SOCIETY FOR DENTAL SCIENCE

Régénération Osseuse
Ingénierie Tissulaire Osseuse

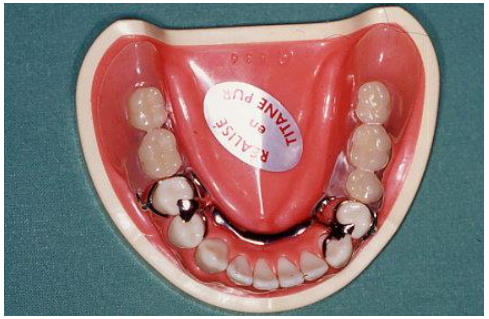
Philippe Lesclous – Pierre Weiss

La Médecine Réparatrice

- https://alliancerm.org/

La Médecine 4R

Replace

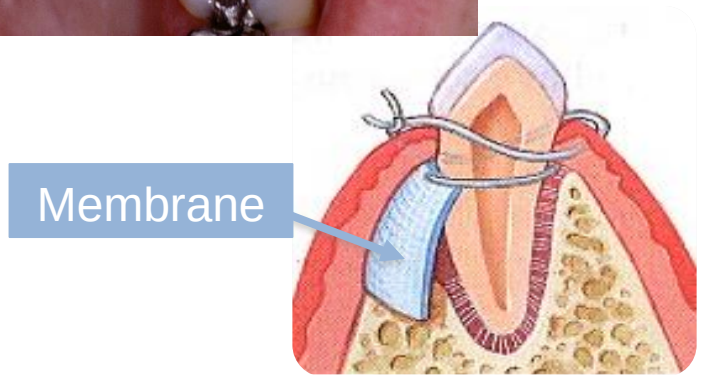


On remplace un organe par un dispositif médical qui rétablit une fonction mécanique et/ou l'esthétique

Repair

On répare une partie d'un organe avec un biomatériau bioactif pour rétablir une fonction mécanique, esthétique et biologique

Regenerate

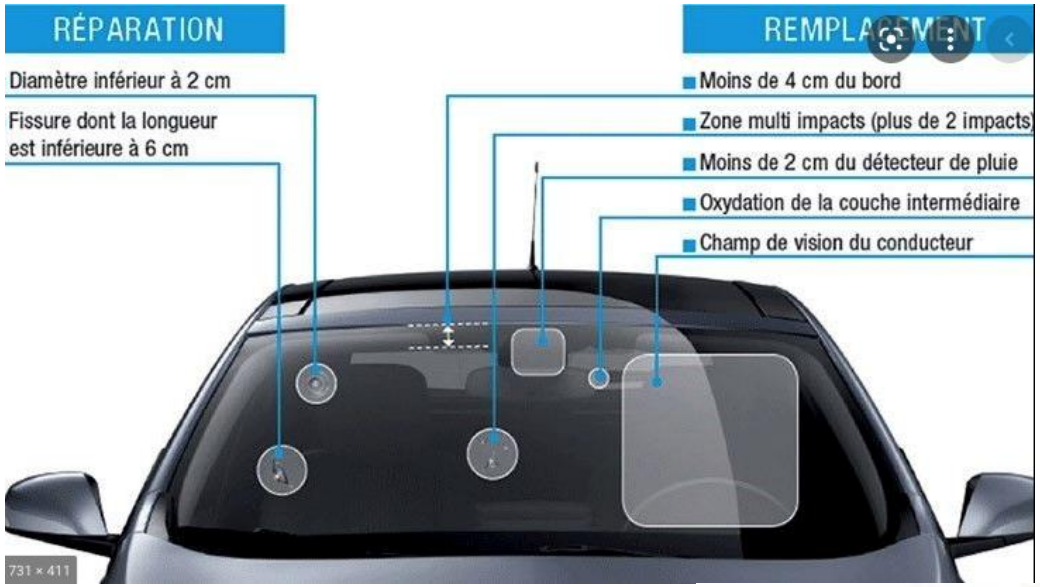


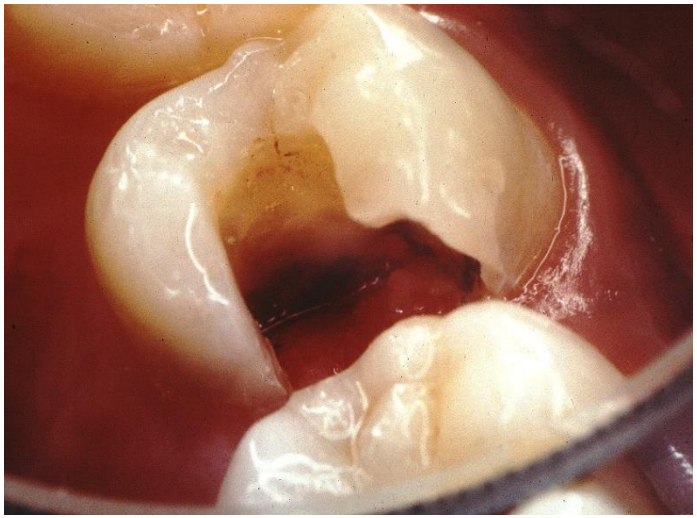
On régénère *ad integrum* une partie d'un organe avec un biomatériau, des cellules, des facteurs de croissance…

Reprogram

On reprogramme des cellules pour leur demander la régénération d'un tissu.

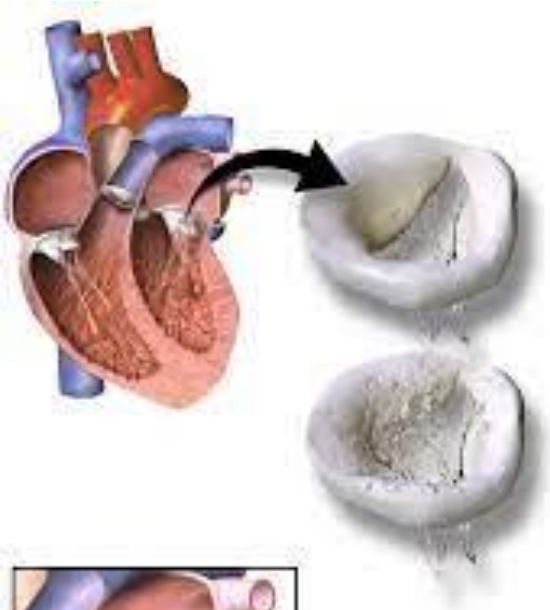
Remplacer ou réparer ?

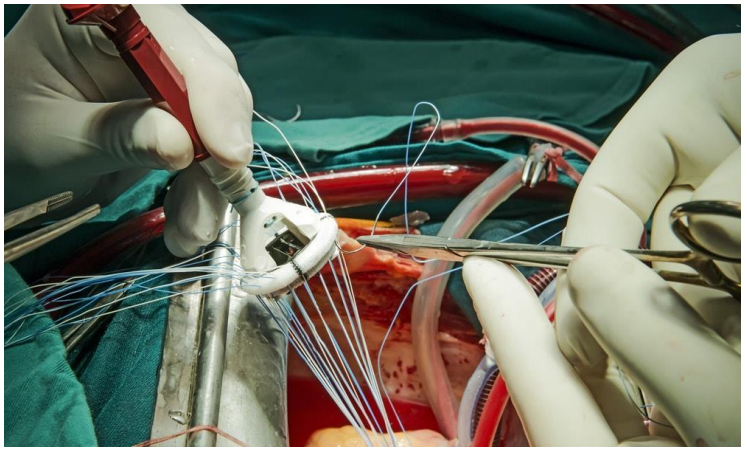




Réparer ou remplacer une dent délabrée

Remplacer ou réparer ?





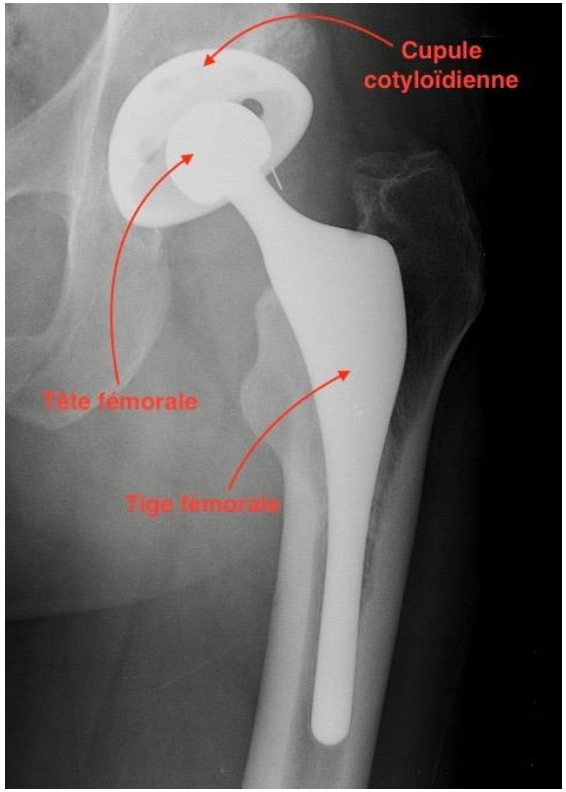
On répare le cœur
On remplace une valve

On remplace le cœur

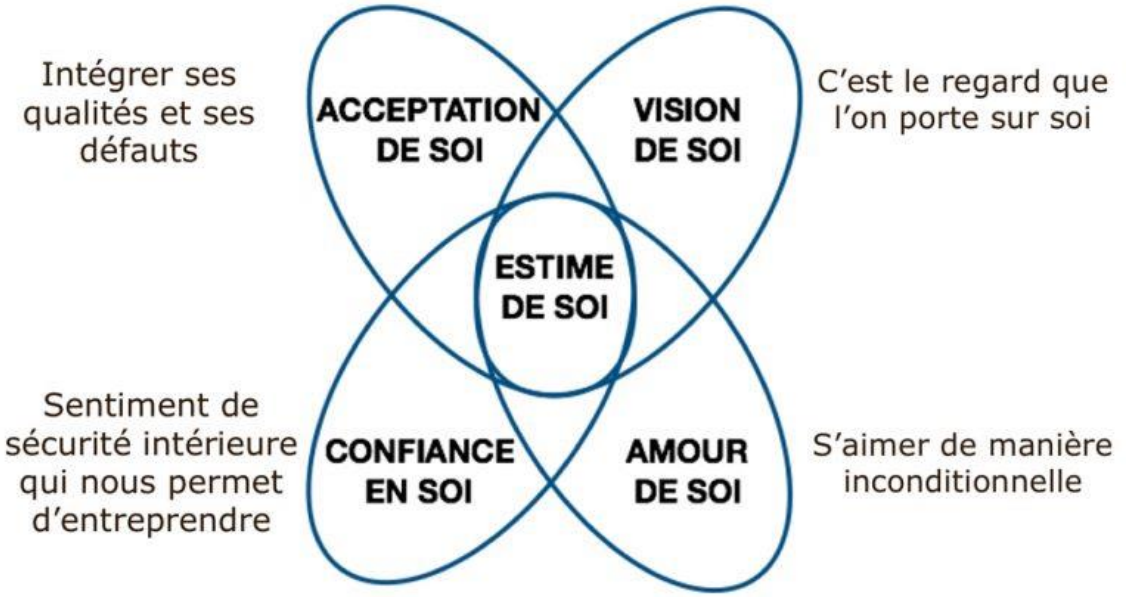
Objectif remplacer ou réparer

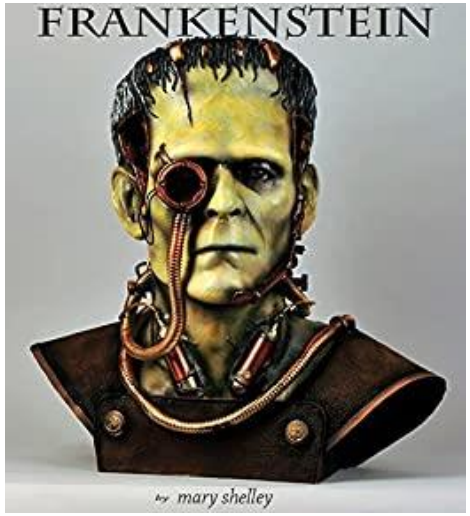
- On répare une partie d'un organe
- On remplace un organe

Pour retrouver une fonction biologique



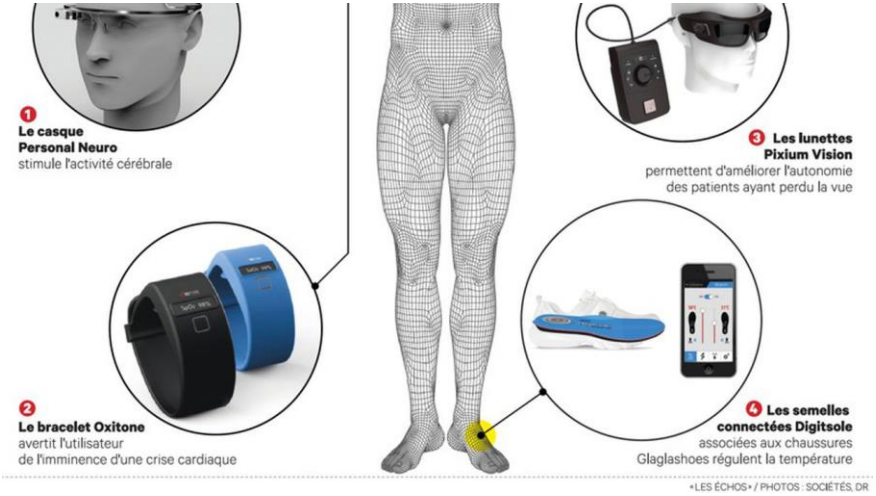
Remplacer ou réparer ?





L'homme augmenté → Le transhumanisme

Le transhumanisme



Le **transhumanisme** est un courant de pensée laïc qui cherche à améliorer la condition humaine et à accélérer l'évolution de la vie intelligente grâce à la science. Les **transhumanistes** considèrent en effet la mort, le vieillissement et la souffrance comme des tares que les nouvelles technologies peuvent enrayer.

