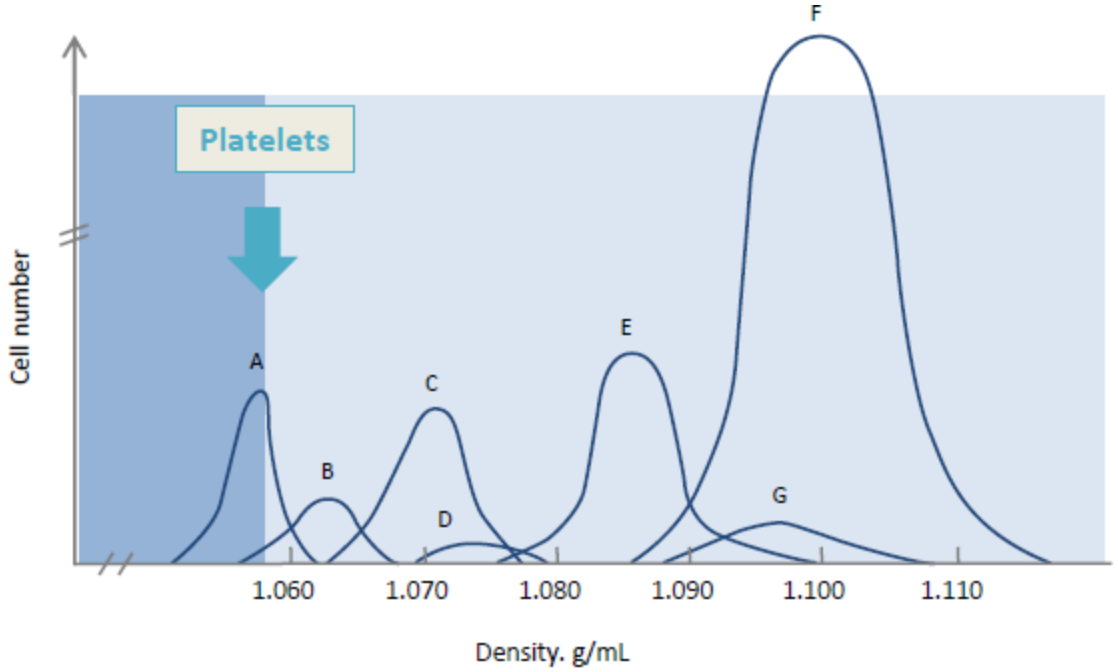
Trekk varsomt ut PRP til det er igjen ca 1ml plasma. Roter indre sprøyte mot klokken.

Sett på sprøytespiss. ACP-produktet er klart for bruk.


Få eller ingen mulige brukerfeil
Reliabel prosedyre
Få trinn i fremstilling
Bruker vennlig
Enkel håndtering
Tidsbruk
Flere indikasjoner

ACP Fremstilling

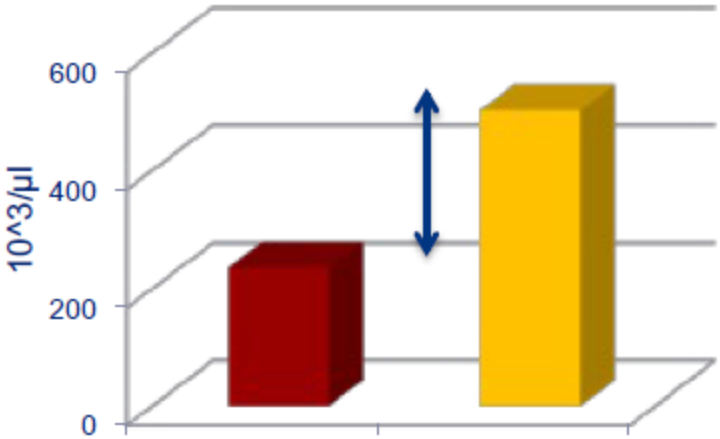


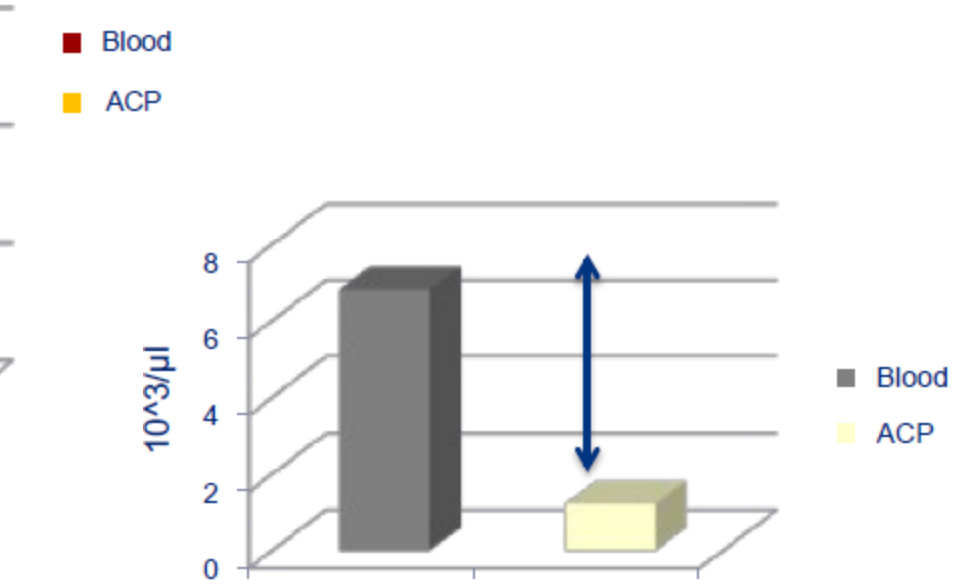


Massetetthetsfordeling av blodkomponentene
A-Blodplater
B-Monocytter
C-Lymphocytter
D-Basofiler
E-Nøytrofiler
F-Erythrocytter
G-Eosinofiler

PRP er fremstilt ved seperasjon av blodplater (A) fra andre celletyper. Noe overlapping av blodplater og andre celler vil kunne skje grunnet variasjon av massetetthet.

