



ACL: HOW TO IMPROVE OUR RESULTS

BIOLOGIC ENHANCEMENT IN 2024

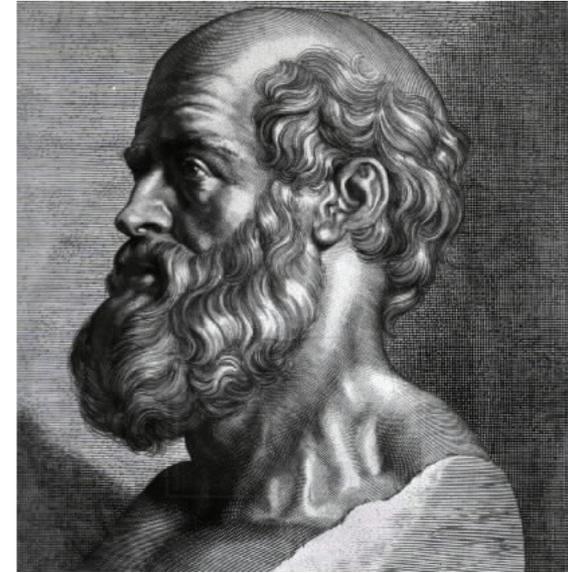
F-X GUNEPIN



HEALING

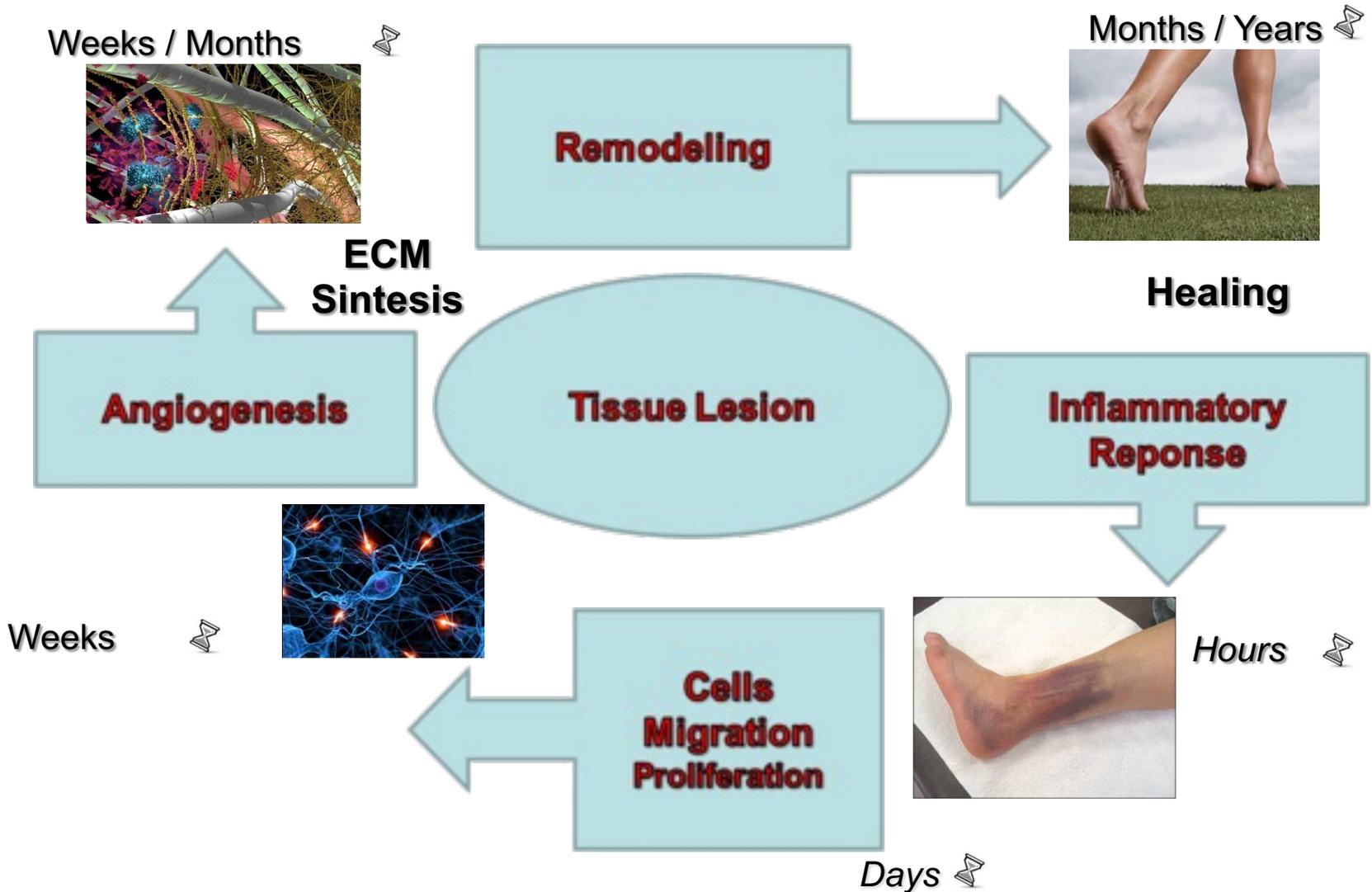
- *“the healing power of nature and the body contains within itself the power to rebalance the humors and to heal itself”*