Définition | Transhumanisme | Futura Tech
https://www.futura-sciences.com › Tech › Définitions

Définitions

- Biomatériau (D. Williams, 1987) :
  - Matériau non vivant utilisé dans un dispositif médical
  - Destiné à interagir avec les systèmes biologiques

- Cela n'est plus vrai, les biomatériaux peuvent être vivants en les fonctionnalisant : c'est l'ingénierie tissulaire

ALTERNATIVES AUX GREFFES

- BIOMATERIAUX
  - Petites cavités
  - Diffusion des protéines et migration des cellules hôtes dans le matériau
  - Adhésion cellulaire puis remodelage

- INGÉNIERIE TISSULAIRE
  - Grosses pertes de substances
  - Cellules du patient multipliées *in vitro*
  - Réimplantées

Maladie génétique :
La fente labio-palatine

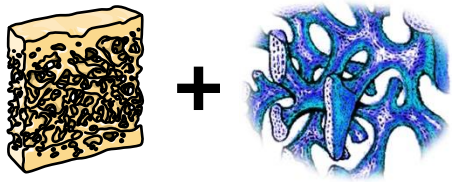
Limites actuelles de la greffe osseuse autologue

- Taux d'échec de la greffe osseuse
  - Enfant : 0%
  - Adulte: 10%

- Morbidité tibiale
  - Douleur: 5 jours
  - Boiterie: 10 jours
  - Cicatrice visible: 13%

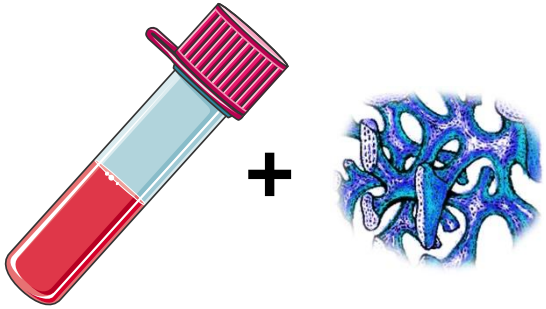
Corre P *et al*. Intérêt du site de prélèvement tibial médio-proximal dans l'alvéoloplastie secondaire: expérience de 55 cas chez l'enfant. Rev Stomatol Chir Maxillofac. 2011 Nov;112(5):280-5

Greffe osseuse = Gold standard

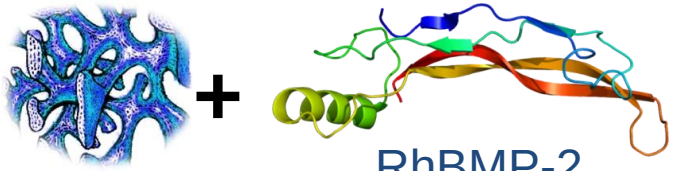


Expansion osseuse :

Greffe + Biomatériaux

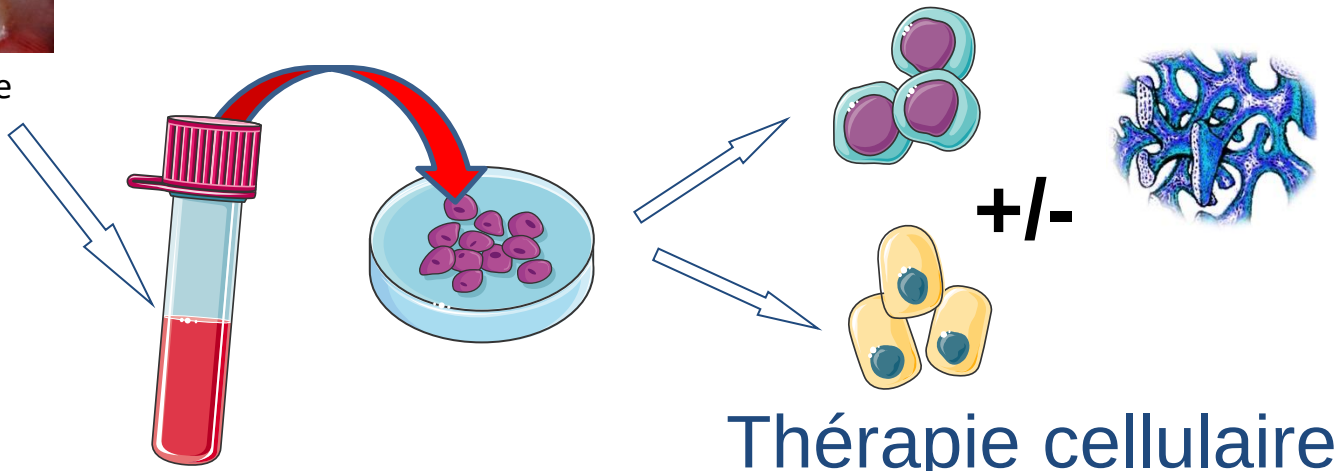


Moelle osseuse totale + Biomatériaux



RhBMP-2

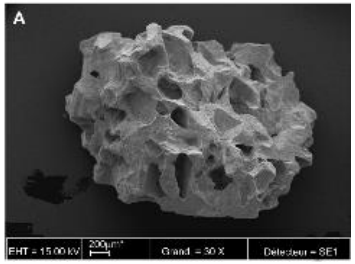
Pr. Pierre Corre

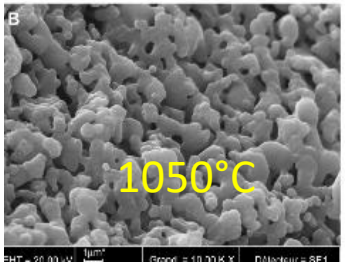


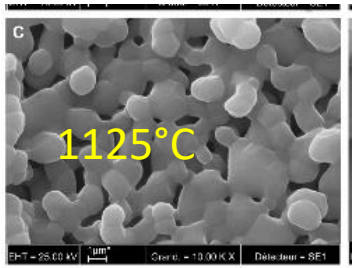
Thérapie cellulaire / ITO

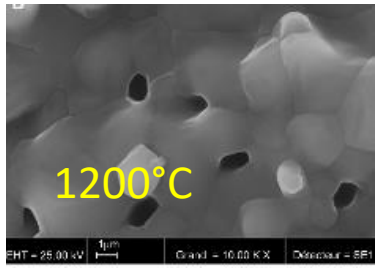
Design des biomatériaux et des systèmes combinés

1- Bioactive calcium phosphate ceramics

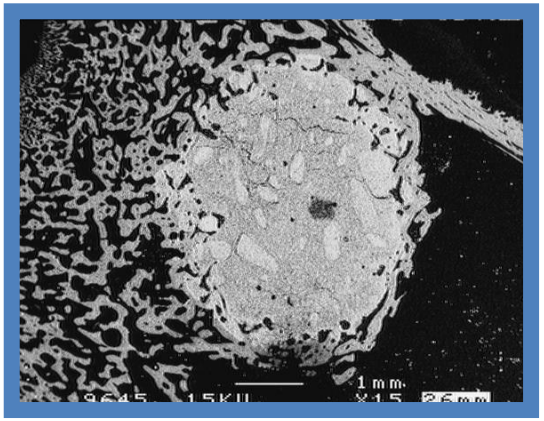




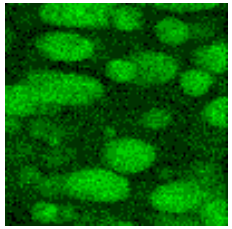




2- CaP cements and IBS



3- Self-setting hydrogels



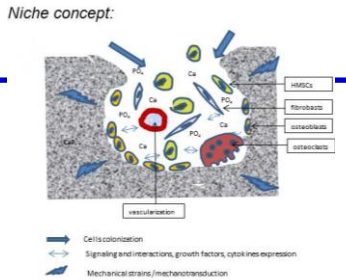
Liquide visqueux

Hydrogel

Granules de CaP

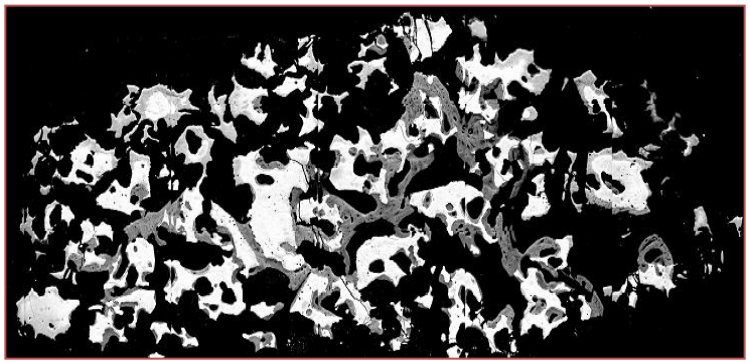
Composite

Biocéramiques pures



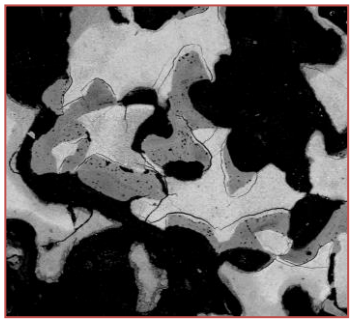
Pre-clinical studies

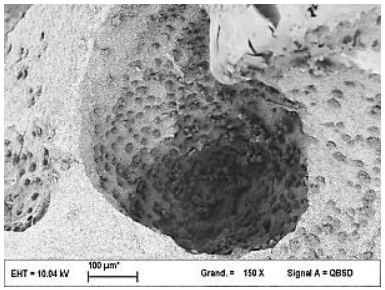
Bioceramics Smart Template for bone regeneration
The niche concept / BCP+



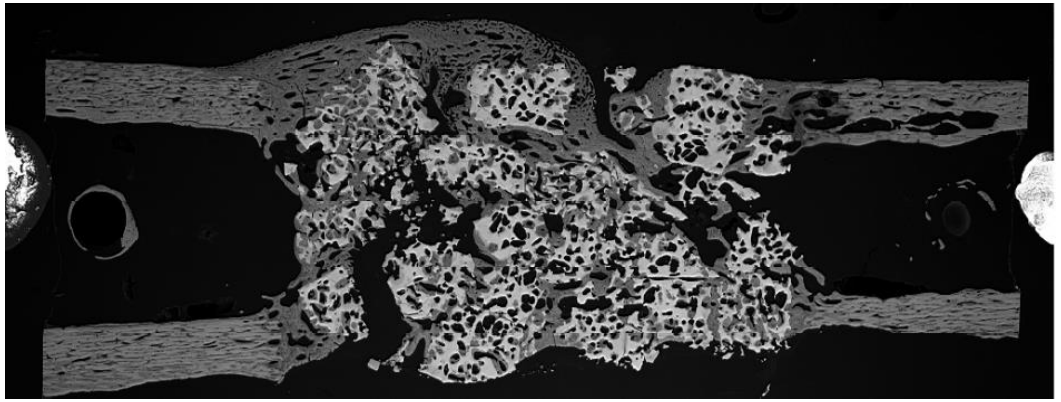
Muscular area / Granules MBCP 1-2mm 6 months in goat

Specific Osteogenic/osteoinductive propertiesof Bioceramic Smart Template (MBCP+)





Segmental defect (2.5 cm) in metatarsus of sheep after 12 weeks regenerated with autologous MSC and granules



Miramond T et al.. **J Biomater Appl**, **2014**
Miramond T et al. **IRBM**, **2013**
Daculsi G, et al. **IRBM**, **2012**.
Daculsi G et al. **J Aust Ceram Soc**, **2011**.
Daculsi G et al. **J Mater Sci Mater Med**, **2010**.

Les substituts osseux injectables (PCa)

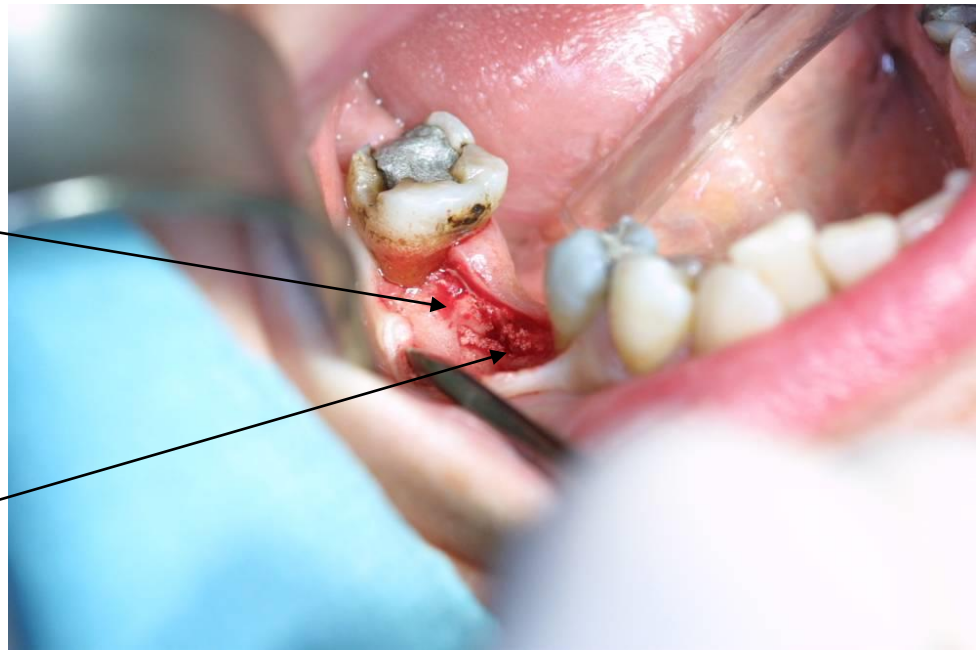
- Phosphates de calcium suspension
- Même phase minérale que le tissu osseux
- Non toxiques et biocompatibles
- Moulables ou injectables
- Remplissage complet de la cavité
- Contact intime entre le biomatériau et les tissus environnants

Résultats cliniques

No inflammation after 3 years
The width and the height seem to be conserved

Hard bone on the border
and the surface of the socket

A small amount of soft tissue
was present at the interface of
gum and bone



Produit mis sur le marché

ELSEVIER

Available online at www.sciencedirect.com
ScienceDirect
Biomaterials 28 (2007) 3295–3305

Biomaterials
www.elsevier.com/locate/biomaterials

The safety and efficacy of an injectable bone substitute in dental sockets demonstrated in a human clinical trial

Pierre Weiss[a,b,c,*], Pierre Layrolle[a,b], Léon Philippe Clergeau[b,c], Bénédicte Enckel[b,c], Paul Pilet[a,c], Yves Amouriq[b,c], Guy Daculsi[a,b], Bernard Giumelli[b,c]

Biomatlante
Biologics Solutions

Les substituts osseux injectables (ciment)

CIMENT

POUDRE + LIQUIDE

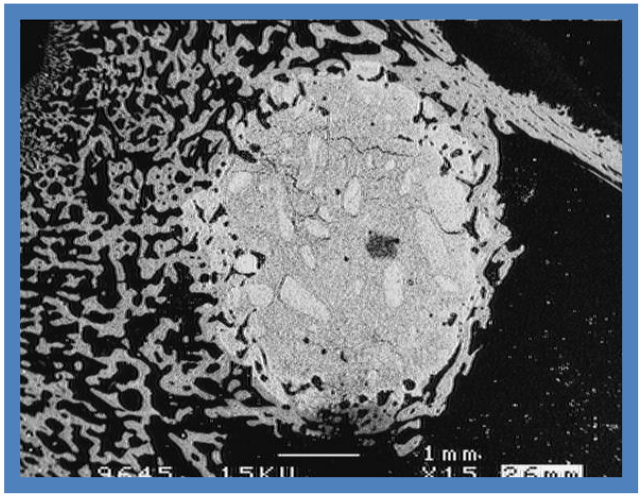
→ Manipulation du mélange 1 mn

Pâte plastique

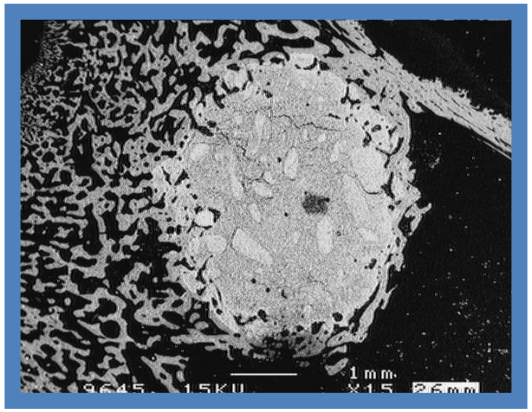
→ Mûrissement 2 mn (injection)
Temps de prise 5 mn