Platekonsentrasjon venstre / leukocyttnivå høyre

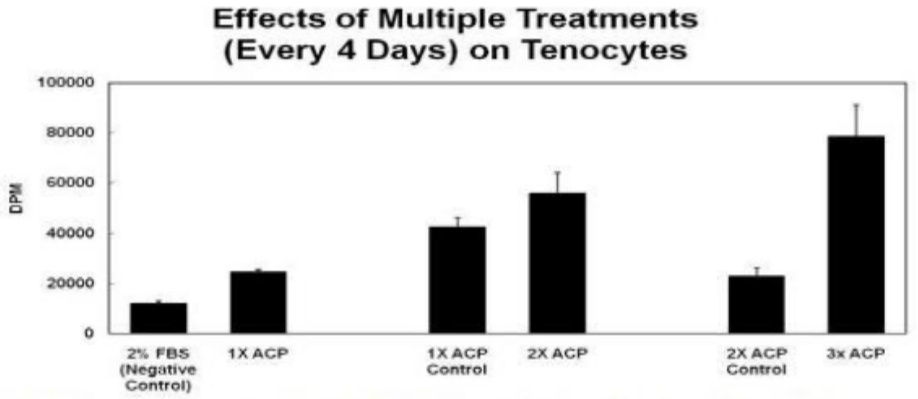




04 Bruk

Injeksjons frekvens og antall

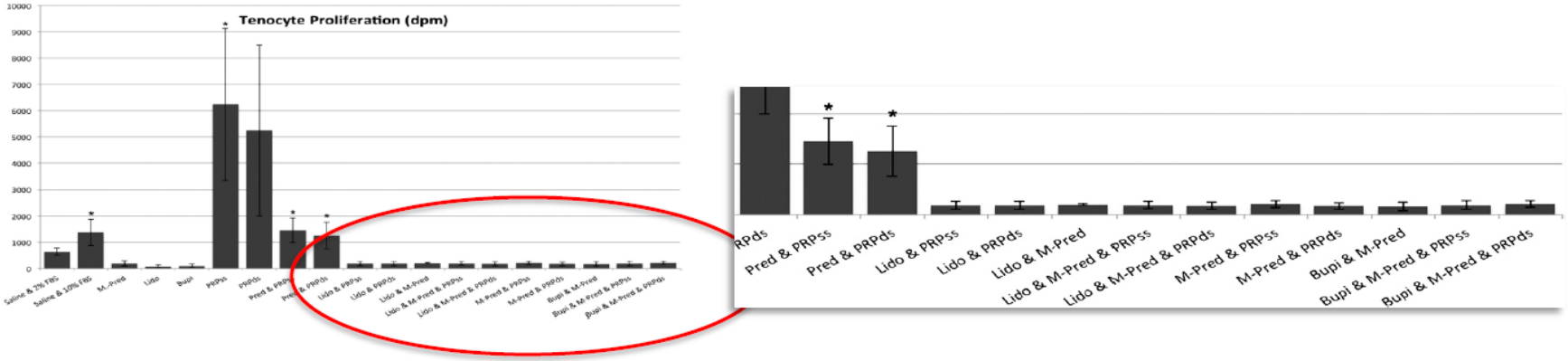
- Multiple injeksjoner viser økt effekt
- Anbefaling: 2-5 injeksjoner med ACP avhengig av indikasjon



Mazzocca AD. Biological healing enhancement in shoulder surgery using autologous growth factors. 14th ESSKA Congress 2010, Oslo
DeLong et al., Update on platelet-rich plasma, Current Orthopaedic Practice 2011

- (Artrose: 3 injeksjoner)

