BIOMAT

CRÉER RÉPARER RÉGÉNÉRER

4th BIOMAT congress 2021

& BIOMAT Young Scientists' Day

Bourg Saint Maurice, October 18th-22nd, 2021

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4th BIOMAT Congress

& BIOMAT Young Scientists' Day

Book of Abstracts

Bourg Saint-Maurice (France)

October 18th – 22nd 2021

Sponsors

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RÉPARER L'HUMAIN
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European Society for Biomaterials

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National Organizing Committee

- Joëlle Amédée (BIOTIS, INSERM U1026, Bordeaux)
- Pierre Weiss (RMeS, INSERM U1229, Nantes)
- Reine Bareille (Retraitée Ingénieur Inserm, Bordeaux)
- Nicolas Blanchemain (ADDS, INSERM U1008, Lille)
- Jérôme Chevalier (MATEIS, UMR 5510, Lyon)
- Didier Mainard (IMOPA, UMR 7365, Nancy)
- Emmanuel Pauthe (ERRMECe, EA 1391, Cergy)
- Astrid Pinzano (IMOPA, UMR 7365, Nancy)
- Didier Letourneur (LVTS, UMR_S1148, Paris)

Local Organizing Committee (*BIOMAT Young scientists*)

- Jérôme Sohier (LBTI, UMR 5305, Lyon)
- David Marchat (sainbiose, Mines Saint Etienne, U1059, Saint-Etienne)
- Catherine Picart (IRIG, U1292 Biosanté, EMR 5000 BRM, Grenoble)
- *Teresa Simon-Yarza (LVTS, UMR_S1148, Paris)*
- *Bruno Paiva dos Santos (BIOTIS, INSERM U1026, Bordeaux)*
- *Vianney Delplace (RMeS, UMR 1229, Nantes)*
- *Mathilde Maillard (Mateis, UMR 5510, INSA, Lyon)*
- *Phuong-Anh Dang (C3M, ESPCI, Paris)*
- *Maxime Gobin (ERRMECe, Cergy-Pontoise)*

Welcome

The 4th BIOMAT Congress (BIOMAT 2021) is taking place in Bourg saint Maurice (Savoie), in the heart of the French Alps. The logistical and scientific organization of this meeting has been ensured by biomaterials researchers of the region Auvergne-Rhône-Alpes and members of the national association BIOMAT.

The organizing committee would like to thank all participants of the BIOMAT Congress!

More than 120 biomaterials scientists, clinicians and industrials from several countries (UK, Germany, Canada, The Netherlands, Belgium, Luxembourg and France) will join the meeting. The aim of the Congress is to bring together and provide meeting and exchange opportunities to students, clinicians, researchers and companies working in the field of biomaterials development and evaluation. It focuses principally on i) The European and international cooperation's with 12 invited speakers from Europe and France, a special emphasis on European projects experience, funding and experiences, and a Special seminar on an Intereg project; ii) The training of students and young researchers (more than 80) with, for the first time, a dedicated BIOMAT Young Scientists' Day that provides educational and exchange opportunities around experts in medical devices, career choices, funding, and round tables; iii) The interaction with industrials of the field (4 invited industrials). This and more, embedded in a rich scientific program.

The conference is composed of plenary conferences given by distinguished researchers from Europe to open 7 sessions scheduled during 4 days. 35 oral presentations (29 from young researchers) and more than 30 posters have been selected by the scientific committee. The posters will be displayed over the entire course of the congress, highlighted by 15 flash presentation in two dedicated sessions. Awards will be attributed by BIOMAT, the GDR Réparer l'Humain and Rheolution for the best student poster and best student oral presentations.

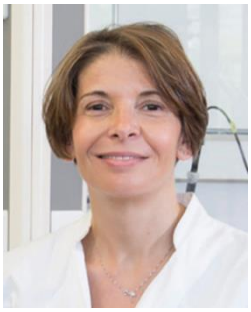
We encourage you to interact, discover and exchange during the Congress, the breaks and the Thursday's free times (hiking in the mountains, guided visits of historic and industrial sites, sports or *farniente*). Just enjoy to learn, meet, share and discuss around science and the beautiful area of Bourg-Saint-Maurice!"

We wish you an enjoyable BIOMAT Conference, in many respects.

On behalf of the organizing committee.

Invited Speakers

Tuesday, October 19th, 2021



Pr. Rachel Auzély-Velty

Cermav, UPR5301, Grenoble, France

Plenary session

Dr. Denys DURAND-VIEL

DM Experts, Paris, France

Educational Session 1

Medical device regulation

Dr. Jérôme Guicheux

RMeS, UMRS 1229, Nantes, France

Educational Session 2

Research career and strategy in academia

Pr. Catherine PICART

IRIG, U1292 Biosanté, EMR 5000 BRM, Grenoble

Educational Session 3

Find and apply for funding

Dr. Nicolas Courtois

ANTHOGYR, Salanches

Educational Session 4

Career in industry

Wednesday, October 20th, 2021

Pr. Peter DUBRUEL

Ghent University, Ghent, Belgium

"One size fits all: the story of the Interreg project DERMA"

Pr. Catherine PICART

IRIG-CEA, INSERM U1292, Grenoble

"Biomaterials for bone regeneration and in vitro studies of cell signaling"

Pr. Lorenzo MORONI

Maastricht University, Maastricht, The Netherlands

"From scaffold design for stem cell fate "control" / persuasion to bioprinting"

Dr. Luciano VIDAL

Ecole Centrale Nantes, Nantes, France

"Customized 3D Printed Scaffold for Bone Regeneration : Lab to Clinic"

Thursday, October 21st, 2021

Pr. Katja SCHENKE-LAYLAND

Univ. of Tübingen, Tübingen, Germany

"FLIM, Raman imaging and microspectroscopy for real-time monitoring"

Dr. Baptiste CHARBONNIER

RMeS, INSERM UMRS 1229, Nantes, France

"Deep-learning for image analysis: It's time to step our game up!"

Morgan DOS SANTOS

Labskin creations, Lyon, France

Audrey CHERBLANC

Healshape, Lyon, France

Cyril van ROBAIS

Rheolution, La Rochelle, France

"Soft matter analytics with the new ElastoSens Bio, a technology that enlarges research boundaries"

Thursday, October 21st, 2021

Night conference

Pr. Alain CRIBIER

CHU Rouen, Rouen, France

"Remplacer une valve cardiaque sans opérer, c'est possible. Le développement du TAVI, une odyssée de 20 ans

Le Professeur Alain Cribier a été pendant 15 ans Chef du Service de Cardiologie de l'Hôpital Charles Nicolle, Université de Rouen. Il est depuis 2011 Professeur Emérite et depuis 2015 Co-Directeur Médical du Rouen Normandie Training Center qu'il a contribué à créer.

Ses études médicales ont été réalisées à Paris. Il a rejoint le CHU de Rouen comme interne en 1972. Après un stage comme Fellow au Cedars-Sinaî Medical Center de Los Angeles, il a suivi à Rouen la filière classique hospitalo-universitaire en cardiologie, a été nommé Professeur en 1993 puis a dirigé les Soins Intensif et le Cathétérisme Cardiaque jusqu'à prendre la direction du service de Cardiologie, succédant au Professeur Brice Letac en 2003.

Il est largement reconnu dans le monde pour ses innovations thérapeutiques a diffusion mondiale en cardiologie interventionnelle, ayant réalisé la première dilatation valvulaire aortique pour le rétrécissement aortique calcifié en 1985, la mise au point d'un dilatateur valvulaire mitral métallique en 1992 pour le traitement du rétrécissement mitral dans les pays en développement, et surtout pour avoir développé après 15 ans de recherche, la technique de remplacement valvulaire aortique percutanée (TAVI : Transcatheter Aortic Valve Implantation) avec une première mondiale en Avril 2002 à Rouen. Cette dernière innovation a constitué une véritable révolution thérapeutique en permettant de remplacer la valve aortique sans chirurgie, donc sans ouvrir la poitrine, en utilisant des techniques usuelles de cathétérisme cardiaque, sous anesthésie locale. Cette technique de rupture connaît une extraordinaire expansion mondiale avec en 20 ans, plus de 1.500.000 patients traités dans 75 pays. Elle a été validée depuis 2007 par la Communauté Européenne, et depuis 2011 par la Food and Drug Administration (FDA) qui a en 2019 étendu les indications à tous les patients de plus de 65 ans.

Le Professeur Cribier a de multiples titres et fonctions scientifiques, et il a reçu de très nombreux prix et distinctions parmi les plus honorifiques en France et dans le monde pour l'ensemble de ses travaux, dont la Médaille d'Or de la Société Européenne de Cardiologie en 2016 et le prestigieux prix Lefoulon Delalande de l'Institut de France en Juin 2017. Il a publié plus de 800 articles sur la cardiologie interventionnelle et sur ses innovations thérapeutiques.

CURRICULUM VITAE Pr Alain Cribier

FONCTIONS UNIVERSITAIRES ET ACADEMIQUES

- Né à Paris, 01/25/1945. Etudes médicales à Paris
- 1976: Docteur en médecine
- 1983: Professeur des Universités, Université de Rouen
- Depuis 2011: Professeur Emérite, Université de Rouen

FONCTIONS CLINIQUES

- 1972: Interne, CHU de Rouen
- 1976: Diplôme de spécialité : Cardiologie
- 1976: Research Fellow, Cedars Sinaï Medical Center, Los Angeles, Cal, USA
- 1978: Chef de Clinique, CHU de Rouen, Cardiologie
- 1981: Praticien Hospitalier, CHU de Rouen, Cardiologie
- 1983: Chef de Service: Soins Intensifs et Cathétérisme Cardiaque
- 1993-2012 : Chef du Service de Cardiologie, CHU de Rouen
- **ACTUELLEMENT:**
    - Praticien Hospitalier Associé Hôpital Charles Nicolle, Rouen
    - Co-Directeur Médical du "Rouen Normandie Médical Training Center"

TITRES ET FONCTIONS SCIENTIFIQUES

- Member of the National Institute of Health and Medical Research (INSERM) Rouen University
- Associated Member of the French Society of Cardiology
- Fellow of the American College of Cardiology
- Fellow of the European Society of Cardiology
- Fellow of the Asian Pacific Vascular Society
- Member of the American Society of Interventional Cardiology
- Member of the Executive Committee of the Structural Heart Disease Council
- Member of the British Society of Interventional Cardiology
- Member of the European Society of Geriatric
- Member of the Russian Society of Interventional Radiology and Endovascular Surgery
- President of the Interventional Cardiology Group of the French Society of Cardiology (2003-05)
- Medical Director of the Rouen Normandy Multidisciplinary Medical Training Center 2015
- Member of the French Academy of Medicine: 2012

PRIX ET DISTINCTIONS

- 1988: Scientific Achievement Award, Columbus, Ohio, USA
- 1996: BARD Trophee, French Society of Cardiology, Paris, France
- **1998: Andreas Gruentzig Award, French Society of Cardiology, Paris, France**
- **2003: ETHICA Award, Euro-PCR, Paris, France**
- 2006: Louis Sudler Lectureship, Rush University, Chicago, USA
- 2008: John Codina Award, Barcelona, Spain
- 2009: Scientific Achievement Award, Tel-Aviv, Israël
- 2009: Scientific Achievement Award, Indo-European Congress, Amsterdam, Hollande

- 2010: Silver Medal Award, European Society of Cardiology, Stockholm, Sueden
- 2010**: Career Achievement Award, Transcatheter Cardiovascular Therapeutics, Washington, USA**
- 2010: Trophee of the Interventional Cardiology Group, Paris, France
- 2010: Trophee of the Victories in Medicine, Paris, France
- **2011: Laennec Award, French Society of Cardiology, Paris, France**
- 2012: Career Achievement Award, Tel Aviv, Israëli Society of Cardiology
- 2013: Scientific Achievement Award, Hammamet, Tunisian Society of Cardiology
- 2013: Career Achievement Award, Guadalajara, Mexico
- **2013: Maseri Florio Lecture Award, ACC, San Francisco, USA**
- 2013: Paul Wood Lecture Award, British Cardiology Society, Londres, UK
- **2013: Ray G. Fish Award, Texas Heart Institute, Houston, TX, USA**
- 2014: Career Achievement Award, German Society of Cardiology, Manheim, Germany
- 2015: Life Time Achievement Award, India-Live meeting, Madras, India
- 2015: Eliot Corday International Prize on Heart Research, Cedars-Sinaï Medical Center, Los Angeles, USA
- 2016: Legend of Medicine Lecture Award, C3 Cardiology meeting, Orlando, USA
- **2016: Gold Medal of the European Society of Cardiology, ESC meeting, Roma, Italy**
- **2017: Grand Prix de la Fondation l'Institut de France : Lefoulon Delalande**
- 2017: Prix Stote Serco, Katowice, Poland
- 2017: Prix Scientifique de la Société Catalane de Cardiologie, Barcelone, Espagne
- 2018: Mikamo Lecture Award, 82nd congress of the Japanese Circulation Society, Osaka, japan
- 2018: Chien Foundation Award, CIT meeting, Suzhou, China
- 2018: Cardiovascular Translational Medicine Award, ISCTR-TCT Meeting, San Diego, Cal, USA

DECORATIONS NATIONALES

- Chevalier de l'Ordre de la Légion d'Honneur
- Chevalier de l'Ordre des Palmes Académiques

PRINCIPALES INNOVATIONS MEDICALES A DIFFUSION MONDIALE

1985 : La dilatation aortique par ballonnet pour le traitement du rétrécissement valvulaire aortique
1997 : Le dilatateur mitral métallique pour le traitement du rétrécissement valvulaire mitral
2002 : Le remplacement de la valve aortique par cathétérisme cardiaque (TAVI) pour le traitement du rétrécissement aortique

Plus de 800 publications internationales

Friday, October 22nd, 2021

Pr. Jeroen LEIJTEN

Univ. Of Twente, Enschede, The Netherlands

"Cell fate controlling micromaterials for the engineering of multiscale tissues"

Dr. Laurent PIEUCHOT

Univ. de Haute-Alsace, IS2M-CNRS 7361, Mulhouse, France

"Curvature-guided migration in single cells and epithelia"

Conference Program

BIOMAT Young Scientists' Day

Monday, October 18th, 2021

16:00 - 19:25	Welcome 'BIOMAT young scientists' day - Hotel Base Camp Lodge - Bourg Saint Maurice
19:30 - 23:00	Dinner and welcome party Young scientists → *Restaurant BC7*

Tuesday, October 19th, 2021

09:30 – 9:35	Opening Young BIOMAT scientists' day
09:35 – 10:30	**Pr. Rachel AUZÉLY-VELTY - Plenary session**
10:30 – 11:00	Coffee break
11:00 – 12:00	**Dr. Denys DURANT-VIEL –** Educational Session 1 – Medical device regulation
12:00 – 13:30	Lunch
13:30 – 14:30	**Dr. Jérôme GUICHEUX–** Educational Session 2 – Research career and strategy in academia
14:30 – 15:15	**Pr. Catherine PICART–** Educational Session 3 – Find and apply for funding
15:15 – 16:00	**Dr. Nicolas COURTOIS–** Educational Session 4 – Career in industry
16:00 – 16:30	Coffee break
16:30 – 18:00	Round tables
19:30 – 23:00	Closing dinner Young BIOMAT scientists' day → *Restaurant BC7*

Conference Program

BIOMAT 2021

Tuesday, October 19th, 2021

16:00 – 18 :00	Welcome and registration BIOMAT congress - Base Camp Lodge Hotel - Bourg Saint Maurice
20 :00 - 22:00	Welcome diner/cocktail BIOMAT congress → *Bar/lounge mezzanine*

Wednesday, October 20th, 2021 → *Mont-Blanc room*

08:15 - 08:25	Opening BIOMAT congress
08:30 – 10:00	**'European and international research' session (1st part)** ***Chairs: Peter Dubruel and Teresa Simon-Yarza***
08:30- 09:00	**I1 - Pr. Peter DUBRUEL**, "One size fits all: the story of the Interreg project DERMA" *(Ghent University)*
09:00 - 09:15	**O1* - Phuong Anh DANG**, *"*Design of thermosensitive injectable chitosan-based hydrogels for cell delivery"*, (Chimie Moléculaire, Macromoléculaire, Matériaux, ESPCI Paris)*
09:15 - 09:30	**O2* - Quentin MULLER**, "Fabrication of Hyaluronan-based Matrices, Functionalized with Laminin Derived Peptides, to Sustain Cellular Adherence and Axonal Growth in Bone Regeneration Applications''*, (BioTis U1026, Bordeaux)*
09:30 - 09:45	**O3* - Fabien NATIVEL**, "Intra-articular injection of mesenchymal stromal cell encapsulated in micro-molded alginate particules for the treatment of post-traumatic osteoarthristis: a preliminary study in rabbit knee", *(RMeS, INSERM UMRS 1229, Nantes)*.
09:45 - 10:00	**FLASH presentations**
10:00 - 10:30	Coffee break and posters
10:30 - 11:35	**'European and international research session' (2nd part)** ***Chairs: Peter Dubruel and Teresa Simon-Yarza***
10:30 - 10:50	**I2 - Pr. Catherine PICART**, ''Biomatériaux pour la régénération osseuse et l'étude de la signalisation cellulaire'', *(IRIG, INSERM U1292 Biosanté, EMR 5000 BRM, Grenoble)*.
10:50 - 11:05	**O4* - Naïma AHMED OMAR**, "Bone tissue engineering strategies using pullulan and/or dextran-based materials: a systematic review of pre-clinical studies", *(U1026 Biotis Inserm Bordeaux)*.
11:05 - 11:20	**O5* - Lison ROCHER**, "Extrusion and expansion of PLLA/WS2NT tubes for bioresorbable stent application", *(School of Mechanical and Aerospace Engineering, Queen's University Belfast)*.

11:20 - 11:35	**O6* - Marie-Stella M'BENGUE**, "Evaluation of a medical grade thermoplastic polyurethane in the conception of a 3d-printed custom-made aortic stentgraft", *(UMR 8207 - U1008, Lille)*.
11:35 - 12:00	**Coline PINESE,** Interreg Cardiopatch : une aventure européenne, *(IBMM, Montpellier)*.
12:00 - 12:45	**BIOMAT general assembly**
12:45 - 14:00	Lunch → *Restaurant BC7*
14:00 - 15:45	**'Scaffold design, lab to clinic' session (1st part)** ***Chairs: Jean-Daniel Malcor and Delphine Logeart-Avramoglou***
14:00 - 14:30	**I3 - Pr. Lorenzo MORONI**, "From scaffold design for stem cell fate "control"/persuasion to bioprinting", *(Maastricht University)*.
14:30 - 14:45	**O7 - Christophe HÉLARY**, "Dense Collagen/PLGA Composite Hydrogels as Medicated Wound Dressings for the Treatment of Cutaneous Chronic Wounds: In Vitro and In Vivo Evaluation", *(LCMCP, Sorbonne Université, UMR 7574)*.
14:45 - 15:00	**O8 - Christopher YUSEF**, "Development of a contraction-resistant dermal substitute based on collagen and a polymeric scaffold", *(IBMM, Montpellier)*.
15:00 - 15:15	**O09* - Estelle PALIERSE**, ''Hydroxyapatite coated membranes for the design of surgical adhesives'', *(Chimie Moléculaire, Macrom. et Matériaux, UMR7167, Paris)*.
15:15 – 15:30	**O10* - Diane POTART**, "Implantation and sterilisation of a new tissue-engineered vascular graft", *(BioTis U1026, Université de Bordeaux)*.
15:30 - 15:45	**O11 - Amélia JORDAO,** pour Marion GRADWOHL "Evaluation of poly-L-lactid-co-glycolid (PLGA) as a potential biomaterial for autologous breast reconstruction: in vitro and in vivo degradation studies", *(INSERM UMR S1172, Lille)*.
15:45 - 16:10	Coffee break and posters
16:10 - 18:15	**'Scaffold design, lab to clinic' session (2nd part)** ***Chairs: Jean-Daniel Malcor and Delphine Logeart-Avramoglou***
16:10 - 16:30	**I4 - Dr. Luciano VIDAL**, "Customized 3D Printed Scaffold for Bone Regeneration: "Lab to Clinic" -
16:30 - 16:45	**O12* - Carole BAROU**, "Fabrication of injectable calcium phosphate cements containing PLGA microspheres for drug delivery", *(IEM-UMR 5635, Univ Montpellier, Montpellier)*.
16:45 - 17:00	**O13* - Pierre WEISS**, pour Marie-Michèle GERMAINI, "Development of a printable composite formulation of phosphocalcic cement and hyaluronic acid for cleft lip and palate repair", *(RMeS, INSERM UMRS 1229, Nantes).*
17:00 - 17:15	**O14* - Joanna BABILOTTE**, "Sandwich cellularization approach for bone tissue engineering", *(Univ. Bordeaux, INSERM, BioTis U1026)*.
17:15 - 17:30	**O15* - Charlotte GAROT**, "Influence of scaffold geometry on bmp-2 incorporation and in vivo bone regeneration", *(IRIG, INSERM U1292 Biosanté, EMR 5000 BRM, Grenoble)*.

17:30 - 17:45	**O16* - Julie CHEVRIER**, "A combination of selective laser melting and surface mechanical attrition treatment for metallic materials manufacturing", *(EA 4691, Reims).*
17:45 - 18:00	**O17 - Sébastien BLANQUER**, "From 3D to 4D printing with biocompatible synthetic hydrogels", *(ICGM, Montpellier)*.
18:00 - 18:15	**O18* - Lucas LEMARIÉ**, "Alginate-gelatin hydrogels as a tool to control the fate of induced pluripotent stem cells", *(SEGULA Technologies, Lyon)*.
19:15 - 22:30	**Gala Diner** → *Restaurant BC7*

Thursday, October 21st, 2021 → *Mont-Blanc room*

08:30 - 10:00	**'Data analysis, monitoring and modeling' session** ***Chairs: Joelle Amédée and Emmanuel Pauthe***
08:30 - 09:00	**I5 - Pr. Katja SCHENKE-LAYLAND** "FLIM, Raman imaging and microspectroscopy for real-time monitoring", *(University of Tübingen)*.
09:00 - 09:15	**O19* - Marie DUBUS**," Increase in bone regeneration using calcium phosphate-chitosan-hyaluronic acid hybrid material", *(BIOS, EA 4691, Reims)*.
09:15 - 09:30	**O20* - Eirini CHATZOPOULOU**, "Dental pulp stem cells enhance the maturation of an engineered microvascular network for tissue regeneration: an in vivo study", (EA 2496, Montrouge).
09:30 - 09:45	**O21 – Frédéric MALLEIN-GERIN**, "Contrast-enhanced computed tomography for non-invasive monitoring of tissue-engineered cartilage implants.", (LBTI, UMR 5305, Lyon).
09:45 - 10:00	**O22* - Moustoifa SAÏD,** "An 10dine-labeled injectable hyaluronic acid hydrogel: a radiopaque biopolymer to track the fate of bioscaffold in cell therapy applications", *(Univ. Grenoble Alpes, Inserm, U1216, Grenoble)*.
10:00 - 10:15	**FLASH presentations**
10:15 - 10:40	Coffee break and posters
10:40 -12:00	**'Data analysis, monitoring and modeling' session – part 2** ***Chairs: Joelle Amédée and Emmanuel Pauthe***
10:40 -11:00	**I6* - Dr. Baptiste CHARBONNIER**, "Deep-learning for image analysis: It's time to step our game up!", *(RMeS, INSERM UMRS 1229, Nantes)*.
11:00 -11:15	**O23 - Francisco FERNANDES** "Porous yet dense, using ice to shape biomimetic materials for 3D cell culture applications", *(LCMCP, Paris)*.
11:15 -11:30	**O24* - Océane SÉNEPART**, "Croissance axonale stimulée par modification de surface à l'aide de procédés chimiques et physiques", *(LCMCP, Saints Pères Paris Institute Neurosciences)*.
11:30 - 11:45	**O25 – Lucie BAILLY**, "Hydrogels oscillants en interaction fluide/structure : vers le design de plis vocaux biomimetiques", *(Laboratoire sols, solides, structures – risques, Grenoble)*.
11:45 - 12:00	**O26* - Oeyo MAEZTU REDIN**, "In vivo study and wear model to predict the damage and resistance of reconstructed ACL", *(Centre des Matériaux, MINES ParisTech)*.
12:00 - 13:00	**Industrial session** ***Chair: Pierre Weiss***
	Morgan DOS SANTOS (Labskin creation), **Audrey CHERBLANC** (Healshape), et **Cyril VAN ROBAIS** (Rheolution: Soft matter analytics with the new ElastoSens Bio, a technology that enlarges research boundaries)
13:00 - 14:10	Lunch → *Restaurant BC7*

14:30 - 18:30	Get together activities - How beautiful is the mountain !
19:00 - 20:00	Diner → *Restaurant BC7*
20:00 - 21:00	**Night conference** ***Chairs: Jérôme Sohier and Didier Letourneur***

I7 - Pr. Alain CRIBIER, "Remplacer une valve cardiaque sans opérer, c'est possible. Le développement du TAVI, une odyssée de 20 ans", *(CHU Rouen)*.

Friday, October 22nd, 2021 → *Mont-Blanc room*

08:30 - 10:15	**'Architectures and cell fate' session** ***Chairs: Karine Anselme and David Eglin***
08:30 - 09:00	**I8 – Pr. Jeroen LEIJTEN**, "Cell fate controlling micromaterials for the engineering of multiscale tissues", *(University Of Twente)*.
09:00 - 09:15	**O27* - Léa THORAVAL**, "Evaluation of cu2+ doping potential to control the calcium-phosphate particles-induced acute inflammatory response in bone site", *(Biomatériaux et inflammation en site osseux - EA 4691)*.
09:15 - 09:30	**O28* - Steve PAPA**, "Femtosecond lasers structured titanium dental implants in regulating bacterial adhesion", *(INSERM U1059-SAINBIOSE, St-Etienne)*.
09:30 - 09:45	**O29 - Halima KERDJOUDJ**, "An expected antibacterial and immunomodulatory properties of acellular Wharton's jelly matrix", *(EA 4691, BIOS, Reims)*.
09:45 - 10:00	**O30* - Marie CAMMAN**, "Dense 3D printed collagen hydrogels mimicking extracellular matrix for tissue engineering applications", *(LCMCP, Sorbonne Université, CNRS, UMR 7574, Paris)*.
10:00 - 10:15	**O31* - Rémy GAUTHIER**, "Influence of cellular mechanical environment on periodontal ligament fibroblasts behavior: an in situ investigation", *(LMI, UMR CNRS 5615, Lyon)*.
10:15 - 10:40	Coffee break and posters
10:40 - 12:00	**'Architectures and cell fate' session – part 2** ***Chairs: Karine Anselme and David Eglin***
10:40 - 11:00	**I9 - Dr. Laurent PIEUCHOT**, "Curvature-guided migration in single cells and epithelia", *(Univ. de Haute-Alsace, IS2M-CNRS 7361, Mulhouse)*.
11:00 - 11:15	**O32 - Thomas DOS SANTOS,** "développement d'auto-assemblages protéiques pour la conception de matériaux intelligents", *(Univ. de Haute-Alsace, IS2M-CNRS 7361, Mulhouse)*.
11:15 - 11:30	**O33* - Louise GRIVEAU**, "Design of injectable and porous hydrogels and their potential as support for skeletal muscle tissue engineering", *(IBCP, LBTI, CNRS UMR 5305, Lyon)*.
11:30 - 11:45	**O34* - Arvind RATHORE**, "hydrogel coating for biofuel cells to enhance biocompatibility and long-term functionality", *(Inserm, Univ. Bordeaux, U1026 Biotis)*.
11:45 - 12:00	**O35* - Pauline BREGIGEON**, "A new platform for culture and electroporation of 3D cell constructs based on a porous scaffold", *(Laboratoire Ampère, Paris)*.
12:00 - 12:30	**Closure ceremony and awards**
12:30 - 14:00	Lunch box

Posters

P1* - **ALOUI Eya**, "ALBUPAD technology: Salt-assisted compaction for the design of new biodegradable albumin-based materials"

P2* - **BELABBES Karima**, " Design of hybrid peptide / polymer nanofibers for soft tissues regeneration"

P3* - **BELAID** Habib, "Development of a 3d printed scaffold allowing multiple drug delivery for the treatment of bone metastasis in breast cancers"

P4* - **CALDERON Rosa**, "Development of a curcumin loaded-NLCs hydrogel system for topical applications"

P5* - **CARRÉ Albane**, "Super-critical co2 decellularization strategy: a novel approach to develop cardiac 3-dimensional biohybrid matrice."