Trauma → hematoma → Healing



Hippocrate

TISSUE HEALING



FAILURE TO HEAL

- What fraction of the hematoma is active
- How to activate or restart tissue repair
- Improve or accelerate physiological processes



NEW CONCEPTS

- Activate cells in place
- Bring cells



**NEW JOBS
BIOENGINEERING**

NEW JOBS → BIOENGINEERING

- **Identify natural repair mechanisms**
- **Compensate for a deficiency:**
- **Partial (correction of disorders or gaps)**
- **Total**

- **Knowledge of cell biology**
- **Knowledge of histology**
- **Knowledge of biochemistry**

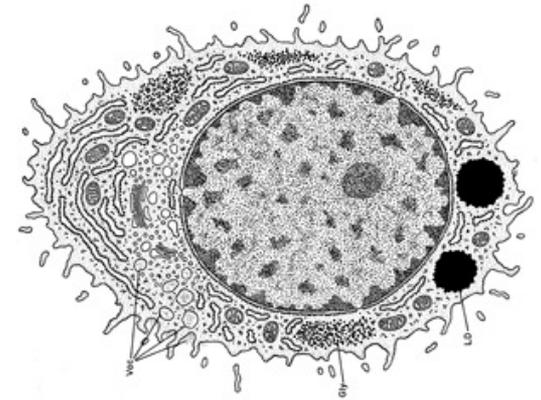
→ Put down the scalpel and took out the microscope

RECONSTRUCTION ≠ REGENERATION

- Natural reconstitution of organic tissues after destruction
- Find the initial properties of the native tissue
- Two main pathways around the cell:
 - ➔ Stimulate the cells present = Activation proteins
 - ➔ Bring in new cells

CELLS STIMULATION: HOW

- The cell will be activated by local factors:
 - Hormones
 - Level 0²
 - Activation proteins
 - Drugs
 - Vitamins
- It will secrete the fundamental substance and the fibers of the three-dimensional matrix of its fabric
- ? It is also necessary to have fuel and oxidant