ACP i kombinasjon med lokal anestesi eller kortison

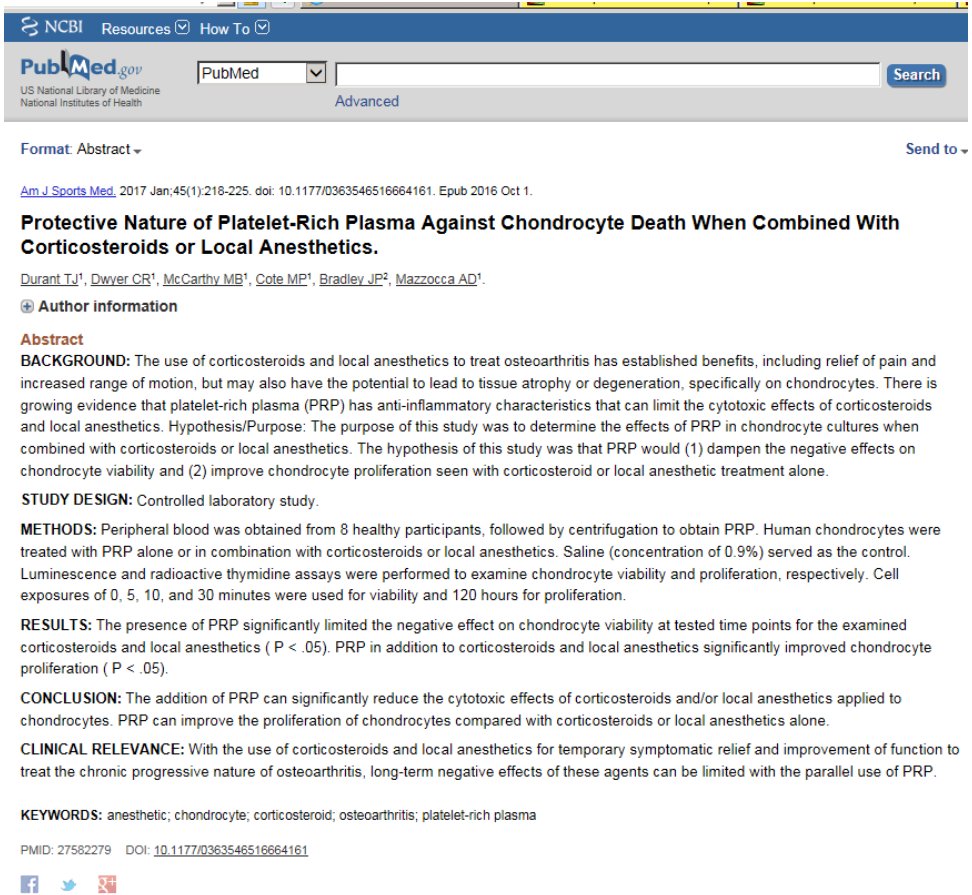


- Redusert celleprolifering
- Anbefaling: Injeksjon med ACP uten lokal anestesi (alternativt; is-spray eller subcutan bedøvelse

Carofino et al., Corticosteroids and Local Anesthetics Decrease Positive Effects of Platelet-Rich Plasma: An In Vitro Study on Human Tendon Cells, Arthroscopy 2012

MEN!

- Injeksjon av ACP kan redusere cytoksiske effekten av kortison og/eller lokal anestesi på chondrocytter



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Am J Sports Med. 2017 Jan;45(1):218-225. doi: 10.1177/0363546516664161. Epub 2016 Oct 1.

Protective Nature of Platelet-Rich Plasma Against Chondrocyte Death When Combined With Corticosteroids or Local Anesthetics.

Durant TJ[1], Dwyer CR[1], McCarthy MB[1], Cote MP[1], Bradley JP[2], Mazzocca AD[1].

Author information

Abstract

BACKGROUND: The use of corticosteroids and local anesthetics to treat osteoarthritis has established benefits, including relief of pain and increased range of motion, but may also have the potential to lead to tissue atrophy or degeneration, specifically on chondrocytes. There is growing evidence that platelet-rich plasma (PRP) has anti-inflammatory characteristics that can limit the cytotoxic effects of corticosteroids and local anesthetics. Hypothesis/Purpose: The purpose of this study was to determine the effects of PRP in chondrocyte cultures when combined with corticosteroids or local anesthetics. The hypothesis of this study was that PRP would (1) dampen the negative effects on chondrocyte viability and (2) improve chondrocyte proliferation seen with corticosteroid or local anesthetic treatment alone.

STUDY DESIGN: Controlled laboratory study.

METHODS: Peripheral blood was obtained from 8 healthy participants, followed by centrifugation to obtain PRP. Human chondrocytes were treated with PRP alone or in combination with corticosteroids or local anesthetics. Saline (concentration of 0.9%) served as the control. Luminescence and radioactive thymidine assays were performed to examine chondrocyte viability and proliferation, respectively. Cell exposures of 0, 5, 10, and 30 minutes were used for viability and 120 hours for proliferation.

RESULTS: The presence of PRP significantly limited the negative effect on chondrocyte viability at tested time points for the examined corticosteroids and local anesthetics ($P < .05$). PRP in addition to corticosteroids and local anesthetics significantly improved chondrocyte proliferation ($P < .05$).

CONCLUSION: The addition of PRP can significantly reduce the cytotoxic effects of corticosteroids and/or local anesthetics applied to chondrocytes. PRP can improve the proliferation of chondrocytes compared with corticosteroids or local anesthetics alone.

CLINICAL RELEVANCE: With the use of corticosteroids and local anesthetics for temporary symptomatic relief and improvement of function to treat the chronic progressive nature of osteoarthritis, long-term negative effects of these agents can be limited with the parallel use of PRP.