P6* - **CHIJCHEAPAZA - FLORES Henry**, "Hydrogel based on chitosan/polycyclodextrin/cinnamaldehyde for the treatment of diabetic foot ulcers"

P7* - **CHUZEVILLE Lauriane**, "Ecological and scalable synthesis of CaCO3 nanoparticles stable in aqueous media using bio-sourced materials for applications in biomedicine"

P8* - **CONINX Simon**, "Boron neutron capture therapy assisted by boron-enriched polysaccharide nanogels"

P9* - **D'ARROS Cyril**, "FDBS (freeze dried bone scaffold), the osteogenic synthetic platform for bone regeneration"

P10* - **DE GAUDEMARIS Imbert**, "Etude du role du pyrocarbone dans la regeneration du cartilage articulaire"

P11* - **DELLAQUILA Alessandra**, "Vascularized 3d polysaccharide-based scaffolds as model of liver sinusoid"

P12* - **DHAYER Mélanie**, "Ingenierie tissulaire pour la reconstruction mammaire a l'aide de tricots bioresorbables en pla/pcl"

P13 - **DROCHON Agnes**, "Mechanical characterization of a rotating bioreactor for tissue engineering"

P14* - **FROMAGER Bénédicte**, "3D membrane of electropsun fibers for cell therapies"

P15* - **GOBIN Maxime**, "Development of antibiofilm dressings with natural active ingredients for the treatment of infected wounds"

P16* - **GRIBOVA Varvara**, "Antibacterial and anti-inflammatory hydrogels: towards multifunctionality"

P17* - **GROSJEAN Mathilde**, "Design of degradable star-shaped copolymers for the conception of bioresorbable anti-inflammatory patchs"

P18* - **KAWECKI Fabien**, "Inter-donor variability evaluation of human cell-assembled extracellular matrices"

P19* - **KENGOUM Pedie Claude Elvire**, "Suivie non intrusif du rythme cardiaque au travers des deformations d'un polymere : caracterisation de la mousse polyurethane"

P20* - **LAGNEAU Nathan**, "Investigating SPAAC for the design of polysaccharide-based hydrogels: a most versatile platform for cell culture"

P21 - **MALCOR Jean-Daniel**, "Triple-helical peptides for cartilage tissue engineering"

P22* - **MASSONIE Mathilde**, " Conception of photopolymerisable, degradable and bioactive polymeric ink for meniscus regeneration"

P23 - **MICHEL Raphaël**, "Design of composite hydrogels for bioprinting : molecular interactions, rheological behavior and printability"

P24* - **BOREL Orianne**, "Optimisation and use of a bioprinted model to study biomaterials for bone regeneration"

P25* - **OUEDRAOGO Sidzigui**, "Synthesis and characterization of polyethylene glycol based hydrogels for anti-inflammatory drugs release"

P26* - **PALOMINO DURAND Carla**, "Chitosan-fibronectin hydrogel for application in tissue engineering"

P27* - **RANGANATH Sindhu**, "Bilateral double site (calvaria and mandibular) critical size bone defect model in rabbit for evaluation of craniofacial tissue regeneration"

P28 - **REFFUVEILLE Fany**, "Etude de l'adherence de staphylococcus aureus sur diverses surfaces liees au contexte osseux"

P29* - **ROQUART Maïlie**, "Photopolymerization of degradable PEG-based hydrogels with adjustable swelling and mechanical properties"

P30* - **ROTA Solène**, "Animal bone matrices purification based on modified supercritical co2 fluid processes: biochemical charaterizations and bone tissular regeneration capacities"

P31* - **ROUDIER Gaëtan**, "How to build a better Tissue-Engineered Vascular Graft woven from Cell-Assembled Extracellular Matrix yarn?"

P32* - **VERGNAUD Florestan**, "Superparamagnetic and bioactive nanoparticles for bone cancer treatment"

*** Young researcher**

FLASH presentation

Abstracts

Oral presentations

Wednesday, October 20th, 2021

‘European and international research’ session

O1: DESIGN OF THERMOSENSITIVE INJECTABLE CHITOSAN-BASED HYDROGELS FOR CELL DELIVERY

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Keywords: injectable hydrogel, thermosensitive, cell delivery

ABSTRACT

Cell-laden injectable hydrogels are highly valuable delivery vehicles for cell therapies: (i) they provide a temporary scaffold to injected cells in order to ensure their viability and to stimulate their activity; (ii) theycan be administrated in a minimally invasive manner and fill-in the defects in hardly accessible and fragiletissues [1]. Thermosensitive mixtures of chitosan (CS) and organic salts such as beta-glycerophosphate (βGP) exhibit interesting features for such applications. They can be held liquid at room temperature andneutral pH while exhibiting a rapid sol/gel transition at body temperature [2]. However, these systems arenot appropriate for cell delivery because fast gelation and physiological pH requires high βGP concentrations, which induces cytotoxic levels of osmolarity [3]. Here, we propose to modify thisformulation to render it suitable for *in vivo* cell injection. Our approach consists in partially replace βGP by ammonium hydrogen phosphate (AHP), another salt which induces less osmolarity [4]. In a systematic study, we explored formulation parameters governing the pH, the osmolarity and the gelation kinetics of the mixture CS/βGP/AHP. Based on those results, we report a rational guide to prepare formulations compatible with cell injection having various CS concentrations, which is a key parameter to tune properties of the hydrogels such as porosity, mechanical strength and kinetics of gel degradation. The cytocompatibility of these optimized formulations was assessed *in vitro*: Encapsulation of two cellular models, pre-osteoblastic cell line MC3T3 and primary gingival human fibroblasts, showed homogeneousdispersions and good viability up to 24 h. These results collectively show the potential of CS/βGP/AHP system as a cell-laden injectable matrix. In further studies, tunability of hydrogel properties will be explored to design adjustable systems for various types of cells.

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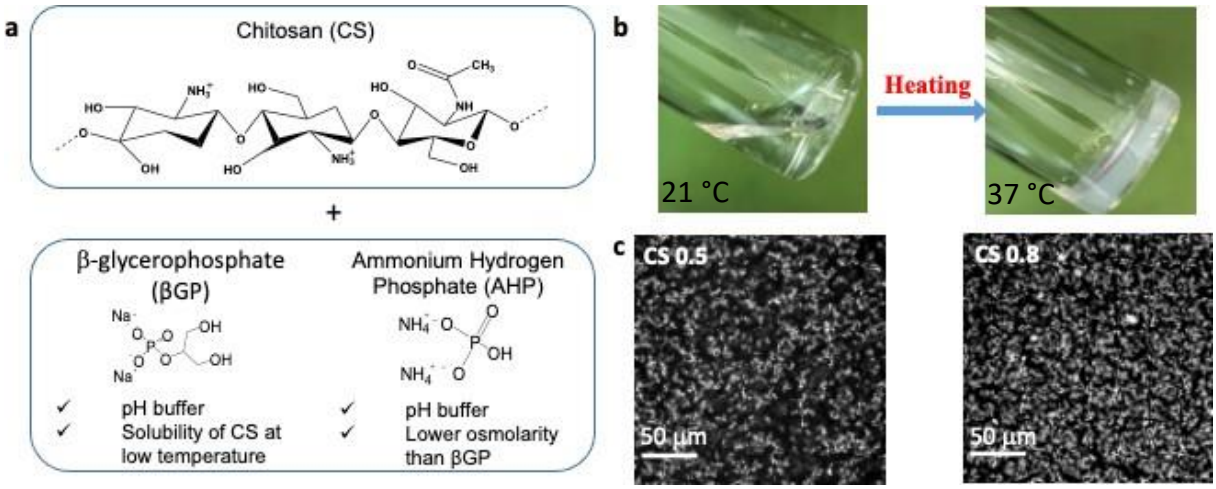

Figure 1. a) Composition of the studied thermosensitive system CS/βGP/AHP; b) Photographs showing the sol/gel transition; c) Confocal micrographs of fluorescently-labeled CS/βGP/AHP hydrogels having CS concentrations of 0.5 and 0.8 wt%.

O2: FABRICATION OF HYALURONAN-BASED MATRICES, FUNCTIONALIZED WITH LAMININ DERIVED PEPTIDES, TO SUSTAIN CELLULAR ADHERENCE AND AXONAL GROWTH IN BONE REGENERATION APPLICATIONS

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Keywords: Bone Regeneration, Bioprinting, Induced-Pluripotent Stem Cells

After blood, bone remains the most transplanted organ, in cases of bone trauma and resection. Also, from many years, bone tissue-engineering strategies were mainly focused on osteogenesis and shown limited clinical success. Only recently, focus has been drawn on the importance of neurovascular modulation to attain fully functional tissues. Here, we explore the 3D fabrication of a cell-free scaffold, designed to support the intricate orchestration between vascularization, innervation and bone healing, in a regeneration scenario. We focused on a hyaluronan-based matrix functionalized with laminin derived peptides, characterized by i) rheology,
ii) able to be bioprinted and iii) support endothelial and neuronal cell adhesion and maturation.

The tyramine-modified hyaluronan-based matrix (HA-Tyr) was formed with combined enzyme-mediated cross-linking (H_2O_2 – HRP) and visible light cross-linking (Eosin Y) (1), formulated with different peptide concentrations (i.e. 0, 0.5 and 1 mg/mL). The first crosslinking was used to pre-jellify, and enable microextrusion bioprinting, and the second to set the bioprinted structure. Rheological evaluation was performed before and after light crosslinking. The linear domain, frequency scan, was used to determine the strain range where the structure of the gel was not modified, the gel character, the viscoelasticity properties and the tan δ value (G''/G') (2,3). *In vitro* evaluation was performed, after the light cross-linking, by seeding human umbilical vein endothelial cells (HUVECs), human bone marrow mesenchymal stem cells (MSCs) or human induced-pluripotent stem cells-derived sensory neurons (iPS-SN) on the top of the matrix. Phenotypical characterization was performed using cell-specific immunolabelling.

After the first polymerization, as expected, we observed a weak crosslinking of HA-Tyr, the addition of peptides showed to decrease the viscoelastic properties of the composite hydrogel, with decreased G' and G" values. Following the second polymerization of HA-Tyr we observed a higher crosslinking efficacy, and again, a lower elastic modulus when peptides were associated within the matrix. In terms of *in vitro* results, the addition of peptide shows to support HUVEC, MSC and iPS-SN cell adhesion, metabolic activity, phenotype and axonal growth. The maintain of metabolic activity allow us to conclude to an absence of cytotoxic effect (direct or soluble) by the matrices. Further studies are ongoing and will enable to improve the capacity of this biomaterial to sustain the interplay between angio/neurogenesis for bone regeneration.

This project is a part of the cmRNAbone project, who had received funding from the European Union's Horizon 2020 research and innovation program under grant agreement No 874790.

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O3: INTRA-ARTICULAR INJECTION OF MESENCHYMAL STROMAL CELL ENCAPSULATEDIN MICRO-MOLDED ALGINATE PARTICULES FOR THE TREATMENT OF POST- TRAUMATIC OSTEOARTHRISTIS: A PRELIMINARY STUDY IN RABBIT KNEE

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Keywords: Hydrogel, Cell therapy, anti-OA factors

Osteoarthritis (OA) is a degenerative and inflammatory disease that affects the whole joint. Mesenchymal Stromal Cells (MSCs) are clinically used for their anti-inflammatory and immuno-modulatory properties and are considered an attractive tool for the intra-articular (IA) treatment of OA. Considering the risk of cell leakage and death after IA injection, MSC encapsulation in cytoprotective hydrogels appears as a promising solution to overcome these limitations and to provide MSCs with a suitable 3D microenvironment supporting their biological activity. In this context, we evaluated the anti-OA efficacy of alginate-based microencapsulated human MSCs in an in vivo model.
Human adipose stromal cells (hASCs) were encapsulated via a micro-molding method (Figure 1). Cell loading in 2% (w/v) alginate micro-molded hydrogels was performed by centrifugation (300g, 2min) followed by crosslinking with Ca2+. The anti-OA efficacy of microencapsulated hASCs was investigated in a post-traumatic OA model, set up by performing anterior cruciate ligament transection (ACLT) in adults rabbits. Eight weeks after surgery, destabilized joints were randomly assigned to 4 groups and were injected (26G needle) with 200 µL of either PBS, blank microparticles, non-encapsulated cells (5 x 105 hASCs), or microencapsulated cells (5 x 105 hASCs). Six weeks after injection, rabbits were euthanized and all destabilized (right) and sham-operated (left contralateral) joints were dissected and analyzed for OA severity. Histological sections of samples were analyzed after Safranin-O staining and quantitatively assessed according to a modified OARSI scoring system. Immunohistochemical detection of NITEGE was performed to assess the extracellular matrix degradation.
All destabilized joints exhibited a significantly increased modified OARSI score, ranging from 7.4±0.4 for encapsulated cells to 8.9±0.2 for PBS, compared to 4.8±0.4 for CL sham joints. Of interest, the modified OARSI scoring has shown a tendency toward a reduced severity of OA lesions after injection of microencapsulated cells. Semi-quantitative analysis of NITEGE immunostaining revealed a significant increase in all destabilized joints that were injected with PBS or blank microparticles, in comparison with sham ones. On the contrary, NITEGE immunostaining in destabilized joints that were injected with non- encapsulated or encapsulated hASC revealed a significant marked reduction in matrix degradation.

In this study, we were able to encapsulate hASCs in micro-molded alginate microparticles and demonstrated that this encapsulation process allowed hASCs to exert their anti-OA properties in a rabbit model of post-traumatic OA. Further studies are now warranted to investigate the therapeutic efficacy of microencapsulated hASCs in the long-term.

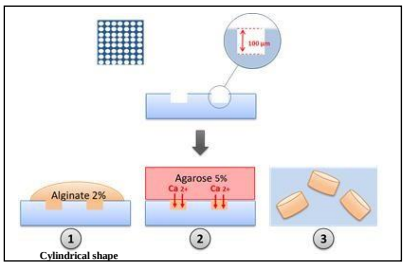

Figure 1: Microparticles were manufactured by pouring a sterile alginate solution (2% w/v) onto PDMS micromolds, followed by ionic cross-liking using an agarose gel loaded with 100 mM of $CaCl_2$. PDMS: Polydimethylsiloxane

O4: BONE TISSUE ENGINEERING STRATEGIES USING PULLULAN AND/OR DEXTRAN-BASED MATERIALS: A SYSTEMATIC REVIEW OF PRE-CLINICAL STUDIES.

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Key words: Pullulan; Dextran; Bone tissue engineering

Abstract

Improving bone regeneration after traumatic injuries, pathologies or tumours resection remains a surgical challenge. To date, autologous bone graft is considered as the gold standard. However, due to the inherent limitations of this technique (limited availability, donor site injury and morbidity), there is a growing interest in the development of new materials for bone regeneration since these last decades. Dextran and pullulan are both natural hydrophilic polysaccharides. As they display unique biological and physico-chemical properties, dextran and pullulan-based biomaterials became highly attractive and promising alternative biomaterials for bone tissue engineering. This systematic review aimed to identifyand sum up in preclinical studies the different strategies of pullulan and/or dextran-based substitutes used for bone tissue engineering. An electronic search in Pubmed, Scopus and Web of Science databases was conducted and the selection of articles was performed following PRISMA guidelines. This systematicreview led to the inclusion of 26 articles taking into consideration the studies in which pullulan and/or dextran-based biomaterials were used to promote bone regeneration in animal models. Among the 26 studies included, 14 focused on dextran-based materials for bone regeneration, six used pullulansubstitutes and six reported the use of a combination of pullulan and dextran. Several strategies have been employed to further enhance their potential for bone regeneration, mainly through their fabrication processes or the addition of various elements to these scaffolds. Different types of applications were thus reported in the included studies: pullulan and/or dextran-based biomaterials were used either as potential cell and/or growths factors carrier system, as bone filling substitutes or as a membrane for guided bone regeneration. Four routes of administration of these biomaterials in implantation sites were also identified. Finally, the diverse fabrication processes of pullulan and/or dextran-based materials (functionalization methods, reticulation process) and their application usages to promote bone regeneration were discussed.

O5: Extrusion and expansion of PLLA/WS_2NT tubes for bioresorbable stent application

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Keywords: Bioresorbable stent, SAXS/WAXS, polylactide, tungsten disulfide nanotubes, tube extrusion,blow molding.

ABSTRACT

Coronary artery disease has remained the leading cause of death worldwide for the past 20 years [1]. To cure this disease, bioresorbable stents (BRS) can treat the injured artery and fully resorb when the support is no longer needed. This alternative would avoid late-stage complications observed with permanent metallic stents [2], regain the artery vasomotor function [3], and enable reoperation. A poly(L-lactide) (PLLA) nanocomposite could respond to two current unmet needs in (PLLA)-based BRS to improve its clinical outcomes: increasing strength to enable thinner devices and improving radiopacity to enable imaging during implantation. In this study, Tungsten disulphide nanotubes (WS2NTs)/PLLA nanocomposites were studied after tube extrusion and during tube expansion (or blow molding), two main steps of a BRS industrial manufacturing process. PLLA tubes reinforced with 0.5 and3 wt % of nanotubes were extruded following different processes to improve the nanotubes dispersion. High resolution computed tomography (µ-CT) combined with scanning electron microscopy (SEM) were used to perform a representative analysis of dispersion. The most promising tubes were expanded during in-situ collection of small- and wide-angle X-ray scatterings (SAXS/WAXS) to observe the microstructure forming.

SEM and µ-CT results presented complementary information regarding nanotubes dispersion and allowed the identification of the best extrusion and loading conditions (Fig. 1). During the extrusionprocess, the high-shear setup allowed a stronger mixing of the nanoparticles with the polymer and resulted in a better state of dispersion. A pre-dispersion of the nanotubes before extrusion improved deglomeration without having to increase the shear in the barrel, which mitigated risks to damage and shorten the nanotubes observed on SEM images. The nanofiller loading also influenced dispersion: 0.5 wt% loading dispersed better and formed fewer agglomerates compared to a high loading (3 wt%). DSCdata revealed an efficient cooling of the tubes during extrusion and a strong nucleation effect from the nanotubes. The tubes loaded with 0.5 wt% of nanotubes and extruded with high-shear setup had the fewest number of agglomerates and were selected for the next step of tube expansion.

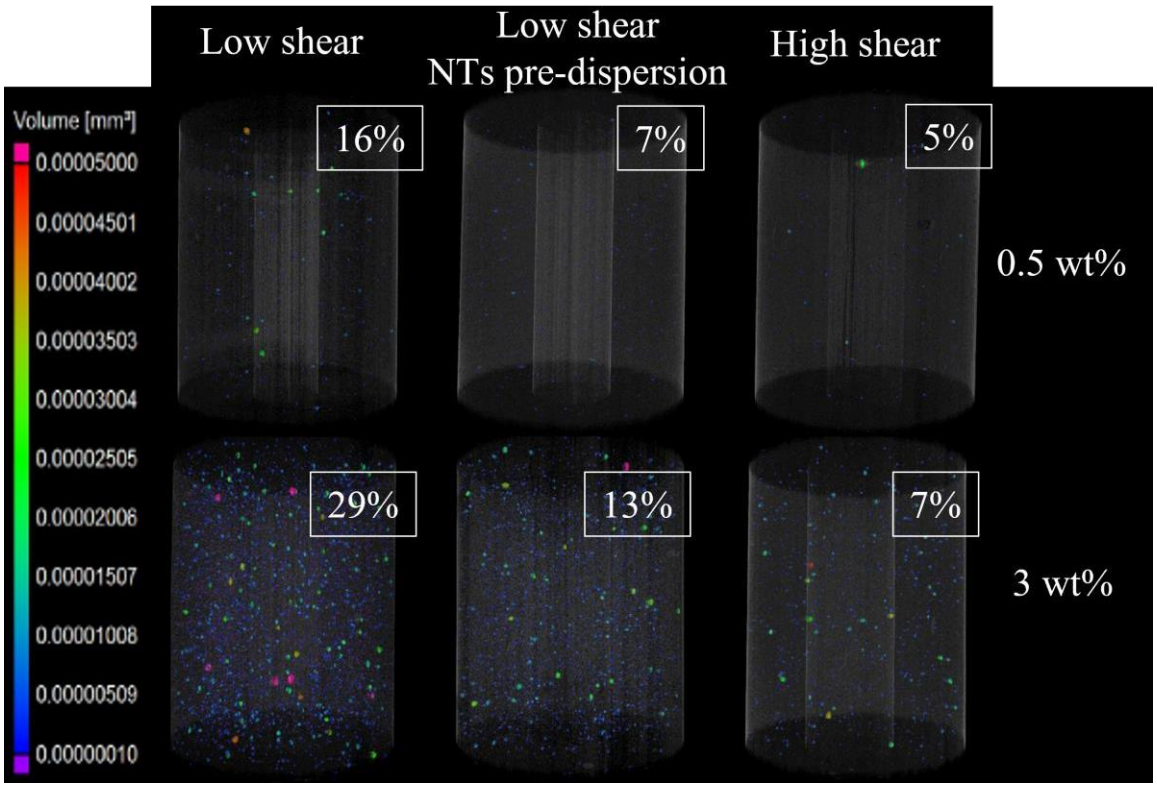

Figure 1: µ-CT images resulting from the inclusion analysis with the percentageof nanotubes mixed with the polymer that remain agglomerated

The SAXS/WAXS data indicated that, despite the high strain happening in the circumferential direction during the tube expansion, the nanotubes remained highly aligned in the extrusion direction while the PLLA crystals formed with their c-axis along the stretching direction (Fig. 2).

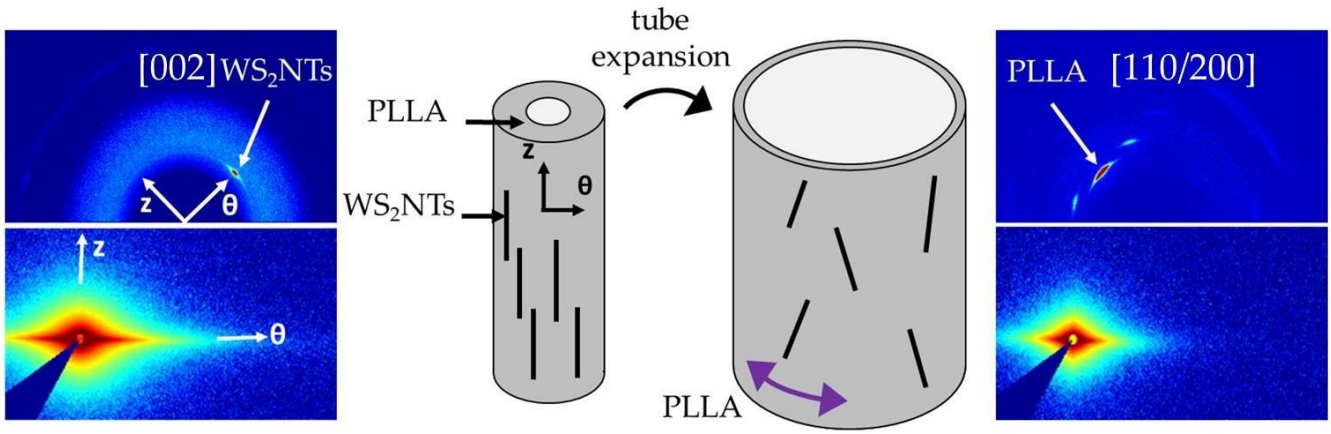

Figure 2 : WAXS (top) and SAXS (bottom) 2D patterns of PLLA/WS_2NT tubesbefore and after tube expansion

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O6: EVALUATION OF A MEDICAL GRADE THERMOPLASTIC POLYURETHANE IN THECONCEPTION OF A 3D-PRINTED CUSTOM-MADE AORTIC STENTGRAFT

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Introduction: The use of fenestrated stentgrafts in endovascular repair (FEVAR) of abdominal aortic aneurysms (AAA) shows limitations in manufacturing time (8-12 weeks), cost (15-20 k€), and patient customization. Providing a custom-made (CM) medical device made by 3D-printing (3DP) would solvethese issues. In this context, thermoplastic polyurethane (TPU) appears as an excellent raw material. Synthesized from a macrodiol (soft segment, SS) and a diisocyanate (hard segment, HS), this polymeris already used as a biomaterial. For it to be implantable in the long term, TPU must be biocompatible,sterilizable and maintain its integrity over time. Thus, our objective is to evaluate this polymer through the manufacturing process and assess its stability in a pro-oxidative medium.

Experimental: Impact of gamma sterilization at a dose of 40 kGy (γ-40 kGy) and susceptibility of TPU to degradation by reactive oxygen species (ROS) have been investigated on 3DP samples. The controlgroup (0 kGy) and the sterilized group (γ-40 kGy) were exposed to a 25% H_2O_2 solution under reflux for 6 hours to simulate the inflammatory response of macrophage cells. Surfaces of samples were observed under scanning electron microscope (SEM). Surface properties were investigated by water contact angle (WCA) measurements and infrared (ATR-FTIR) spectroscopy. Molecular weights were determined by gel permeation chromatography (GPC) coupled with a differential refractometer. Thermomechanical properties were assessed by differential scanning calorimetry (DSC) and tensile tests. Biocompatibility was evaluated by a cytotoxicity assay according to ISO10993-5 and hemolysis assay according to ISO10993-4. Surface of samples after whole blood contact were observed under SEM.

Results: Increase of molecular weights, augmentation of HS glass transition temperature and toughening suggests that reticulation occurs in TPU after gamma sterilization. Peak emergence at 1636 cm^{-1} in ATR-FTIR spectra show oxidation degradation in TPU. High cell viability and low hemolysis rates confirm that TPU remains biocompatible through the manufacturing process and after H_2O_2 exposure. SEM observation after blood contact shows inhibition of platelet activation after gamma sterilization.

Conclusions: Our study shows the feasibility of using TPU as a raw material in the conception of a 3DPCM aortic stentgraft. The manufacturing process would seem to have low impact on the properties ofTPU regarding our application as it is sterilizable and it remains biocompatible. After H_2O_2 exposure, itwas shown that TPU is susceptible to oxidation degradation by ROS. Further studies should investigate long term mechanical stability and toxicity analysis of degradation products and extractables.

Acknowledgments: I-SITE scholarship call for project "Expand", sustained program (FEDERATE).

Keywords: Fenestrated endovascular repair (FEVAR), Additive manufacturing, Polymer characterization.

Wednesday, October 20th, 2021

‘Scaffold design, lab to clinic’ session

O7: DENSE COLLAGEN/PLGA COMPOSITE HYDROGELS AS MEDICATED WOUND DRESSINGS FORTHE TREATMENT OF CUTANEOUS CHRONIC WOUNDS: IN VITRO AND IN VIVO EVALUATION

Xiaolin Wang [1], Olivier Ronsin [2], Basile Gravez [3], Nicolette Farman [3], Tristan Baumberger [2], Frédéric Jaisser [2], Thibaud Coradin [1], Christophe Hélary [1]

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3 Centre de Recherche des Cordeliers – Sorbonne Université – INSERM UMRS 1138

Key words: **Composites, Collagen, Drug delivery**

Cutaneous chronic wounds are characterized by the absence of healing after six weeks. The classic treatment is the debridement of the wound bed followed by a compression method. When the treatment is not efficient enough, the application of wound dressings is required. To date, no dressings are appropriated to treat the different kinds and stages of wounds. Nowadays, research orientation is towards medicated wound dressings incorporating therapeutic molecules within biomaterials in order to favor skin repair or to prevent infection. In this study, dense collagen/PLGA composite hydrogels have been developed to deliver dexamethasone or spironolactone in a controlled manner to modulate inflammation in the wound bed. To evaluate composite hydrogels as a novel medicated wound dressing, hydrogel stability, mechanical properties, drug loading and release kinetic have been analyzed. Then, the in vivo performance of composites was evaluated in a pig model over 10 days. Dense fibrillar collagen hydrogels concentrated at 40 mg/mL were incubated in a PLGA solution (7 KDa) containing dexamethasone or spironolactone for 24 hours. Then, the mixtures were rinsed in PBS to closely associate the hydrophobic polymer with the collagen network (Fig 1A). This procedure enabled to obtain composites with high mechanical properties and an improved resistance against in vitro degradation by collagenase. The elastic modulus measured in composites was two times higher than that measured in pure collagen hydrogels. After rehydration, the composite hydrogels swelled up to 10 times their dried weight and recovered their original shape. The ultrastructural analysis by scanning electronic microscopy revealed the presence of PLGA particles associated with collagen fibrils (Fig 1B). Compared to pure collagen hydrogels, the drug loading in composites was 5 times higher and the release rate was constant over the first two weeks (Fig 1C). Unlike pure collagen hydrogels, no burst release was detected. The released drug from composites retained its activity, thereby evidencing the absence of degradation during the compositesynthesis. Cell viability experiments showed the absence of cytotoxic effect of composites hydrogels on fibroblasts and keratinocytes. Subsequently, the effect of PLGA/collagen composite hydrogels wasevaluated in vivo in a model of impaired wound healing in pig. Spironolactone loaded composite hydrogels improved wound closure by 50% and permitted a complete re-epithelialization after 6 days(Fig 1D). Taken together, these results show that dense collagen/PLGA composite hydrogels are promising medicated wound dressings for the treatment of chronic wounds as they deliver constant doses of drugs favoring skin repair.