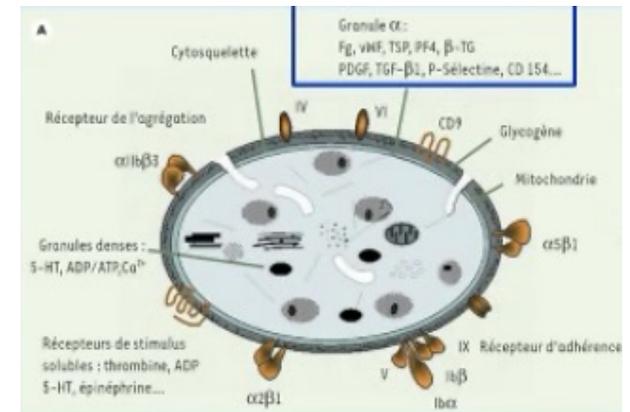
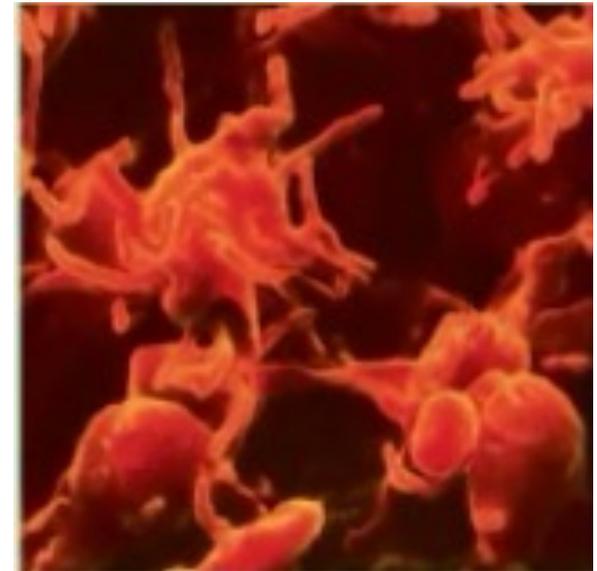


SUBSTITUTION WITH FETAL CALF SERUM (BOVINE SPONGIFORM ENCEPHALOPATHY)

- Autologous or Allogenic Serum = PRP
 - Stute et al., Exp. Hematology, 2004
 - Shahdadfar et al., Stem Cells, 2005
- Platelet Lysate
 - Doucet et al., J. Cell Physiol., 2005

PLATELETS & ALPHA GRANULATIONS

- Activated by thrombin
- Hemostatic role:
 - Adhesive properties
 - Contractility
- Alpha granules:
 - Growth factors
 - Released by activation of plt

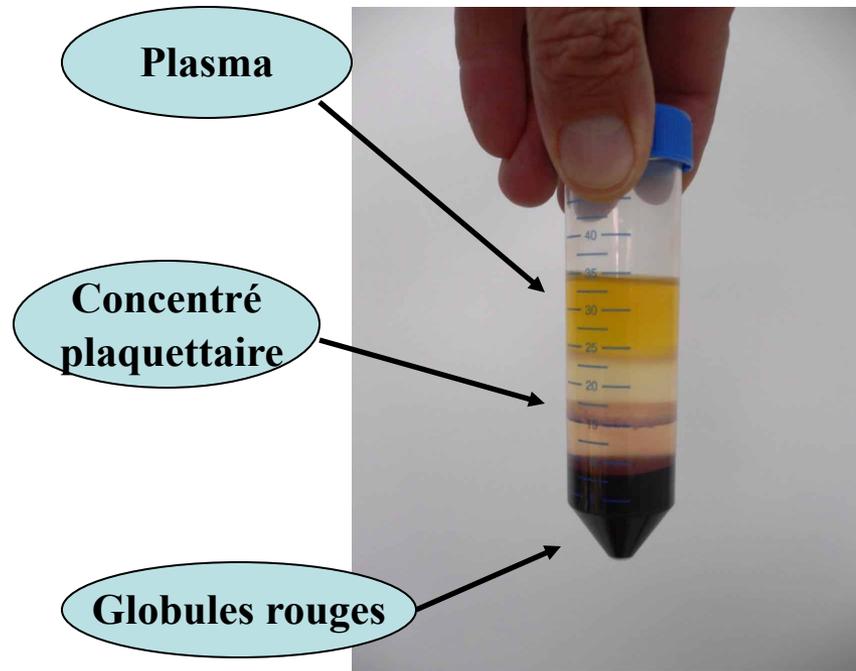


THE CONTENTS OF THE TOOLKIT

A GREAT FERTILIZER

Facteur	Tissus/Cellules Cibles	Fonction
PDGF-AB(Platelet Derived Growth Factor):	Fibroblastes, <u>chondrocytes</u> , ostéoblastes, <u>myocytes</u>	Croissance cellulaires, recrutement différenciation, sécrétion cytokine
TGF (Transforming Growth Factor β)	Endothélium, fibroblastes, monocytes, <u>osteoblastes</u>	Synthèse collagène, régulation croissance cellulaire et apoptose, différenciation, chimiotactisme
IGF (Insulin Like Growth Factor)	Os, endothélium, <u>kératinocyte</u> , fibroblastes	Croissance cellulaire, différenciation, recrutement, synthèse collagène, migration cellulaire, <u>néoangiogénèse</u>
FGF (Fibroblast Growth Factors)	Endothélium, <u>myocytes</u> , fibroblastes	Croissance cellulaire
VEGF (Vascular Endothelial Growth Factors)	Endothélium	Croissance cellulaire, migration, <u>néoangiogénèse</u>