KEYWORDS: anesthetic; chondrocyte; corticosteroid; osteoarthritis; platelet-rich plasma

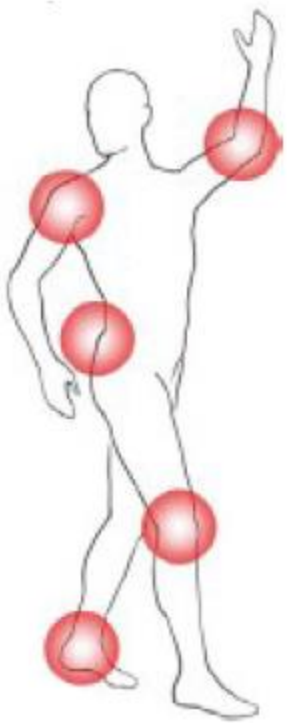
PMID: 27582279 DOI: 10.1177/0363546516664161

Arthrex

Målsetting

- Raskere regenerasjon
- Mindre smerter
- Bedret funksjon

- Økt aktivtetsnivå



Indikasjoner

- Akutte
  - Seneskader
  - Ligamentskader
  - Muskelskader
- Kroniske
  - **Artrose**
  - Tendinopatier
    - patella, achilles, epicondyl, plantar fascie

05 Evidens


Arthrex White Papers ACP (Autologous Conditioned Plasma)
Reviews
Arthrex
Publikationen ACP (Autologous Conditioned Plasma)
Klinische Studien
Tierstudien
In Vitro Studien

Review – Kanchanatawan (KSSTA, 2015, level 1)

- PRP bedre WOMAC total score, IKDC score og EQ-VAS score enn HA
- PRP gruppe mindre utsatt for «adverse events» enn HA gruppen

- PRP bedre WOMAC total score, IKDC score og EQ-VAS score enn placebo
- Ingen statistiske forskjeller i «adverse events» sammenlignet med placebo

- Konklusjon: PRP injeksjon mer effektiv enn HA og placebo i reduksjon av symptomer, bedret funksjon, og bedre QOL hos pasienter med mild og moderat OA i kneet som ikke responderer på konvensjonell behandling, og bør derfor foreslås som behandlingsvalg.

Knee Surg Sports Traumatol Arthrosc
DOI 10.1007/s00167-015-3784-4

KNEE

Short-term outcomes of platelet-rich plasma injection for treatment of osteoarthritis of the knee

Wichan Kanchanatawan[1] · Alisara Arirachakaran[2] · Kornkit Chaijenkij[3] · Niti Prasathaporn[4] · Manusak Boonard[5] · Peerapong Piyapittayanun[2] · Jatupon Kongtharvonskul[6]

Received: 5 May 2015 / Accepted: 8 September 2015

Abstract
Purpose To compare the clinical outcomes of osteoarthritis indices (WOMAC and Lequesne scores) and adverse events in the treatment of osteoarthritis (OA) of the knee with platelet-rich plasma (PRP) versus hyaluronic acid (HA) or placebo.
Methods A systematic review and meta-regression were performed to compare outcomes between PRP injections versus HA or placebo. Relevant randomized control trials were identified from Medline and Scopus from date of inception to 13 August 2015.
Results Nine of 551 studies were eligible; 6, 5, 5, 5, 2, 2, 2 and 7 studies were included in pooling of WOMAC total, pain, stiffness and function scores, Lequesne score, IKDC score, EQ-VAS score and adverse events in OA knee patients, respectively. The PRP injections had −15.4 (95 % CI −28.6, −2.3, $p = 0.021$), lower mean WOMAC total scores, and 8.83 (95 % CI 5.88, 11.78, $p < 0.001$), 7.37 (95 % CI 4.33, 10.05, $p = 0.021$) higher mean IKDC and EQ-VAS scores when compared to HA injections. However, PRP injections had no significant differences in WOMAC pain, stiffness and function scores, as well as Lequesne score and adverse events when compared to HA or placebo.
Conclusion In short-term outcomes (≤1 year), PRP injection has improved functional outcomes (WOMAC total scores, IKDC score and EQ-VAS) when compared to HA and placebo, but has no statistically significant difference in adverse events when compared to HA and placebo. This study suggests that PRP injection is more efficacious than HA injection and placebo in reducing symptoms and improving function and quality of life. It has the potential to be the treatment of choice in patients with mild-to-moderate OA of the knee who have not responded to conventional treatment.

Electronic supplementary material The online version of this article (doi:10.1007/s00167-015-3784-4) contains supplementary material, which is available to authorized users.

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OA Knee ACP level 1 –Smith (AJSM, 2016)

- RCT, double-blindet
- FDA godkjent
- 30 pasienter
- 3 injeksjoner, ukentlig intervall
- Atrose grad 2-3; WOMAC

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

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

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

Background: Platelet-rich plasma (PRP) injections have become an intriguing treatment option for osteoarthritis (OA), particularly OA of the knee. Despite the plethora of PRP-related citations, there is a paucity of high-level evidence that is comparable, cohort specific, dose controlled, injection protocol controlled, and double-blinded.

Purpose: To determine the safety and efficacy of leukocyte-poor PRP autologous conditioned plasma (ACP) for knee OA treatment through a feasibility trial regulated by the US Food and Drug Administration (FDA).

Study Design: Randomized controlled trial; Level of evidence, 1.

Methods: In accordance with FDA protocol, patient selection was based on strict inclusion/exclusion criteria; 114 patients were screened, and 30 were ultimately included in the study. These patients were randomized to receive either ACP (n = 15) or saline placebo (n = 15) for a series of 3 weekly injections. Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores served as the primary efficacy outcome measure. Patients were followed for 1 year.

Results: No adverse events were reported for ACP administration. Furthermore, the results demonstrated no statistically significant difference in baseline WOMAC scores between the 2 groups. However, in the ACP group, WOMAC scores at 1 week were significantly decreased compared with baseline scores, and the scores for this group remained significantly lower throughout the study duration. At the study conclusion (12 months), subjects in the ACP group had improved their overall WOMAC scores by 78% from their baseline score, compared with 7% for the placebo group.