Pâte rigide

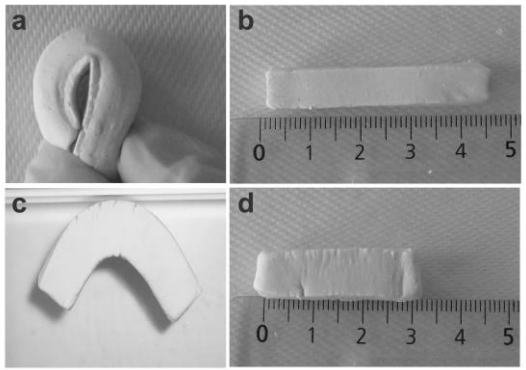
Masse solide → **Durcissement**
Résistance mécanique finale
24 Heures : 44 MPa
mais dense et fragile



Les substituts osseux injectables (ciment)



Increase handling and ductile properties of CPC



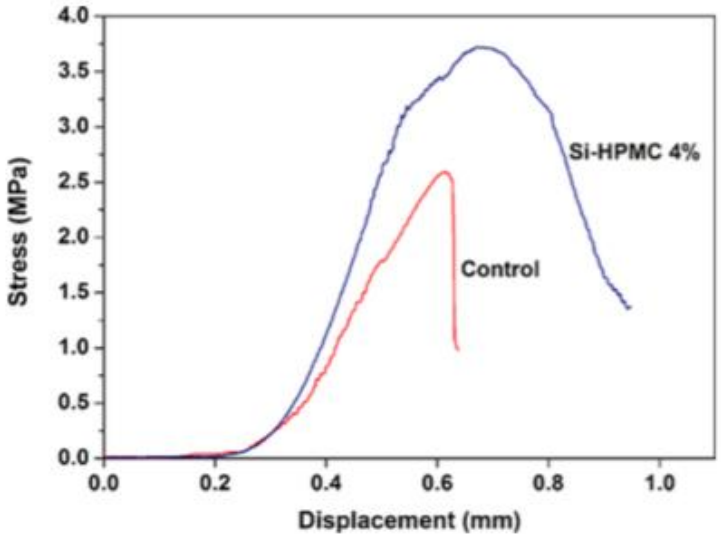
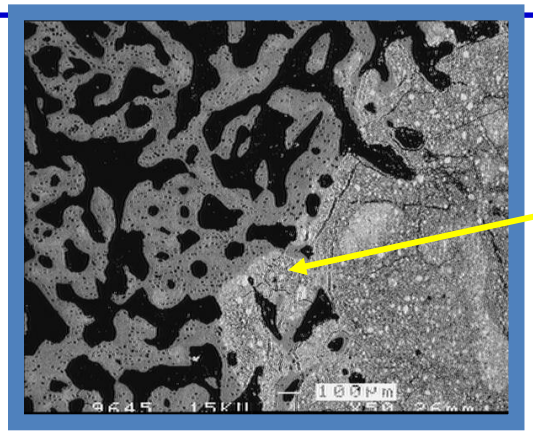
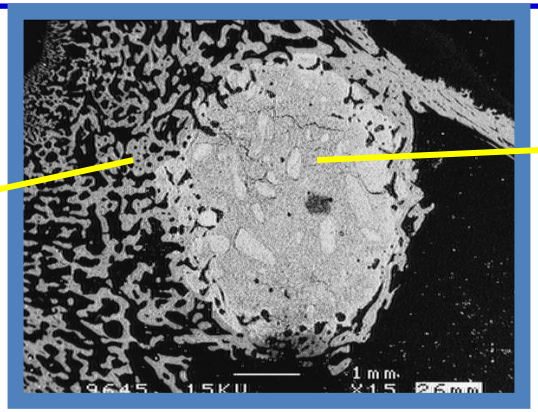


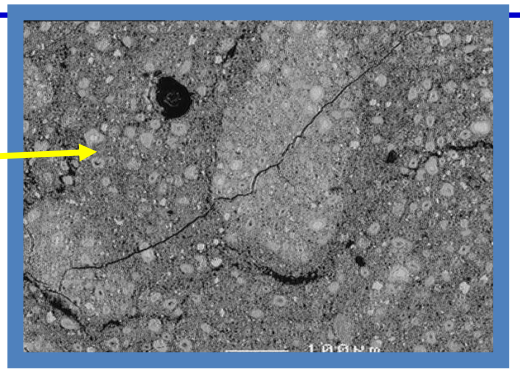
Fig. 7. Stress vs. crosshead displacement curves of the control cement and Si-HPMC composite cement (L/P = 1.0).

Liu W. et al. Acta Biomater. 2013.
Liu W. et al. Acta Biomater. 2014.

Les substituts osseux injectables (ciment)







Acta Biomaterialia 31 (2016) 326–338

Contents lists available at ScienceDirect

Acta Biomaterialia

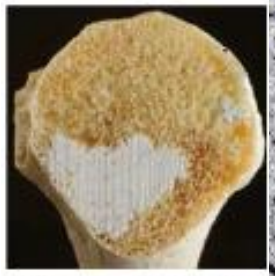
journal homepage: www.elsevier.com/locate/actabiomat

Full length article

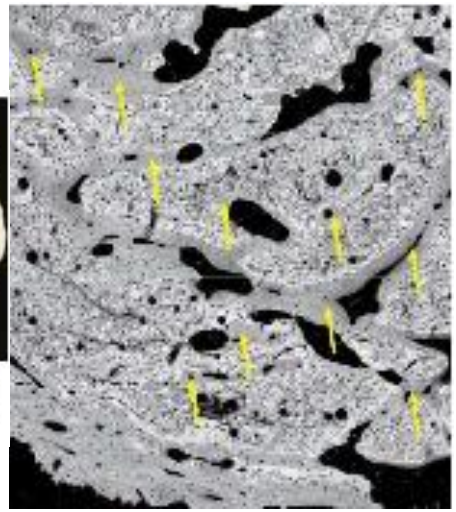
A simple and effective approach to prepare injectable macroporous calcium phosphate cement for bone repair: Syringe-foaming using a viscous hydrophilic polymeric solution

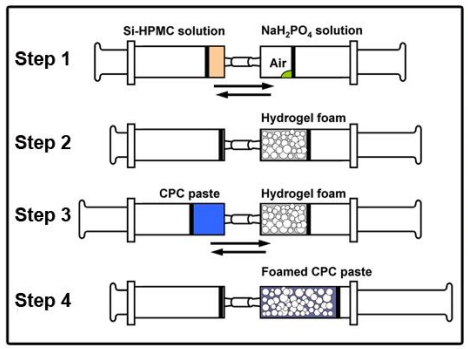
Jingtao Zhang [a,b,1], Weizhen Liu [a,b,1], Olivier Gauthier [c], Sophie Sourice [a], Paul Pilet [a,e], Gildas Rethore [a,e], Khalid Khairoun [a], Jean-Michel Bouler [d], Franck Tancret [b], Pierre Weiss [a,e,*]

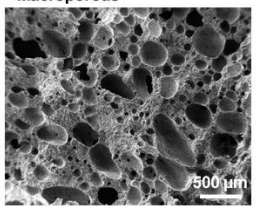
Increase Bioactivity of CPC : Macroporosity

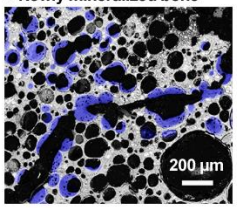


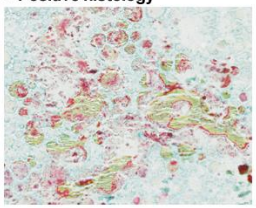
Pénétration de Graftys® HBS dans les trabécules





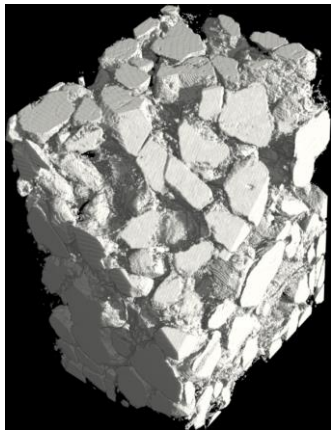




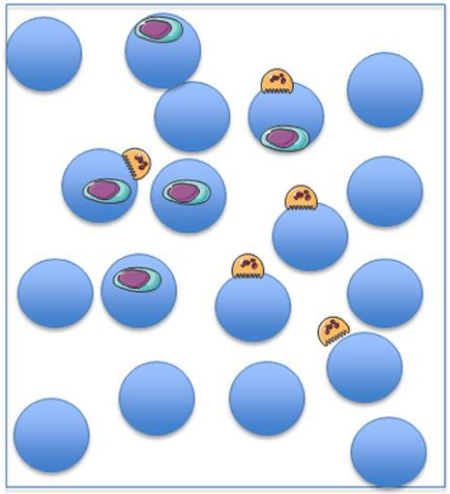


Macroporous and highly resorbable apatitic calcium-phosphate cement
Khairoun I, Weiss P, Bouler JM
Application WO2008023254

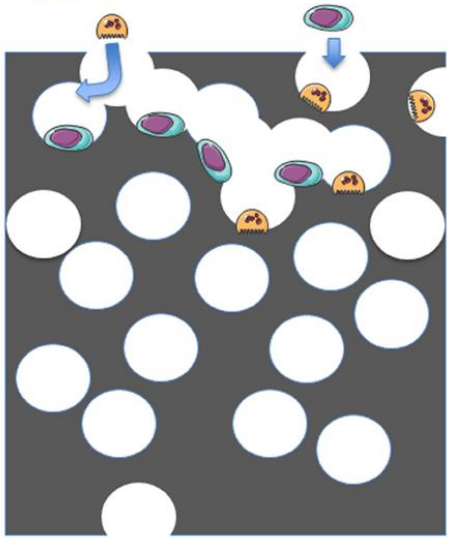
Les substituts osseux injectables

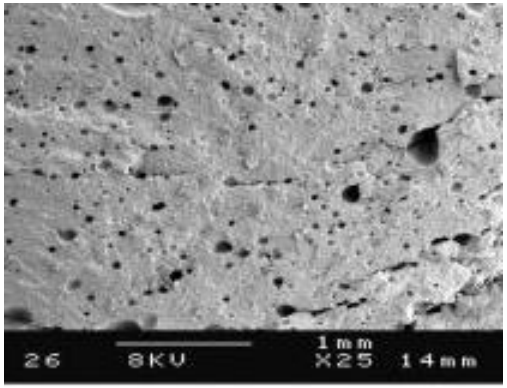


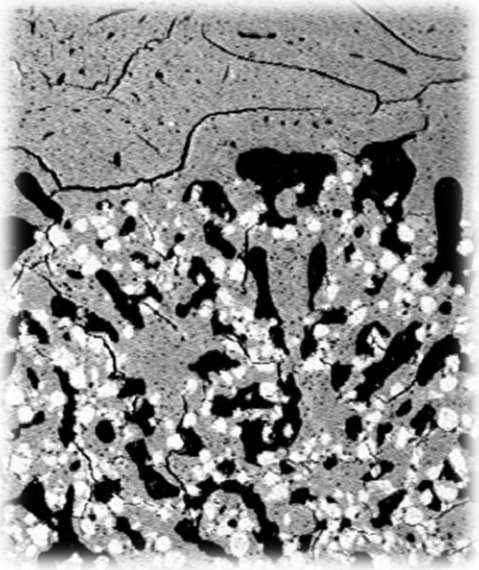
Classe I

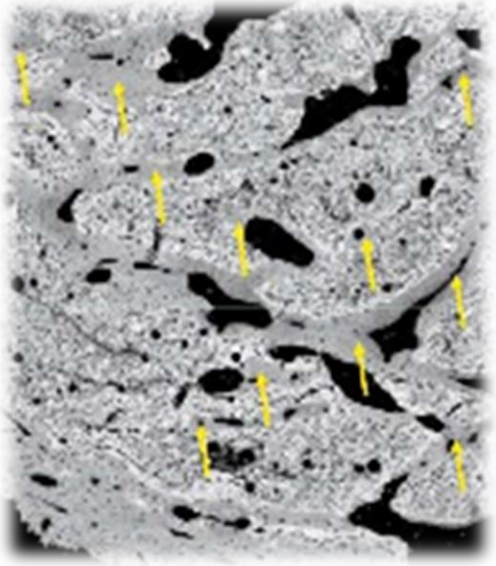


Classe II









Commercialized injectable bone subtitutes

Biological properties

Mechanical properties

In'Oss™ MBCP™

Injectable suspensions

MBCP™ Putty - In'Oss™

+ Biocompatibility
+ Injectability
+ Osteoconduction

- Mechanical properties

Hydroxyapatite + Phosphate Tricalcique Bêta (ßTCP)
+ viscous liquid = 2% HPMC

Biomatlante
Biologics Solutions

WO 9521634 (A1) Injectable Bone Substitute : WEISS P, DACULSI G,, DELECRIN J, GRIMANDI G ET PASSUTI N

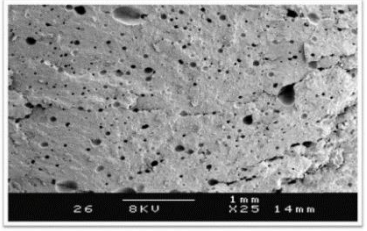
Solid materials

Graftys® QuickSet

Transfer Mix : 2 min Inject

+ Biocompatibility
+ Injectability
+ mechanical properties

- Porosity = HPMC particules
- Osteoconduction



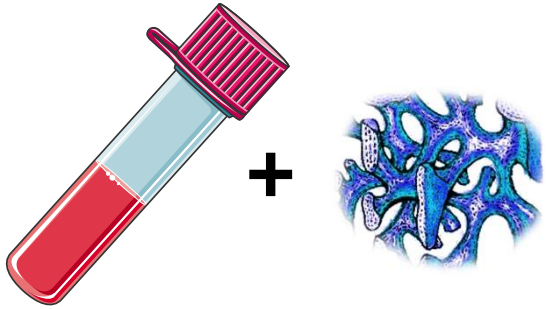
calcium phosphate salts + HydroxyPropylMethylCellulose (HPMC)) + Na_2HPO_4

Graftys®

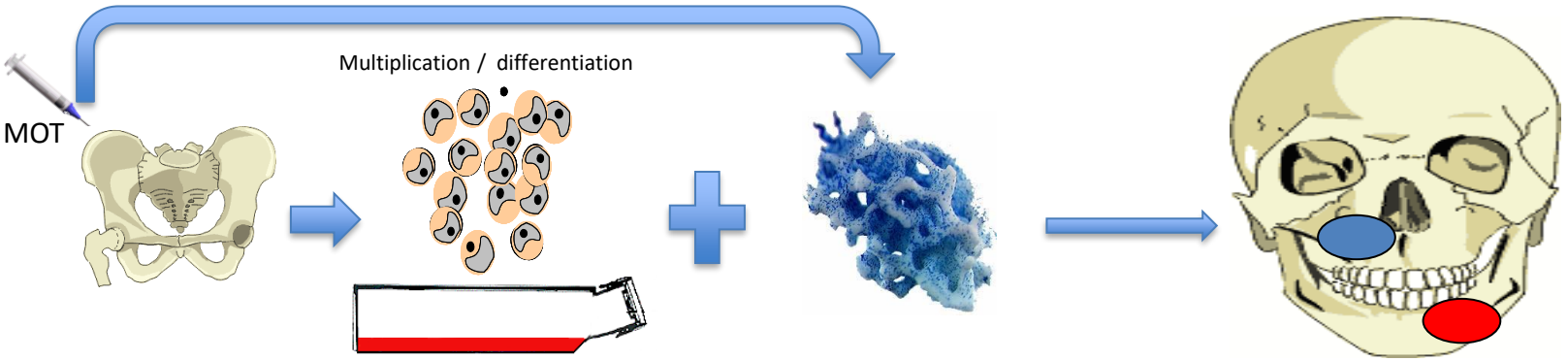
WO 20081023254 A1, 2008, Macroporous and highly resorbable apatitic calcrtm-phosphate cement, WEISS P, KHAIROUN I, BOULER JM