Venipuncture of blood which will be centrifuged



COMPOSITION

- 3 to 8 times the circulating platelet count
- 150,000 to 400,000/ μl circulating blood

- Centrifugation speed
- Number of centrifugations
- Extraction methods
- Activation mode



difficult to compare

IN VITRO

- Fibroblast proliferation
- Collagen synthesis
- Neoangiogenesis
- Cellular differentiation
- Inducer of healing in poorly vascularized tissues with low mitotic activity
- Zhang J et al; Am J Sports Med. 2010

**PHENOTYPE
MESENCHYMAL UNCHANGED**

**USE OF PRP
FOR CELL CULTURES:**

- ➔ NO CELLULAR ABNORMALITY**
- ➔ GREATER CELL PROLIFERATION**

ACL

- Improve healing in partial injuries or repairs
- Improve regeneration of classic grafts
- Bioengineered grafts

IMPROVE HEALING

[Orthop J Sports Med.](#) 2017 Jan; 5(1): 2325967116681724.

PMCID: PMC5298533

Published online 2017 Jan 25. doi: [10.1177/2325967116681724](https://doi.org/10.1177/2325967116681724)

PMID: [28210653](https://pubmed.ncbi.nlm.nih.gov/28210653/)

Biologic Approaches for the Treatment of Partial Tears of the Anterior Cruciate Ligament

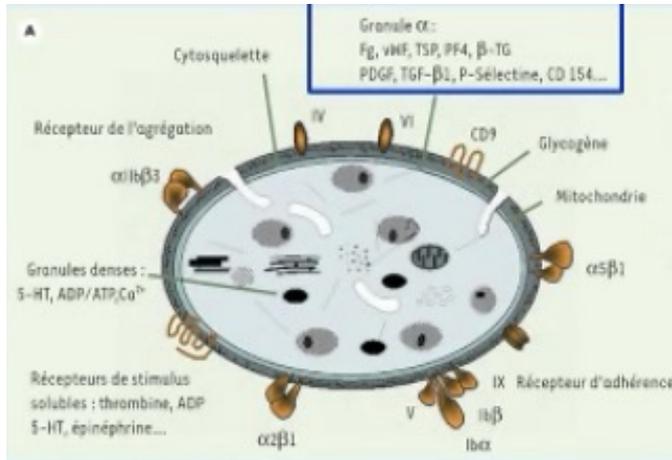
A Current Concepts Review

[Ignacio Dallo](#), MD,* [Jorge Chahla](#), MD,† [Justin J. Mitchell](#), MD,† [Cecilia Pascual-Garrido](#), MD,‡ [John A. Feagin](#), MD,†
and [Robert F. LaPrade](#), MD, PhD†§||

Growth factor + ACL repair

The potential benefits of these biological augmentation approaches for partial ACL tears **are improved healing,** better proprioception, and a faster return to sport and activities of daily living when compared with standard reconstruction procedures. However, **long-term studies with larger cohorts of patients and with technique validation are necessary to assess the real effect of these approaches.**

IMPROVE REGENERATION OF CLASSIC GRAFTS



This article presents the current data on the use of **platelet-rich plasma in the reconstruction** of the anterior cruciate ligament. Although the findings are not conclusive, the use of autologous platelet-rich plasma is shown to be safe, reproducible, and effective in **mimicking the natural processes** of soft tissue and bone healing

The Future: Optimizing the Healing Environment in Anterior Cruciate Ligament Reconstruction

Sánchez, Mikel MD^{*}; Anitua, Eduardo MD[†]; Lopez-Vidriero, Emilio MD[‡]; Andía, Isabel PhD[†]

[Author Information](#) ☺

Sports Medicine and Arthroscopy Review 18(1):p 48-53, March 2010. | DOI: 10.1097/JSA.0b013e3181c0ccd5

IMPROVE REGENERATION OF CLASSIC GRAFTS

> [Arthroscopy](#). 2010 Apr;26(4):470-80. doi: 10.1016/j.arthro.2009.08.019. Epub 2010 Jan 15.