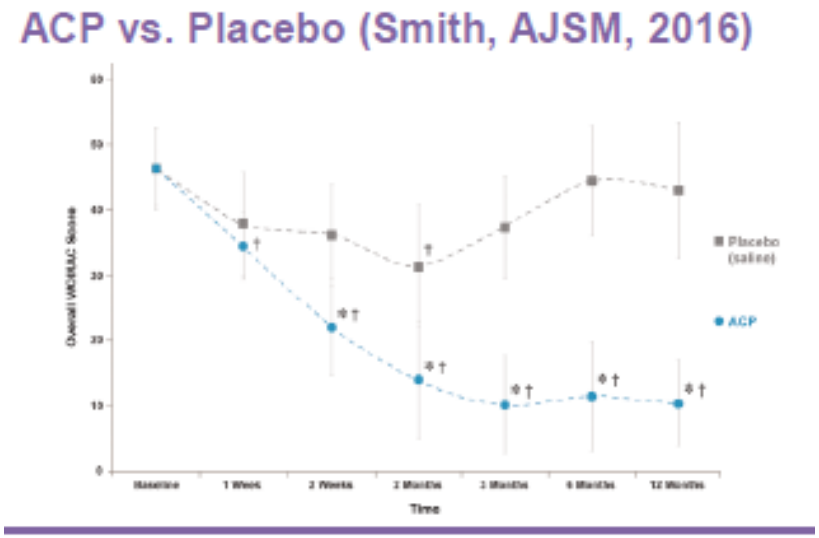
Conclusion: ACP is safe and provides quantifiable benefits for pain relief and functional improvement with regard to knee OA. No adverse events were reported for ACP administration. After 1 year, WOMAC scores for the ACP subjects had improved by 78% from their baseline score, whereas scores for the placebo control group had improved by only 7%. Other joints affected with OA may also benefit from this treatment.

Keywords: FDA; autologous conditioned plasma; leukocyte-poor platelet-rich plasma; placebo; saline control; WOMAC; osteoarthritis; level 1

Arthrex

OA Knee ACP level 1 –Smith (AJSM, 2016)

- Fra uke 2(!), ACP signifikant bedre enn placebo opp til 12 måneder
- ACP-gruppen bedret WOMAC score med 78% fra baseline vs. 7% for placebo-gruppen
- Ingen «adverse events»



OA Knee – Li Dai (JARS, 2017)

- Meta-analyse for å evaluere effekt av PRP-injeksjon for artrose
- Systematisk litteraturereview, Level 1
- 10 RCT studier inkludert, totalt 1069
- Konklusjon: dagens evidens indikerer at, sammenlignet med HA og saltvann, har intra-artikulære PRP injeksjoner bedre virkning i smerte og funksjon 1år (!) etter behandling

Meta-analysis

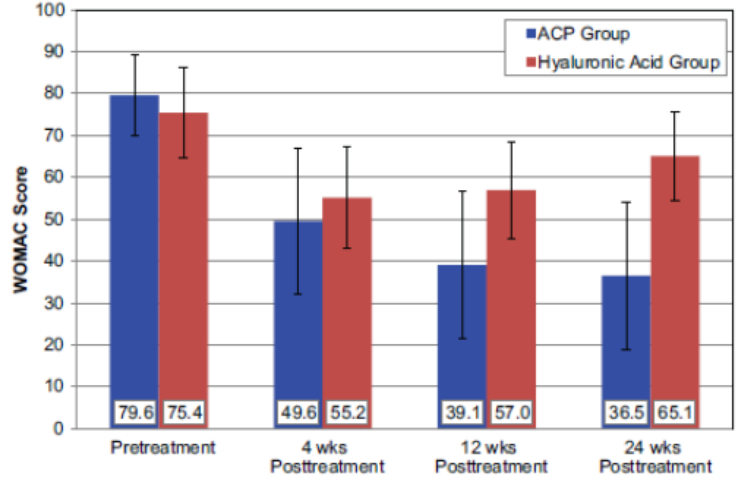
Efficacy of Platelet-Rich Plasma in the Treatment of Knee Osteoarthritis: A Meta-analysis of Randomized Controlled Trials

Wen-Li Dai, M.Sc., Ai-Guo Zhou, M.D., Hua Zhang, M.D., and Jian Zhang, M.D.

Purpose: To use meta-analysis techniques to evaluate the efficacy and safety of platelet-rich plasma (PRP) injections for the treatment knee of osteoarthritis (OA). **Methods:** We performed a systematic literature search in PubMed, Embase, Scopus, and the Cochrane database through April 2016 to identify Level I randomized controlled trials that evaluated the clinical efficacy of PRP versus control treatments for knee OA. The primary outcomes were Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain and function scores. The primary outcomes were compared with their minimum clinically important differences (MCID)—defined as the smallest difference perceived as important by the average patient. **Results:** We included 10 randomized controlled trials with a total of 1069 patients. Our analysis showed that at 6 months postinjection, PRP and hyaluronic acid (HA) had similar effects with respect to pain relief (WOMAC pain score) and functional improvement (WOMAC function score, WOMAC total score, International Knee Documentation Committee score, Lequesne score). At 12 months postinjection, however, PRP was associated with significantly better pain relief (WOMAC pain score, mean difference −2.83, 95% confidence interval [CI] −4.26 to −1.39, $P = .0001$) and functional improvement (WOMAC function score, mean difference −12.53, 95% CI −14.58 to −10.47, $P < .00001$; WOMAC total score, International Knee Documentation Committee score, Lequesne score, standardized mean difference 1.05, 95% CI 0.21-1.89, $P = .01$) than HA, and the effect sizes of WOMAC pain and function scores at 12 months exceeded the MCID (−0.79 for WOMAC pain and −2.85 for WOMAC function score). Compared with saline, PRP was more effective for pain relief (WOMAC pain score) and functional improvement (WOMAC function score) at 6 months and 12 months postinjection, and the effect sizes of WOMAC pain and function scores at 6 months and 12 months exceeded the MCID. We also found that PRP did not increase the risk of adverse events compared with HA and saline. **Conclusions:** Current evidence indicates that, compared with HA and saline, intra-articular PRP injection may have more benefit in pain relief and functional improvement in patients with symptomatic knee OA at 1 year post-injection. **Level of Evidence:** Level I, meta-analysis of Level I studies.