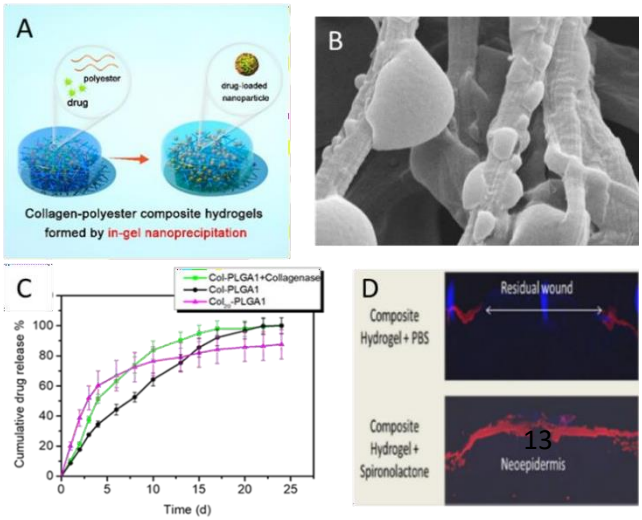

Figure 1: Collagen/PLGA composite hydrogels as novel wound dressings.
(A): process of fabrication.
(B): Ultrastructure analysed by sem.
(C): Drug release kinetic.
(D) Wound reepithelialization promoted by spironolactone released from composite hydrogels

O8: DEVELOPMENT OF A CONTRACTION-RESISTANT DERMAL SUBSTITUTE BASED ONCOLLAGEN AND A POLYMERIC SCAFFOLD

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Keywords: collagen gels, contraction, hybrid scaffolds

ABSTRACT

Current strategies in dermal healing involve the use of tissue-engineered scaffolds to avoid tissue grafting and their subsequent potential drawbacks (e.g. donor-site pain, patient morbidity) [1]. Collagen-based templates are widely used as implantable dermal substitutes due to their excellent resemblance with the extracellular matrix and their biocompatible, non-toxic and cost-effective features [2]. However, their lack of sufficient strength to withstand the rapid cell-mediated contraction remains a major problem for the efficiency of suchscaffolds, potentially leading to undesirable (and excessive) scarring, impaired tissue functionand poor cosmesis [3]. For instance, collagen matrices seeded with normal human dermal fibroblasts (NHDF) contract around 50% of their initial size in the initial 48 h and up to 20% within the first week (Figure 1). In this work, we aim to: i) produce a hybrid dermal substitute based on collagen and a polymeric scaffold and ii) evaluate the impact of the latter on the contraction of the dermal substitute. Particularly, we investigated 1) the formulation ofcollagen gels and the factors influencing their contraction (such as NHDF seeding density, floating or restrained models) 2) the synthesis and processing of a polymeric scaffold with appropriate mechanical properties and that can be physically incorporated into the gel while also facilitating cellular adhesion, infiltration and proliferation, and 3) the coupling of both moieties (gel + polymer) to evaluate the contraction of the dermal substitute. The structure ofthis hybrid dermal substitute was evaluated by optical and scanning electron microscopies, while tensile tests and rheology (Elastosens® technology) were used to evaluate their mechanical characteristics. Finally, the proliferation, cell distribution and differentiation of NHDF in such materials were also investigated.

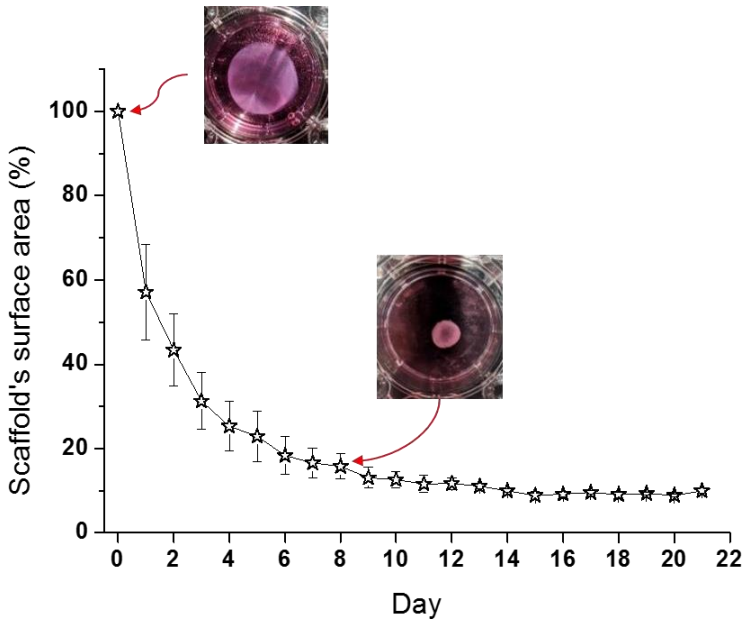

Figure 1. Contraction of NHDF-seeded collagen gels over time (*unpublished data*).

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O9: HYDROXYAPATITE COATED MEMBRANES FOR THE DESIGN OF SURGICAL ADHESIVES

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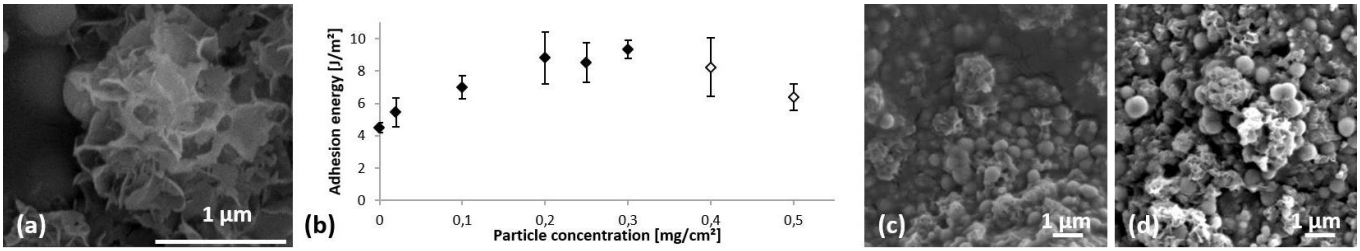
Keywords: tissue adhesives, hydrogels, hydroxyapatite coatings

ABSTRACT

The fixation of hydrogels to the wet and soft surface of internal organs is a challenge to develop implantable devices. A promising approach is the adhesion by bridging nanoparticles placed at the hydrogel-tissue interface. In this approach, adhesion is created by the adsorption of the macromolecules composing the hydrogel and the tissue to the surface of the particles [1,2]. Recently, procoagulant silica nanoparticle coatings have been shown to enhance the adhesion of PEG hydrogel membranes on living pig livers, especially in the presence of blood through the formation of an interfacial clot [3]. Unfortunately, silica nanoparticles may present toxicity issues that limit their potential use *in vivo*. Hydroxyapatite particles are an interesting alternate system having a higher biocompatibility. It has been demonstrated that hydroxyapatite nanoparticles deposited as suspensions or assembled into plates can be used to glue hydrogels or tissues [4]. Here, we show that coatings of nanostructured hydroxyapatite particles enhance the adhesion between hydrogel membranes and living tissues. For that, we developed a deposition method of biomimetically grown hydroxyapatite particles (Fig. 1a) on PEG-based hydrogel membranes where the homogeneity and density of thecoating can be finely tuned. Using *ex vivo* peeling experiments on pig liver capsules, we show that the adhesion energy increases with the surface concentration of the hydroxyapatite coating and reaches a maximum for 0.2-0.3 mg/cm² (Fig. 1b). Microscopic analysis of the coatings before and after peeling showed that the particles are anchored in the PEG hydrogel with little transfer from the coating to the tissue (Fig. 1c, d). Preliminary results of *in vivo* studies in a porcine model illustrate the potential of these adhesive membranes for surgery.

Figure 1. (a) SEM image of nanostructured hydroxyapatite particles; (b) Adhesion energy measured by 90° peeling test on fresh liver capsule ex vivo as a function of the surface particle concentration; (c-d) SEM observations of hydroxyapatite coatings before (c) and after (d) peeling.



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O10: IMPLANTATION AND STERILIZATION OF A TISSUE-ENGINEERED VASCULAR GRAFT

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[1]BioTis, INSERM U1026, Université de Bordeaux, Bordeaux, France**Keywords:** Tissue engineering ; cardiovascular ; cell-assembled matrix

ABSTRACT:
To meet the clinical need for small vascular graft, we propose a new human and textile- based Tissue-Engineered Blood Vessel (TEBV). Vessels were produced by weaving yarn of Cell-Assembled extracellular Matrix (CAM) synthetized in vitro by skin fibroblasts. Study objectives were to 1) find the best sterilization method to simplify TEBVs production whilepreserving its biomechanical and biological properties, and 2) assess the human TEBV functionality in an immunodeficient rat model.
Well-organized human CAM sheets were produced in vitro after two months of culture with 20% bovine serum and 500 mM ascorbate. Sheets were cut into 5 mm wide ribbons that were sterilized using gamma irradiation (dry or wet, with high or low dose rates), electron beam irradiation, ethylene oxide (EtO), or supercritical carbon dioxide (scCO2). Ribbons (16 cm long, n=8/condition) were implanted subcutaneously in immunodeficient rats (4/rat) and tensile tests were performed after 2, 4, 12, and 24 weeks. TEBVs (8 mm long, 1.6 mm inner diameter) were woven from 2 mm-wide ribbons and implanted in abdominal aortas of immunodeficient rats. Before implantation, the strength of the gamma-wet group was significantly lower than control (sterile production group) by 34%, while the EtO group was stronger (+20% of control). After five months, the gamma-wet group remained the weakest,while scCO2 group seemed to be stronger than other conditions.
Small TEBVs (8 mm long, 1.6 mm inner diameter) were manually woven from 2 mm-wide CAM ribbons and implanted in abdominal aortas of immunodeficient rat. Preliminary surgeries demonstrated graft implantability and the absence of transmural leakage. At thistime, 6 grafts have been successfully implanted and are still functional after 3 months.
In conclusion, ribbons can be sterilized while preserving satisfying mechanical properties,and be assembled into promising grafts.

O11: Evaluation of poly-L-lactid-co-glycolid (PLGA) as a potential biomaterial for autologous breast reconstruction: *in vitro* and *in vivo* degradation studies

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Keywords: Tissue Engineering Chamber, Additive Manufacturing, Bioabsorbable polymer

INTRODUCTION:

Tissue engineering chamber (TEC) using fat flap from the patient's own tissue could be a promising solution to restore large volume of mature and vascularized adipose tissue (AT)[1,2] and a therapeutic alternative to breast reconstruction. Here, we addressed the possibility of using poly-L-lactid-co- glycolid acid for optimum 3D printed TEC conception and adipose tissue growth. *In vitro* and *in vivo* degradation of PLGA were evaluated as well as adipose tissue growth inside of the chamber.

EXPERIMENTAL METHOD:

Medical grade PLGA 85:15 (Mw: 2,70E+05 g/mol, amorphous) was used to manufacture TECs with a Fused Deposition Modelling printer. *In vitro* degradation study was performed in PBS (37°C, pH 7,4) according to ISO 13781 (2017). For *in vivo* study, TECs were implanted subcutaneously in the dorso- lumbar region of rats (n=13), a subcutaneous pedicled fat flap was then dissected (V=340mm^3) to fit inside the 3D printed chamber (V=2168mm^3). Iterative Magnetic Resonance Imaging (MRI) were performed on rat at different time points to measure fat flap volume. At each respective time point, degraded implants were evaluated by Differential Scanning Calorimetry (DSC) and Gel Permeation Chromatography (GPC) to follow changes in crystallinity and molecular weight over time and mass loss was evaluated as well.

RESULTS ANS DISCUSSION:

After 6 months of implantation, the volume of the adipose tissue under the TEC revealed a significantincrease from 340 mm3 to 1219±523 mm^3. One-third of rats showed a 4-fold increase (up to a maximum of 5-fold increase) in the volume under the TEC. The maximum percentage of infill was 84% due to a progressive time-dependent TEC deformation that finally reduced the available volume.The mean crystallinity *in vitro* and *in vivo* increased slightly at 3 months to 3,3±0,34 % ($p<0,001$) and 4,0±2,0 % ($p<0,05$), respectively. The molecular weight of PLGA decreased with degradation time: by 3 months the Mw of in vitro and in vivo degraded samples had decreased to 1,55±0,074E+05 g/mol ($p<0,0001$) and 1,21±0,27E+05 g/mol ($p<0,05$) respectively.

CONCLUSION:

PLGA could be used as a biomaterial for TEC conception as it enables significant adipose tissue ingrowth. Nevertheless, PLGA implant underwent rapid degradation which was characterized by early loss of the TEC mechanical integrity that limit the available volume for AT reconstruction.

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O12: Fabrication of injectable calcium phosphate cementscontaining PLGA microspheres for drug delivery

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Keywords: Injectable cement, Bone regeneration, Drug delivery.

ABSTRACT

Bone is a living tissue which undergoes constant remodelling and whose performance are altered by various diseases such as osteoporosis, fibrous dysplasia or cancer metastases… In addition to be painful for patients, these diseases lead to pathological fractures, which require multidisciplinary approaches for their treatment. In many cases, a bone substitute material is used to fix the damaged tissue and to provide the mechanical support needed for the skeleton. The use of synthetic biomaterials like methyl methacrylate (PMMA) resin or calcium phosphate cement (CPC) has a great interest to repair bone defects. Therapeutic arsenal is constantly supplemented with novel interventional techniques to propose alternatives, less invasive than the surgical procedure.

The goal of this work was to propose a biodegradable injectable biomaterial, which not only assures the mechanical function but may also allows the local release of drugs for bone regeneration and/or inhibition of cancer cell proliferation. Indeed, such local delivery can achieve drug targeting to obtain a selective accumulation in the bone lesion and surpass the dose-limiting side effects to healthy tissues of standard medication.

We therefore developed injectable CPC with various formulations and incorporated degradable biopolymer microspheres into the inorganic matrix. We have chosen poly (lactic-co-glycolic acid) (PLGA)suited as biocompatible and biodegradable material, and being FDA approved. The controlled porosity created by the microspheres allowed a modulation of the cement degradation time and improved the osteoconduction of the substitute material. The percentage and the size of microspheres influenced on the physicochemical, as well the biological properties. Our study focused on the effects of PLGA addition into the cement (e.g. setting time, injectability, cohesion behaviour, mechanical properties, degradationability…). We also addressed the opacity of CPC by ZrO_2 doping, which is of importance to allow monitoring of the injection by the clinician.

Furthermore, polymeric microspheres were used as drug carriers for a selective estrogen receptor modulator (SERM) indicated for the treatment and prevention of osteoporosis and breast cancer. This SERM shows poor bioavailability due to its limited water solubility and extensive intestinal/hepatic first- pass metabolism. We have achieved the loading of the SERM in PLGA microspheres by double emulsion process. Biological properties of the combined CPC were analysed on various cell lines including hFOB

1.19 and MCF-7 cells. Altogether, this SERM-loaded CPC appears as a promising material and its biocompatibility and bioefficacy are currently validated using an *in vivo* model based on bone defect in rat vertebrae [1].

[1] Habib BELAID *et al (2021)* _ Fabrication of injectable calcium phosphate cements containing PLGA microspheres

(Submitted to materials science and engineering C)

O13: DEVELOPMENT OF A PRINTABLE COMPOSITE FORMULATION OF PHOSPHOCALCIC CEMENT AND HYALURONIC ACID FOR CLEFT LIP AND PALATE REPAIR

Marie-Michèle Germaini[1], Pierre Weiss[1], Sofiane Belhabib[2], Sofiane Guessasma[3], Helene Gautier[1], Remi Deterre[2], Steven Nedellec[4], Joëlle Véziers[1], Boris Halgand[1], Thierry Rouillon[1], Valérie Geoffroy[1]and Pierre Corre[1,5]

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Keywords: phosphocalcic cement, hyaluronic acid, additive manufacturing

ABSTRACT

Context: Autologous graft is the gold standard procedure for alveolar repair causing morbidity, pain and scar. To date, various bone tissue engineering strategies have been tested to replace bone graft with unpredictable results. Tridimensional printing of synthetic biomaterial is a ground-breaking technology for personalized medicine.
Objective: Our goal is to develop a printable formulation, biocompatible, ductile, sterilizable, osteoconductive, ideally osteoinductive and finally absorbable for bone regeneration.
Materials and Methods: Alpha tricalcium phosphate has been mixed with a physical hydrogel ofhyaluronic acid (HA). Rheological properties of the composite material including viscosity, pseudoplasticity, thixotropic and self-healing properties have been assessed thanks to striated and plate geometries on a RS300 rheometer. Young modulus, compressive and flexural strength, ductility (percentage of deformation) have been measured thanks to a texture analyzer. BIOX cellInk commercial 3D-printer was used for performing the printing thanks to a pneumatic extrusion process. Viability (live and dead), metabolic activity (CCK8 test) cell adhesion (focal adhesion contacts) and proliferation (EdU tests) were assessed using human BMSCs and L929 cells.
Results: The composite cement/HA formulation was printed by direct ink writing with a resolution of 200-250 microns (Figure 1 (A)). In contrary to the pristine cement that is not printable, the composite formulation exhibited acceptable pseudoplasticity, thixotropic and self-healing properties (more than 60% of recovery after 1 min) that avoids the use of a binder that requires debinding step. This formulation is self-hardening at room temperature, the earliest self-hardening occurs from 1h (measured by Gillmore needle). The X-ray diffractogram showed a phase transformation of alpha TCP by calcium deficient apatite on both materials. Bioactivity of the composite formulation was demonstrated through nanosheet-like shape apatite crystals formation from 1h after soaking in cell culture medium (Figure 1 (B)). Mechanical properties determinations were in the range of those of trabecular bone and with a rate of deformation of 17% 4 days after demoulding for cement/HA against 3% for the cement. Biocompatibility has been validated with 96% of cell survival for cement/HA against 83% for cement. Cell adhesion and proliferation were evidenced on both materials.
Conclusion: These results are promising indicators for the development of a wide-use printing formulation for bone grafting procedures. This composite formulation (patent UE Patent 20315185,7- 1109) is straightforward to prepare with the use of only biocompatible reagent. It is cost-effective and can be used with whatever the commercial printer by extrusion process. It possesses interestingfriendly-handling properties. In vivo investigations are in progress.

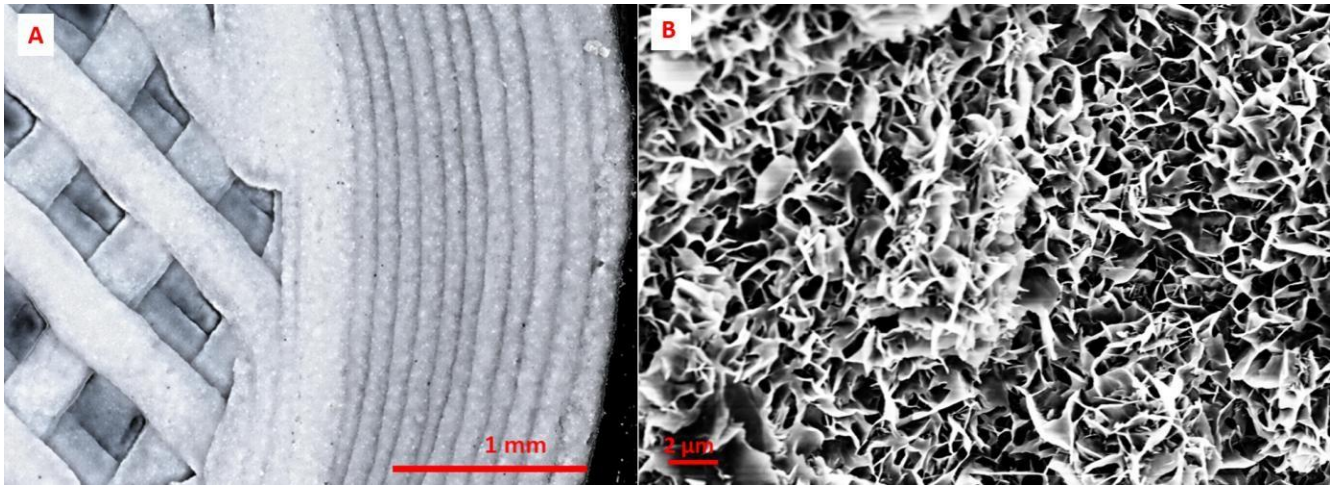

Figure 1: (A) 3D printing by direct ink writing of the cement/HA formulation; (B): SEM image of thesurface of cement/HA formulation after 1h of soaking in the cell culture medium.

O14: SANDWICH CELLULARIZATION APPROACH FOR BONE TISSUE ENGINEERING

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Keywords: Layer-by-layer, Fused Deposition Modeling, Composite

ABSTRACT

Treatment of large bone defect require a specific bone regenerative strategy. Tissue engineering approach suggests to use engineered scaffold with cells and suitable biochemical and physicochemical factors to develop a material with improved bioactivity. The main issue with these strategies is linked to the difficulty to obtain an efficient and homogeneous cell seeding. The conventional approach involves seeding cells onto a macroporous scaffold and expect cell colonization to form composite tissue constructs. Many limitations have been observed using this approach, due to slow vascularization and limited diffusion of nutrients, a low cell density and non-uniform cell distribution is usually observed.

To overcome this current issue our suggestion is a layer-by-layer (LBL) cellularization approach, also called "sandwich" approach. Previous studies have shown that LBL fabrication approach, based onthe assembly of small-seeded blocks, provided more efficient cell repartition in 3D compared to conventional methods [1].

For our purpose we developed a new material, made of medical grade Poly(lactic-co-glycolic) acid (PLGA)mixed with 10% (w/w) hydroxyapatite nanoparticles (HA) for 3D printing by Fused Deposition Modelling(FDM). The developed materials were printable with appropriate resolution and showed favourable properties and relevant cellular response for bone tissue engineering applications [2].

Based on our previous results, the aim of this work was to evaluate the potential benefits of a LBL cellularized scaffold for bone tissue engineering preclinical applications. Stromal vascular fraction isolated from rat adipose tissue were used as a rich stem cell source [3]. Cell colonization, proliferation and differentiation were compared with the conventional approach and our LBL approach. Both approaches were also applied in a calvaria bone defect model to assess the bone reparation potential.

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O15: INFLUENCE OF SCAFFOLD GEOMETRY ON BMP-2 INCORPORATION AND *IN VIVO* BONE REGENERATION

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Keywords: Bone tissue engineering, 3D printing, bone morphogenetic protein 2

RÉSUMÉ DES TRAVAUX

Critical-size bone defects are unable to heal by themselves during the patient's lifetime. Currently, autologous bone graft is the gold standard solution to treat such defects, but it is associated with some limitations such as limited availability, high postoperative donor-site morbidity and inconsistency of repair in very large bone defect [1]. To address this issue, we designed three scaffolds (cylinders 25mm long and 14mm in diameter) with different geometries to repair a long-segmental critical-size sheep metatarsal bone defect (**Figure 1**): (i) geometry Lines with 880µm cubic pores and a central cylinder holeof 5mm in diameter (**Figure 1A**) ; (ii) geometry Gyroid, a triply-periodic minimal surface design with a poresize of about 1mm and a central cylinder hole of 5mm in diameter (**Figure 1B**) ; (iii) geometry Double Lines, with 1.2mm cubic pores in the outer of the cylinder while its center (7mm in diameter) had a gyroidpore shape with 2mm pores (**Figure 1C**).

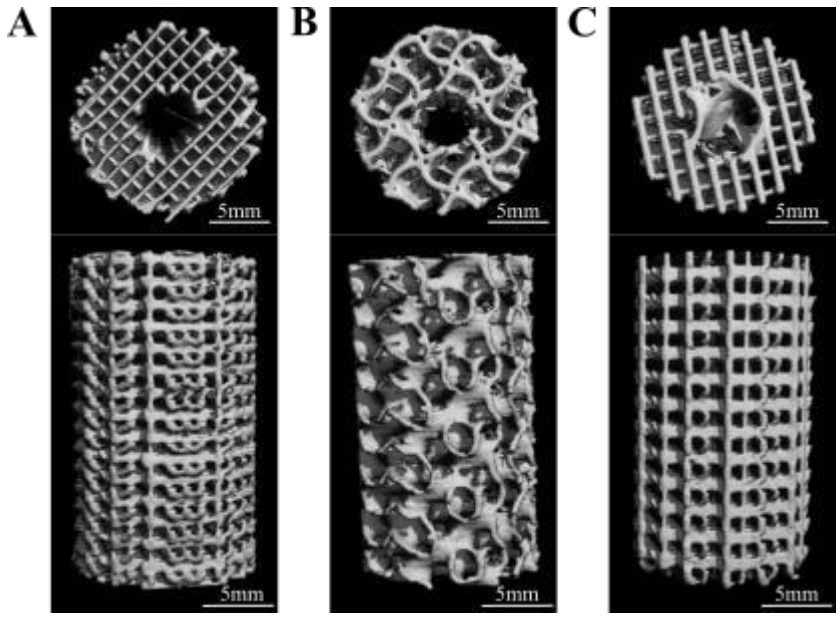

Figure 1. µCT scans of the three different scaffold geometries. (A) Lines, (B) Gyroid, and (C) Double Lines.

The surfaces of these geometries, measured using micro-computed tomography (µCT), were all different.The 3D-printed scaffolds made of clinical-grade PLA were coated with a polyelectrolyte film and loaded with BMP-2 at a targeted surface dose of 9.2 µg/cm². The quantification of BMP-2 with a UV-Vis spectrophotometer showed that the geometry Lines had the lowest incorporated BMP-2 surface dose while the geometry Gyroid had the highest. Surprisingly, the scaffolds with different surfaces incorporated a similar quantity of BMP-2 per implant, suggesting that scaffold geometry influenced BMP- 2 incorporation in the polyelectrolyte film. Two scaffolds of each geometry

were implanted in six sheep,with one implant per sheep. Interestingly, X-ray radiographs and µCT scans showed that despite its lowest incorporated BMP-2 surface dose, the geometry Lines presented the fastest and strongest bone formation, leading to a full bridging of the defect. The geometry Gyroid only led to a partial bridging of the defect and the geometry Double Lines did not allow bone repair (**Figure 2**).