Ingénierie Tissulaire Osseuse

Réparation osseuse de l'os hypotrophique et de l'os ischémique

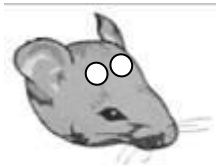


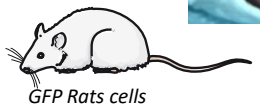
Moelle osseuse totale +
Biomatériau



Ingénierie Tissulaire Osseuse

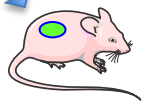
Genetic disease



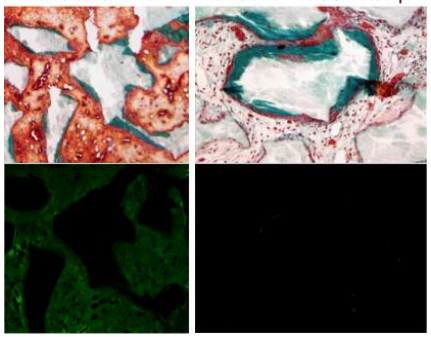


GFP Rats cells

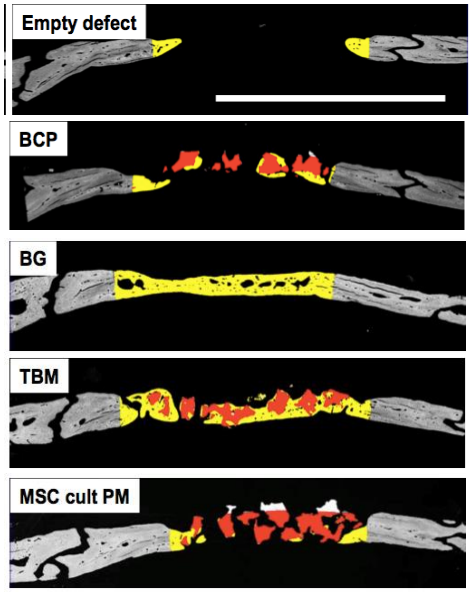
8 weeks



GROUP C: TBM GROUP D : MSC extemp.

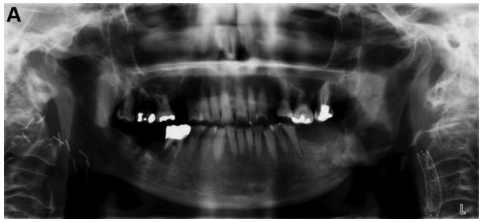


Corre P, PLoS ONE. 2013

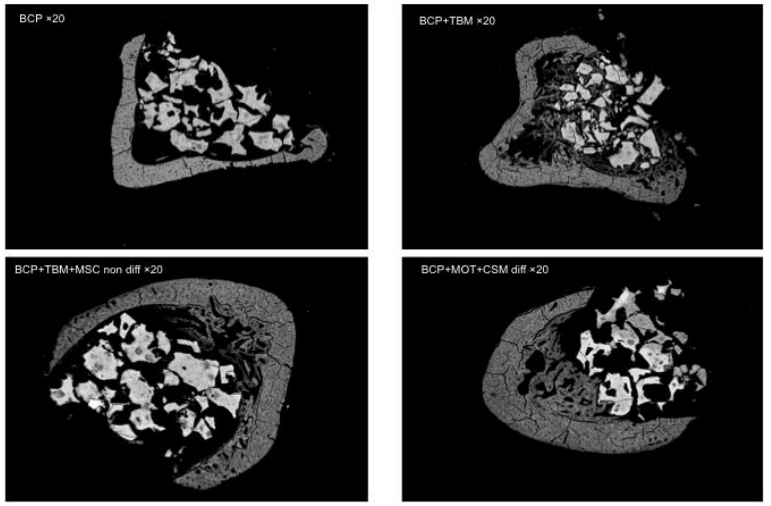


Corre P., Acta Biomaterialia 2015

ORN



Irradiated bone



1 mm

Thery A. Journal of Cranio-Maxillo-Facial Surgery. 2015
Michel G. Calcified Tissue Int 2015
Blery P J Mater Sci: Mater Med 2014

Total Bone Marrow (TBM) with Calcium phosphate ceramics is the most promising TE strategy for clinical transfer

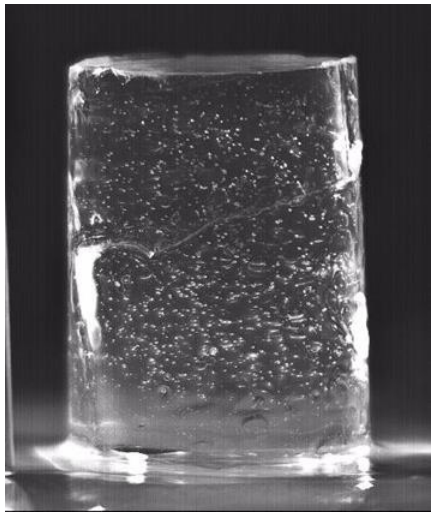
Utilisation d’un hydrogel injectable

Matrices extracellulaires synthétiques

Les hydrogels

Utilisation d'un hydrogel injectable

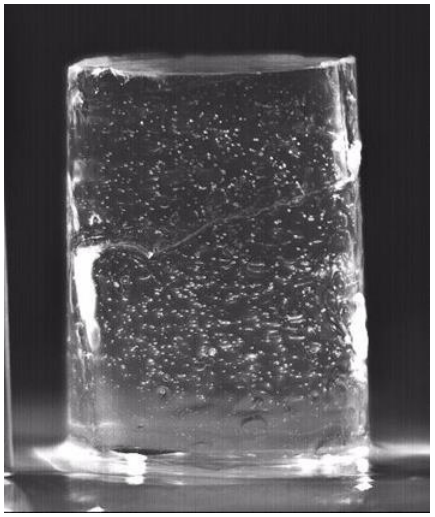
Hydrogel of a
superabsorbent polymer

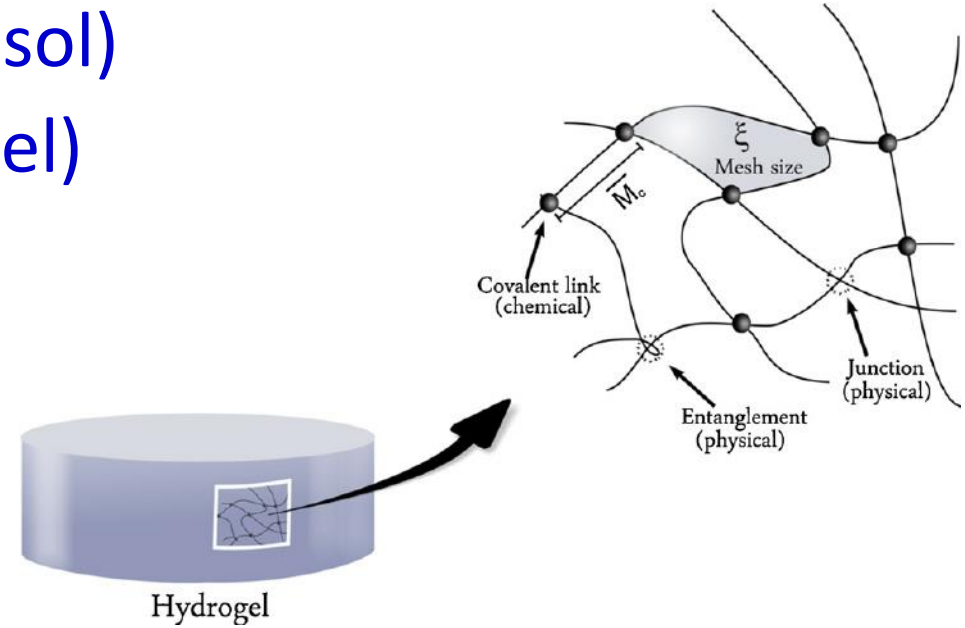


Liquide visqueux ou solide élastique

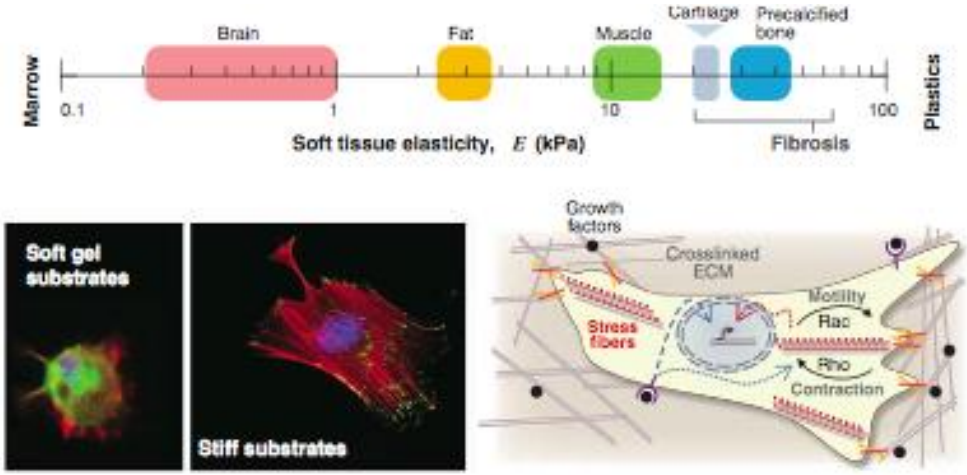
Utilisation d'un hydrogel injectable

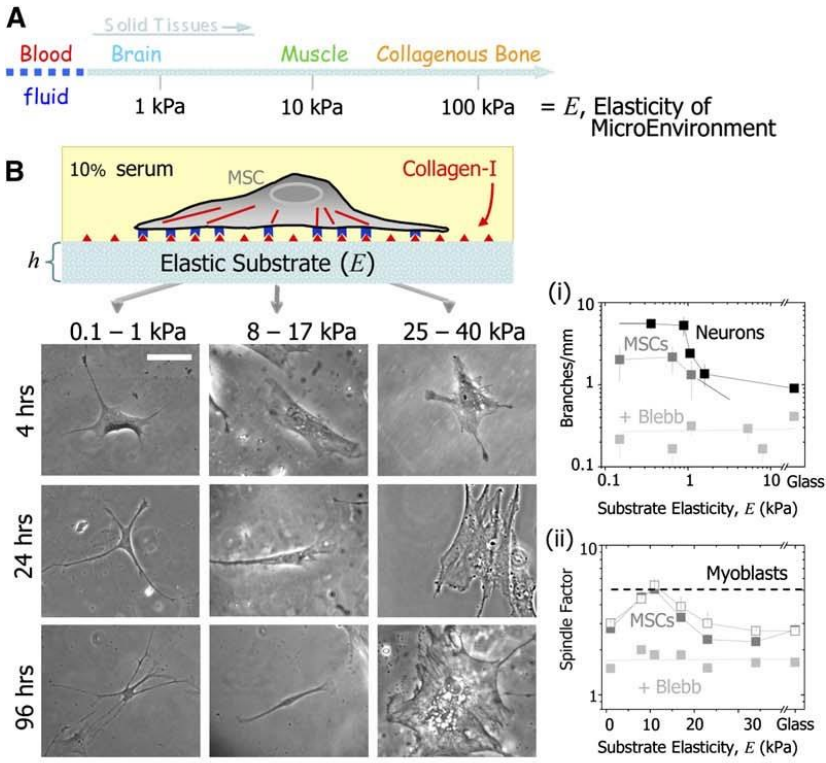
- C'est un liquide visqueux qui a la capacité de devenir solide par réticulation tridimensionnelle des chaines macromoléculaires.
- C'est un réseau tridimensionnel qui contient une grande quantité d'eau.
- Liquide visqueux (sol)
- -> Solide fragile (gel)





Rigidité du substrat: capacité de différenciation cellulaire





⑩Discher et al. Growth factors, matrices, and forces combine and control stem cells. Science (2009) vol. 324 (5935) pp. 1673-7

Matrix Elasticity Directs Stem Cell Lineage Specification

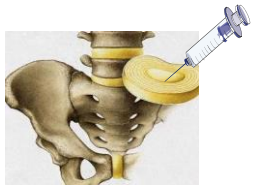
Adam J. Engler,[1,2] Shamik Sen,[1,2] H. Lee Sweeney,[1] and Dennis E. Discher[1,2,3,4,*]
[1]Pennsylvania Muscle Institute
[2]School of Engineering and Applied Science
[3]Cell & Molecular Biology Graduate Group
[4]Physics Graduate Group
University of Pennsylvania, Philadelphia, PA 19104, USA
*Contact: discher@seas.upenn.edu

DOI 10.1016/j.cell.2006.06.044

Rigidité du substrat

Stiffness (E)

10^3 Pa



10^3 - 10^4 Pa

Si-HPMC

-

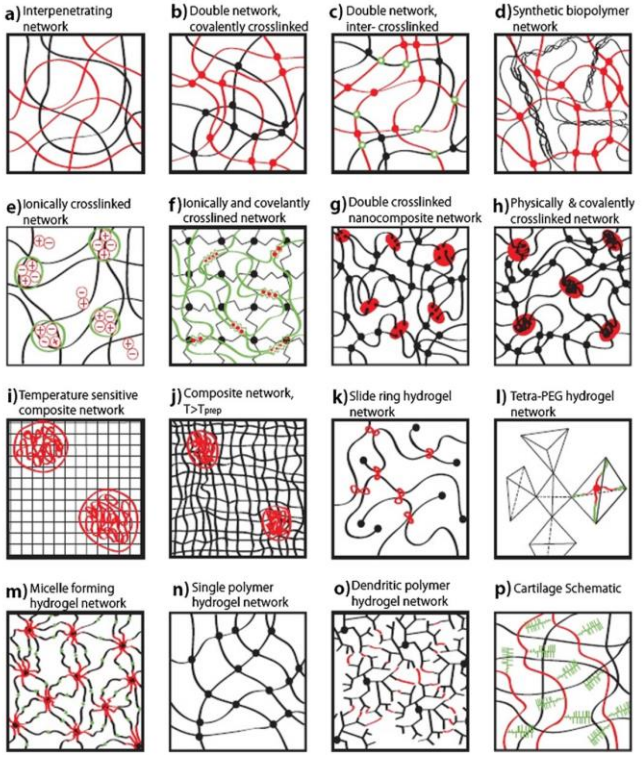
10^5 - 10^6 Pa

Cartilage Intervertebral Disc

-

>10^6 Pa

Bone



- **Modified Polysaccharides (10^3 - 10^4 Pa)**
- **Protein aggregates gels (10^4 Pa)**
- **Dense Suspension of proteins micro gels (10^5 Pa)**
- **Mélanges like IPN gels (10^5 Pa)**

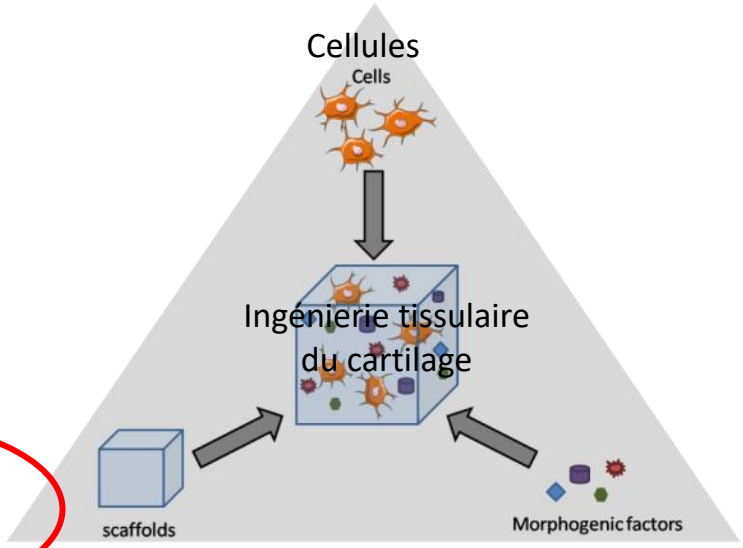
But stiffness is not enough to characterize the mechanical properties..