ACP vs. HA level 1 – Cerza (AJSM, 2012)

- RCT studie
- 120 pasienter
- 4injeksjoner, ukentlig intervall
- Artrose grad 1-3, WOMAC



- ACP signifikant bedre enn behandling med HA opp til 6 måneder
- Behandling med HA virket ikke til å ha god effekt på pasienter med grad 3 gonoatrose

Halpern (CJSM, 2013)

- Se PRP injeksjoner for tidlig artrose motvirke brukshøyde
- Leukocytt fattig system
- Grad 0-2 artrose
- MR og etter 12 måneder

- Konklusjon: Signifikant bedring i smerte og funksjon (WOMAC). MR viste i 73% av tilfellene ingen reduksjon i brusk.

Clinical and MRI Outcomes After Platelet-Rich Plasma Treatment for Knee Osteoarthritis

Brian Halpern, MD, Salma Chaudhury, MD, PhD, MRC, Scott A. Rodeo, MD, Catherine Hayter, MD, Eric Bogner, MD, Hollis G. Potter, MD, and Joseph Nguyen, MPH

Abstract: The purpose of this study was to investigate whether platelet-rich plasma therapy for early knee osteoarthritis is associated with good clinical outcomes and a change in magnetic resonance imaging (MRI) structural appearances. The design was a prospective cohort study following patients 1 year after platelet-rich plasma therapy for knee osteoarthritis. Twenty-two patients were treated with platelet-rich plasma for early osteoarthritis, confirmed with a baseline MRI. Inclusion criteria were Kellgren grade 0–II with knee pain in patients aged 30 to 70 years. All the patients received a 6-mL platelet-rich plasma injection using the Cascade system. Fifteen subjects underwent clinical assessments at baseline, 1 week, and 1, 3, 6, and 12 months, and MRIs at 1 year. Pain scores significantly decreased, whereas functional and clinical scores increased at 6 months and 1 year from baseline. Qualitative MRIs demonstrated no change per compartment in at least 73% of cases at 1 year.

Key Words: knee, osteoarthritis, platelet-rich plasma, magnetic resonance imaging (MRI)

(*Clin J Sport Med* 2013;23:238–239)

the knee. Inclusion criteria were Kellgren grade 0–II, osteoarthritis confirmed by a baseline MRI (some patients also having other intra-articular pathology), with knee pain in patients aged 30 to 70 years. Four patients were lost during the follow-up period, and 1 patient had an additional viscosupplement during the study and so was excluded, resulting in follow-up data for 17 patients with 18 knees injected with platelet-rich plasma. The medial femoral and tibial compartments and patellofemoral joints were affected in all 15 knees with complete MRI data, with 12 patients showing osteoarthritis changes in the lateral tibial and femoral compartments as well. All the patients received a single 6-mL platelet-rich plasma injection, which was concentrated from 20 mL of whole blood using the MTF Cascade system (MTF Sports Medicine, Edison, NJ). The subjects underwent serial clinical assessments at baseline, 1 week, and 1, 3, 6, and 12 months. Visual analog scale (VAS) scores were measured to assess overall knee pain, function, and activities of daily living (ADL) and Western Ontario and McMaster Universities Arthritis Index (WOMAC) scores measured knee pain, stiffness, and ADL.

Magnetic resonance examinations to assess cartilage morphology (with a 1.5 or 3.0-T clinical scanner using fast spin echo images in 3 planes), and Outerbridge scores were graded by 2 musculoskeletal radiologists (C.H. and E.B.) who were blinded as to

Arthrex

Title and comparison

Basic Science

- Buul et al, AJSM, 2011
- Andia et al, Op. Tech. Ortho, 2012
- Smyth et al, Arthroscopy, 2013
- Anitua et al, J Biomed Mat.Res, 2014
- Braun et al, AJSM, 2014
- Sundman et al, AJSM, 2014

Reviews

- Filardo et al, KSSTA 2013
- Koshbin et al, JARS 2013
- Pourcho, Osteoarthritis 2014
- Meheux, Journal of Arthroscopic 2015
- Kanchanatawan, KSSTA 2015

Randomized Controlled Trials

Sanchez et al, Arthroscopy, 2012	PRGF vs. HA
Vaquerizo et al, Jars, 2013	PRGF vs. HA
Filardo et al , Musc. Disorders, 2012	PRP vs. HA
Patel et al, AJSM, 2013	PRP vs. Placebo
Smith et al, AJSM, 2016	ACP vs. Placebo
Cerza et al, AJSM, 2012	ACP vs. HA
Cole et al, study finished tbp 2016	ACP vs. HA

Epicondylitis

- 6 positive RCT studier
  - 3vs. Kortison, 2vs. Lokal anestesi,
    - 1 ACP vs. Kortison

- 1 review som konkluderer
    - PRP mer fordelaktig enn kortison på level 2 evidens.