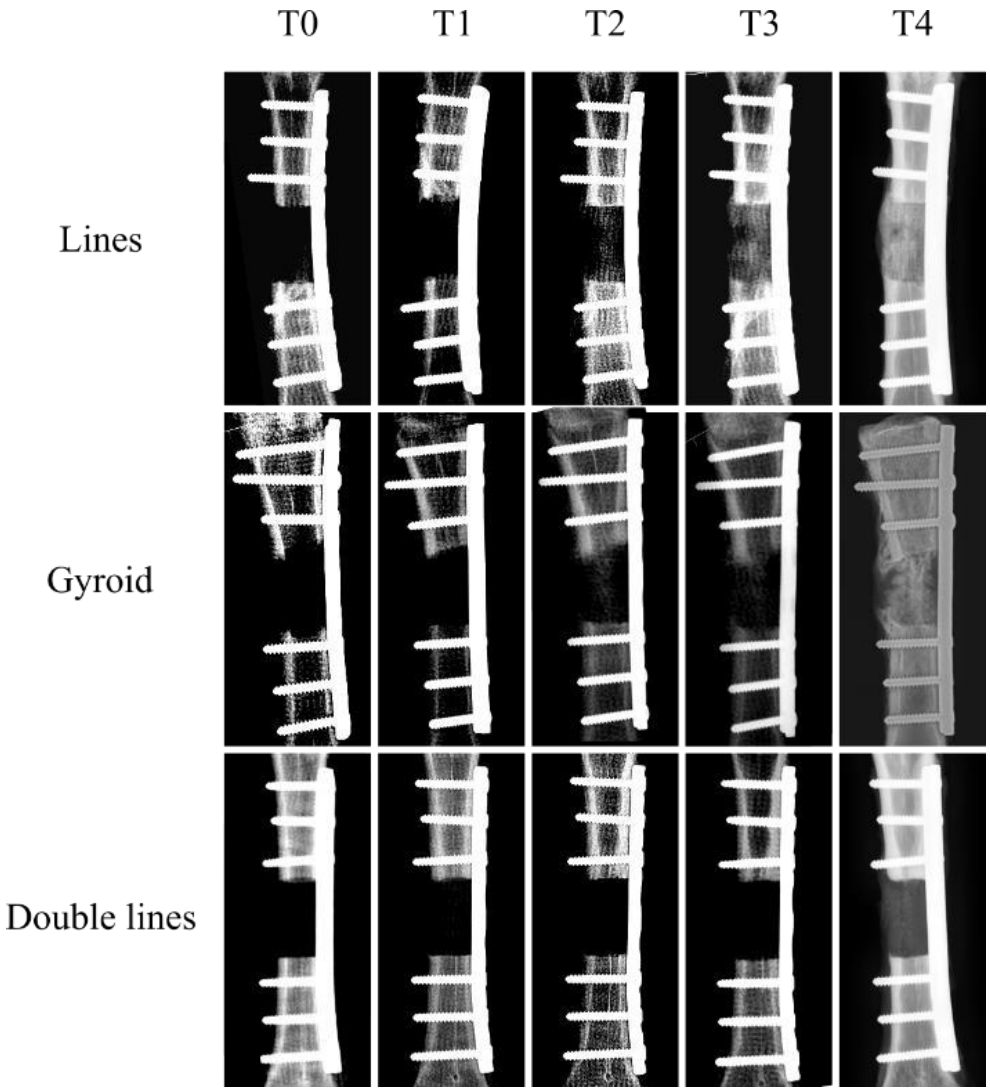

Figure 2. Representative X-ray radiographs of scaffolds implanted in a critical-size sheep metatarsal bonedefect after 0, 1, 2, 3, and 4 months.

Since the quantity of BMP-2 per implant was similar in all scaffolds, this suggests that the scaffold geometry influenced the bone regeneration kinetics and the amount of newly-formed bone. This preliminary study opens perspectives to optimize the scaffold geometry in view of long bone repair. Theoptimization of pore size and shape along with the optimization of the BMP-2 dose could lead to efficient implants with reduced fabrication costs and reduced secondary effects.

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O16: A COMBINATION OF SELECTIVE LASER MELTING AND SURFACE MECHANICAL ATTRITION TREATMENT FORMETALLIC MATERIALS MANUFACTURING

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The use of metallic materials in the medical field has a long history. Although metal implants occupy a dominant position in bone reconstructive surgery, fibrosis and implant-associated infections remain themost severe and devastating risks associated with orthopedic prosthesis failure. To readily fulfill their mission, implants have to fit as much as possible to the native bone characteristics in term of structure and mechanical properties (Young modulus). It was on this scope that selective laser melting (SLM) additive manufacturing technology, started to be investigated as a manufacturing approach to develop porous materials with a complex geometry. Surface Mechanical Attrition Treatment (SMAT) involves a sever deformation of the metal through vibration of spherical shots of steel or ceramic. This surface treatment allows on the one hand the nano-structuring of the material at the surface and on the other hand the increase in the compressive stresses in the subsurface, the whole preventing the propagation of cracks and greatly increasing the life of the parts. The current study aims to evaluate (i) the effect of SMAT treatment on the physical features of SLM manufactured material and (ii) the biological response to SLM manufactured material with or without SMAT treatment. From a microstructural point of view, TA6V parts from SLM consist of α' martensite needles. Our study showed that a 10 min treatment was the best option allowing to obtain a nanostructure of about ten micrometers thick and a homogenization of the roughness (making it possible to avoid machining industrially used to remove the un-melted particles and the supports). This treatment duration is all the more relevant as it is perfectly suited to an industrial application. The biological responses to SMAT-treated material showed a decrease in osteoblast and mesenchymal stem cells (MSCs) number in comparison with raw SLM material. Despite a decrease in the material porosity and an increase in local roughness, SMAT-treated material and raw SLM material did not show the presence of bone-*like* nodules on both materials. Furthermore, these materials did not affect the paracrine function of MSCs (i.e. release of VEGF and OPG). Regarding the bacterial adhesion on the SMAT-treated material, our investigations showed a decrease in *S. aureus* and *P. aeruginosa* adhesion in comparison with the raw SLM material. Taken together, these results suggest that a combination of SLM and SMAT could be a good strategy for future prosthesis manufacturing.

O17: FROM 3D TO 4D PRINTING WITH BIOCOMPATIBLE SYNTHETIC HYDROGELS

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[2] 3D Medlab, Marignane, France **Keywords**: Vat photopolymerization ; Poly(oxazoline) ; Thermo-stimulable**ABSTRACT**

Hydrogels are soft three-dimensional hydrophilic networks able to absorb a large quantity of water without losing their mechanical integrity. The large hydration contributes not only to the biocompatibility but also allows to get closer to the chemical and physical structuration of the biologicaltissue. Therefore, hydrogels are extremely suitable for a variety of applications in pharmaceutical, medical industry and more particularly in tissue engineering.
However, the development of tunable hydrogels able to provide good mechanical properties and sufficient water absorption while maintaining efficient bioactivity remains a huge challenge. Hydrogels based on synthetic polymers can offer such expectations because of their tunable, controlled and reproducible properties (chemistry, structure, porosity, degradability…). A majority of synthetic hydrogels used for biomedical applications are based on poly(ethylene glycol) (PEG). However, several limitations are linked to PEG and an enormous challenge is emerging to substitute the PEG while keepingefficient mechanical properties, improving cell adhesion ability and displaying specific functionalities. Among all the hydrophilic synthetic polymers, the poly(oxazoline) (POx) family tends to be the best substitute of PEG. POx are qualified as pseudo-peptides with high chemical versatility and simple post- functionalization which gives them a huge advantage. Moreover, POx are recognized for their biocompatibility and their significant improved bioresponse compared to PEG [1]. Consequently, POx based hydrogels are considerably growing in the domain of additive manufacturing for tissue engineering[2]. We therefore investigated the potential of POx based hydrogel to be used in vat photopolymerization such as stereolithography, and highlighted their potential in biomedical applications.

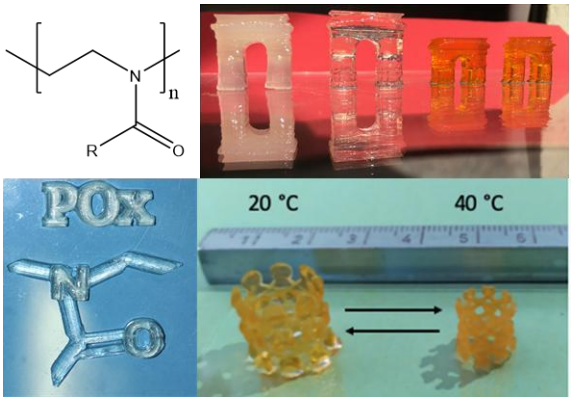

Figure 1. POx hydrogels in 3D and 4D printing.

Various POx polymers have been successfully synthesized by ring opening polymerization, with different targeted molecular weight and functionalization ratios. Typical chemical functionalizations led not only to remarkable mechanical properties for hydrogel material, but also specific thermo-stimulable hydrogel which showed great potential in 4D printing.

The fabricated structures have been characterized in terms of physical and mechanical properties (Figure1). We then demonstrated the promising bioactivity of such materials, and we opened the investigationstoward biofabrication area with POx hydrogels.

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O18: ALGINATE-GELATIN HYDROGELS AS A TOOL TO CONTROL THE FATE OF INDUCED PLURIPOTENT STEM CELLS

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Keywords : Hydrogels, iPS cells, Mecanosensitivity

ABSTRACT

3D bio-printing is a cellular engineering process of great potential in regenerative medicine, especially for autografting [1],[2]. Among the different 3D bioprinting techniques, Liquid Extrusion Deposition (LDM) is an economic bioprocess offering the possibility to accurately control cell density [3],[4], which allows to produce complex 3D tissues with high resolution and cell concentration close to tissues of interest [6]. In addition, the shear induced during extrusion process as recently been proposed as a mean to control the fate of printed cells. This is particularly relevant when using induced pluripotent stem cell (iPS), or stem cells, which differentiation in bio-printed tissues is related to the composition, physico-chemical properties and structure of the biomaterial used as a matrix. [6].

Since LDM is a complex bioprocess encompassing 3 entities (bioprinting method, biomaterial used and nature of the cells [7]), it is mandatory to evaluate the interactions between each entity in view of creating pre-mature organoids.In a first step towards this goal, the aims of this study were (i) to evaluate the suitability of a novel hydrogel ink in view of LDM printing, and (ii) determine its suitability as substrate for induced pluripotent stem cell (iPS).

The cells used here were hiPSC AG08C5, donated by the neuromyogen institute (Lyon). To investigate the impact of hydrogel stiffness on iPS fate, two alginate/gelatin bioinks (AGs and AGh) with significantly different stiffness were formulated from a previously developed fibrinogen-alginate- gelatin bioink [2]. Variation of alginate/gelatin ratios and post-crosslinking (alginate chelation) allowed to increase the rigidity gap between both formulations by 2 orders of magnitude (Figure 1, A). Since theviscosity of the gelatin is thermo-dependent, it was possible to reach a printable viscosity of the hydrogels in a range comprised between 15 and 37°C (Figure 1, B). In addition, a rheo-thinning profile was observed which could limit the generation of intense shear stresses during printing.

The incorporation of iPS cells at high concentration (2.10^6 cells.mL^{-1}) in both AGs and AGh formulations was possible, as shown in Figure 3, with an important cell survival observed up to 8 days. Control group was cultivated in mTeSR medium on Matrigel-coated plate. Unlike the control, cells in the hydrogels remained round, indicating a low cell-matrix interaction. This suggests that the cellular adhesion patterns present in the bioinks via gelatin (RGD type) were not adequate or sufficient for the iPS cells.

To conclude, these bioinks formulation show great rheological and mechanical properties for 3D printing, which makes them an interesting tool to understand the mechanical differentiation of iPS in 3D. Ongoing work now focuses on the optimization of the cell-material interaction through incorporation of various ligands within the bioink, prior to studying iPS differentiation within.

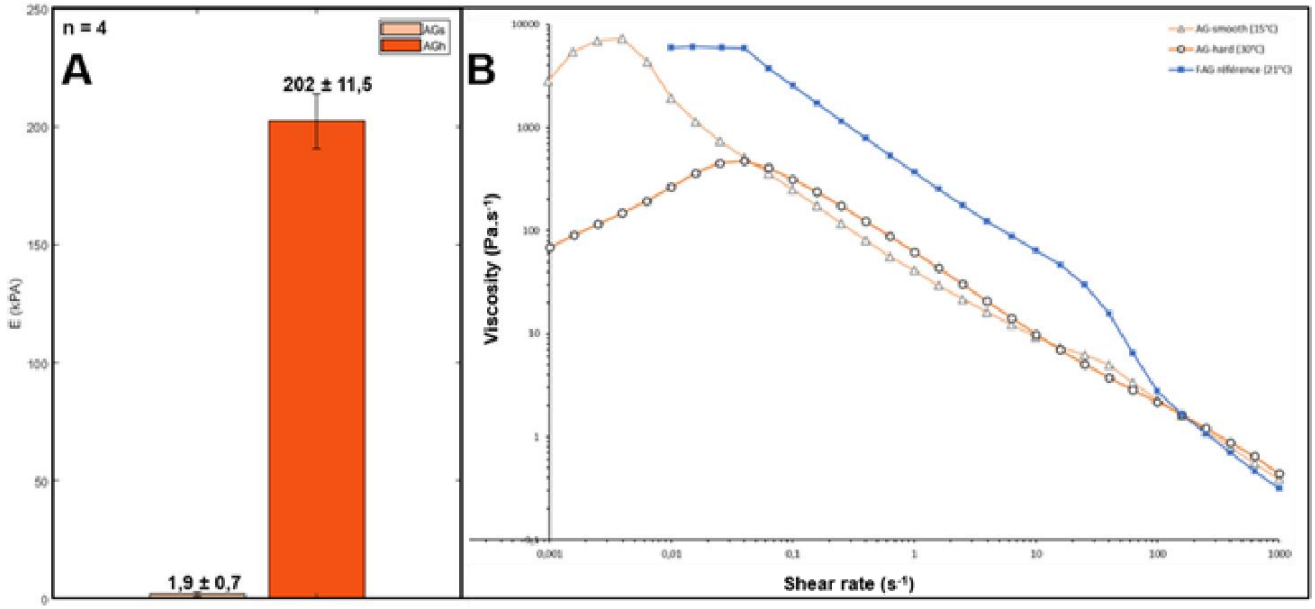

Figure 1: Rheological and mechanical characterizations of the hydrogel formulations. (A) Young Module measured on both AGs (0.5%Alg-2%Gel) and Agh (5%Alg-10%Gel) formulations in post crosslinking (1% CaCl2 for 30mn) after 24h at 37°C. Measurements performed by DMA compression tests, 8 mm geometry, with a DHR2 rheometer. (B) Study of the rheological profile of the 2 formulations AGs and AGh compared to the FAG reference (3d.FAB, Villeurbanne), measure by shear in sweep with a rheometer (DHR2, TA)

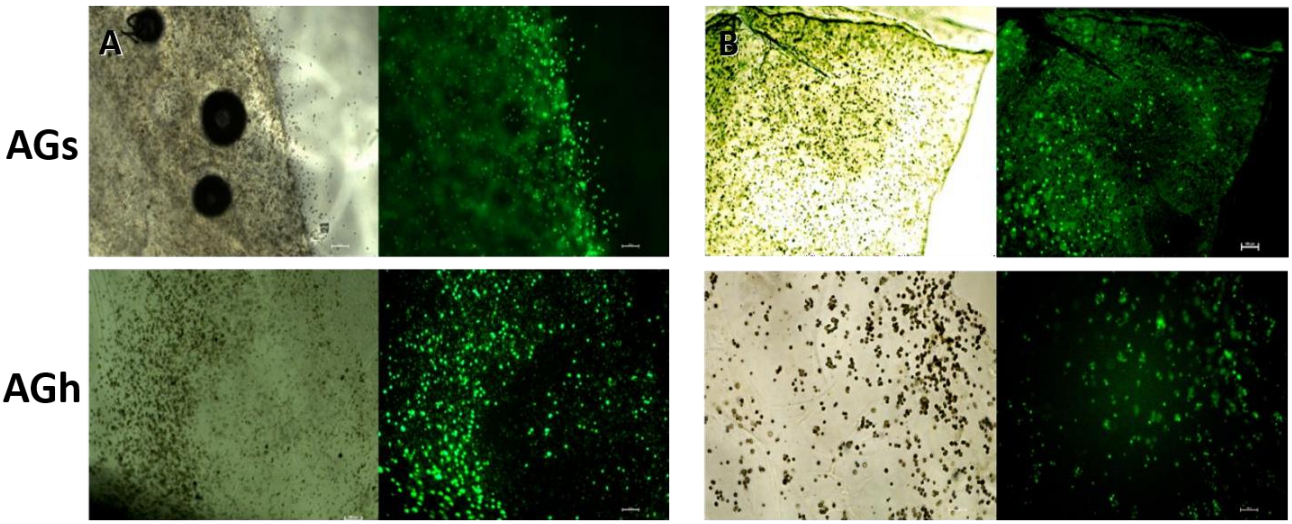

Figure 2 : Calcein labelling of iPS cells (AG0538 obtained by retrotranscription of fibroblasts, NeuroMyoGene Institute, Lyon) incorporate in AGh and Ags formulations. (A) Comparison optical and fluorescent observation (calcein AM) at D1. (B) Comparison optical and fluorescent observation (calcein AM) a D8

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Thursday, October 21st, 2021

'Data analysis, monitoring and modeling' session

O19: INCREASE IN BONE REGENERATION USING CALCIUM PHOSPHATE-CHITOSAN-HYALURONIC ACIDHYBRID MATERIAL

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Mots clefs : Hybrid coating, bone regeneration, *in vivo* calvaria model

RÉSUMÉ DES TRAVAUX

Guided bone regeneration (GBR) is one of the most attractive technique for restoring oral bone defects, where an occlusive membrane is positioned over the bone graft material, providing space maintenance required to seclude soft tissue infiltration and to promote bone regeneration. However, bone regeneration is in many cases impeded by a lack of an adequate tissue vascularization and/or by bacterial contamination. Therefore, a multifunctional membrane that kills bacteria and drives bone healing is urgently sought. Herein, we used simultaneous spray coating of interacting species (SSCIS) process to build a bone inspired coating made of calcium phosphate-chitosan-hyaluronic acid on one side of a GBR membrane. The resulting hybrid coating is composed of amorphous calcium phosphate and carbonated poorly crystalline hydroxyapatite, wrapped within chitosan/hyaluronic acid polysaccharide complex. Hybrid coating possesses excellent bioactivity and capability of inducing an overwhelmingly positive response of stromal cells and monocytes in favor of bone regeneration [1-3]. Furthermore, the antibacterial experiments showed that the hybrid coating provides contact-killing properties by disturbing the cell wall integrity of Gram-positive and Gram-negative bacteria. Its combination with stromal cells, able to release antibacterial agents and mediators of the innate immune response, constitutes an excellent strategy for fighting bacteria [1,4]. A preclinical *in vivo* studywas therefore conducted in rat calvaria bone defect (6 mm of diameter) and the newly formed bone was characterized 8 weeks post implantation. µCT reconstructions showed that hybrid coated membrane favored bone regeneration, as we observed a two-fold increase in bone volume/total volume ratios *vs.* uncoated membrane (p<0.005). The histological characterizations revealed the presence of mineralized collagen (Masson's Trichrome and Von Kossa stain), and immunohistochemistry analysis highlighted a bone vascularization. However, second harmonic generation analysis showed that the newly formed collagen was not fully organized. Despite an increase in the stiffness of the newly formed bone with hybrid coated membrane (*vs*. uncoated membrane), the obtained values were lower than those for native bone (approximately 5 times less). These significant data shed light on the regenerative potential of such bioinspired hybrid coating, providing a suitable environment for bone regeneration and vascularization, as well as an ideal strategyto prevent bone implant-associated infections.

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O20: Dental pulp stem cells enhance the maturation of an engineered microvascular network for tissue regeneration: an in vivo study

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*** co-first, β co-last**

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Keywords: Tissue engineering, pre-vascularization, DPSCs.

ABSTRACT

One of the main challenges of tissue engineering is the rapid perfusion of the implanted tissue construct for providing nutrients and oxygen to the damaged organ. Pre-vascularizing tissue constructs *in vitro* with capillaries that can rapidly anastomose to the host vessels[1] upon implantation is a promising strategy. Using stem or progenitor cells is an appealing option since they both release proangiogenic factors[2] and can also be recruited as perivascular cells to promote vessel maturation[3,4]. The aim of the present study was to investigate the capacity of dental pulp stem cells derived from deciduous teeth (SHED) to promote capillary formation and stabilization in a tissue construct grafted *in vivo*. We here studied 3 conditions in which the tissue construct was held in a human tooth slice and cultured for 96h *invitro* prior to subcutaneous implantation in nude mice[2]: 1) a mixture of EC and SHED (EC-SHED), 2)EC treated with SHED conditioned medium (EC-SHED-CM), and 3) SHED alone as control. Angiogenesis was then investigated at 4 weeks using micro-CT following intracardiac contrast agent injection and characterized by immunohistochemistry (von Willebrand Factor, Podocalyxin, Collagen IV). The pre-vascularized construct EC-SHED showed significantly increased vascularization and innervation when compared to the other groups. In addition, the presence of SHED i) favored the stabilization of the engineered vessels via their recruitment as perivascular cells and secretion of type IV collagen in the vascular basement membrane, and ii) decreased cell apoptosis within the constructs as evidenced by TUNEL assay. Furthermore, the engineered vessels were perfused by blood cells, supporting the interest of pre-vascularization using SHED for tissue engineering applications[5].

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O21: CONTRAST-ENHANCED COMPUTED TOMOGRAPHY FOR NON-INVASIVEMONITORING OF TISSUE-ENGINEERED CARTILAGE IMPLANTS

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Keywords: cartilage tissue engineering, biomaterials, 3D imaging

The avascular nature of the cartilage impedes the spontaneous healing of chondral injuries. These lesions can progress to more serious degenerative articular conditions as in the case of osteoarthritis.As no efficient cure for cartilage lesions exist yet, cartilage tissue engineering has emerged as a promising method aiming at repairing joint defects and restoring articular function. Currently, assessment on the quality and composition of the engineered cartilage mainly relies on destructive methods, such as immunohistology. Therefore, there is a need for the development of techniques that allow for longitudinal imaging and non-destructive monitoring of cartilage-engineered constructs. Contrast-enhanced computed tomography (CECT) is a young field of research but it has a high potential within the field of biomedical research because of its minimally invasive character and its possibility to produce 3D datasets that allow structural analysis of biological tissues. This method has been introduced for the evaluation of cartilage integrity, *ex vivo*, following the explantation of joints of animal or human cadavers. Here we tested the possibility of using the CECT to non-invasively monitor the stability of tissue-engineered cartilage implants, using a large animal model.

Cartilage constructs, prepared *in vitro* with autologous chondrocytes combined with hydrogels, were implanted in articular defects created in the femoral condyles of cynomolgus monkeys. The joints were monitored non-invasively by CECT and a 3D surface rendering of the joints was built from 2D section images. The joints were first examined 40 days before implantation to obtain reference images of healthy joints and, after the creation of the defects, 6 days before implantation to obtain reference images of empty defects. The joints were then imaged 41 days and 82 days after implantation, the final phase of the study when the animals were euthanized and the joints treated for histological examination.

The 3D surface rendering of the joints predicted over the course of the study was in good concordance with our final macroscopic and histological observations. To our knowledge, our study is the first to show 3D surface rendering of cartilage grafts on live animals. We have successfully demonstrated theefficacy of this method to non-invasively investigate the cartilage implant integration in an experimental model that is very close to humans, particularly in mimicking the native biomechanics of the joints. This opens the possibility that CECT-based 3D imaging may be used to survey postoperatively tissue-engineered cartilage implants in human patients.

O22: AN IODINE-LABELED INJECTABLE HYALURONIC ACID HYDROGEL: A RADIOPAQUE BIOPOLYMER TO TRACK THE FATE OF BIOSCAFFOLD IN CELL THERAPY APPLICATIONS

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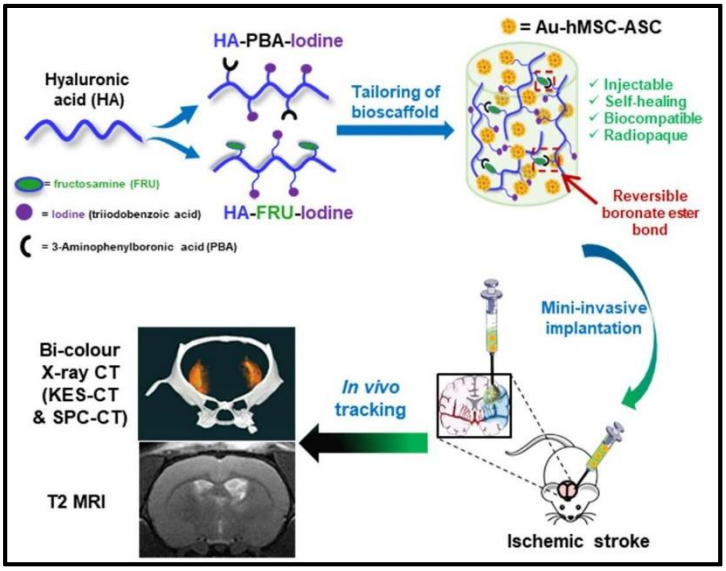
Key words: Injectable hydrogel, Cell therapy, bi-colour imaging techniques

Cell therapy has recently emerged as a promising approach to treat ischemic stroke by replacing the lost cells and by stimulating endogenous self-repairing mechanisms[1]. Unfortunately, a major issue in stem cell transplantation is the substantial loss of transplanted cells, which can be as much as 80-99% of the total number of grafted cells[2].To overcome these issues, injectable hydrogels combined with stem cells have sparked great interest as they can improve cell retention at the lesion site and survival[3]. For this purpose, we proposed to use a recently developed hyaluronic acid (HA) hydrogel, that exhibits self-healing and injectability properties, as a biomimetic scaffold for delivery of transplanted cells in the brain lesion[4]. As a combined advanced therapy medicinal product candidate, an *in vivo* follow-up is required to monitor both the fate of the hydrogel scaffold and cells in a long temporal window.

In this context, a radiopaque iodinated-labeled HA hydrogel (HA-I) was synthesized for bi-colour imaging using K-Edge subtraction computed tomography (KES-CT) and spectral photon-counting computed tomography (SPCCT). This hydrogel was simply prepared by mixing two modified HA partners in physiological conditions that can self-crosslink *via* boronate ester bond formation.

Human adipose-derived mesenchymal stem cells (hASC) encapsulated in the hydrogel showed high viability. In addition, the hydrogel could be easily injected in the brain and monitored by a magnetic resonance image (MRI). Finally, gold-labeled hASC (Au-hASC) were embedded within HA-I hydrogel, then intracerebrally injected in healthy rats. An *in vivo* tracking using the bi-colour X-ray imaging techniques showed both the HA-I hydrogel and theAu-hASC in the brain. In conclusion, bi-colour images were obtained showing the grafted Au- hASC encapsulated in the HA-I hydrogel in the brainof rats.



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O23: Porous yet dense, using ice to shape biomimetic materials for 3D cell culture applications

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Keywords : Ice-templating, collagen, 3D cell culture

ABSTRACT

Three dimensional cell culture scaffolds are expected to bridge the gap between traditional *in vitro* cell culture and *invivo* models. Here, we report recent results in the development of new 3D cell culture systems based on ice templatingof biopolymer solutions. Ice templating relies on the use of controlled ice crystal growth to create porosity. The process is easy to implement, cost effective and applicable to a wide range of materials. Since it relies on the use of low temperatures to shape materials, ice templating has sparked growing interest to shape biological matter which isparticularly prone to thermal denaturation, ranging from biomolecules up to living cells[1,2].

Here we explore how ice templating can be modulated to induce the supramolecular assembly of type I collagen - exhibiting the textural and mechanical features of the extracellular matrix[3] – while imposing a controlled macroporous structure that favors cell colonization, as well as nutrient and gas diffusion. The unlikely combination of macroporosity and local high concentration developed during freezing[4] provides a beneficial setting to create materials that gather the advantages of dense collagen matrices without presenting their common limitations such as hypoxic zones due to limited gas diffusion.