Nano/Micro particles ➔ Modulate Si-HPMC rheological and mechanical properties

Définition de l'Ingénierie Tissulaire

Un nouveau domaine biomédical regroupant les principes de la biologie cellulaire et du génie biologique, qui permet de reconstruire des structures proches des tissus à partir de cellules vivantes pour des usages *in vivo* ou *ex vivo*. Le concept clef est la reproduction, avec des caractéristiques simplifiées, de l'architecture tissulaire, qui conduit à une intégration immédiate et interactive de ces tissus dans le corps humain

(Auger, Canada)



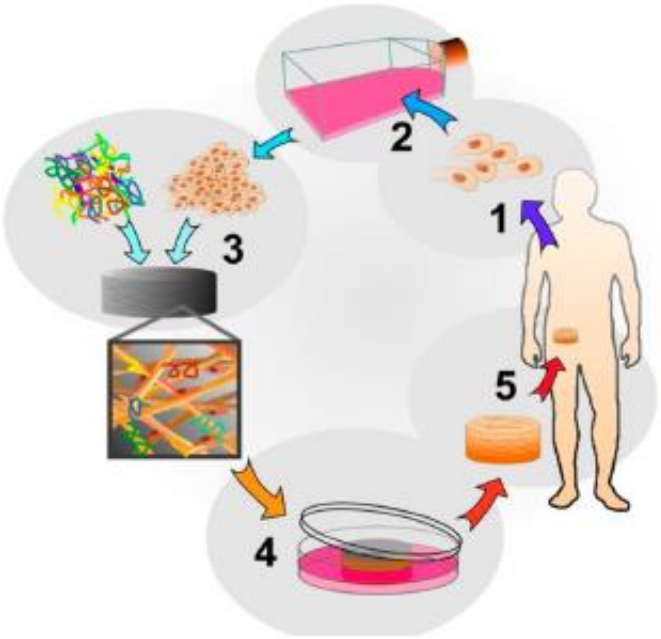
Biomatériaux/
matrices

Morphogènes

Merceron, Vinatier, Guicheux. Joint Bone Spine 2008
Vinatier, Guicheux. Trends Biotechnol 2009
Vinatier, Guicheux, Noël Curr Stem Cell Res Ther 2009

Ingénierie Tissulaire Osseuse

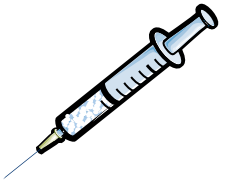
L'INGÉNIERIE TISSULAIRE



➢ Restaurer, maintenir ou améliorer les propriétés et fonctions d'un tissu

De Boer et al., Tissue Eng 2008

PROPRIÉTÉS DU MATÉRIAU IDÉAL



1. Injectable
Chirurgie mini-invasive

2. Stérilisable
Stable et pas de modification chimique

3. Biocompatible
Pas de cytotoxicité, immunogénicité et limiter l'inflammation

4. Propriétés mécaniques adaptées
Matériau peu fragile

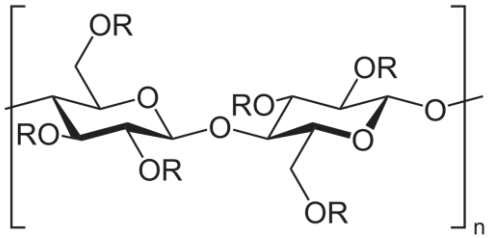
5. Ostéoconducteur
Permettre la formation osseuse à sa surface

6. Macroporeux
Favoriser la colonisation cellulaire dans le matériau

7. Ostéoinducteur
Capacité du matériau à attirer et différencier des cellules souches

Les hydrogels : l'HPMC silanisé

➢ L'hydroxypropylmethylcellulose



R = –H, $–CH_3$, $–CH_2–CHOH–CH_3$

Éther de cellulose, peu cher

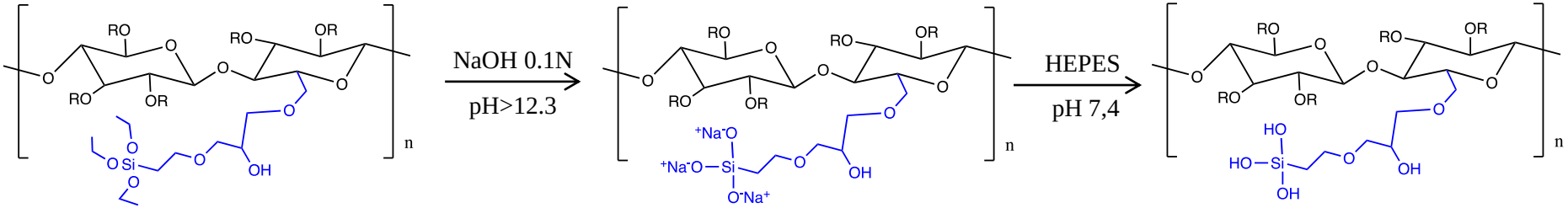
Inerte

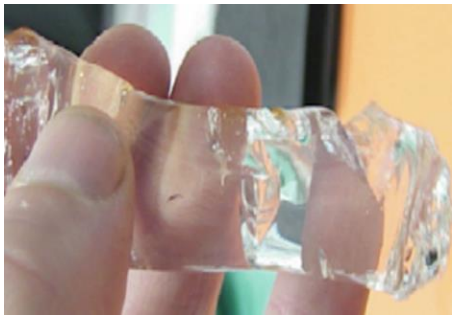
Non toxique

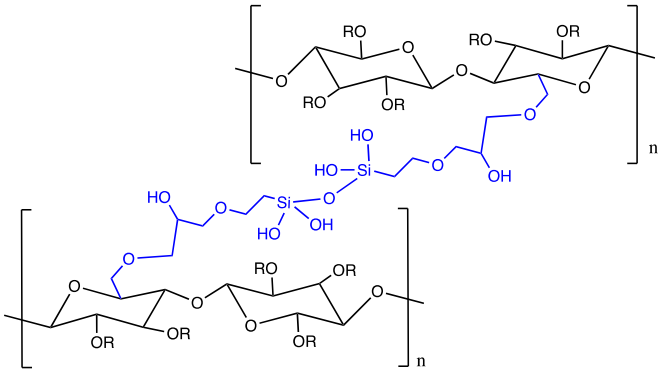
Excipient courant,
Grade Pharmacopée Européenne

➢ L'hydroxypropylmethylcellulose **silanisé**

Injectable







Condensation

Auto-réticulant
Bio-orthogonal

Bourges *et al.* ACIS 2002

Application en Parodontologie

Photo-crosslinkable membrane for Guided Periodontal Tissue Regeneration

Pauline Marie Chichiricco[1, 2], Raphael Riva[1], Jean-Michel Thomassin[1], Xavier Struillou[2], Catherine Le Visage[2], Christine Pierre Weiss[2, 3]

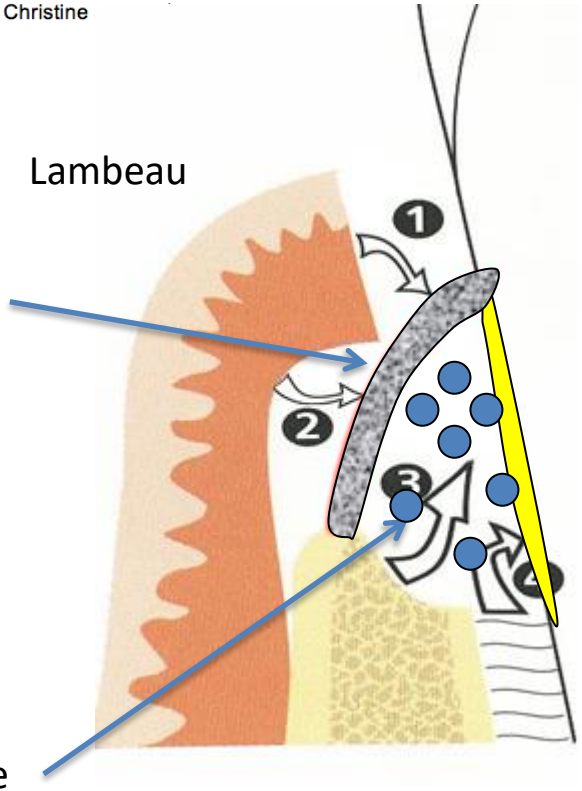
[1] Center for Education and Research on Macromolecules (CERM), CESAM Research Unit, University of Liège, Belgium,

[2] INSERM, U1229 Regenerative Medicine and Skeleton (RMeS), School of Dental Surgery, Université de Nantes, France

[3] CHU Nantes, PHU4 OTONN, France

Membrane :
Hydrogel
injectable réticulé

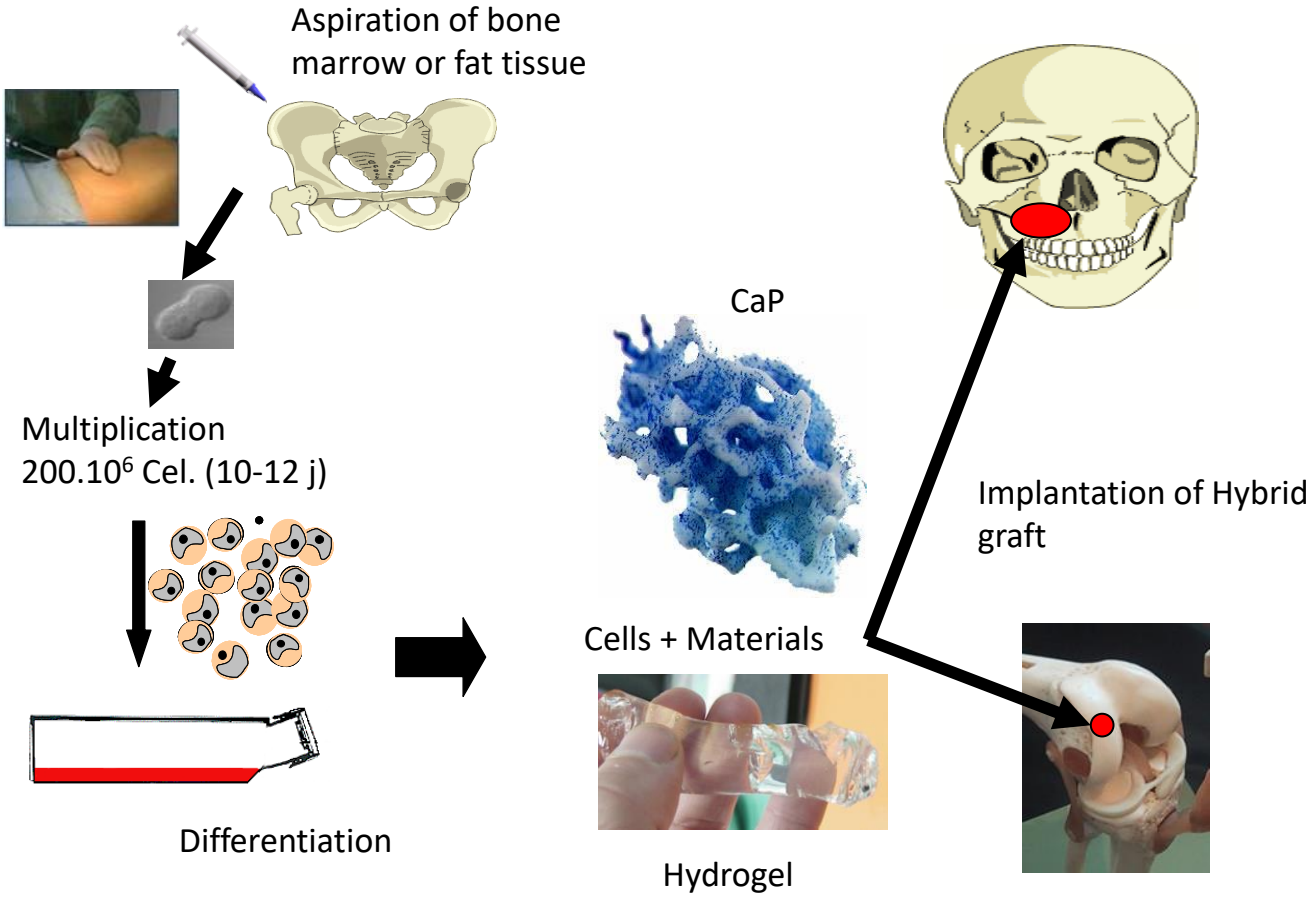
rempart mécanique
contre les cellules
épithéliales



- Protocole rapide et simple
- Contrôle spatial de la différentiation tissulaire ?