Ligamentization of tendon grafts treated with an endogenous preparation rich in growth factors: gross morphology and histology

Mikel Sánchez ¹, Eduardo Anitua, Juan Azofra, Roberto Prado, Francisco Muruzabal, Isabel Andia

The use of PRGF influenced the histologic characteristics of tendon grafts, resulting in more remodeling compared with untreated grafts. We have shown temporal histologic changes during the 6- to 24-month postoperative period of graft maturation, with newly formed **connective tissue enveloping most grafts treated with PRGF.**

No functional difference

Not only Growth factor

Comparative Study > [Am J Sports Med.](#) 2013 Aug;41(8):1762-70.

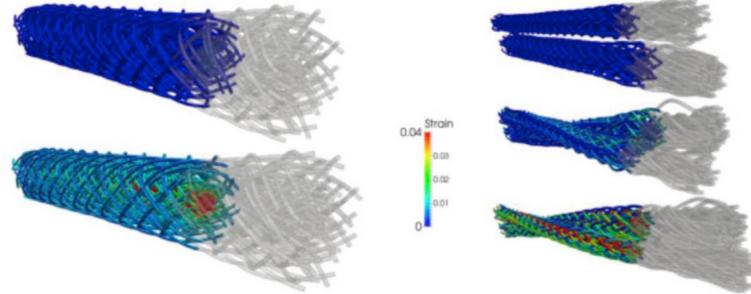
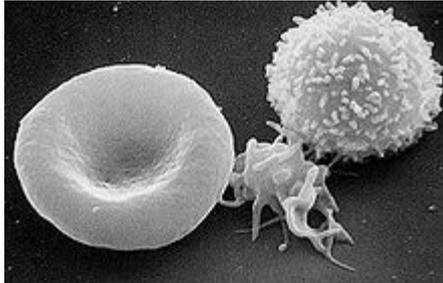
doi: 10.1177/0363546513483446. Epub 2013 Jul 15.

Use of a bioactive scaffold to stimulate anterior cruciate ligament healing also minimizes posttraumatic osteoarthritis after surgery

[Martha M Murray](#)¹, [Braden C Fleming](#)

**Bioactive collagen
Porcine model**

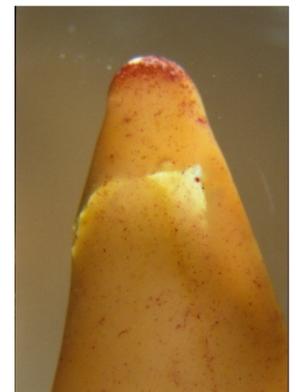
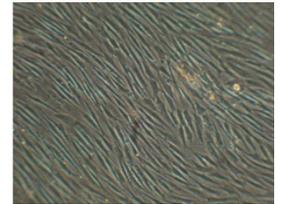
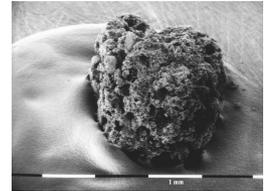
BIOENGINEERING



- Reproduce Cellular component
 - Fundamental substance
 - Three-dimensional matrix
 - Cells culture (Mesenchymal stem cells or fibroblast)

MODEL FOR THE BONE

- 3D matrix
- A cellular component
- Fundamental substance → PRP
 - Nutrient
 - Activation proteine



The effects of short-term hypoxia on human mesenchymal stem cell proliferation, viability and p16^{INK4A} mRNA expression: Investigation using a simple hypoxic culture system with a deoxidizing agent

[Akira Ito](#),^{1,2} [Tomoki Aoyama](#),³ [Makoto Yoshizawa](#),⁴ [Momoko Nagai](#),¹ [Junichi Tajino](#),¹ [Shoki Yamaguchi](#),^{1,2}
[Hirotaka Iijima](#),¹ [Xiangkai Zhang](#),¹ and [Hiroschi Kuroki](#)¹