- Fleste studier er med leukocytt-rik PRP

Epicondylitis

ACP vs. Steroid betamethasone (Lebiedzinski, SICOT, 2015)

RCT, 99 pasienter, single injeksjon, DASH

Etter 6 uker, 6 måneder, og 12måneder ACP signifikant bedre

ACP vs. Operasjon (Ford, HAND, 2015)

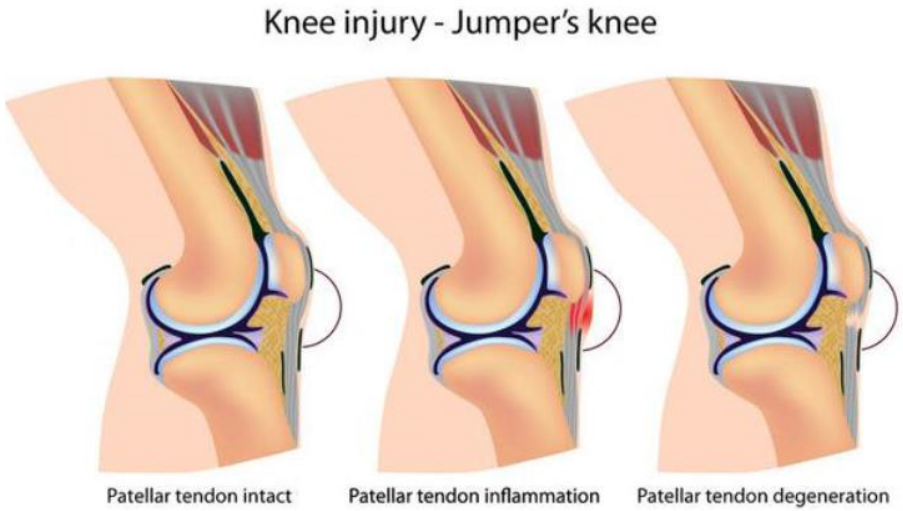
Retrospektiv sammenligning, 78 pasienter, single injeksjon vs kirurgisk release

Samme outcome i smerte og retur til jobb.

Men; ACP ingen risiko, anestesi, rehabilitering

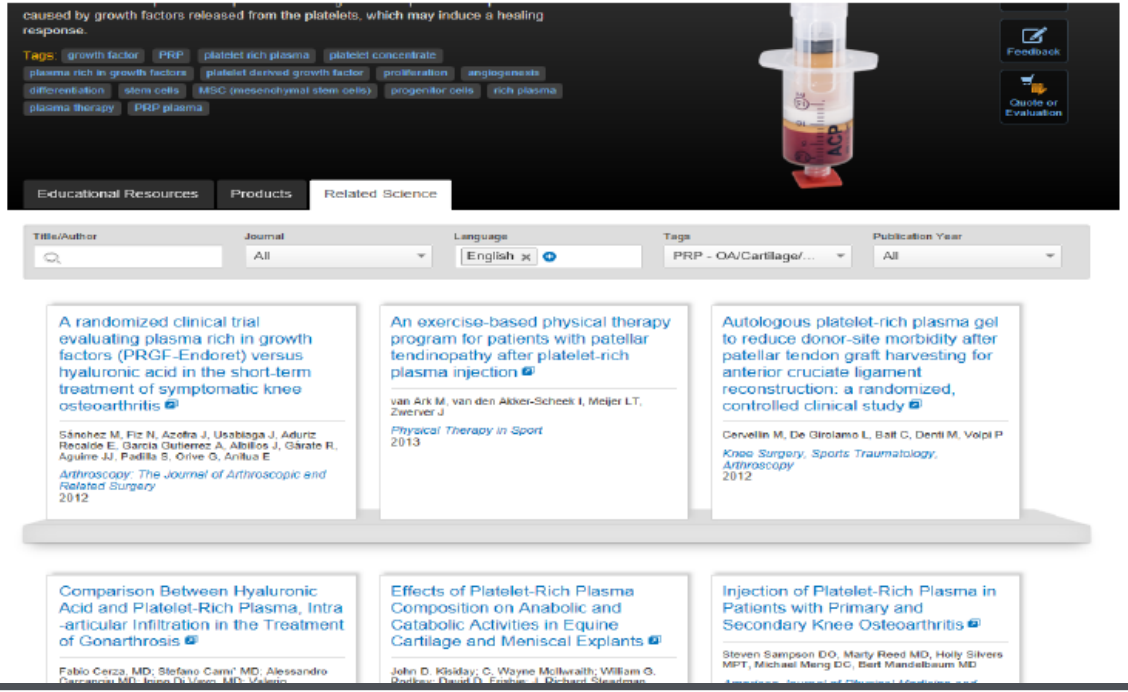
Variable	PRP (%)	Surgery (%)	*p* value
Pain improvement	89.3	84	0.733
Percent pain reduction	61.1	55	0.566
Associated symptom improvement[a]	85.7	88	0.880
Residual associated symptoms[b]	14.3	10	0.686
Lateral epicondyle tenderness	64.3	44	0.137
Pain with resisted extension	35.7	30	0.431
Full elbow ROM	100	100	–
Return to full activity	82.1	82	0.987
Postop complications[c]	0	0	–
Secondary intervention	7.2	6	0.925