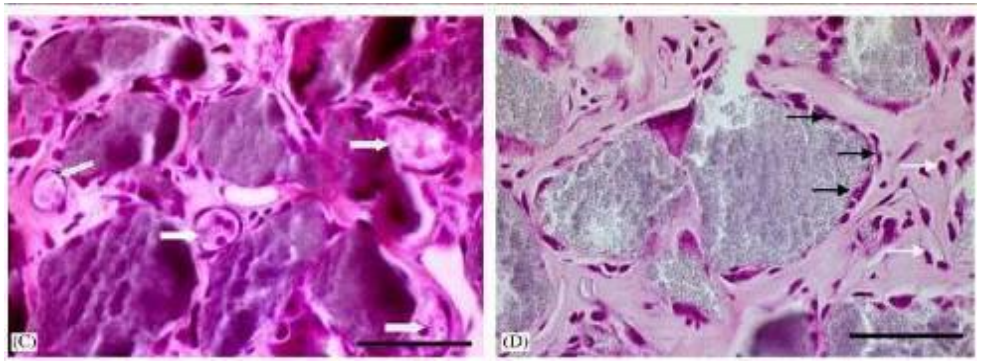
IBS : Suspension injectable de CaP = repousse osseuse rapide

Application en régénération articulaire et osseuse



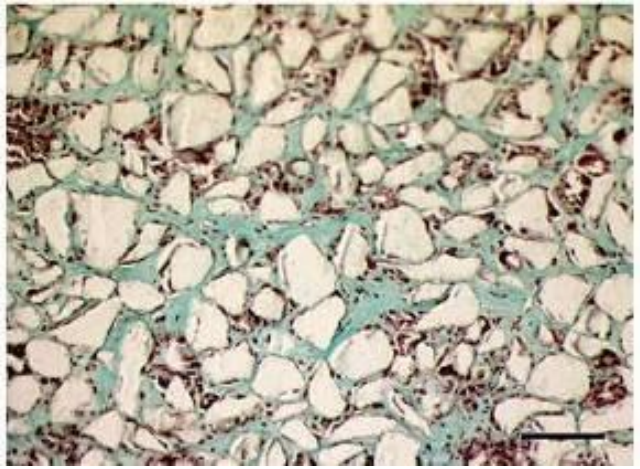
Ingénierie tissulaire osseuse *in vivo HPMC*

BMSC with Si-HPMC / BCP formulation implanted under skin of mice for 4 weeks



Blood vessels

Osteoblasts and osteocytes



Goldner staining paraffin sections

Ectopic bone formation
was available in mice model

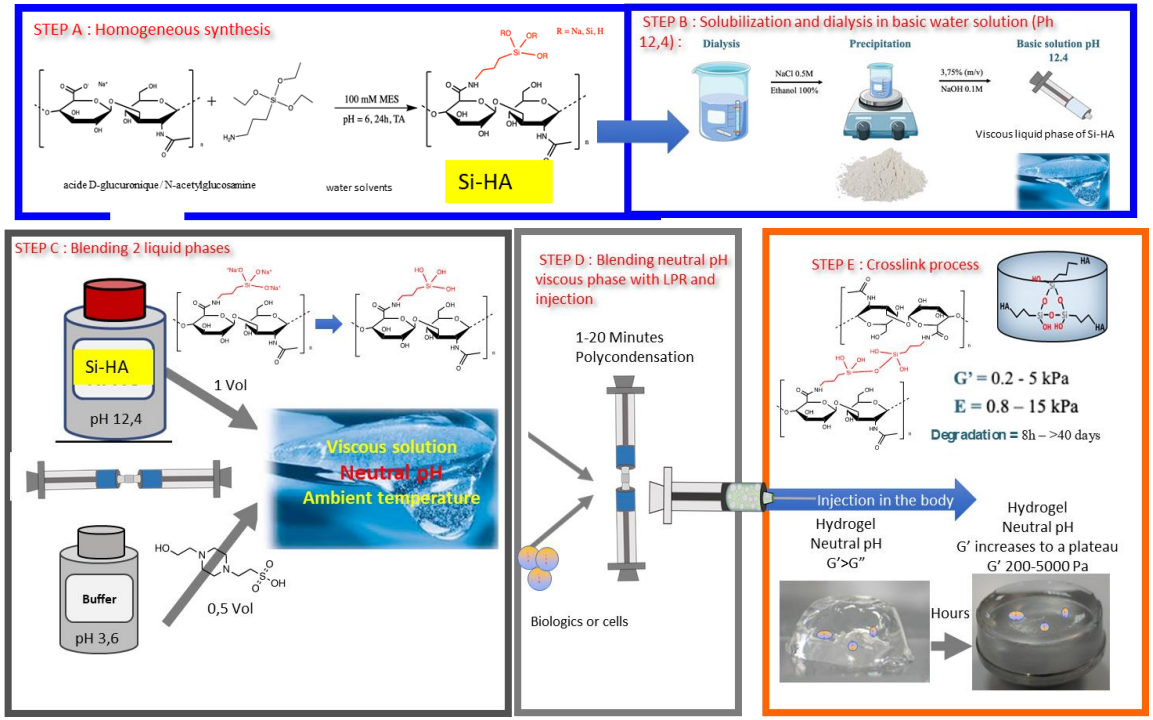
Available online at www.sciencedirect.com
SCIENCE DIRECT
Biomaterials

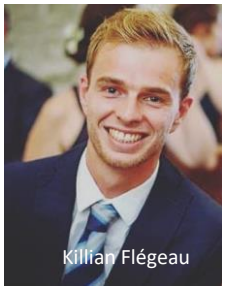
Ectopic bone formation using an injectable biphasic calcium phosphate/Si-HPMC hydrogel composite loaded with undifferentiated bone marrow stromal cells

Christophe Trojani[a,b], Florian Boukhechba[a], Jean-Claude Scimeca[a], Fanny Vandenbos[c], Jean-François Michiels[c], Guy Daculsi[d], Pascal Boileau[b], Pierre Weiss[d], Georges F. Carle[a], Nathalie Rochet[a,*]

Ingénierie tissulaire osseuse *in vivo*

Acide hyaluronique





FULL PAPER

ADVANCED HEALTHCARE MATERIALS
www.advhealthmat.de

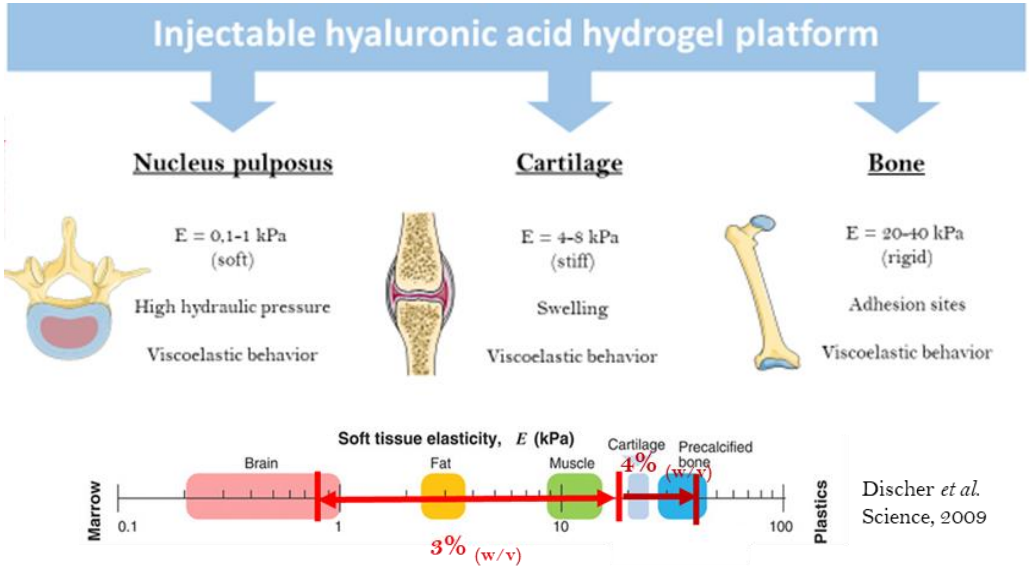
Check for updates

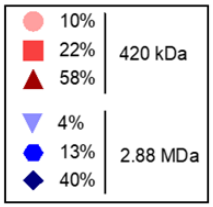
In Situ Forming, Silanized Hyaluronic Acid Hydrogels with Fine Control Over Mechanical Properties and In Vivo Degradation for Tissue Engineering Applications

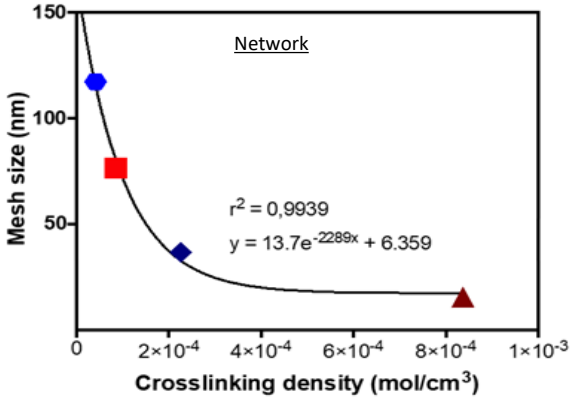
*Killian Flegeau, Claire Toquet, Gildas Rethore, Cyril d'Arros, Léa Messager, Boris Halgand, Davy Dupont, Florent Autrusseau, Julie Lesoeur, Joëlle Veziers, Pascal Bordat, Anthony Bresin, Jérôme Guicheux, Vianney Delplace, Hélène Gautier, and Pierre Weiss**

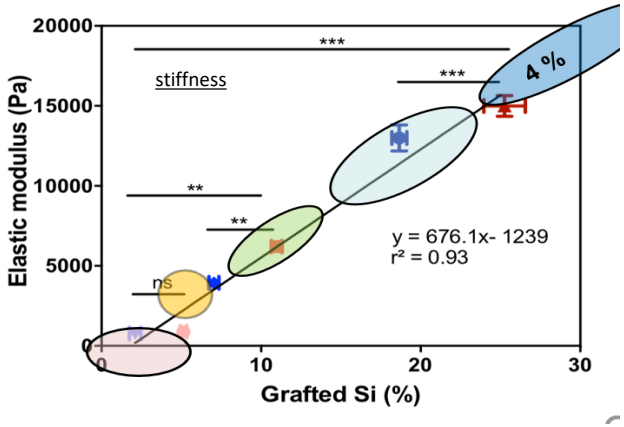
Ingénierie tissulaire osseuse *in vivo*

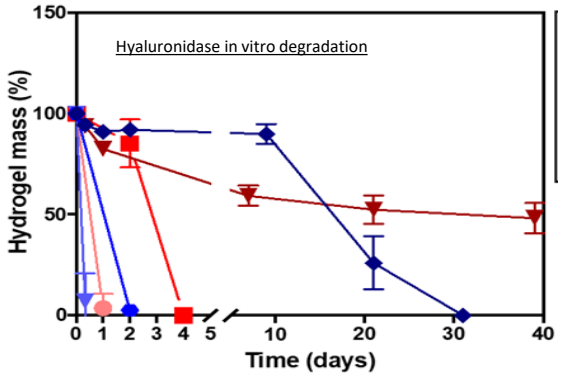
Acide hyaluronique





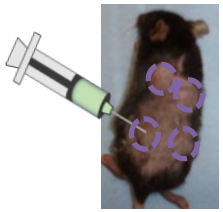


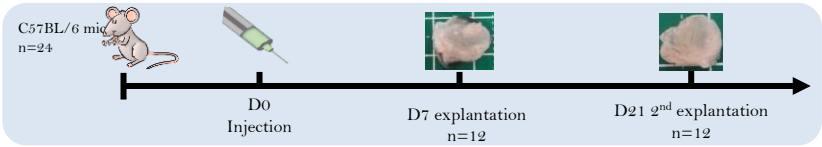


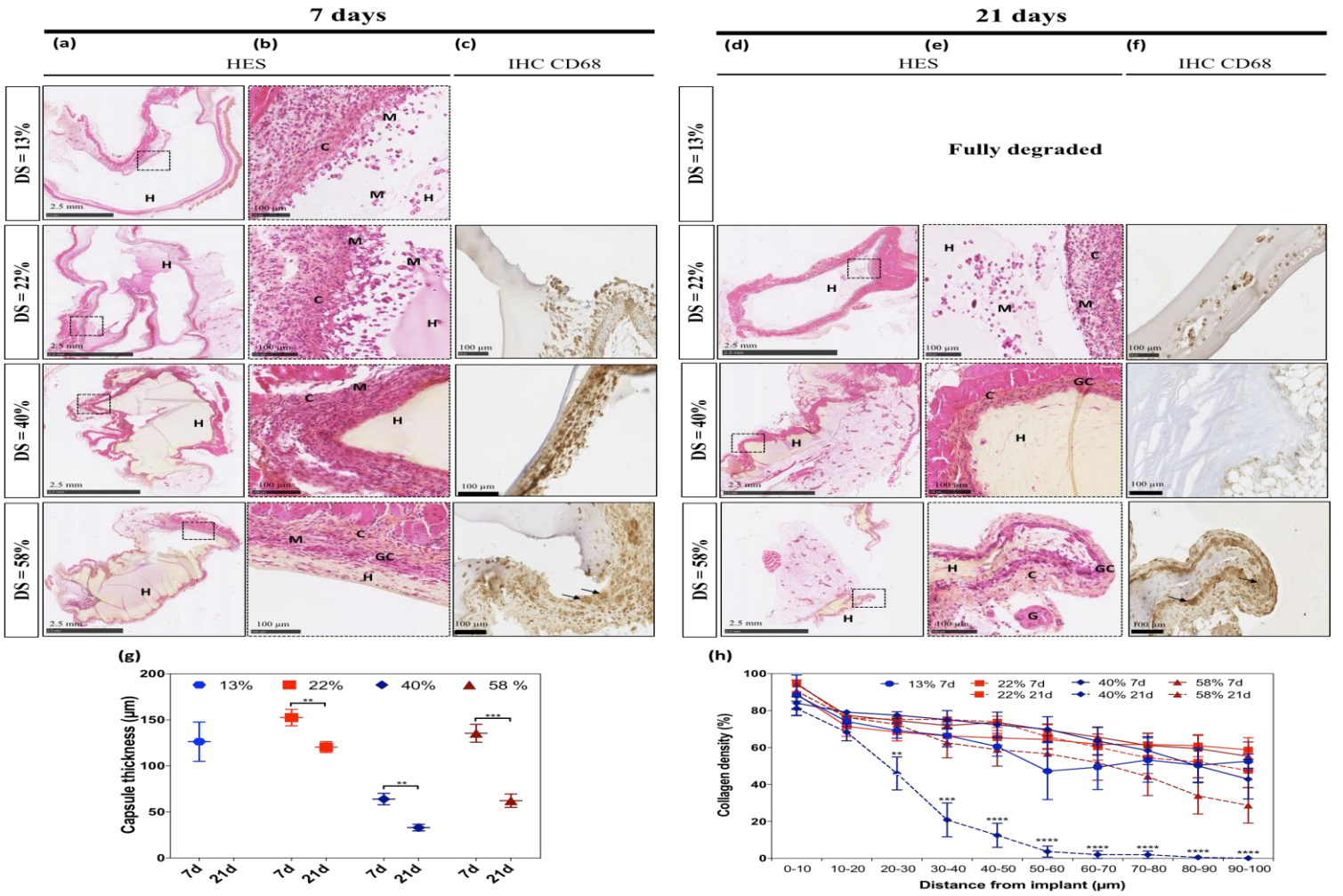


Tunable properties for each targeted tissues

Subcutaneous implantation

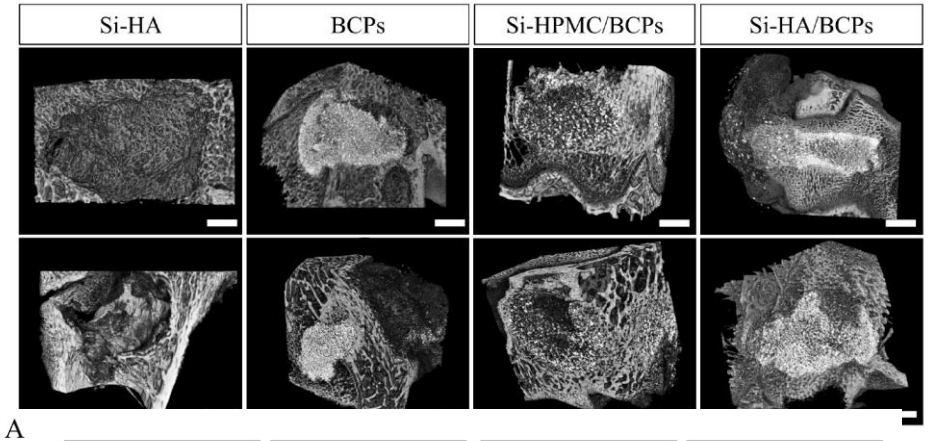






Ingénierie tissulaire osseuse *in vivo*

Acide hyaluronique et PCa



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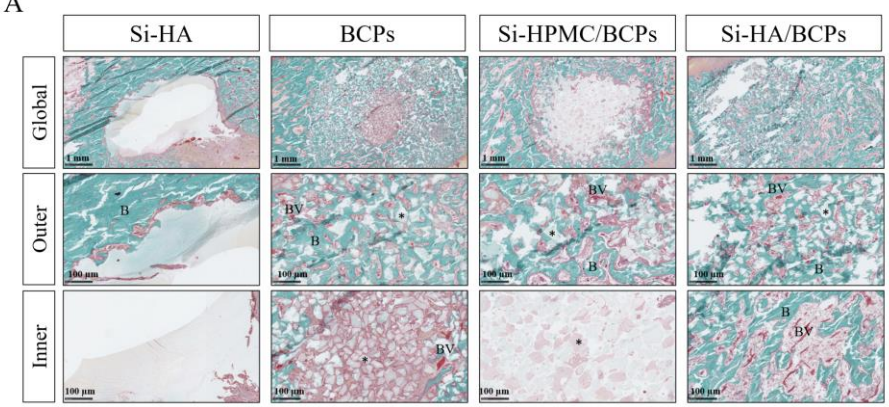