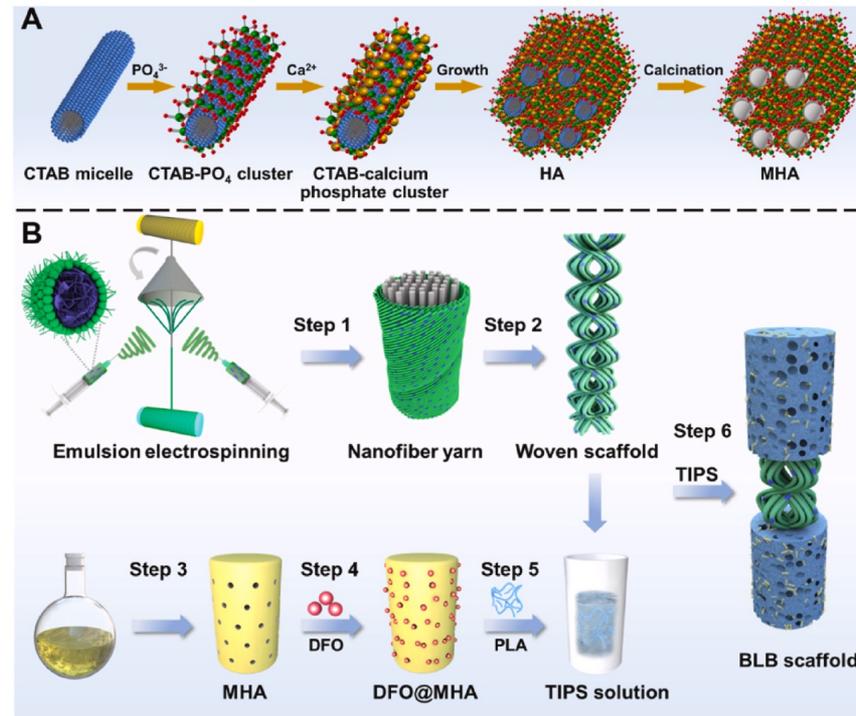


difficult training
easier war



Multiphasic bone-ligament-bone integrated scaffold enhances ligamentization and graft-bone integration after anterior cruciate ligament reconstruction

Xianrui Xie^{a,c,1}, Jiangyu Cai^{b,d,1}, Dan Li^a, Yujie Chen^a, Chunhua Wang^c, Guige Hou^c, Thorsten Steinberg^e, Bernd Rolauffs^f, Mohamed EL-Newehy^g, Hany EL-Hamshary^g, Jia Jiang^{b,****}, Xiumei Mo^{a,c,*}, Jinzhong Zhao^{b,**}, Jinglei Wu^{a,c,***}



CONCLUSION

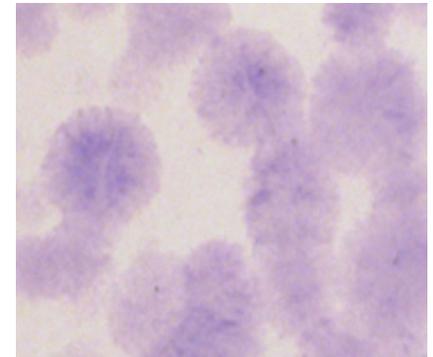
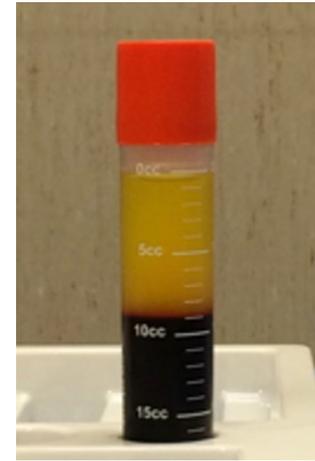
stimulate healing with PRP :

➔ available but low level of evidence

use cell cultures

➔ impossible in France but effective in vitro

3D scaffold?



15th Advanced Course
on **Knee Surgery**

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February
2024