Patella tendinopati



- Review: Clinical Application of PRP in Pattelar Tendinopathy (Jeong, BMRI, 2014)
  - Statistisk bedring i fleste evalueringsscore observert etter PRP behandling
  - PRP er ikke bare effektiv på kort sikt (6mnd), men også stabilt gode resultater på 12mnd og opp til 4 år

Arthrex Database (www.arthrex.com)



Take home messages

- ACP et Arthrex produkt
- To sprøyter i en
- Lukket system – sterilt
- Kroppens eget virkestoff
- Anti-inflammatorisk virkning
- «Pro-healing»
- Multiple injeksjoner, viser bedre effekt en enkel
- God evidens på artrose og degenerative senelidelser

Takk for oppmerksomheten!

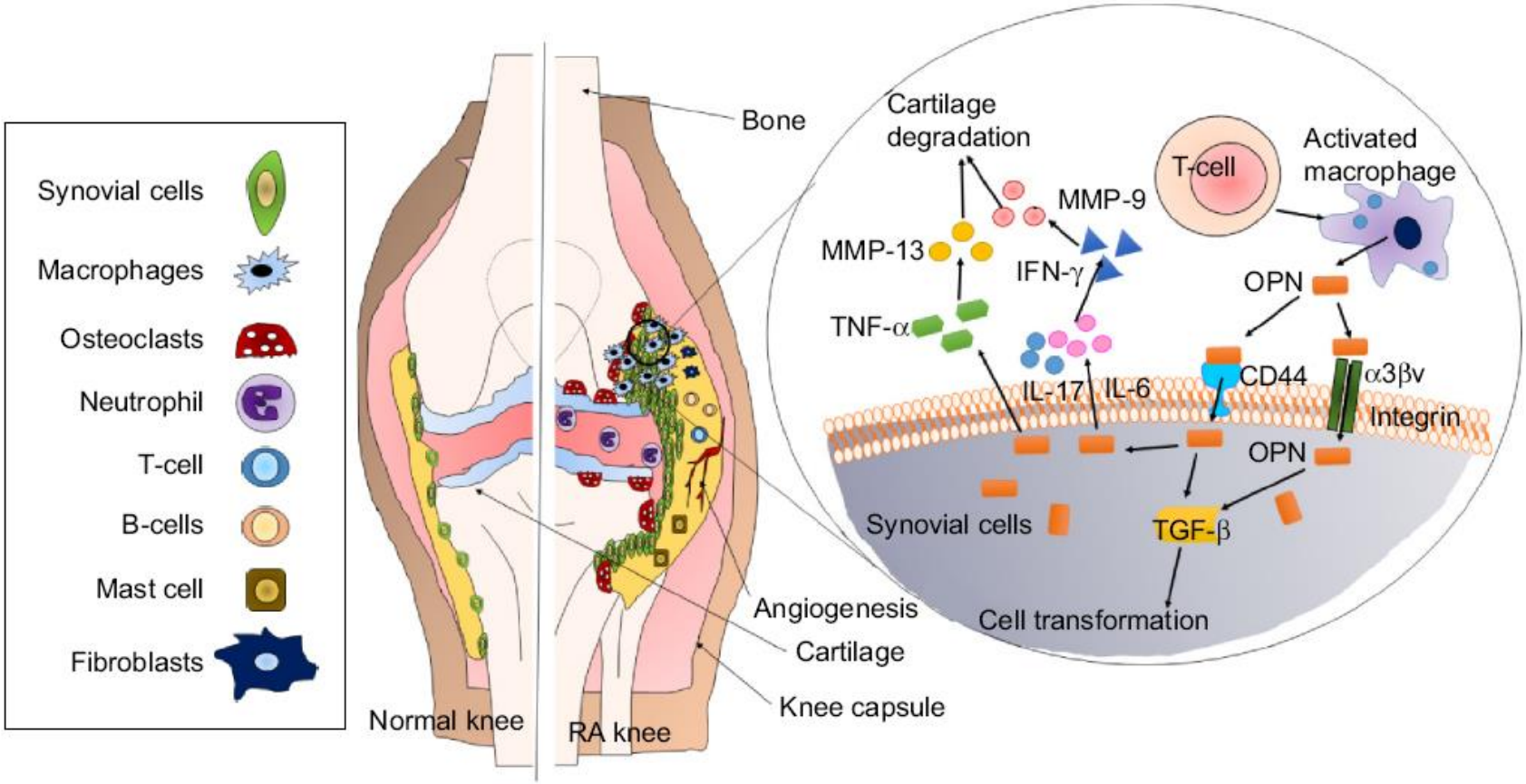


Figure 2 Role and importance of osteopontin in arthritis.

Notes: Osteopontin (OPN) is highly expressed in the synovial fluid and in bones, which leads to production of pro-inflammatory cytokines and attachment of osteoclasts to the bone matrix. OPN is known to interact with CD44 and integrin receptors on cell membrane leading to activation of TGF-β signaling and further activation of pro-inflammatory cytokines such as IL-17, IL-6, and TNF-α. Pro-inflammatory cytokines lead to cartilage degradation.

Abbreviations: IL, interleukin; MMP, matrix metalloproteinase; TGF-β, transforming growth factor β; TNF-α, tumor necrosis factor alpha.