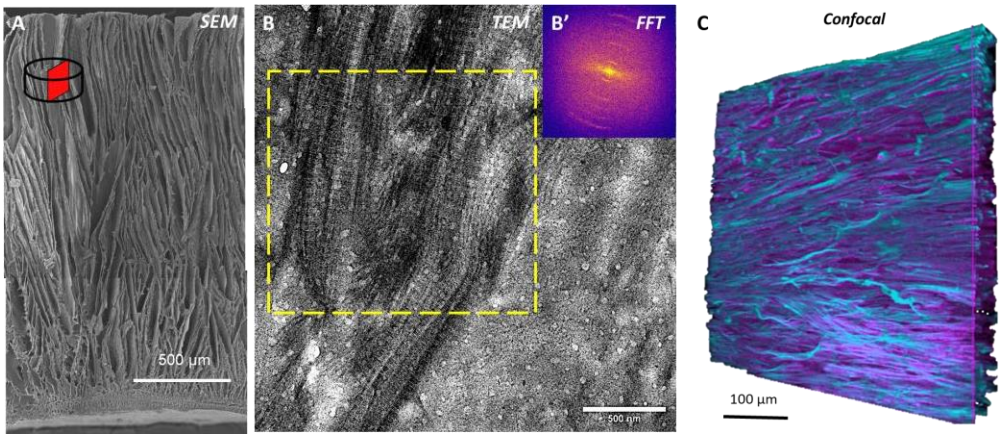

Figure 1. Multiscale organization of collagen matrices shaped by ice. A) Macroporous collagen matrix obtained by icetemplating observed under SEM. B) Fibrillar motifs of macroporous collagen matrix observed under TEM. B') 2D FFT ofdashed yellow region highlighting the fibrillar motifs and orientation. C) NHDF colonization of ice templated collagen scaffold. SHG and fluorescence 3D reconstitution from confocal microscopy[3]. Magenta codes for collagen SHG signal and cyan codes for actin.

We will discuss how the motifs developed during freezing enable successful migration and colonization of human fibroblasts (NHDF) and C2C12 murine myoblasts across the 3D biomimetic collagen scaffolds. Moreover we will discuss recent results showing the how these porous matrices compare with equivalent non-porous collagen matrices in termsof kinetics and extent of collonization[5], opens an exciting pathway to achieve new biomimetic 3D cell culture materials systems with enhanced physiological relevance.

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O24 : CROISSANCE AXONALE STIMULÉE PAR MODIFICATION DE SURFACE ÀL'AIDE DE PROCÉDÉS CHIMIQUES ET PHYSIQUES

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Mots clés : régénération axonale, biomatériaux, fonctionnalisation de surface

Les maladies dégénératives progressives et les lésions du cerveau ou de la moelle épinière affectent, indifféremment, les personnes jeunes et en bonne santé, ainsi que les personnes âgées. Ces maladies conduisent à des situations ravageuses qui touchent dans le monde des milliers d'individus par an. De nombreuses stratégies visant à réduire les blessures secondaireset l'inflammation ainsi que le remplacement des oligodendrocytes "myélinisantes" ont été favorisées. Cependant, les thérapies de remplacement cellulaire ou d'ablation, dans le cas de tumeurs ou d'AVC, avec le risque évident de détruire des tissus sains, sont favorisées depuis longtemps. Bien que ces stratégies ont été clairement désignées comme axes prioritaires par larecherche pour la "réparation du cerveau", la régénération axonale et son guidage restent la voie par "excellence" de la recherche pour la réparation du nerf.

Mon projet de recherche vise à l'élaboration d'un dispositif implantable et électroactif pour la réparation du nerf dans le système nerveux central et périphérique. A ce jour, l'utilisation d'un champ électrique (CE) pour la réparation du nerf a démontré sa pertinence, car elle augmente et dirige la croissance des neurites. [1] Cependant, les paramètres influençant cette croissance et son guidage, tels que l'amplitude du CE, la rigidité du substrat et son énergie d'adhésion, n'ont pas été étudiés. Dans un premier temps, l'objectif sera l'optimisation de l'effet du CE localsur les processus de neuritogénèse et de la régénération, grâce à un dispositif expérimental original, aisément (bio)fonctionalisable et permettant l'application de méthodes d'imagerie et decaractérisation physiques innovantes, associée à des études biologiques in vitro approfondies.

Ce projet a d'abord nécessité un approfondissement des connaissances concernant l'effet d'unchamp électrique local et d'une fonctionnalisation de la surface d'adhésion sur le contrôle de lacroissance axonale et des propriétés mécaniques des cellules. [2] La conception d'un dispositifde stimulation 2D des cellules a permis de caractériser ces propriétés diverses, de comprendre l'effet de la modification chimique de surface sur les cellules [3] et d'exciter les motoneurones de manière à constater l'effet du champ électrique. Nous observons actuellement un effet positif de cette stimulation sur les cellules étudiées et travaillons à une caractérisation approfondie. Ces derniers résultats laissent penser que l'usage d'une combinaison de stimulations chimique et physique de la surface pourrait conduire à un traitement intéressant pour la thérapie régénérative.

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O25: HYDROGELS OSCILLANTS EN INTERACTION FLUIDE/STRUCTURE : VERS LE DESIGN DE PLIS VOCAUX BIOMIMETIQUES

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Mots clefs : plis vocaux ; hydrogels oscillants; interaction fluide/structure

Introduction – En cas de cancers laryngés avancés, la restauration des capacités phonatoires des patients par des implants artificiels capables de mimer les vibrations des plis vocaux reste un défi scientifique, clinique et sociétal. Ce défi nécessite le développement de matériaux capables d'imiter les caractéristiques vibromécaniques des plis vocaux humains ou "cordes vocales" : capacités (i) d'endurer de grandes déformations réversibles sous chargements multiaxiaux [1], (ii) de vibrer dans une large gamme de fréquences fondamentales (50 à 1500 Hz). Les hydrogels sont des candidats attrayants en raison de leurs propriétés élastiques ajustables, et de leur teneur en eau comparable à celle des tissus [2,3]. Cependant, leurs propriétés vibratoires restent peu étudiées à ce jour, ou dans des configurationsmécaniques encore bien éloignées de la réalité physiologique. L'objectif de ce travail est d'élaborer des hydrogels aux propriétés mécaniques contrôlées, capables de reproduire les auto-oscillations caractéristiques du pli vocal humain en interaction fluide/structure.

Méthodes – Une première formulation d'hydrogels à base de gélatine porcine à 10 %m/v et d'un agent réticulant de concentration ajustable a été optimisée, en tenant compte des propriétés mécaniques des tissus natifs des plis vocaux et de celles des maquettes *in vitro* de la littérature. Les hydrogels et matériaux de référence ont d'abord été testés à l'aide d'une machine de traction uniaxiale. Trois modes dechargement ont été étudiés, comme précédemment sur les tissus natifs [4] : traction, compression, cisaillement. Dans un second temps, ces matériaux ont été mis en forme dans une géométrie 3D réaliste du pli vocal à l'aide de moules imprimés en 3D, puis leur capacité à auto-osciller a été mise à l'épreuve grâce à un banc d'essais dédiéà flux d'air contrôlé.

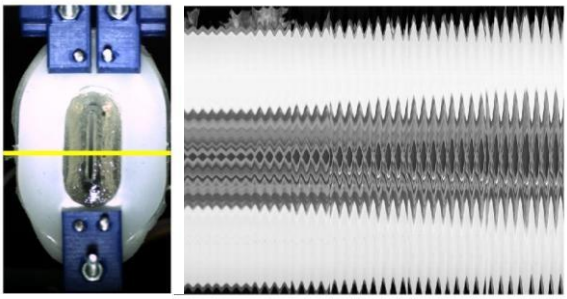

Figure 1: Illustration d'une maquette 3D de pli vocal à base d'hydrogel, et pattern vibratoire associé en fonction du temps.

Résultats – L'optimisation de la formulation chimique des hydrogels permet d'approcher les propriétés mécaniques en compression et cisaillement du pli vocal, et des silicones élastomères de référence utilisés *in vitro*. La comparaison reste satisfaisante en traction entre les différents matériaux de synthèse étudiés, isotropes. Des patterns vibratoires très prometteurs ont été obtenus pour les hydrogels ainsi optimisés (Fig. 1), capables d'osciller à basses fréquences à des pressions d'air sous-glottique proches de la réalité physiologique. Si cette étude montre le lien entre propriétés matériaux et performances aéro-acoustiques des plis vocaux de synthèse, la mise en œuvre de futurs hydrogels 3D oscillants et nanostructurés devrait permettre de reproduire les propriétés non-linéaires anisotropes du tissu natif en traction, et de vibrer dans une plus large gamme de fréquences.

Remerciements: ANR MICROVOICE N° ANR-17-CE19-0015-01.

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O26: IN VIVO STUDY AND WEAR MODEL TO PREDICT THE DAMAGE ANDRESISTANCE OF RECONSTRUCTED ACL

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Keywords: anterior cruciate ligament, implant damage, surgery planning

Anterior cruciate ligament (ACL) reconstruction is a common surgical procedure with overall good outcomes. Nonetheless, the ætiology of ACL reconstruction failure is often unclear. Impingement —interference of the implant with other structures like bone — is considered a major main reason of failure. Impingement is highly sensitive to anatomical variability and graft positioning during surgery.These uncertainties raise a special concern for preclinical trials, since the anatomy of sheep, standard animal model used for ACL grafts, is particularly prone to ACL impingement. In this study, we used a sheep model of arthroscopic ACL reconstruction to explore the origin of implant damage. For that, 7 sheep underwent ACL reconstruction using tendon autografts. The limbs were explantedat three months after implantation. For each specimen, low-dose biplanar radiographs were obtained with EOS and 3D reconstructions were performed using a reconstruction algorithm. The cadaveric sheep knee specimens were then tested in vitro using a specific motorized device previously developed to obtain knee kinematics in flexion-extension. Graft damage was characterized by necropsy observations and ultimate tensile strength (UTS) measurements. The 3D images and kinematic data were used to construct a digital model of each knee (Figure 1). Strain, torsion angle and impingement volume underwent by the graft during a knee bending cycle were computed from the position of the femur and tibia during flexion-extension. When compared to UTS, these geometrical criteria, however, fail to explain the resistance of the grafts in vivo. A wear model was thus proposed integrating kinematic data. Wear against the femoral surface showed a strong negative correlation with UTS and explained the differences in UTS among the specimens (Figure 2). The simplicity of this wear criterion permits its direct use in surgery planning as a way to minimise the risk of implant failure. Its application to sheep anatomy provides a straightforward wayto increase efficiency and predictive power of preclinical testing, reduce the costs, time and numberof animals.

Figure 1: 3D images of femur and tibia and real kinematic data used to build a patient-specific model of knee flexioncycle

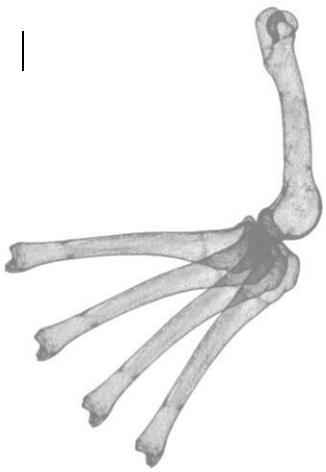
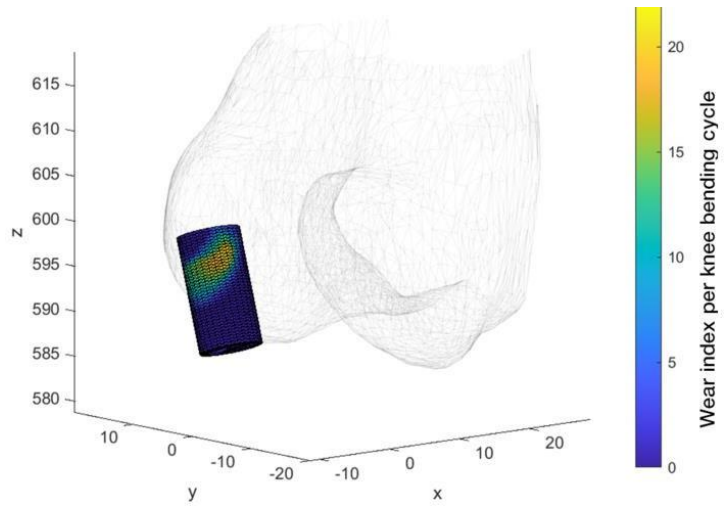


Figure 2. Model results (left) were compared to experimental data (right). Wear criterion captures the damage zones ofthe implant (triangle on the graft in the right image)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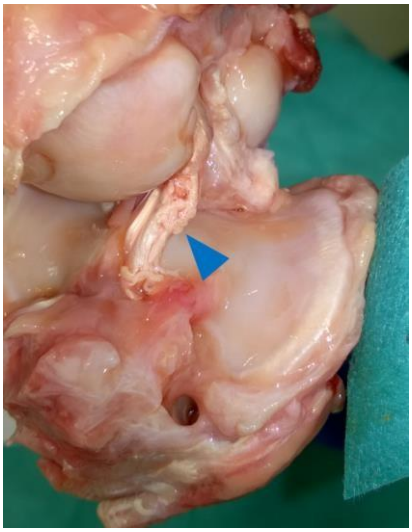
Wear index per knee bending cycle



Friday, October 22nd, 2021

‘Architectures and cell fate’ session

O27: EVALUATION OF CU^{2+} DOPING POTENTIAL TO CONTROL THE CALCIUM- PHOSPHATE PARTICLES-INDUCED ACUTE INFLAMMATORY RESPONSE INBONE SITE

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Keywords: Cu^{2+}-doped CaP, acute inflammation, PMN

Introduction

Calcium phosphates (CaP) are widely used as prosthesis coating and bone substitute. Cationic substitutions (e.g., Sr^{2+}, Zn^{2+}) in CaP have been shown to control the biomaterial particles- induced inflammatory process [1-2]. Copper ion (Cu^{2+}) is known for its antibacterial potential and Cu-doped CaP has been demonstrated biocompatible in previous studies [3-4]. The presentwork aims to evaluate *in vitro* the effect of copper on CaP-mediated human primary neutrophilsactivation and biomaterial-induced recruitment of blood neutrophils *in vivo*.

Materials and methods

Cu-doped or undoped CaP powders obtained by two different processes (*i.e.*, sol-gel (SG) and aqueous precipitation (AP)), were studied. Human primary neutrophils (PMNs) were isolated from blood (n=9-12 healthy donors) then cultured in the presence of CaP particles alone, or inco-stimulation with lipopolysaccharide (LPS). IL-8 and TNF-α concentrations were determined in conditioned culture supernatants by ELISA, MMP9-related gelatinolytic activity was examined by zymography and cell viability assessed by measuring lactate dehydrogenase activity. Neutrophil Extracellular Traps (NETs) formation was imaged thanks to Scanning Electron Microscopy. Using the air pouch model, the ability of doped and undoped powders tomodulate PMNs recruitment *in vivo* was investigated (n=10-16 mice). Recruited-cells in the air-pouch were collected, numbered then identified thanks to flow cytometry.

Results and discussion

CaP SE powders were well tolerated as we only noticed a slight variation in LDH activity whilethe increase in LDH signal observed with AP samples seemed to be reduced in the presence ofcopper. Cu-doped samples stimulated the release of IL-8, exhibiting a copper dose-dependent effect, especially with LPS co-stimulation. All CaP materials failed to induce the production ofTNF-α by neutrophils, but tended to decrease its concentration in LPS-stimulated PMNs supernatants. Undoped samples generated an increase in MMP9-related gelatinolytic activity which was not potentiate by LPS addition, whereas in this latter condition Cu-doped samples reduced the gelatinolytic activity. *In vivo,* all powders induced an increased recruitment of totalleukocytes. Cu-doped AP samples increased the PMNs recruitment compared to undoped samples whereas monocytes/macrophages recruitment was decreased.
We demonstrated here a robust immunomodulatory effect of Cu-doped CaP powders, that occurs independently of the synthesis route. Our study suggests that such doped samples may be interesting to maintain a moderate level of inflammation to ensure the bacterial clearance byPMNs besides of anti-microbial potential of the material in infected bone context.

Acknowledgments

Authors would like to thank Institut Carnot MICA and « Fondation des Gueules Cassées » forfunding the project and the URCA PICT platform for imagery.

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O28: FEMTOSECOND LASERS STRUCTURED TITANIUM DENTAL IMPLANTSIN REGULATING BACTERIAL ADHESION

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Biological complications related to bacterial engraftment on rough titanium are an issue in the design of new functionalized dental implants. Specific bio-inspired nano- topographies are described to limit bacterial adhesion and growth. By fine-tuning femtosecond lasers (FSL) parameters, we aim to design nanoscale textured surfaces withunique antibacterial properties. In an oral biology context, bacteria of interest are*Streptococcus mutans* (*S.mutans*) and *Porphyromonas gingivalis* (*P.gingivalis*), known to be associated with peri-implantitis and dental implants failure.

Samples made of Titanium (Ti6-Al4V), are irradiated at 3 different FSL wavelengths (namely 1030-515-257 nm), to produce various types of Laser-Induced Periodic Surface Structures (LIPSS), which periodicity are ranging from 600nm to 160nm. We investigate *S.mutans* and *P.gingivalis* adhesion after 24 to 48 hours to textured surfaces by comparison to mirror polished titanium samples.

We revealed that LIPSS periodicity and morphology (linear or radial) are determinant for anti-bacterial properties. When LIPSS period is larger than bacteria's diameter (600nm LIPSS obtained with a 1030nm wavelength), *S.mutans* (≈325nm) and *P.gingivalis* (≈200nm) are mechanically retained in LIPSS valleys, interestingly if LIPSS period is smaller than bacteria diameter (LIPSS ≤300 nm), the surface becomes more repulsive than mirror polished titanium. Additionally, we demonstrate that nanospikes-like texturing, obtained by breaking the linear periodicity of LIPSS with radial polarization at 1030 nm, also increase the antibacterial properties of titanium.

In conclusion, as it gives the possibility to reduce areas of contact between biomaterials and bacteria, FSL appears as an innovative tool to produce anti-bacterial nano-LIPSS giving the opportunity to improve the natural bacteriostatic properties of titanium, and sodecrease dental implants failure.

Keywords: Femtosecond lasers, Laser-Induced Periodic Surface Structures, antibacterialtextured surfaces.

O29: An expected antibacterial and immunomodulatory properties of acellularWharton's jelly matrix.

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Of all biologic matrices, decellularized tissues have emerged as a promising tool in the fields of regenerative medicine. Few empirical clinical studies have shown that human Wharton's jelly (WJ) of the human umbilical cord promotes wound closure and reduces wound-related infections. It was in this scope that we investigated if decellularized (DC)-WJ could be used as an engineered biomaterial. Following thefull removal of cell membranes and nuclei moieties from Wharton's jelly (WJ) tissue, no major alterations in the ECM components (*i.e.* collagen, GAG content and growth factors), physical (*i.e.* porosity and swelling) and mechanical (*i.e.* linear tensile modulus) properties were noticed. Interestingly, an increase in macromolecules and growth factors release was observed for DC-WJ, assuring thus a suitable bioactive matrix for cell maintenance upon recellularization. Based on the *in vitro* and *in vivo* biodegradability and stromal cell homing capabilities, DC-WJ provided an ideal substrate for stromal cells adhesion and colonization. In comparison with devitalized (DV)-WJ, our results showed bacteriostatic and antiadhesive effect of DC-WJ on Gram positive (*S. aureus* and *S. epidermidis*) as well as Gram negative (*E. coli* and
P. aeruginosa) strains. Although DC-WJ activated the neutrophils and monocytes in comparable magnitude than DV-WJ, macrophages modulated their phenotypes and polarization states from the resting M0 phenotype to the hybrid M1/M2 phenotype in the presence of DC- WJ. M1 phenotype was predominant in the presence of DV-WJ. Finally, the subcutaneous implantation of DC-WJ showed a total resorption afterthree weeks of implantation without any sign of foreign body reaction. Used as a membrane for guided bone regeneration, few bone regeneration evidence was found at the marginal area of the a rat calvarial defect. The limited bone regeneration could be attributed to the immunomodulatory properties in favor of M2 phenotype but alsoto lack of sufficient mechanical strength and collapse of the membrane into bone defect area. These significant data shed light on the potential regenerative application of DC-WJ in providing a suitable biomaterial for soft tissue regenerative medicine and an ideal strategy to prevent wound-associated infections. An increasein the mechanical features of DC-WJ in hydrated conditions is in progress.

O30: DENSE 3D PRINTED COLLAGEN HYDROGELS MIMICKING EXTRACELLULAR MATRIXFOR TISSUE ENGINEERING APPLICATIONS

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Keywords : Collagen, anisotropy, porosity, extracellular matrix

ABSTRACT

Thanks to its biocompatibility and its biodegradability, collagen I is broadly used in tissue engineering to develop biomaterials such as dermal substitutes, scaffolds for neurons guidance or cardiac patches[1]. Collagen based hydrogels, usually fabricated from low concentrated collagen solutions, are characterized by poor mechanical properties and low physical stability with a significant shrinkage by encapsulated cells[2]. To circumvent these drawbacks, the addition of synthetic polymers or cross-linking are required to improve collagen hydrogel properties[3]. An original approach is to increase collagen concentration. Dense collagen hydrogels concentrated at 30 mg.mL^{-1} exhibit high mechanical properties, do not shrink and are stable over several weeks after *in vivo* implantation[4]. However, their high collagen concentration limits cell colonization and vascularization from the host. In this study, macroporous dense collagen I hydrogels have been developed to mimic extracellular matrix physical properties while favoring cell migration. In addition, intrinsic anisotropy of collagen fibrils has been set up within hydrogels to favor cell alignment which is required for axon growth or cardiomyocyte organotypic growth. Dense fibrillar collagen hydrogels concentrated at 30 mg/ml were 3D printed to create the suitable shape required for specific applications. By tuning the extrusion velocity of the concentrated collagen solution within a selected buffer bath, 3D printing allowed to generate constructs exhibiting a collagen molecules alignment (intrinsic anisotropy). The modulation of the fibrillogenesis conditions by incubation in PBS and/or ammonia impacted the diameter of aligned fibrils and the hydrogel mechanical properties. The phosphate buffer enable anisotropy occurrence while ammonia improved mechanical properties. Cells seeded on top of hydrogel layers were sensitive to anisotropy since human fibroblasts aligned along the axis of 3D printed constructs (Figure 1). The 3D printing scaffolds, consisting of 1-10 layers of aligned collagen, exhibited an intrinsic porosity of 50-100 µm in diameter between the different layers (Figure 2-B). This porosity is an asset for colonization by endothelial cells. In addition, a macroporous hydrogel is more easily integrated *in vivo*. To increase the scaffold porosity, macroporous channels were added with sacrificial matrix printing or needles molding (Figure 2-C) to create channels ranging from 100-500 µm. These bigger channels were set up for a cardiac tissue engineering application. Indeed, cardiomyocytes need a larger volume to adopt their organotypic organization. Taken together, these results demonstrate the usefulness of 3D printing of dense collagen solutions to develop anisotropic and porous biomimetic scaffolds with a specific shape for tissue engineering applications.

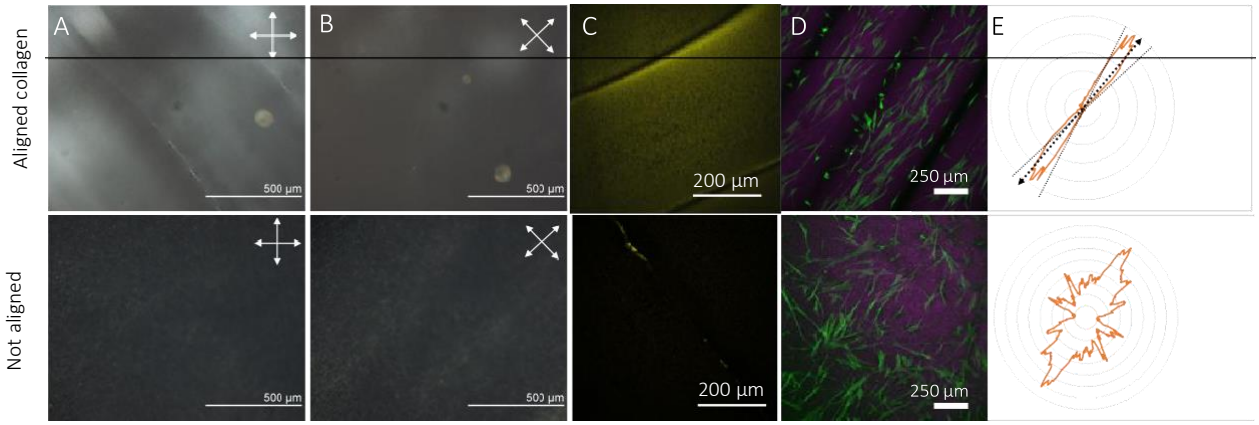

Figure 1: Comparison of aligned and not aligned collagen. A-B Polarized light microscopy with a 45° rotation between the two images, collagen birefringence must be observed if aligned. C- Second harmonic generation microscopy, signal intensity is proportional to collagen quantity and alignment. D- Normal human dermal fibroblasts cultivated for 48h on the collagen samples and immunostained with Phalloidin (green). Purple corresponds to SHG signal acquired simultaneously. E – Cell orientation analyzed by Image J Orientation J plug-in. The dark arrow corresponds to filament orientation and the dot lines to a 20° angle around filament orientation.

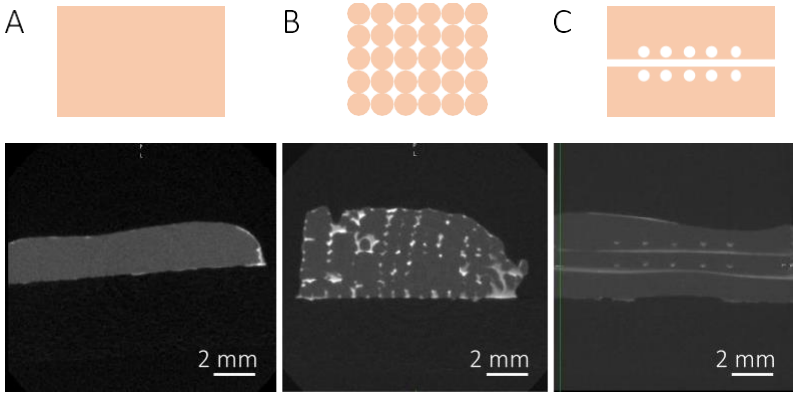

Figure 2: The range of porosity. A- Molded collagen hydrogel, no porosity. B- 3D printed collagen hydrogel, intrinsicporosity between filaments. C- Macroporous channels in molded collagen.

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O31: Influence of cellular mechanical environment on periodontal ligament fibroblasts behavior: an *in situ* investigation

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Keywords: Periodontal regeneration, bioreactor, mechanotransduction

ABSTRACT

Dental loss due to periodontal diseases remains a major issue for clinical dentistry. The further development of periodontal regeneration strategies is still needed. In this context, the scientific community increasingly focus on tissue engineering as a promising technique to elaborate efficient biomaterials. Nevertheless, one has to accurately understand the mechanisms involved in periodontal regeneration to develop a sustainable engineeredproduct that can withstand the periodontal environment. More specifically, the periodontal ligament is subjectedto a complex mechanical environment [1]. It is well known that this mechanical environment has a significant influence on cells behaviour. Thus, we aim to investigate the influence of mechanical solicitations on human periodontal ligament fibroblasts behaviour cultured *in vitro*.

Poly(ε-caprolactone) (PCL) and Poly Lactic-co-Glycolic Acid (PLGA) matrices were chosen as cellular supports. 3D scaffolds were synthetized through electrospinning process associated to a rotating stainless steel, 6 mm in diameter. This resulted in crown shaped matrices, with a wall thickness close to 1 mm. Such a shape was chosen to mimic the shape of the periodontal ligament around the dental root. In that way, the scaffolds can be solicited somewhat in a similar manner as the ligament is, with a compressive load along the main axis of the tooth. Moreover, in that conditions, the cells' activity can be assessed in this specific geometry. These scaffolds morphologies were investigated using a scanning electronic microscope (see figure 1).The mechanical loading device is a recently developed bioreactor allowing an *in situ*monitoring of the cells behaviour under a specific mechanical environment, either compressive or shear loadings (or both) [2]. Using this experimental device, we are able to follow the evolution of the scaffolds' mechanical properties with culture time while assessing physical properties through confocal microscopy combined to fluorescent staining.