ARTICLE

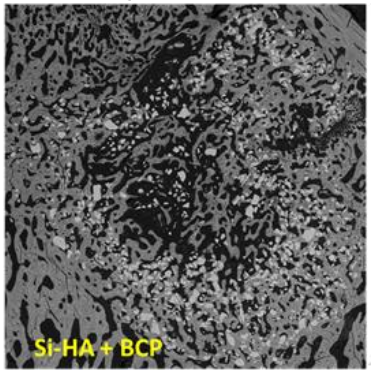
Injectable Silanized Hyaluronic Acid Hydrogel/Biphasic Calcium Phosphate Granule Composites with Improved Handling and Biodegradability Promote Bone Regeneration in Rabbits

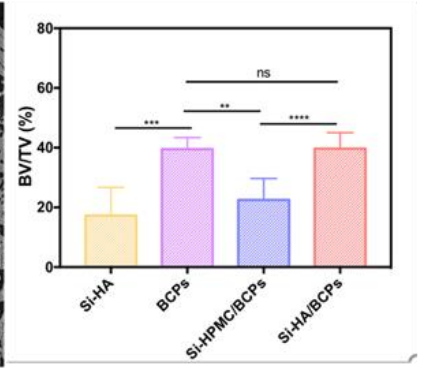
Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

Killian Flegeau[1,2,6], Olivier Gauthier[1,2,8], Gildas Rethore[1,2,3], Florent Autrusseau[1,2,7], Aurélie Schaefer[1,2,5], Julie Lesoeur[1,2,5], Joëlle Veziers[1,3,5], Anthony Brésin[6], Hélène Gautier[1,2,4], Pierre Weiss*[1,2,3].

SEM : Not published data





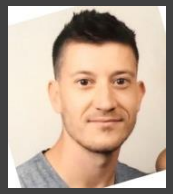
➢ Bone ingrowth

- **Si-HA + BCPs ≃ BCP alone**
- **> Si-HPMC that is low degradable**

Move to CaP BioInks

The Team


Pierre


Arnaud

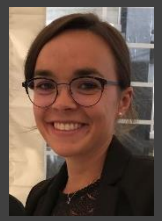

Pierre


Valérie


Maéva


Pierre


Olivier


Léna


Thierry

and more…!

En route vers le 3D printing: fente palatine

ANR GI-JAW

Bench to bedside translational research
→ Innovative solutions for personallized care of cleft deformities

But… what are cleft palate / lip deformities?

- Congenital deformity: 2nd most common malformation after clubfoot
- Occurrence : 1/700 birth

Is alveolar cleft reconstruction still controversial? (Review of literature) 10.1016/j.sdentj.2015.01.006

En route vers le 3D printing: fente palatine

Soft Tissue repair:

- Aesthetic
- Phonation
- Deglutition
- Feeding
- …

Cleft Lip/palate management

Multi-step treatment:

- Soft tissue repair
  @ 3 – 12 months old
- Hard tissue repair
  @ 6 – 9 years old
- Orthodontics
  @ 14+ years old

Is alveolar cleft reconstruction still controversial? (Review of literature) 10.1016/j.sdentj.2015.01.006

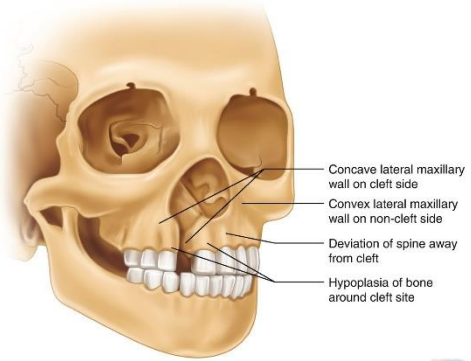
En route vers le 3D printing: fente palatine

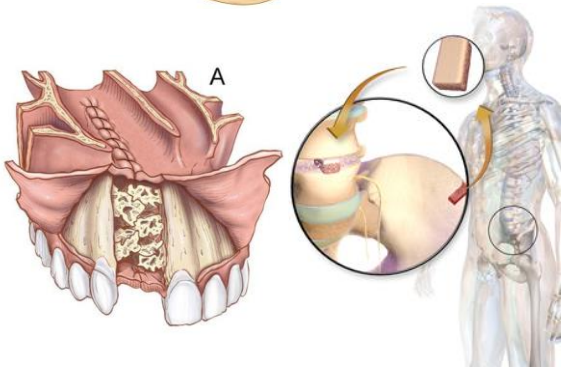
Cleft palate management

Hard Tissue repair:

- Essential for teeth eruption
- …

Standard of care =
autologous bone graft





Associated drawbacks:

- Dammaging healthy bone
- 2nd surgical site
- ↑ surgery time
- ↑ infection risks, morbidity
- Anatomical missmatch
- Graft resorption
- …

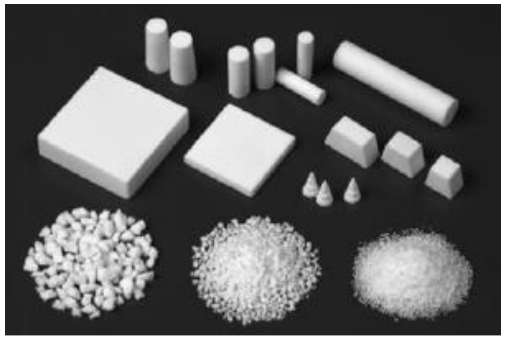
Is alveolar cleft reconstruction still controversial? (Review of literature) 10.1016/j.sdentj.2015.01.006

En route vers le 3D printing: fente palatine

BUT…

- Low biodegradation
- Lack of biological prop.
- Anatomical mismatch
- Micro motions
- Brittle / fragile
- …

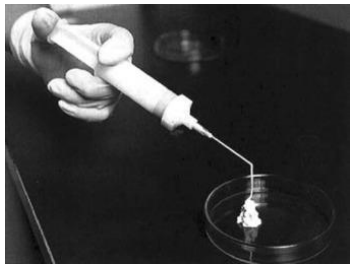
Biomaterial for hard tissue repair



Commercial synthetic bone grafts

- Macroporous bioceramics
- Putties
- Injectable Hydraulic cements

Majority of calcium phosphates-based formulations



Advantages

- +++ Biocompatibility
- +++ Osteoconduction

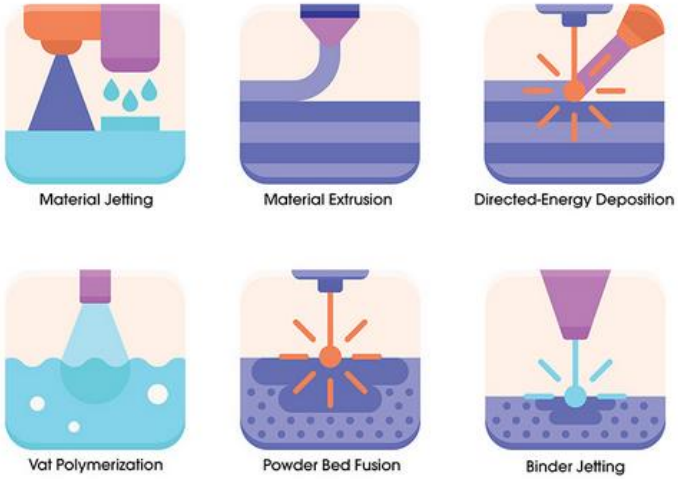
BUT…

- Still lacking of biodegradability
- Still lacking of biological prop.
- Contact bone/scaffold
- Brittle / fragile
- …

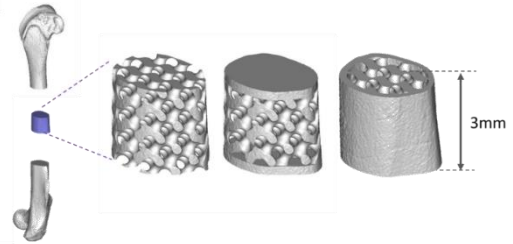
* Copyright "How I met your Mother"

Biomat. for hard tissue repair

Additive manufacturing (AM)



AM synthetic bone grafts



- Patient specific implants
- Wider range of materials
- Possibly improved biodegradation
- Possibly ↑ biological prop.
- Limited anatomical missmatch

En route vers le 3D printing: fente palatine

DEVELOPMENT OF A PRINTABLE COMPOSITE FORMULATION OF PHOSPHOCALCIC CEMENT AND HYALURONIC ACID FOR CLEFT LIP AND PALATE REPAIR

3D refentine

Marie-Michèle Germaini [1]; Pierre Weiss[1]; Sofiane Belhabib[2]; Sofiane Guessasma[3]; Remi Deterre[2]; Helene Gautier[1];

Steven Nedellec[1]; Boris Halgand[1]; Joëlle Veziers[1]; Thierry Rouillon[1]; Pierre Corre[1] and Valérie Geoffroy[1]

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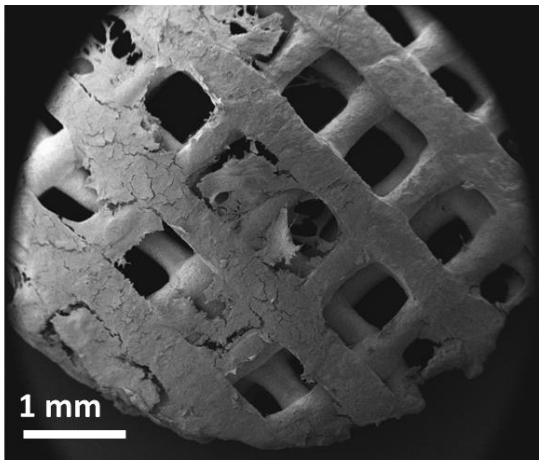
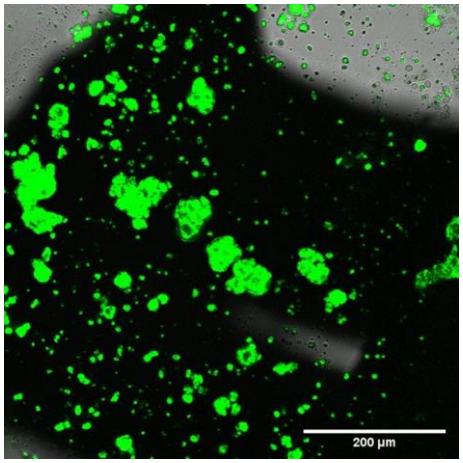
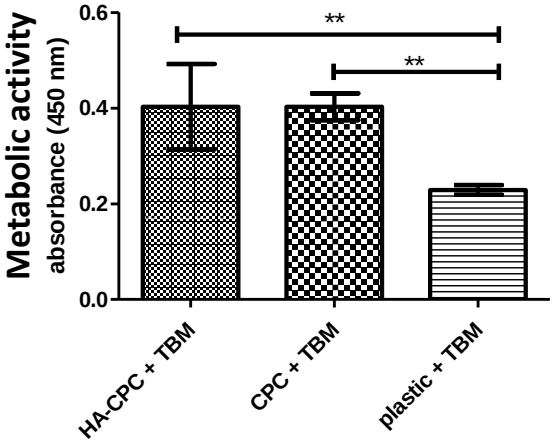
En route vers le 3D printing