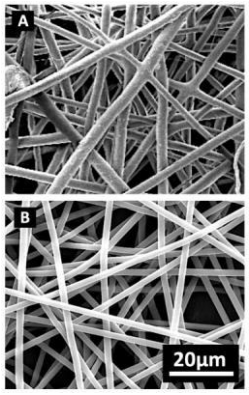

Figure 1 PCL (A) andPLGA (B) matrixes morphology

Human periodontal ligament fibroblasts were cultured in direct contact of the tested scaffold in standard static conditions. After 7 days of incubation, the cellular culture was kept going under dynamic conditions within the bioreactor. Mechanical and physical properties of the dynamically culture scaffolds were then compared to control samples without cells. Moreover, key cellular stress parameters were also assessed within the scaffold before and after the mechanical treatment.

The behaviour of fibroblasts was different between the control and the loaded group, and between the matrixes. This study highlights the importance of considering the cells' mechanical environment when developing biomaterials for periodontal ligament regeneration through tissue engineering strategy.

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O32: DEVELOPPEMENT D'AUTO-ASSEMBLAGES PROTEIQUES POUR LACONCEPTION DE MATERIAUX INTELLIGENTS

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Mots-clés : Particules virales, RGD, Devenir cellulaire

RESUME

Les organismes vivants ont développé au cours de l'évolution une très large gamme de protéines capables de s'auto-assembler et de former des objets 3D de forme et de fonction spécifiques. Différentes structures biologiques sont issues de ces auto-assemblages comme les capsides de virus ou les éléments du cytosquelette des cellules (microtubules, filaments d'actine). Certaines capsides de virus, produites *in vitro*, forment des nanoparticules auto-assemblées non infectieuses appelées VLPs (Virus Like Particles). Organisées à partir de l'association répétée de monomères, ces particules constituent spontanément des architectures moléculaires répétitives et bien définies ayant un intérêt particulier en médecine et dans le domaine des nanotechnologies.

Nous présentons ici l'élaboration de VLPs dérivées du bactériophage AP205 modifiées génétiquement pour permettre le contrôle du comportement cellulaire à la surface de matériaux. Ces capsides virales sont constituées de 180 monomères dont les parties N- et C- terminales sont exposées à la surface et permettent de présenter des peptides bioactifs.

Nous avons généré par clonage des variant d'AP205 présentant le peptide d'adhésion RDGet le peptide ostéogénique dBMP2. Les VLPs ont été produites en système d'expression bactérien et purifiées par affinité et chromatographie d'exclusion stérique. Leur visualisation par microscopie électronique à transmission montre que les protéines de capsides modifiéess'assemblent bien en particules de 30 nm de diamètre. L'adsorption des particules RGD sur une surface de PDMS permet l'adhésion de cellules de souris C2C12. La stœchiométrie et la concentration en motifs RGD présentés donnent la possibilité de contrôler l'étalement et le nombre de cellules sur les surfaces de culture. Des peptides de différentiation ont égalementété ajoutés avec succès sur la VLP et les propriétés ostéoinductrices de ces particules ont étéétudiées. Les résultats obtenus montrent l'intérêt d'utiliser les VLPs recombinantes pour moduler le comportement cellulaire. Nous discuterons également de la formation de particules d'AP205 multifonctionnelles et de leur valorisation dans la conception de nouveaux biomatériaux.

O33: DESIGN OF INJECTABLE AND POROUS HYDROGELS AND THEIR POTENTIAL AS SUPPORT FOR SKELETAL MUSCLE TISSUE ENGINEERING

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Keywords : Injectable-porous hydrogels; Skeletal muscle regeneration

Volumetric muscle loss (VML) resulting from traumatic incidents drastically decreases muscle regeneration capacity and lacks treatments[1]. Injectable hydrogels are promising therapeutic candidates, but their regeneration potential is strongly reliant on the presence of a porosity to allow cell infiltration[3] and efficient vascularization. Therefore, the aims of this study were (1) to create a porosity inside a recently developed poly-lysine dendrimers (DGL)/NHS-polyethylene glycol (PEG) hydrogel, through a novel biocompatible effervescent approach suitable with its injection and (2) to evaluate the ability of this new formulation to sustain muscle cells progenitor (myoblasts) proliferation and differentiation, for skeletal muscle regeneration purposes.

Effervescent porous hydrogels (EPH) were prepared by dissolving acetic acid (Aa) and potassium carbonate (Kc) to DGL and PEG solution precursors with a surfactant (Fig 1A). We found that with the correct ratio of Aa and Kc, a spontaneous, homogeneous and interconnected porosity was created remnant of the successful entrapment of stabilized CO_2 bubbles in solid hydrogels through a simultaneous cross-linking (Fig. 1B). The use of sole precursor solutions allows to inject the formulations with a dual syringe and a static mixer. Resultant injectable porous hydrogels were proven cytocompatible (Fig. 1C) and biocompatible by subcutaneous injection in mice (Fig. 1D and E) with extensive vascularization (Fig. 1F).

EPH suitability for myoblasts differentiation was assessed by seeding primary human myoblasts[2] (phMs) on the top of 2 mm thick EPH cylinders. Formation of skeletal muscle cells (myotubes) was appreciated with myosin heavy chain (MyHC) and α-actinin antibodies staining after 6 and 14 days in serum-depleted medium showing an extensive cell fusion with visible striation (Fig 2A, B and C). As a striking result, spontaneous contractions of phMs were observed and maintained up to 6 days. The presence of quiescent satellite cells inside EPHwas evaluated with myogenic regulatory factor Pax7, early stage myogenic marker MyoD and cell cycle marker ki67. Clusters of $Pax7^+/Ki67^-$ and $Pax7^+/MyoD^-$ cells were observed 6,10 and 14 days after differentiation inducement, further consolidating EPH potential to support tissue formation by replenishing stem cell niches[3] (Fig 2D and E).

Hence, we describe here a novel porous hydrogel with potential as scalable solution for VML treatments, providing an optimal support for muscle cells progenitors to differentiate into contractile myotubes, while maintaining a pool of stem cells within a swift and straightforward injectable delivery.

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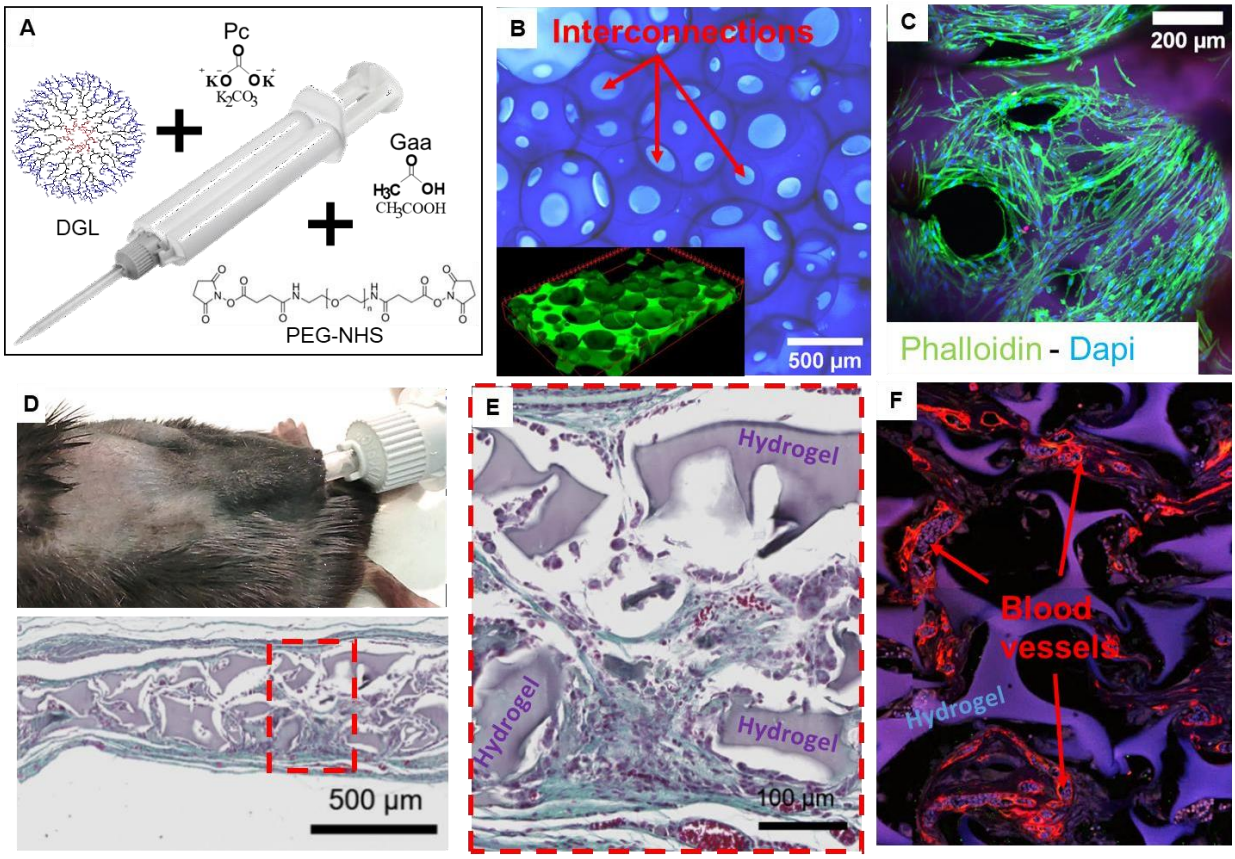

Figure 1 : <u>Formulation of injectable and porous DGL/PEG hydrogel by effervescence</u>
A) System of the dual syringe connected to a static mixer used to form the porous DGL/PEG hydrogel,
B) Formation of an interconnected porous structure made by the successful entrapment of stabilized CO_2 bubbles in solid hydrogel. C) Study of cytocompatibility using primary human fibroblasts (phalloidin in green and dapi in blue). D) Assessment of *in situ* injectability by subcutaneous injection in mice showing E) the formation of an interconnected porosity allowing cellular (in purple) and F) vascular infiltration.

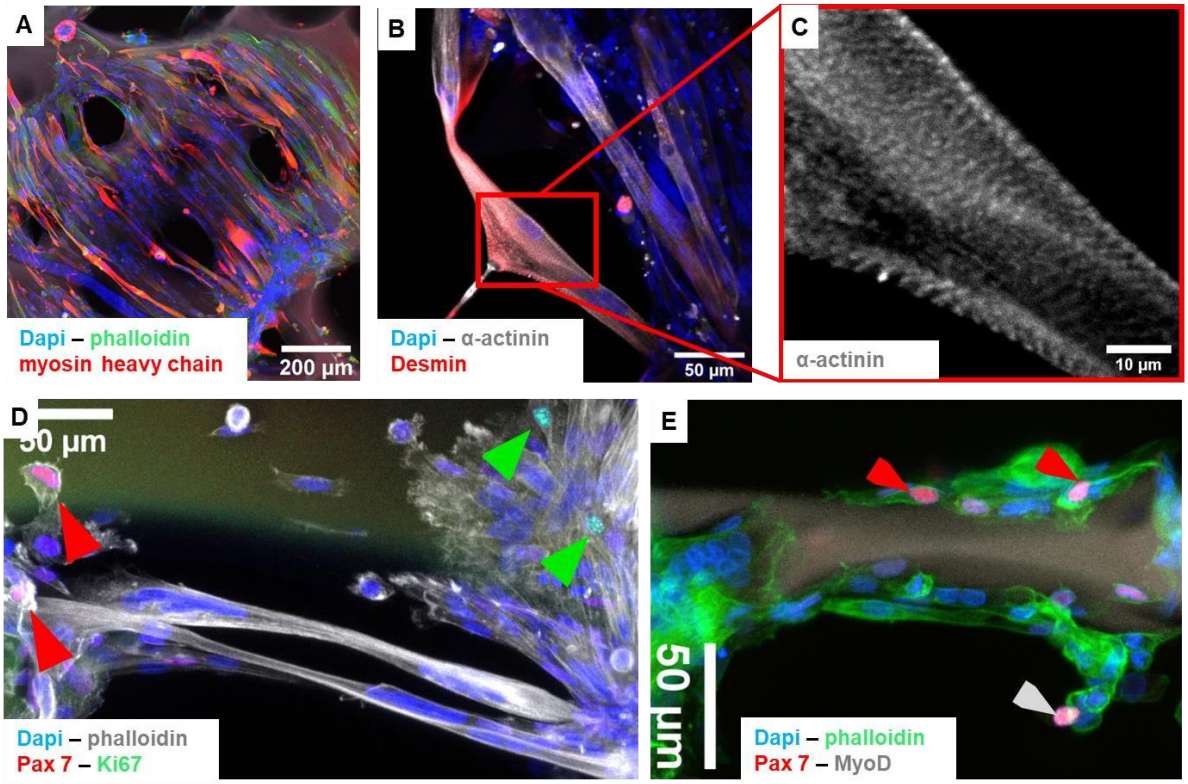

Figure 2 : **Human primary myoblasts inside EPH after 6 days in differentiation**. A) Observation of an extensive myotubes formation (myosin heavy chain in red), B and C) Formation of sarcomeres inside myotubes visible with alpha-actinin staining (in grey) showing myotubes maturation,
D) Observation of mononucleated Pax 7 positive cells (red arrows), non proliferative (Ki67 negative) and E) not entering differentiation (MyoD negative). Green arrows: Ki67 positive cells, Grey arrow :myoD positive cells

O34: HYDROGEL COATING FOR BIOFUEL CELLS TO ENHANCE BIOCOMPATIBILITY AND LONG-TERM FUNCTIONALITY

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Keywords: Hydrogels, Coating, Biocompatibility, Biofuel Cells

ABSTRACT

Miniaturized electrochemical enzymatic biofuel cells hold great potential to power the future generation of implantable medical devices such as continuous glucose monitoring systems. These biofuel cells have potential to harvest energy from the physiological solutes in the body. However, there are a few limitations to such miniaturized devices, particularly with respect to long-term functionality and biocompatibility in the host environment. Formation of fibrous capsules is one of the biggest problems which hinders diffusion between the biofuel cell and the outer environment.

Low molecular weight hydrogels (LMWHs), when used as a biocompatible coating, can help in designing the biofuel cells with long-term stability and biocompatibility. The initial part of this work is focused on characterization and evaluation of different LMWHs to improve degradation kinetics, limit foreign body reaction and allow efficient angiogenesis. The inflammatory reaction to the LMWHs were checked for the foreign body response upon subcutaneous implantation into mice. The hydrogels showed minimal inflammatory response and the formation of a fibrotic capsule was not observed upon 3 weeks of in vivo study. Optimal tissue integration and enhanced angiogenesis was observed due to a pro-angiogenic molecule released during hydrogel degradation. Following the characterization part of LMWHs, one of the studied hydrogels was chosen and used for the coating of a gold electrode, where both the uniformity and thickness of the coating was optimized in order to minimize interference with the analyte and oxygen diffusion.

To conclude, this work aims at identifying an efficient hydrogel coating that could be used to coat the electrodes of biofuel cells. The coating being angiogenic would help in formation of vessels around the electrode without affecting analyte and gas exchange with the surface. This work is expected to contribute to the long-term monitoring of glucose levels by improving biofuel cell biocompatibility and functionality in diabetic patients.

O35: A NEW PLATFORM FOR CULTURE AND ELECTROPORATION OF 3D CELL CONSTRUCTS BASED ON APOROUS SCAFFOLD

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Keywords : Cell spheroids, Electroporation, Porous hydrogel scaffold

INTRODUCTION

Electroporation (EPN) is a method for introducing molecules into cells based on the application of pulsed electric fields. It opens new perspectives for cancer treatment by electrochemotherapy and electro-genetherapy. The study of EPN effects on *in vitro* 3D tumor models could benefit from the development of new tools providing easiness of use, high throughput and results reproducibility.
In the literature, the proposed approaches consist in fabricating the spheroids using droplet-based microfluidics[1] or hanging drop methods[2] and then introduce them in an electroporation cuvette connected to a pulse generator. Thus, it involves several handling steps, which can potentially damage spheroids.
We present a new platform enabling culture of spheroids of similar size and shape, easy introduction offluid and subsequent electroporation inside a unique device integrating a porous hydrogel scaffold.

EXPERIMENTAL

In the device we developed, colorectal adenocarcinoma HT29 cells were seeded in porous microstructured gel after solidification and demolding (Figure 1a) and let grown for 3 days until they filled the microwells[3] (Figure 1b). After placing the hydrogel between two electrodes (Figure 1c) with tubing allowing for the injection of EPN buffer supplemented with an anticancer drug (bleomycin, 20µg/mL), EPN was performed by applying sine burst waveforms whose relevance has recently been demonstrated[4]. To evaluate cellular viability 3 days after EPN, cells were marked with two fluorescent agents: fluorescein diacetate and propidium iodide.

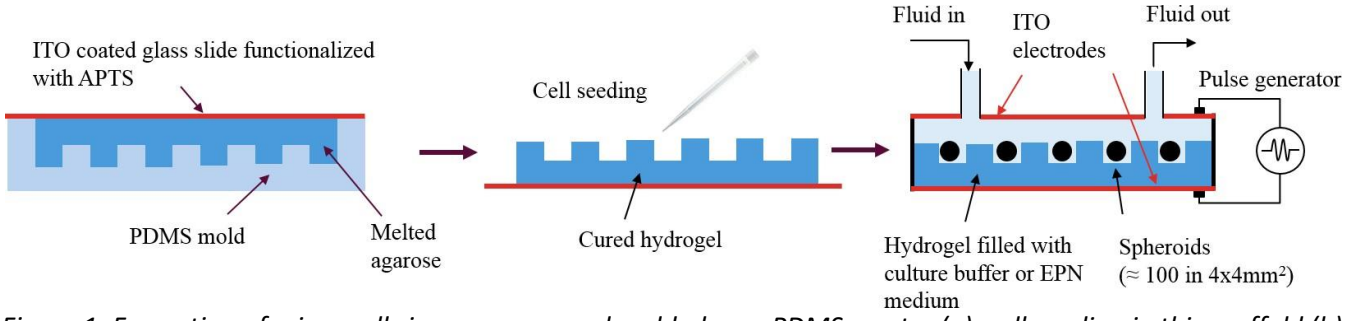

Figure 1: Formation of microwells in an agarose gel molded on a PDMS master (a), cell seeding in this scaffold (b), integration into a microfluidic device composed of two facing electrodes with apertures for fluid inlet and outlet (c).

RESULTS AND DISCUSSION

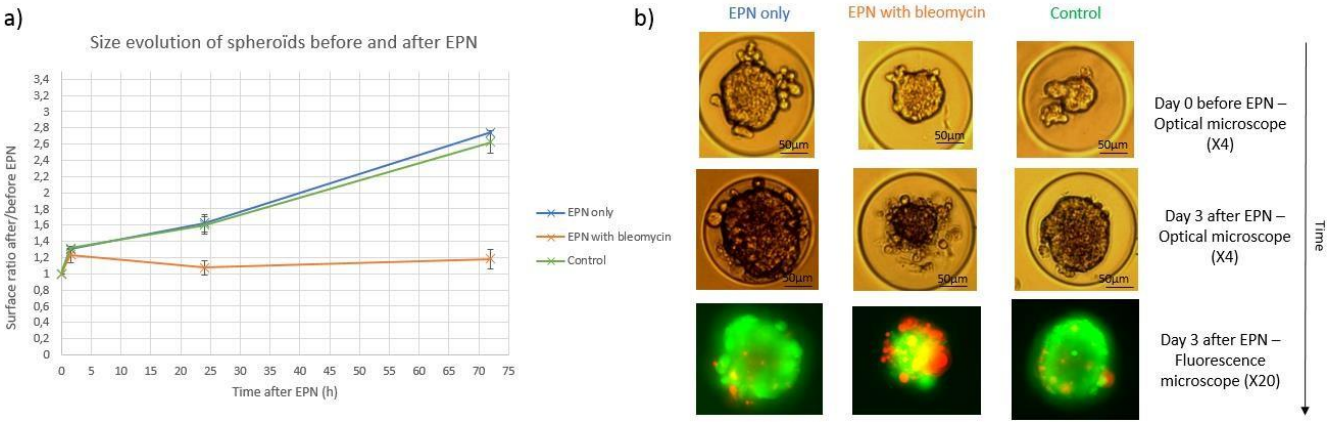

Figure 2 : Evolution of the size of the spheroïds during the experiments (a) and visualization of the size and viability of cells (b) after EPN with or without anticancer drug.

Figure 2a represents the size evolution of spheroids, measured on ImageJ, showing that spheroid growthis inhibited in presence of bleomycin, contrary to the control and EPN without bleomycin groups. This isalso visible on figure 2b, along with the cell viability results suggesting mortality is higher in presence of bleomycin, as the red fluorescence is more present.

After this first application of our device, we intend to study and optimize the kinetics of medium diffusion by changing the hydrogel properties, and to apply EPN to other types of cells, including non-cancerous ones, for sake of comparison.

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ACKNOWLEDGEMENTS

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Abstracts

Poster presentations

Wednesday, October 20th, 2021

FLASH presentations

P1: ALBUPAD technology: Salt-assisted compaction for the design of newbiodegradable albumin-based materials

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Keywords: albumin, material, biocompatible, drug delivery, antimicrobial activity

ABSTRACT

A new era in the design of implantable natural materials should emerge to deal simultaneously with issues related to the toxicity of degradation products, inflammation, infections, and controlled release of loaded drugs. Albumin membranes formulated by evaporation in the presence of salt represent a new class of materials (European patent application EP3811982). In the present study, solutions of bovine serum albumin (BSA) and various salts are evaporatedat 37 °C and pH 6 in order to prepare albumin-based material. Among others, NaBr allows the formation of stable and water-insoluble albumin membranes, thus providing a solid material exclusively composed of albumin after thorough washing. The conditions for obtaining BSA/NaBr membranes are assessed, and the molar ratio salt/albumin proves to be a key parameter for their formation. The Young modulus (E) of the materials lies around 0.86 ± 0.13 MPa. In vitro and in vivo assays show that these albumin membranes are biodegradable and biocompatible, do not induce an inflammatory response, and allow cell adhesion and proliferation. Furthermore, these materials are successfully loaded with antimicrobial active substances. The loaded membranes exhibit antimicrobial properties on *S. aureus* and *E. coli.* Therefore, due to their interesting properties, these materials are suitable candidates for the development of biodegradable implantable devices as well as active scaffolds for tissue engineering.

P4: DEVELOPMENT OF A CURCUMIN LOADED-NLCs HYDROGEL SYSTEM FOR TOPICAL APPLICATIONS

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Keywords : wound healing, nanostructured lipid carriers, natural antioxidant delivery

ABSTRACT

The balance of prooxidant-antioxidant reactions plays a crucial role in the regulation of skin physiological processes, especially during wound-healing. In standard conditions acute wounds heal in few weeks. However, an uncontroled oxidative stress may hinder the normal wound-healing process by perpetuating tissue damage.
Curcumin is a natural active ingredient known by its capacity to efficiently act at the wound site by controlling the toxicity of radicals and through the activation of cytoprotective signaling pathways in dermal cells, thus contributing to the regeneration of the skin barrier function [1]. However, the efficient topical application of active curcumin at cutaneous tissues is hindered by its low solubility in aqueous systems and the need to avoid its degradation (especially by heat and light) during its formulation.

In this work, Nanostructured Lipid Carriers (NLCs) [2] were developed as an encapsulating drug system aimed to prevent the drawbacks of curcumin stability and to favor its delivery to the skin. This would allow its topical application at the wound site by being incorporated into a dynamic hydrogel matrix.

A stable NLCs formulation composed of negatively charged nanoparticles of an average size of about 300 nm was obtained. The curcumin encapsulation efficiency was more than 80% and the preservation of the antioxidant properties during the preparation process was demonstrated. Furthermore, curcumin release was studied in different biological media and reached 75 % in 72 hours.
The viability of dermal cells involved in the wound-healing process was assessed after 24 hours of contact. Developped NLCs were found to be non toxic to fibroblasts and keratinocytes at concentrations below 0.54 mg/mL (containing 10 µM of curcumin) and 1.1 mg/mL (containing 20 µM), respectively.
Finally, NLCs were successfully introduced into a carbopol hydrogel. Rheological analysis revealed that the mechanical properties of the gel were not disturbed.

Overall, our results demonstrated the feasibility of combining a natural compound-loaded NLCs and a hydrogel support into a multiscale platform in order to achieve the controlled release of the natural compound.
The developed system is highly compatible and promising for a topical application. Most of all, it preserves the antioxidant properties of curcumin and controls its release towards dermal cells. Such behavior has been demonstrated to be a key feature in order to achieve pro wound-healing effects [3]. Currently, the ability to promote cell migration and proliferation in *in-vitro* wound-healing tests is under assessment.

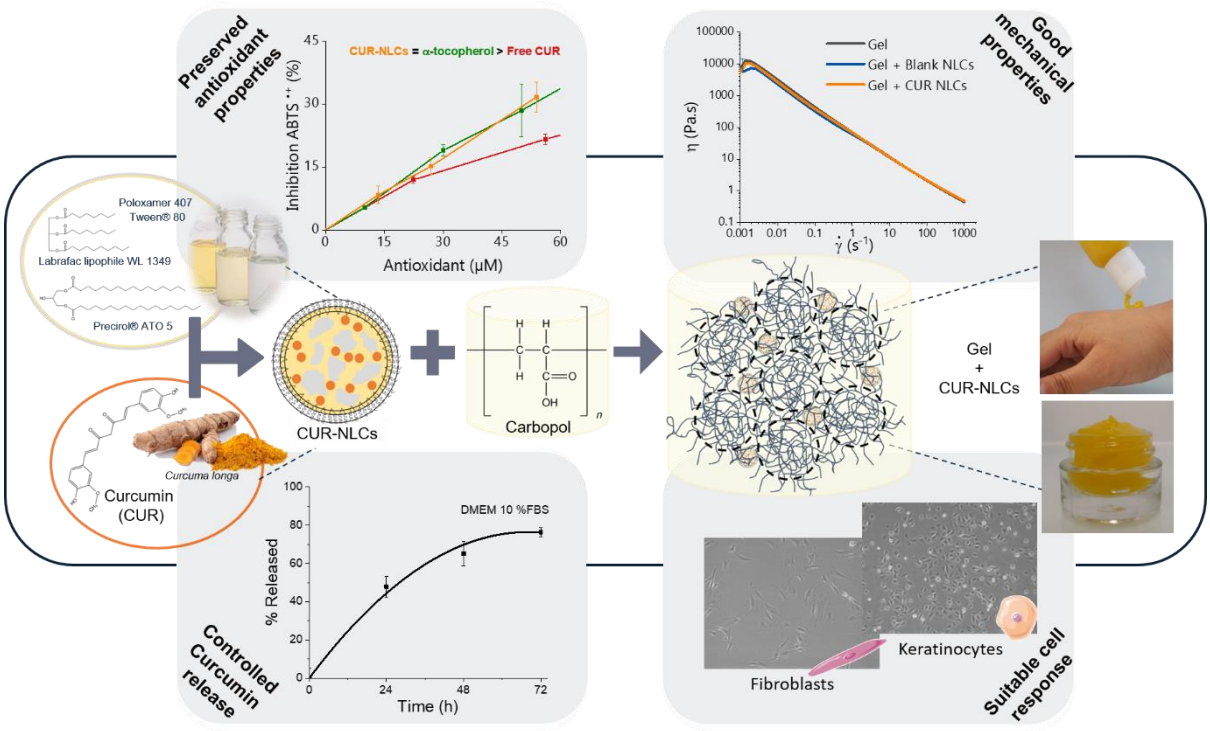

Figure 1: Schematic representation of the Curcumin loaded NLCs/hydrogel system developed and its main characteristics.

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P5: SUPER-CRITICAL CO_2 DECELLULARIZATION STRATEGY: A NOVELAPPROACH TO DEVELOP CARDIAC 3-DIMENSIONAL BIOHYBRID MATRICE.

Albane Carré[1], Raphaëlle Savoire[2], Pascal Subra-Paternault[2], Teresa Simon-Yarza[1]

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Keywords: decellularization, super critical CO_2, biohybrid 3D material.

Since 2008, super-critical CO_2 ($scCO_2$) fluid extraction has been shown to be an effective method for tissue decellularization[1], with numerous advantages such as the conservation of the tissue organizationand the majority of the proteins and small molecules contained in the extracellular matrix (ECM)[2,3]. Using low pressure and temperature and the addition of a polar co-solvent (ethanol; EtOH), this methodis based on 3 main steps: 1) the ethanol diffusion through the porous material facilitated by the $scCO_2$ flux; 2) the cell membranes disruption and intracellular material leakage provoked by the ethanol; 3) the cellular debris evacuation by the $scCO_2$ flux.
Our goal is to use this innovative decellularization method to develop a biohybrid material, combining a polysaccharide-based 3D hydrogel, mimicking the native tissue physical-chemical properties, and adeposition of cardiac cell secreted ECM, containing natural proteins, glycoproteins and proteoglycans.
The polysaccharide-based 3D porous hydrogels were obtained by chemical cross-linking of dextran and pullulan, sodium chloride and freeze-drying were used as chemical and physical porosity factors and the addition of a low percentage of gelatin to ensure cell adhesion. Fibroblasts were vacuum seededin the lyophilized hydrogels at high concentration to maximize the cellularization homogeneity withinthe porous network. Once the cells secreted a sufficient quantity of ECM, usually after 10 days of culture, different $scCO_2$-EtOH treatment protocols were tested. Preliminary experiments, using "harsh" parameters of 30 MPa of a 33.4 wt% $scCO_2$-EtOH70% immersive flux during 1h20min, followed by an 8.5 MPa $scCO_2$ flux only, resulted in a completely plasticized sample. Microscopic observations suggested that the contraction of the sample made the cells inaccessible, limiting the disruptive effect of ethanol and the evacuation of cell debris by the flow of $scCO_2$. To address this issue, a second series of experiments was conducted via the addition of a pretreatment phase (1h in EtOH20%) and the use of a non-immersive contact mode, with "soft" parameters as 17 MPa of a 1.4wt% $scCO_2$-EtOH96% during 2h. Consequently, the samples weren't plasticized and microscopic observations showed a qualitative improvement regarding the decellularization.
These results encourage us to continue to adapt this new decellularization method to engineer a 3D biohybrid cardiac scaffold for tissue repair.

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P7: ECOLOGICAL AND SCALABLE SYNTHESIS OF $CACO_3$ NANOPARTICLES STABLE IN AQUEOUS MEDIA USING BIO-SOURCED MATERIALS FOR APPLICATIONS IN BIOMEDICINE

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Mots clefs : Calcium carbonate, nanoparticles, biomedicine

RÉSUMÉ DES TRAVAUX

Recent years have seen growing the interest in calcium carbonate (CaCO3) colloids for various applications in the biomedical field, including bone and tooth disorders, drug and gene delivery, tumour and inflammatory therapies, and medical imaging1-4. Their attractiveness stands in their unique sensitivity to the mildly acidic pH of some tumor and inflammatory environments2,4-6. The major impediment to their extended development in the biomedical field is the high instability of CaCO3 particles at nanosize in aqueous media, which greatly affects their ability to target tumoral and inflammatory sites through the enhanced permeation and retention effect. Indeed in presence of water, CaCO3 nanoparticles rapidly aggregate and crystallise into microparticles7.

Various techniques have been developed in the last years to overcome this limitation. Current research aims to preserve a particle diameter under 300nm with a homogeneous size dispersion to preserve the targeting properties inherent to nanoparticles in biomedicine. However, some challenges remain to develop a green, scalable, and cost-effective processes.

Our work contributes to the solution with a facile process using the natural electrostatic affinity of negatively charged phospholipids for CaCO3 materials, to produce nanoparticles stable in presence of water with a diameter under 150nm. By investigating several phospholipids as stabiliser, we found a correlation between the phospholipid polar head group charge and the stabilisation efficiency. By rationalising the choice of the phospholipid according to its affinity for CaCO3 nanoparticles, we developed of a time-efficient process using exclusively water and ethanol as solvent mixture. The resulting specific structuration of the selected phospholipids around CaCO3 nanoparticles was imaged by Cryogenic Transmission Electron Microscopy. The correlation between the charge of the phospholipid and the stabilisation efficiency led to the identification of a suitable bio-sourced phospholipid as well as a suitable low-cost biopolymer as stabilisers. Our work also focussed on the adaptation of the process for industrial needs by working on the process upscaling in bulk and continuous flow production.

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P9: FDBS (FREEZE DRIED BONE SCAFFOLD), THE OSTEOGENIC SYNTHETIC PLATFORM FOR BONEREGENERATION

Cyril d'Arros[1,2], Boris Halgand[1,3], Olivier Malard[1,4], Pascal Borget[2] and Guy Daculsi[1] [1]INSERM, UMR 1229, Regenerative Medicine and Skeleton, ONIRIS, Université de Nantes, Nantes, France ;[2]Biomatlante – Advanced Medical Solutions Group plc, ZA des 4 Nations, Vigneux-de-Bretagne, France ;
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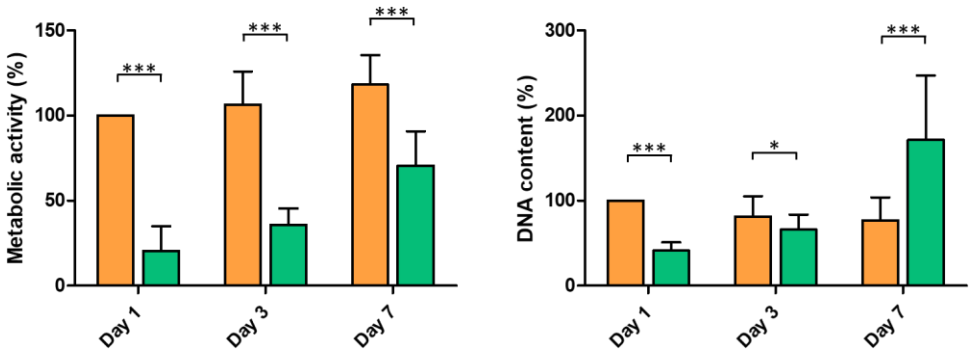
Keywords: Bone regeneration, Tissue engineering, Calcium Phosphate

Many clinical situations need materials to restore and regenerate bone, and able to replace autologous bone graft which is still considered as the gold standard. Different kinds of synthetic bone graft substitutes are largely used for more than 30 years in clinical situations. A first generation of medicaldevices concerns the biomaterials in solid shape (inserts, sticks, granules), and a second one improvingthe usability for the surgeons with injectable/moldable properties (cements, putties) but not easilysuitable for tissue engineering approaches. In highly critical bone defects, the use of cell sources (blood,total bone marrow, stem cells) is particularly interesting to improve the osteogenicity of the medicaldevice. In this way, FDBS (for Freeze Dried Bone Scaffold) is a new bone substitute combining all benefitsof the previous medical device's generation with high handling properties and allowing association withcell sources and/or any other molecules (such as antibiotics, and growth factors contained in platelet richplasma for example).
FDBS is a powder containing Biphasic Calcium Phosphate granules (MBCP®+ with a ratio 20/80 of HA/β- TCP) embedded in a water-soluble polymer (HPMC, Hydroxypropylmethylcellulose). The FDBS formulation gives the opportunity to the clinicians to rehydrate the dried powder with the most appropriate reconstitution medium regarding the clinical indication.
A first *in vitro* experiment (n=3) demonstrated interesting results of cytocompatibility with proliferation of mesenchymal stem cells mixed into FDBS during one week of 3D cell culture (figure on-below). After one day the value of metabolic activity for FDBS is about 20% compared to the positive control (BCP granules at 1 day) probably due to the mixing step during rehydration of FDBS powder compared to theseeding of the cell suspension onto the BCP granules. At day 3 and 7, the metabolic activity increased slightly for FDBS compared to BCP. The DNA dosage demonstrated an increase at day 3 and 7 for FDBS mixing, but stable quantity for the BCP control. A second *in vitro* experiment (n=3) conducted for one month showed an important potential for osteogenic differentiation of MSCs with an increase of the alkaline phosphatase at a proteomic level for FDBS condition with a slight shift in time compared to BCPgranules (positive control) especially in osteogenic medium (data not shown).

Figure: Viability of MSCs on BCP (orange) and FDBS (green) with 1,000,000 cells by 0.1g of material

FDBS could be a versatile platform for bone tissue engineering (stem cells or other strategies such as the release of growth factors; ongoing study).



P10: ETUDE DU ROLE DU PYROCARBONE DANS LA REGENERATION DU CARTILAGE ARTICULAIRE

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Mots clefs : Cartilage, Pyrocarbone, Culture cellulaire primaire, régénération tissulaire

RÉSUMÉ DES TRAVAUX

Les pathologies dégénératives de l'épaule sont actuellement traitées par une Arthroplastie Totale de l'Epaule (ATE) ou Hémi-Arthroplastie (HAE). Cependant, beaucoup d'inquiétudes subsistent concernant la préservation du cartilage et du stock osseux.
Pour tenter de résoudre ce problème, une nouvelle génération d'implant d'interposition d'épaule en pyrocarbone a été développée. Les résultats cliniques (1) sont très encourageants et des études *in vitro* récentes (2) sur des cultures cellulaires montrent que les surfaces en pyrocarbone ont un pouvoir chondrogénique et ostéogenique important.

Nous avons pour objectif d'étudier si les surfaces en pyrocarbone pourraient avoir un potentiel pour régénérer du cartilage humain. Nous avons mis en place des cultures cellulaires primaires de chondrocytes issus de tête fémorales et de labrum humain (en collaboration avec l'hôpital Edouard Herriot). Nous avons réalisé ces cultures au contact de 2 plaques de pyrocarbone ou de 2 plaques de plastique PMMA (polyméthacrylate de méthyl non traité), espacées de 500 µm, durant 17 jours.
Les premiers résultats semblent montrer que les cellules du labrum prolifèrent plus que les cellules de la tête fémorale (voir figure 1) et que cette prolifération est environ 3 fois plus importante sur le pyrocarbone que sur le plastique PMMA. En revanche on observe une nécrose cellulaire au centre des plaques. Cela pourrait être due à une mauvaise diffusion du milieu de culture à l'intérieur de la membrane néoformée pendant les 17 jours de culture. Nous envisageons de contrer ces effets par l'application de sollicitations dynamiques via l'utilisation d'un bioréacteur.

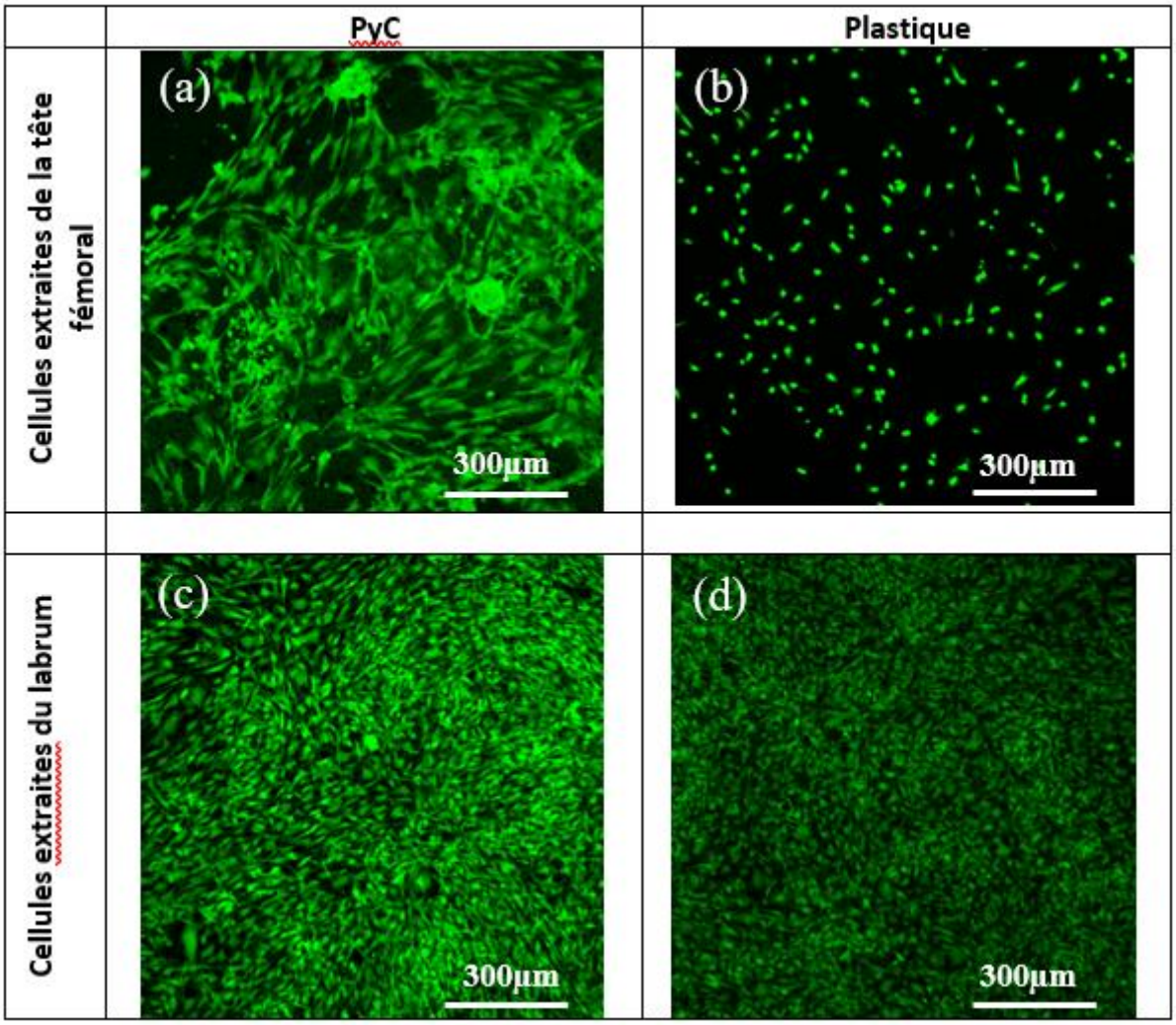

Figure 1. Visualisation en microscopie confocale à fluorescence (marquage live/dead) avec un objectif x5 de cellulesextraites de la tête fémoral (a) et (b) et extraites du labrum (c) et (d) et cultivé entre deux plaques de biomatériaux :Pyrocarbone (a) et (c) et Plastique PMMA (b) et (d) ; (Microscope Zeiss Axio à tête confocale type LSM700)

Par ailleurs, d'autre études sont en cours pour prédire le comportement biologique des chondrocytes humains dans des situations physiologiques et /ou pathologiques.

Pour le financement de cette étude nous remercions : (1) *FEDER : fund of the European Union*, pour leprotocole clinique, (2) *Pyrocarbon Technology Stryker*, pour les échantillons de pyrocarbone

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P11: VASCULARIZED 3D POLYSACCHARIDE-BASED SCAFFOLDS AS MODEL OF LIVER SINUSOID

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Keywords: Vascularized scaffold; Liver sinusoid model; High-resolution imaging.

ABSTRACT

Liver capillaries, known as sinusoids, play a fundamental role in hepatic pathophysiology, such as filtering of molecules from the blood, clearing of wastes and managing the vascular immune response [1]. Despite the recent advances in tissue engineering, the development of 3D *in vitro* models to study the hepatic sinusoid is still hampered by the following drawbacks: (i) fabricating scaffolds with physical properties that mimic the *in vivo* microenvironment, (ii) engineering vascular networks and (ii) imaging 3D cellularized thick constructs without sectioning.

We present here a polysaccharidic scaffold containing channels engineered to create a model of the liver sinusoid and imaged by conventional and high-resolution microscopy (**Figure 1**).

The scaffolds were made of a solution of pullulan and dextran, known to be biocompatible polymers [2], and the channels were fabricated by templating method: briefly, the polysaccharide solution was casted on a custom-made mold containing suture monofilaments (50 µm in diameter). After the cross- linking of the polymeric mixture, the filaments were removed to obtain empty channels within the constructs and then freeze-dried to have a porous structure [3]. Physical, mechanical and chemical properties of the constructs were investigated to assess their capability of mimicking the properties of soft tissues such as the liver. Next, a protocol for selective coating of the channels was optimized to ensure endothelial cells adhesion within the microchannels.

The scaffolds were tested *in vitro* by seeding human umbilical vein endothelial cells (HUVECs) and imaged by confocal and multi-photon microscopy. The presence of a selective collagenic coating was assessed by second harmonic generation (SHG) analysis. Our results confirmed the presence of a specific homogeneous coating of the vascular walls, that allowed endothelial cells to adhere andproliferate in the channels only. The formation of endothelial lumen within the pre-patterned matrices was demonstrated and, more interestingly, we showed the possibility to tune the vasculature formation over time by modulating the cell culture conditions (**Figure 2**).

Current studies are focusing on the integration with other hepatic cells and on perfusion of the matrices to create a dynamic system mimicking the hepatic sinusoid. High-resolution imaging has been further pursued by light sheet fluorescence microscopy to achieve 3D volumetric images of full matrices without the need for sectioning. The development of a complete vascularized and perfusable liver system would give us new insights on liver metabolism *in vitro* and would contribute in engineering functional liver tissue construct for regenerative medicine purposes.

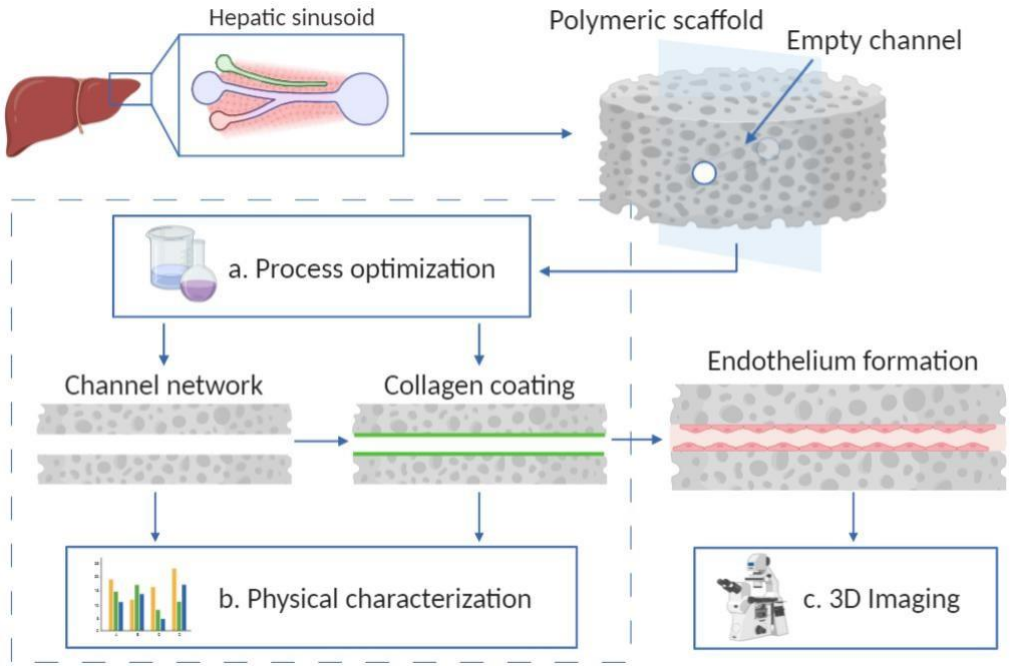

Figure 1. Schematic of the work presented here. The polymeric scaffolds containing an empty channel network have been optimized for both the fabrication and the coating steps (a) and then characterized (b). The constructs have been used as templates to form endothelium within the microchannels, subsequently imaged by different 3D high-resolution imaging techniques (c). Created with BioRender.com

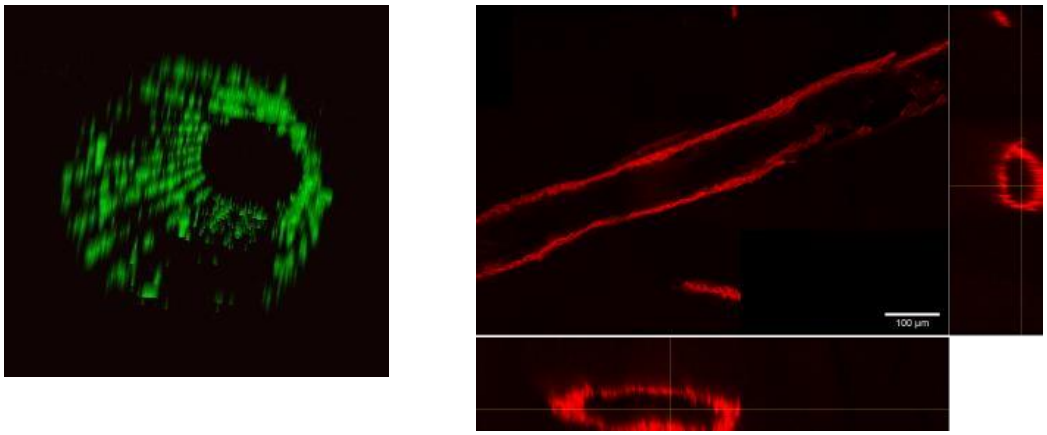

Figure 2. (a) Selective collagen coating of the channel (3D reconstruction, collagen in green), imaged by SHG. (b) Formation of complete endothelial lumen within the scaffold (actin filaments in red), imaged by multiphoton microscopy (cross- section and orthogonal views). Scalebar 100 µm.

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P14: 3D MEMBRANE OF ELECTROPSUN FIBERS FOR CELL THERAPIES

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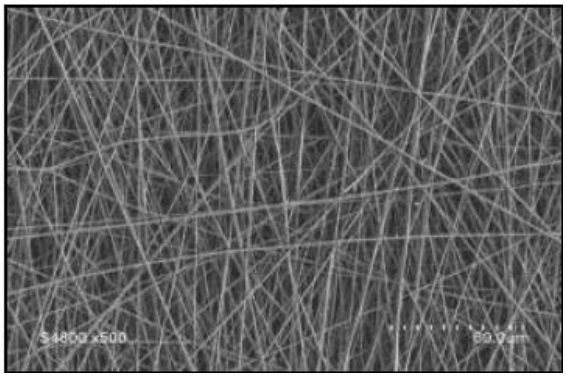
Keywords : Electrospinning, scaffold, cell culture

ABSTRACT

Cell therapy, which is organ or tissue regeneration from injection and growth of stem cells, raises a lot of hope for treatment of diseases. However, the direct injection does not work out so well. Thus, biocompatible membranes, allowing stems cells to growth and differentiate, are needed.

3D membranes of electrospun fibers have been developed by both IEM and INM. Their application extends from drug screening to cell therapies. In fact, this scaffold is purely synthetic, reproductible, low cost to produce and fibers show fluorescence properties, which help for migration studies. Moreover, it is inert and biocompatible, it can be sterilizable and be inserted into well plates. Studies [1-2] have shown that migration and growth of stem cells can be studied realistically since fibres imitate extracellular medium. Finally, chemical and physical properties can be modified independently.



*MEB (*500) of 3D membrane of electrospun fibers*

The main challenges are: a better understanding and characterization of the 3D topology, a total control of links between structures and mechanical properties, a control of the formulation and chemistry surface to induce cell differentiation and better imitate extracellular medium.

As of now, I have produced 3D membranes of aligned and non-aligned electrospun fibers, containing different amounts of mechanical fillers (carbon nanotubes) in order to tune their mechanical properties. Structural characterization of the membranes has been done based on SEM coupled with advanced image processing involving the DiameterJ[3] module of the Image J software. Then force- spectroscopy measurements were made by Atomic Force Microscopy. Finally, the migration of glioblastoma stem cells was studied on the different aligned fibers.

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P15: DEVELOPMENT OF ANTIBIOFILM DRESSINGS WITH NATURAL ACTIVEINGREDIENTS FOR THE TREATMENT OF INFECTED WOUNDS

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Keywords : Natural molecules, Antibiofilm, Dressings

ABSTRACT

Wound healing constitutes a major public health issue. Due to the breach in the skin barrier, woundsare at risk of infection and biofilm development, which complicate their cure. Bacteria in biofilm are difficult to eradicate as they show increased resistance to antibiotics. In the context of chronic and exudative wounds, compresses made out of calcium alginate are commonly used as they favor wound healing thanks to their bioactive properties and high capacity to eliminate wound fluids while maintaining optimal wound moisture. Nevertheless, they do not have antiseptic properties. The project objective was to functionalize calcium alginate dressings with natural molecules conferring antimicrobial and antibiofilm properties against bacteria most commonly found in wounds: *Pseudomonas aeruginosa* and *Staphylococcus aureus*. We focused on three natural molecules: gallic acid (G), carvacrol (K) and curcumin (Q) extracted respectively from galls, oregano and turmeric. First, the efficiency of the natural molecules in solution, individually or in combination, was examined on planktonic bacteria and on 24h-old biofilms. Then, the antibiofilm capacity of compresses functionalized with one or a combination of these molecules was studied.

In solution, we observe a bacterial growth inhibition with the three selected natural compounds, and G and K provide in addition bactericidal properties. G presents strong antibiofilm properties on P. aeruginosa biofilm (5.8 Log reduction CFU/mL (LR)), and a lower activity on S. aureus biofilm, (2,0 LR). Conversely, K has a stronger antibiofilm activity on S. aureus biofilm (6,6 LR) than on P. aeruginosa biofilm (1,9 LR). Q demonstrates no antibiofilm properties either on S. aureus or on P. aeruginosa biofilms. The combination of both G and K increases the antibiofilm effect previously observed on *P. aeruginosa* biofilm and leads to a complete eradication of *S. aureus* biofilm. This combination was also tested on dual-species biofilms of *S. aureus* and *P. aeruginosa* and was shownto exhibit a strong antibiofilm effect (5,4 LR).

In compresses containing one component, we observe antibiofilm efficiency only on *S. aureus* (at least 3,7 LR) and compresses containing combinations of K-G or K-Q have a strong antibiofilm effecton both mono-species biofilms (at least 4,5 LR). Microscopy analysis demonstrate that the antibiofilm effects are due to the destabilization of the biofilm and the ability of the compresses to drain and retain bacteria.

Compresses containing the combinations of natural active ingredients K-G and K-Q may thenrepresent efficient alternatives for the treatment of biofilms in wounds.

P16: ANTIBACTERIAL AND ANTI-INFLAMMATORY HYDROGELS: TOWARDSMULTIFUNCTIONALITY

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Key words: hydrogels, antibacterial, anti-inflammatory

Implantation of biomedical devices is often followed by immune response to the implant, as well as by bacterial, yeast and fungal infections. Inflammation and infection may seriously affect implant functionalities and even may lead to their failure. In this context, new implant materials and coatings dealing with these issues are needed.

Polyarginine (PAR) is a polycationic peptide presenting antimicrobial activity in solution. We have previously described thin films made of hyaluronic acid (HA) and PAR. Such films constructed by layer-by-layer assembly demonstrated antimicrobial and anti-inflammatory properties[1-3].

Recently, we introduced a new formulation of HA-based antimicrobial material: HA hydrogels cross-linked with BDDE (1,4-butanediol diglycidyl ether) and loaded with PAR. Such hydrogels provideda long-lasting antibacterial effect due to a gradual release of PAR. Interestingly, antibacterial activity depended on PAR length, PAR30 (30 arginine units) being the most efficient and PAR200 (200 units) being the less efficient. These hydrogels were non-cytotoxic and could be deposited onto medical devices such as wound dressings and mesh prosthesis. Moreover, first animal experiments were performed and showed good biocompatibility of HA-PAR hydrogels *in vivo*.[4,5]

We are now developing a new system where PAR30 can be used as an immunomodulatory agent. Thus, new HA hydrogels will simultaneously provide antibacterial and anti-inflammatory activity, by killing bacteria and orienting macrophages toward an anti-inflammatory phenotype.

We believe that such multifunctional hydrogels can become a novel tool to prevent implant- related infections, improve tissue regeneration and implant integration.