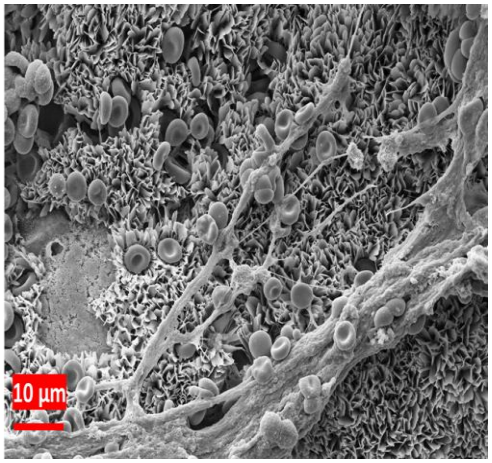


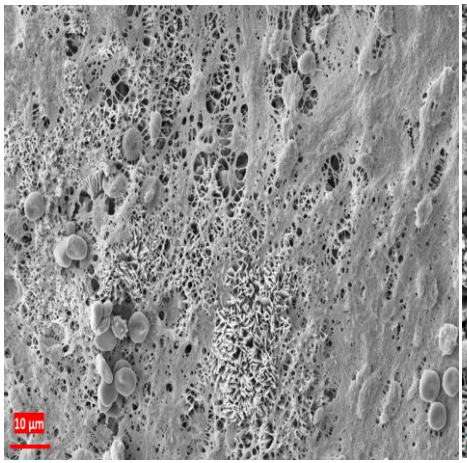
Calcein

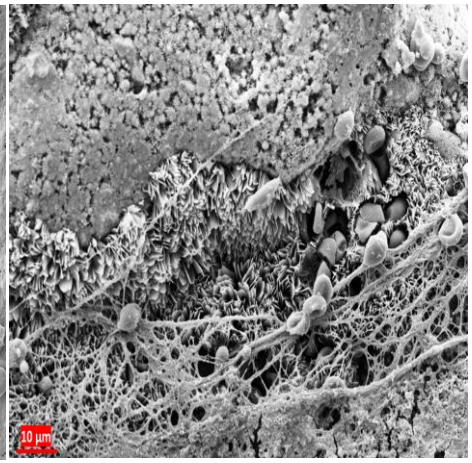


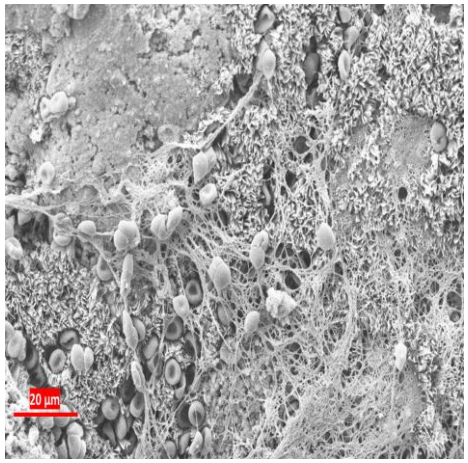


TBM: total bone marrow
40 min of immersion



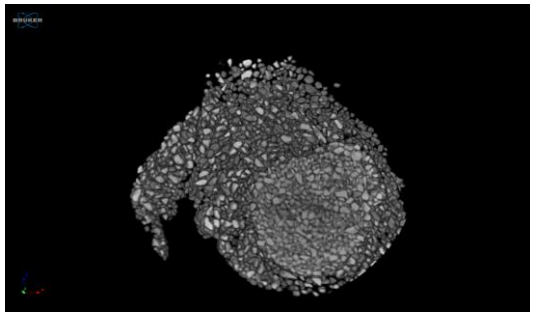


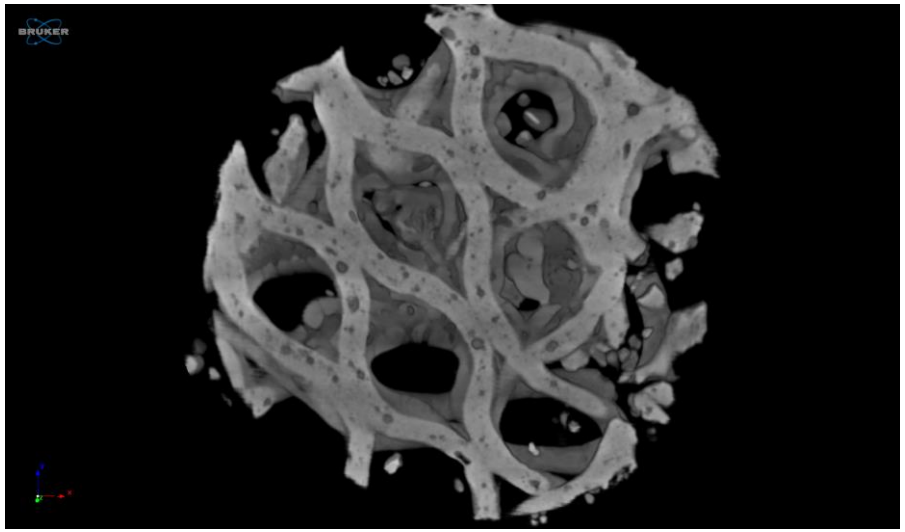


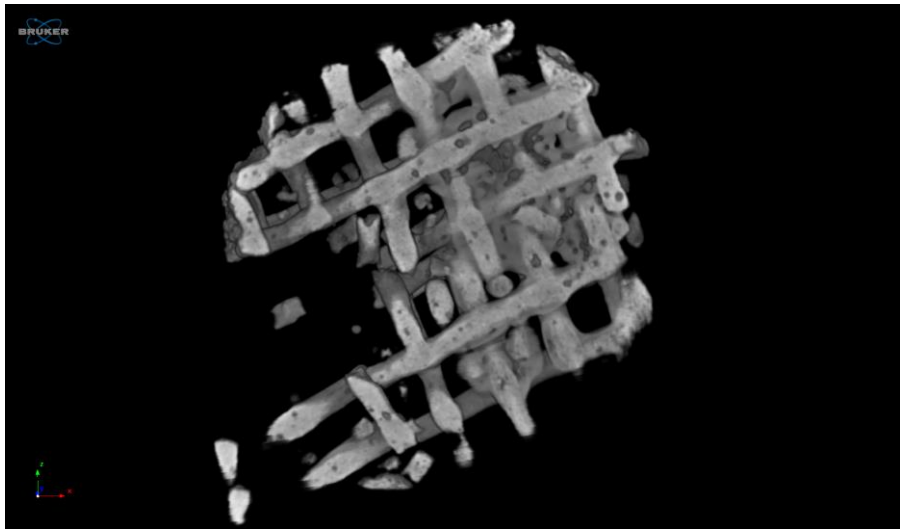


En route vers le 3D printing

+ **Total Bone Marrow**





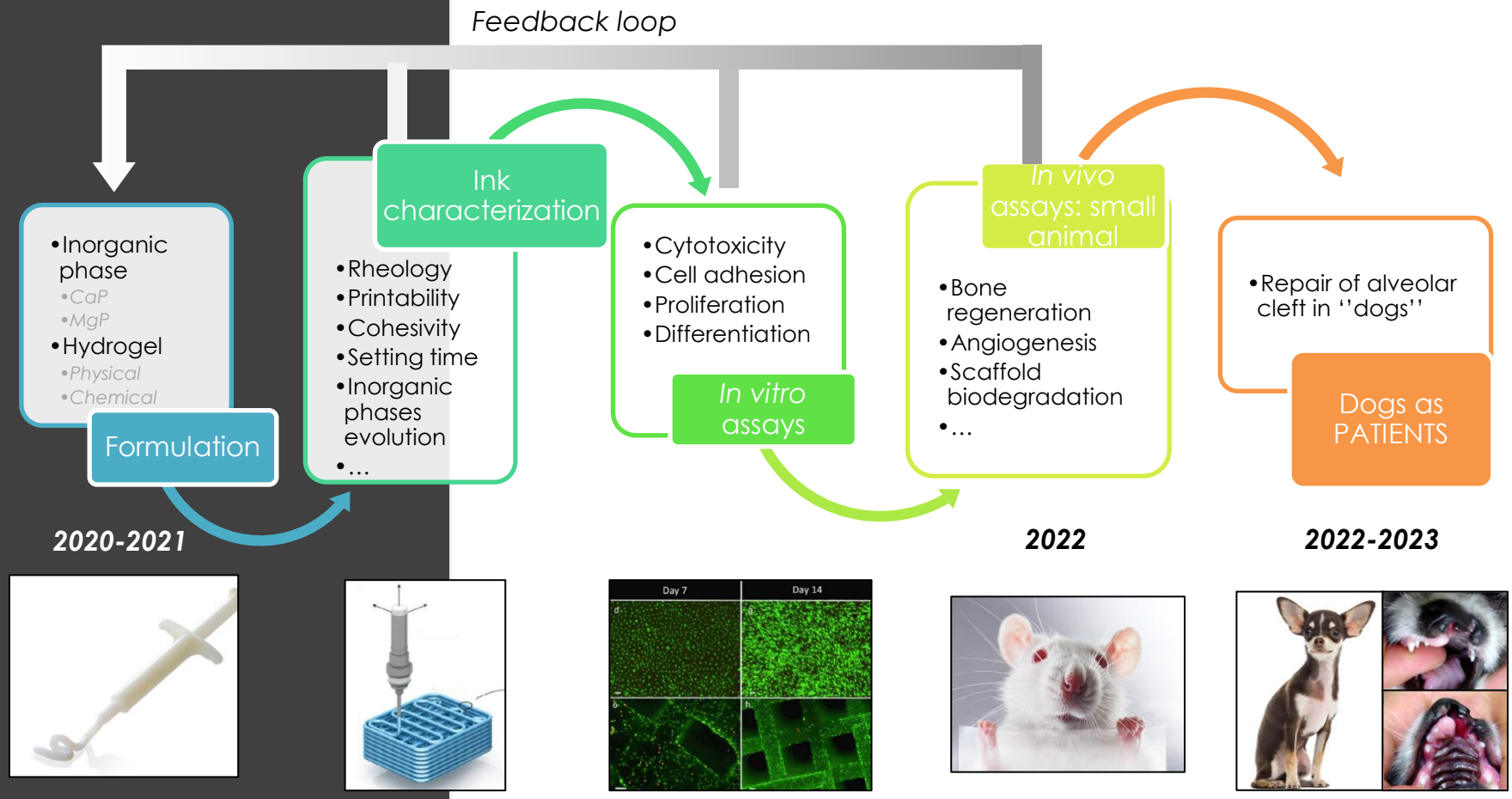


New Bone formation in subcutaneous with TBM but the construct is still fragile

We move to Silated HA covalent hydrogels in the cements : GI JAW program

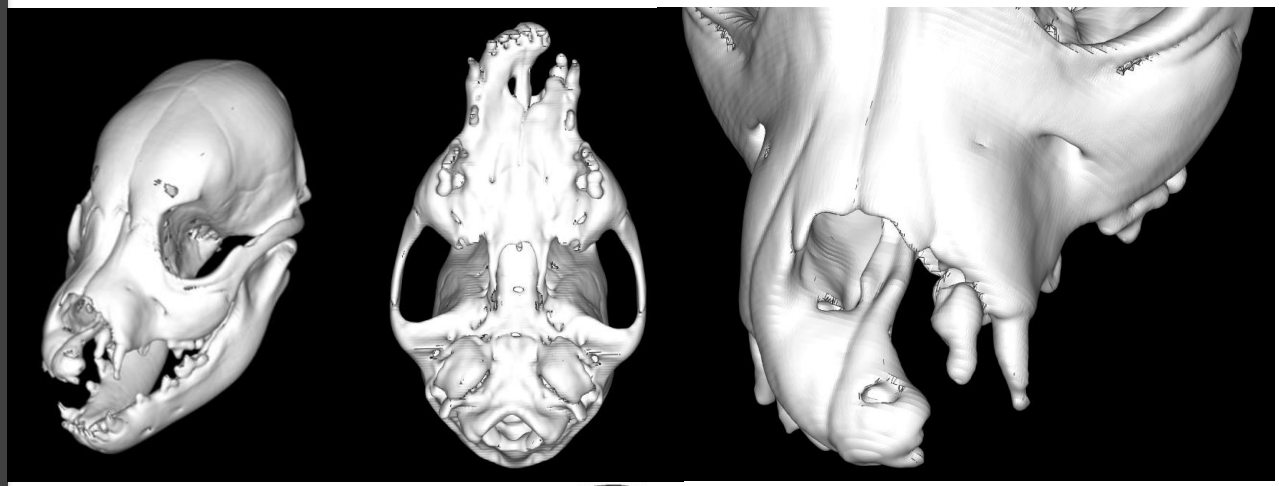
En route vers le 3D printing: fente palatine

GI-JAW Timeline



GI-JAW: 1st Dog patient

3 month-old of American Cocker: '' So Speedy''



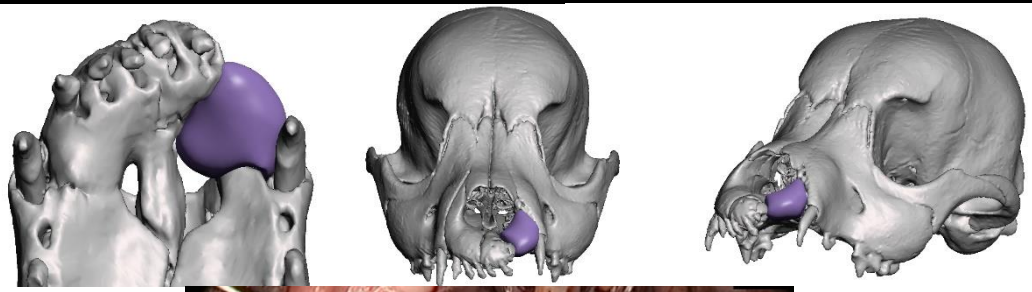

Olivier

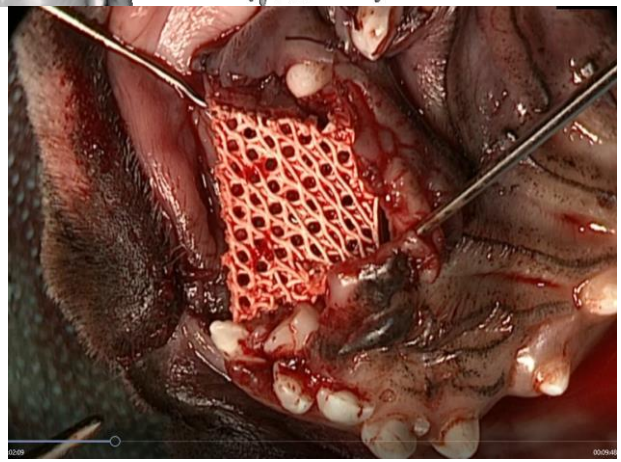

Pierre


Pierre


Léna


Pierre





ITO Les défis

- Ingénierie tissulaire osseuse
  - Moelle Osseuse Totale + Biomatériaux : ++
  - Biomatériaux + Cellules non diff : ---
  - Biomatériaux + Cellules diff : + mais – en territoire Irradié
  - Mort cellulaires? Ischémie dans un biomatériau
  - Cellules hématopoïétiques dans la moelle osseuse totale
  - Rôle des Lymphocytes T et immunologie sur la persistance des cellules implantées

Conclusions

- L'évolution des biomatériaux va vers le biomimétisme

- Les hydrogels sont des copies qui se rapprochent des matrice extracellulaire :
  - Elasticité / tissu
  - Adhésion des cellules et/ou au tissus
  - Contrôle de la dégradation +/-
  - Diffusion des nutriments $O_{2,}$ glucose et des protéines
  - Protection contre l'immunité

Conclusions

Médecine 4 R évolue vers la régénération et la reprogrammation:

SCIENCE ADVANCES | RESEARCH ARTICLE

BIOCHEMISTRY

Efficient healing of large osseous segmental defects using optimized chemically modified messenger RNA encoding BMP-2

Rodolfo E. De La Vega[1,2], Martijn van Griensven[1,2], Wen Zhang[3], Michael J. Coenen[1], Christopher V. Nagelli[1], Joseph A. Panos[1], Carlos J. Peniche Silva[2], Johannes Geiger[3], Christian Plank[3], Christopher H. Evans[1], Elizabeth R. Balmayor[1,4]*

Large segmental osseous defects heal poorly. Recombinant, human bone morphogenetic protein-2 (rhBMP-2) is used clinically to promote bone healing, but it is applied at very high doses that cause adverse side effects and raise costs while providing only incremental benefit. We describe a previously unexplored, alternative approach to bone regeneration using chemically modified messenger RNA (cmRNA). An optimized cmRNA encoding BMP-2 was delivered to critical-sized femoral osteotomies in rats. The cmRNA remained orthotopically localized and generated BMP locally for several days. Defects healed at doses ≥25 μg of BMP-2 cmRNA. By 4 weeks, all animals treated with 50 μg of BMP-2 cmRNA had bridged bone defects without forming the massive callus seen with rhBMP-2. Moreover, such defects recovered normal mechanical strength quicker and initiated bone remodeling faster. cmRNA regenerated bone via endochondral ossification, whereas rhBMP-2 drove intramembranous osteogenesis; cmRNA provides an innovative, safe, and highly translatable technology for bone healing.

SOCIETY FOR DENTAL SCIENCE

Régénération Osseuse
Ingénierie Tissulaire Osseuse

Philippe Lesclous – Pierre Weiss

Merci de votre invitation