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P20: INVESTIGATING SPAAC FOR THE DESIGN OF POLYSACCHARIDE-BASED HYDROGELS:A MOST VERSATILE PLATFORM FOR CELL CULTURE

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Keywords: Hydrogel design, click chemistry, 3D culture

ABSTRACT

Owing to their ability to mimic native cell microenvironments, hydrogels are considered the most suitable scaffolds for 3D cell culture. Yet, most of the existing hydrogel crosslinking strategies (i) require external stimuli or small molecule reagents, (ii) are not entirely bioorthogonal or compatible with physiological conditions, or (iii) have inherent limitations such as poor stability or slow gelation rate, thereby hindering their use. In this context, a new class of versatile, cytocompatible hydrogels that would be easy to synthesize, tune, and use for 3D culture, is most desirable. To address this challenge, we investigated the use of the Strain-Promoted Azide-Alkyne Cycloaddition (SPAAC) as a click and bioorthogonal crosslinkingmechanism for the synthesis of a variety of polysaccharide-based hydrogels.

As a polymer of interest, hyaluronic acid (HA) was first studied. HA was successfully functionalized with either azide or bicyclononyne (BCN) via single-step syntheses, with tunabledegrees of substitution, as confirmed by ^{1}H NMR. By simply mixing HA-azide and HA-BCN together, we obtained stable hydrogels that form within minutes, under physiological conditions (pH 7.2, 37 °C), addressing all the aforementioned issues. Optimizing the HA molecular weight, component ratio, polymer content and substitutions, hydrogels with tunable gelation time (seconds to tens of minutes) and stiffness (0.5 to 25 kPa) were designed.Interestingly, we found that the crosslink density and polymer concentration of these gels canbe finely tuned to maintain minimal to no swelling for months in various media (PBS or DMEM) while tuning their stiffness. We further confirmed that these HA-based hydrogels could degrade enzymatically, and that SPAAC crosslinking can be easily applied to other polysaccharides, such as alginate or chondroitin sulfate, making it a most versatile platform for covalent hydrogel design.

Finally, using a murine cell line (L929 fibroblast cells), we demonstrated the excellent cytocompatibility of these gels (cell viability > 90%), independently of their stiffness, via live/dead confocal imaging. These gels are now being explored for the 3D culture of various cell types such as human mesenchymal stromal cells and induced pluripotent stem cells or murine intervertebral disc-explanted cells, paving the way toward their use in a variety of in vitro applications.

P 24: OPTIMISATION AND USE OF A BIOPRINTED MODEL TO STUDY BIOMATERIALS FOR BONEREGENERATION.

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Mots clefs: Bone regeneration, Tissue engineering, 3D Model

RÉSUMÉ DES TRAVAUX

Craniofacial region is particularly exposed to significant bone loss. Tissue engineering for bone regeneration represents an innovative solution to treat critical craniofacial bone defects by developing constructs that combine cells, biomaterials/scaffolds and bioactive factors. Another application of tissue engineering aims to understand the *in vivo* cellular mechanisms in a three-dimensional controlled system, created by additive manufacturing, as a complement or in replacement of animal models.

Previous *in vivo* studies focused on craniofacial bone healing have shown the good ability of S53P4 bioactive glass, known to have osteostimulative and antimicrobial properties, to repair critical defect even without addition of stem cells.

Here, we present the development of a 3D-bioprinted alginate/gelatin-based model to study the effectof Dense Collagen (DC) scaffold alone or seeded with S53P4 bioactive glass (DC-S53P4) on host cell recruitment during bone repair.

The model was first validated and optimized with fibroblasts before studying primary osteoblasts from 3 different donors and commercially available human umbilical vein endothelial cells (HUVEC). A 21- day follow-up was performed: DC and DC-S53P4 were analyzed at Day 7, Day 14 and Day 21 by fluorescent microscopy and DNA quantification (Hoechst assay). Co-culture experiments Osteoblast+Fibroblasts and HUVECs+Fibroblasts were also conducted to increase the model complexity toward a physiological microenvironment.

As a result, the cells were able to move from the model periphery to the scaffold from D0 to D21. The number of fibroblasts increased significantly ($p < 0,001$) over time and especially from D14. Regarding the osteoblasts, no cells could be detected by Hoechst assay when printed alone (for two donors) evenif some were visible by microscopy at D21. When co-printed with fibroblasts, the percentage of migrated cells was significantly ($p < 0,005$) increased for one donor at D21. HUVECs experiments were replicated. No cells could be detected when printed alone, while their number increased significantly($p < 0,001$) at D21 in the second co-culture set. In all cases, the addition of bioactive glass to the collagen scaffold wasn't significant on cell migration.
While this 3D-bioprinted model has shown encouraging results further optimization is needed to become a reliable tool for studying craniofacial bone regeneration. The study of osteoblasts and HUVECs migration was a first step in its development and co-printing HUVEC+Osteoblasts experiments could be conducted to complete this study. Moreover, histological analyses would be an interesting perspective to complete the results with the study of cell differentiation and matrix deposition.

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P 25: SYNTHESIS AND CHARACTERIZATION OF POLYETHYLENE GLYCOL BASEDHYDROGELS FOR ANTI-INFLAMMATORY DRUGS RELEASE.

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ANR-OPENN: COnception of bioresorbable self-rolled Patchs for the local trEatment of inflammatioNinduced in the coloN after irradiation

Keywords: hydrogel, drug release, PEG.

ABSTRACT

Radiotherapy of abdomino-pelvic tumors induces in 20% of patients late side effects involving a chronic inflammation with an alteration of colon tissue [1, 2]. With the aim to provide a therapeutic solution to this inflammation, we develop a biodegradable self-rolled patch that could be applied locally by colonoscopywithout surgery. This innovative biomaterial is based on the combination of hydrogel and elastomeric layers. This association of two different layers confers tunable mechanical and bio-resorption properties to the patch allowing an unidirectional release of anti-inflammatory drugs (AI) such as Budesonide and Prednisolone toward the ulcerated zone after its unrolling. In this study, the impregnation of AI in hydrogels and their in vitro release kinetics from non-degradable polyethylene glycol derived hydrogels is explored. For that, we used an efficient solvent free microwave-assisted method for poly(ethylene glycol) dimethacrylate (PEGDM) synthesis [3]. After photo-reticulation of the hydrogels by UV (365 nm, 90µW/cm^2, 20min) in presence of Irgacure 2959 photo initiator, AI drugs are loaded through incubating the formulated hydrogels in concentrated drug solutions. After having determined the best approach for loading AI in hydrogels, the loaded hydrogels are soaked in fresh PBS for a release study at 37°C. A particular attention is paid to modifying molecular weight of PEG and PEGDM hydrogels concentration to investigate the effects of these parameters on the hydrogel's behavior. The amount of Budesonide and Prednisolone release was further quantified by Reverse Phase – High Performance Liquid Chromatography (RP-HPLC) coupled to UV detection. Equilibrium swelling studies are also performed for hydrogel mesh size characterization. We demonstrated an efficient release of AI physically entrappedin the linear polyethylene glycol-based hydrogels. The influence of the three-dimensional structure on theamount of total drugs delivered is also verified. Changing hydrogel concentration and molecular weight are convenient handles for tuning mesh size. For further studies, UV photo-crosslinkable copolymers composed of central blocks PEG associated with side blocks of polyesters polylactic acid (PLA)/polycaprolactone (PCL) with a star-shaped topology will be used to develop mucoadhesive and degradable hydrogel-based patches.

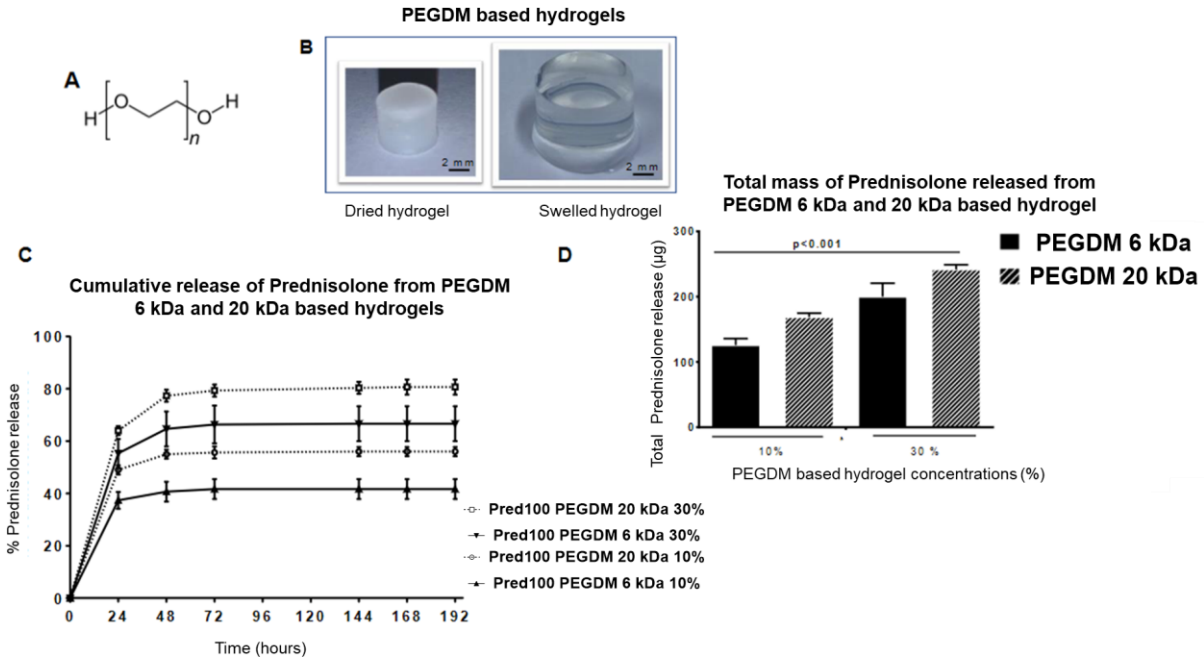

Figure: A) Linear PEG **B**) PEGDM 20 kDa based hydrogel dried and swelled in water **C**) Influence of molecular weight and PEGDM concentration (w/w %) on prednisolone release from hydrogels formedusing 6 kDa and 20 kDa PEGDM. Bars represent average ± standard deviation for n = 3 samples. **D**) Total mass of prednisolone released (n = 3, $p < 0.001$. Results are expressed as mean ± SD and compared between groups by one-way ANOVA with Tukey's test).

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P27: BILATERAL DOUBLE SITE (CALVARIA AND MANDIBULAR) CRITICAL SIZE BONE DEFECTMODEL INRABBIT FOR EVALUATION OF CRANIOFACIAL TISSUE REGENERATION

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Keywords: Critical size defect, Bone regeneration, and 3D implants.

SUMMARY OF THE WORK

Introduction

Most existing preclinical models for evaluating the biomaterial safety and bone-regeneration efficacy are single-site defect models that vary substantially depending on anatomical location. Because of developmental, structural, and functional differences, the mechanism of bone healing varies by anatomical location, which is especially true for maxillofacial wounds (1-2). The novelty of the study was to develop a reproducible preclinical model of bilateral critical-sized defects (CSD) in one rabbitat two distinct anatomical locations (non-load bearing calvaria and load-bearing mandibular). It makes each animal into its own control subject, boosting statistical power for pairwise comparison testing. This bilateral double-site CSD model was validated by comparing the "gold standard" autograft to the sham (no graft) group. Subsequently, a newly developed 3D-Implant (multilayer- stacked polycaprolactone/nano-hydroxyapatite composite (PCL/nHA) composite material, fabricated by melt electrospinning) was implanted to evaluate the utility of this model.

Experimental methods

Twenty healthy adult male New Zealand rabbits, weighing 3.5–4 kg was randomly assigned to a sham or an autograft group (n=10 in each group). The full-thickness calvaria defect (10 mm diameter) and full-thickness mandibular (11 mm diameter) defect on the body of the mandible were created bilaterally with saline irrigation. The defect on one side was filled with autograft debris, and the other side was left empty. For further assessing its utility, 3D-implant was implanted on one side of the rabbits, and the other side was filled by autograft or left empty alternatively. At predetermined time points (4- and 12 weeks) bone defect specimens were harvested and assessed by microcomputed tomography (micro-CT) and histological evaluation.

Results and Conclusion

Micro-CT showed that, in calvaria defect, BV/TV of the autograft group (39.52% ± 5.2% and 47.41% ± 5.4% at 4w and 12w, respectively) was statistically higher (p<0.05) than that of the empty group(15.20% ± 2.3% and 21.24% ± 3.17% at 4w and 12w, respectively) and 3D-implant group (15.7% ±1.44% and 19.46 ± 2.5% at 4w and 12w, respectively); similar tendency of difference was observed in mandible defect between autograft and empty. The developed model was validated as the CSD until 12 weeks based on histological and micro-CT findings. The rabbit has a high tolerancefor the studied bilateral double-site CSD model. The promising results of 3D-implant suggest that this comparative rabbit model could be a useful tool for assessing and comparing the efficacy of new tissue engineering constructs at two different anatomical locations in a single rabbit.

Acknowledgement

The authors would like to thank the Platform Experimental Resources, D.H.U.R.E, University of Lille, fortheir support on animal studies and Mrs M.H Gevaert for technical help on histological analysis. It was supported by the cross-border INTERREG "North-West Europe" fund BONE.

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P32: SUPERPARAMAGNETIC AND BIOACTIVE NANOPARTICLES FOR BONE CANCER TREATMENT

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Keywords: Bioactivity, Bone substitute, Magnetic hyperthermia

ABSTRACT

Most patients who develop primary bone tumors require a surgical intervention. In this respect, the design of a multifunctional material, used as bone substitute, is of high clinical interest to simultaneously treat cancer and promote bone regeneration (Fig. 1).

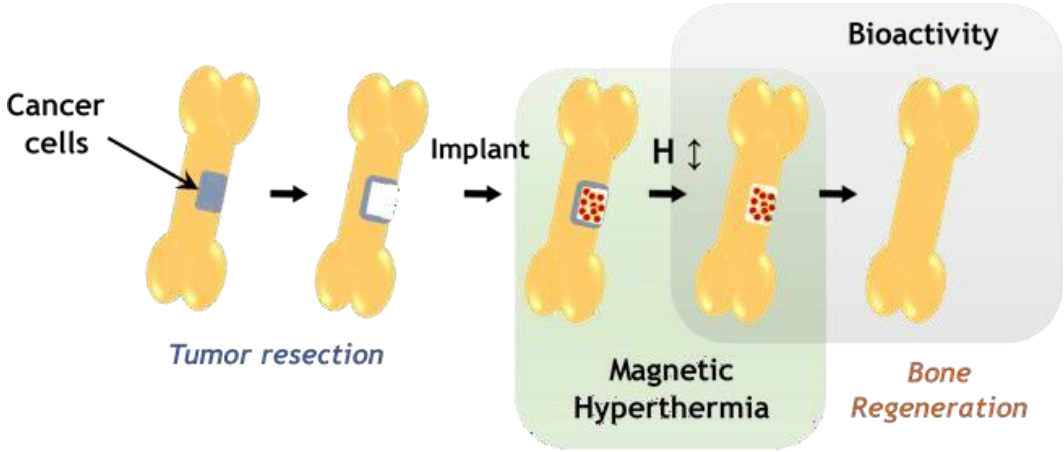

Figure 1 - Schematic representation of bone repair coupled with hyperthermia treatment

Bioactive glass nanoparticles are a promising material for bone tissue regeneration because when implanted, a hydroxyapatite layer (HAp) is quickly formed onto their surface, bonding them to natural bone tissue.[1,2] By coupling the high bioactivity of large specific surface area bioactive glass particles with the heating ability of superparamagnetic iron oxide nanoparticles (SPIONs) under an alternating magnetic field,[3] a multifunctional material could be designed and used to selectively destroy remaining or resurging cancer cells through hyperthermia before promoting bone regeneration.[4]

In this scope, heterostructures consisting of SPIONs encapsulated in dense or porous bioactive glass have been synthesized by sol-gel synthesis and characterized. Both dense and porous γ-Fe_2O_3@SiO_2- CaO core-shell nanoparticles show promising properties. Hyperthermia measurements under an alternating magnetic field (f = 768 kHz and H = 23,9 kA/m) led to a specific loss power (SLP) over 600 W/g_{Fe} for both samples. The porous heterostructures SLP value was found to be slightly lower than theone of the dense heterostructures, which could be explained by a larger clustering of SPIONs (Fig. 2).[5,6]

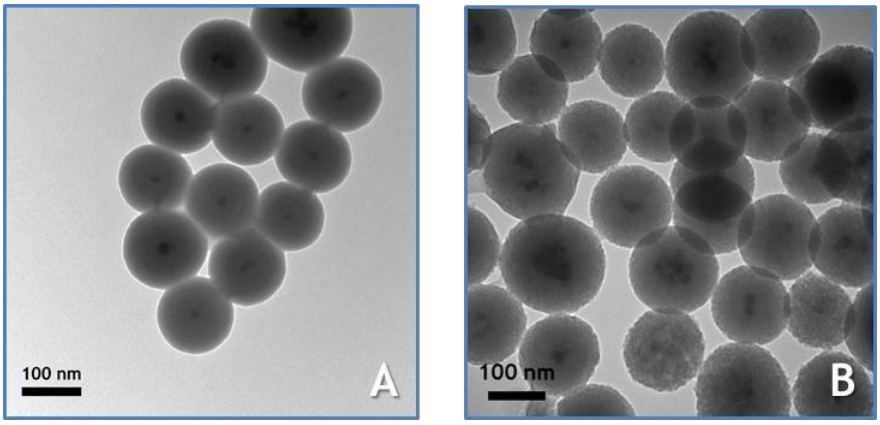

Figure 2 – TEM images of dense (A) and porous (B) γ-Fe_2O_3@SiO_2-CaO core-shell nanoparticles

The samples have been immersed in simulated body fluid (SBF) at 37°C for 7 days to assess their bioactivity. HAp crystals have been detected only after 3 days of immersion for porous heterostructures, revealing their better mineralization kinetics, as expected considering their larger specific surface area.

In conclusion, the shell porosity is not a major drawback for magnetic hyperthermia whereas itprovides a sensible increase in the bioactive glass mineralization kinetics.

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Thursday, October 21st, 2021

FLASH presentations

Other posters

P2: Design of hybrid peptide / polymer nanofibers for soft tissues regeneration

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Keywords: bioactive hybrid nanofibers, biodegradable polymers, electrospinning.

ABSTRACT

Nanofibers are excellent biomimetic supports for tissue regeneration since they mimic the architecture ofthe natural extracellular matrix and provide topographic characteristics necessary to modulate the fate of cells. This work aims to create new implantable and degradable nanofibers composed of PLAs functionalized with bioactive peptides to mimic the physical and biochemical properties of native matrix fibrils for tissue regeneration.
First, we synthesed and characterized star-shaped PLAs functionalized with IPTES (StarPLA-PTES) andbifunctional silylated peptides intented to react together via sol-gel process to create a bioactive network.Subsequently, we produced functional nanofibers by activating the sol-gel reaction during the electrospinning process. We studied the impact of different parameters such as content of IPTES groups and amount of HCL in electrospinning solution on 1/ the formation of the three-dimensional network of polymers composing the nanofibers and 2/ the rate of incorporation of the peptide in this network.
During the fabrication of the nanofibers, we observed that the molecular weight of the polymer and the hydrolysis kinetics of the PTES functions had the most significant impact on the cross-linking of the polymer-peptide network. Interestingly, we noticed that the grafting rate of the peptides was improved with the use of low molecular weight polymers because these polymers have a high content of crosslinking groups (PTES).

In conclusion, we developed a new process to obtain nanofibers composed of a hybrid three-dimensionalnetwork containing degradable polymers covalently bonded with bioactive peptides. Both the polymers and the peptides can be modified to adapt to different disease targets. The continuation of this project will consist in evaluating the biological properties of hybrid nanofibers on skin fibroblasts.

P3: DEVELOPMENT OF A 3D PRINTED SCAFFOLD ALLOWING MULTIPLE DRUG DELIVERY FOR THETREATMENT OF BONE METASTASIS IN BREAST CANCERS

Habib Belaid[1,2], Catherine Teyssier[2], David Cornu[1], Vincent Cavailles[2], Mikhael Bechelany[1]

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Keywords: 3D printing, bone metastasis, drug delivery

ABSTRACT

Breast cancer is the most common invasive cancer in women, and the second main cause of cancer death in women. Metastatic breast cancer, most frequently localized in bone, is causing considerable pain and high patient morbidity. The treatment of bone is challenging due to bone repair, and patients are often treated by implanting a passive artificial junction in addition to a systemic chemotherapy treatment.

3D printing is a powerful tool providing the ability to print bone substitute materials or "scaffolds" designed to mimic the extracellular matrix. The scaffolds need to be biocompatible and bioresorbable with a highly porous and interconnected pore network. The mechanical properties have to match those of the tissues at the site of implantation. For patients with bone metastasis, the scaffold may also allow the controlled and local release of anticancer drugs. One of the strategies to deliver these drugs by the scaffolds is to encapsulate them in microspheres such as Poly (lactic-co-glycolide) or PLGA.

The aim of this work is the development and characterization of novel biomimetic biodegradable 3D printing scaffolds allowing both bone regeneration and inhibition of breast cancer cell proliferation. To this aim, PLGA microspheres have been loaded with Raloxifene Hydrochloride (RH) and Alendronate (AL).These microspheres have been incorporated into a 3D scaffold fabricated using a Stereolithography 3D printer system with a Poly (propylene fumarate) (PPF) photopolymer.

The physicochemical properties of the nanocomposites scaffold have been fully characterized. Biologicaltesting has been carried out in order to confirm the effects of encapsulated drugs on MCF7 cells proliferation. A cell viability test using MG63 cells has been conducted to determine the scaffold biocompatibility and its effects on cell proliferation. The successful cell adhesion was revealed by fluorescent microscopy, and MG63 bone differentiation was monitored by Alizarin red staining and semi-quantitative RT-PCR.
Altogether, our data showed that PLGA microspheres incorporated in PPF scaffolds could be suitable forthe treatment of bone metastasis in breast cancer.

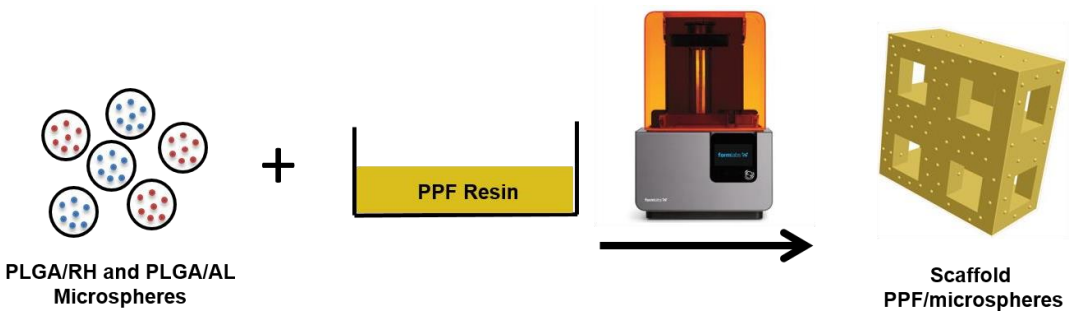

Figure 1. Graphical abstract. Fabrication of PPF/PLGA scaffold.

P6: HYDROGEL BASED ON CHITOSAN/POLYCYCLODEXTRIN/CINNAMALDEHYDE FOR THE TREATMENTOF DIABETIC FOOT ULCERS

Henry Chijcheapaza-Flores[1], Maria José Garcia-Fernandez[1], Mickael Maton[1], Jean-Noël Staelens[2], Nicolas Tabary[2], Frédéric Cazaux[2], Feng Chai[1], Christel Neut[3], Bernard Martel[2], Nicolas Blanchemain[1]

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Diabetic foot ulcers are frequent in diabetic patients. They are considered as severe infections and could lead to more severe complications like osteomyelitis. The wound healing process in patients is becoming increasingly challenging due to poor blood diffusion in the foot, sclerotic tissues, and antibiotic resistance. Traditional treatment is based on debridement, use of wound dressing, and systematic or intravenous antibiotic administration but even under treatment, it could lead to amputations in 25% of cases. In this context, hydrogels have been used in wound healing because of their properties for drug delivery and also their capacity to promote rehydration. At the same time, natural compounds have been used to accelerate the wound healing process, and to improve the efficacy of pharmacological treatments. Recently, cinnamaldehyde (CN, a natural compound obtained from Cinnamon essential oil) has been studied because of its large- spectrum antimicrobial activity. Based on this, our aim is to combine the properties of hydrogels, based on chitosan (CHT) and polymer of β cyclodextrin (PCD), for local delivery of CN in diabetic foot ulcers.

The first step consisted of hydrogel pre-formulation. CHT and PCD powders (<125 µm) were co-milled at different proportions, then suspended in distilled water and acidified lactic Acid (LA) to obtain a hydrogel. The hydrogels were injected with an 18G needle in phosphate-buffered saline (PBS, pH 7.4) for evaluation of structural stability and cohesion. Then, the complexation between cyclodextrins (CD) and CN was studied. CD has been widely used as an excipient to form inclusion complexes for drug delivery and to improve the solubility of molecules with low solubility. In this context, complexation was studied by a phase solubility diagram ("Higuchi and Connors Method") and NMR (H1 and ROESY). Thus, we have proved the inclusion of the aromatic group of CN in the β-CD cavity. The next step consisted of the formulation of CHT/PCD/CN hydrogels. These hydrogels were as well evaluated in PBS for 1h and 24h. Once the hydrogels were optimized, they were characterized by rheology: viscoelastic behavior, recovery, and viscosity. Later, CN release study was performed under dynamic conditions with USP4 apparatus (Sotax®, 37°C, 5 mL/min) coupled with a UV/Vis spectrophotometer (286 nm), and antimicrobial activity was assessed by kill time test.

Finally, results showed a promising hydrogel to use in diabetic foot ulcers. However, further studies are needed to prove its efficacy in an animal model.

Acknowledgments: This project had the funding of the MOBLILEX scholarship Keywords: Hydrogels, drug delivery, diabetic foot ulcers

P8: BORON NEUTRON CAPTURE THERAPY ASSISTED BY BORON-ENRICHED POLYSACCHARIDE NANOGELS

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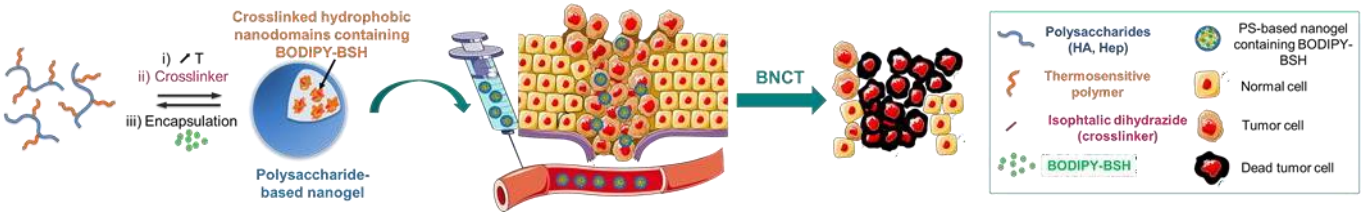
Key words: Nanogels, Polysaccharides, azaBODIPY

Boron Neutron Capture Therapy (BNCT) is an innovative cancer treatment derived from radiotherapy using low energy neutrons to create a fission reaction with a boron isotope: ^{10}B. This reaction releases a high energy α- particle that causes apoptosis in only those cells that have internalized the ^{10}B isotope-containing compound[1]. Currently, this treatment modality is attracting interest due to its accurate targeted action. Today, two boron-richcompounds are being used in clinical BNCT trials: sodium borocaptate (BSH) and L-boronophenylalanine (BPA)[2]. However, these compounds do not demonstrate selective accumulation in tumor, or contains only 1 ^{10}B atom. Therefore, researches aimed at finding novel ^{10}B-containing compounds or nanocarriers of improved target selectivity as well as increased boron load are currently in progress. In this regard, polysaccharides (PS) are interesting carrier candidates due to their biocompatibility, their biodegradability and especially their ability to accumulate in tumor. Taking into account these features, we selected two glycosaminoglycans to design new ^{10}B isotope-containing nanocarriers: hyaluronic acid (HA), which allows a highly efficient targeting due to its recognition by CD44 receptors that are overexpressed by many cancer cells, and heparosan (Hep), due to its "stealth" properties. These polysaccharides were previously modified with thermosensitive co- or terpolymers to produce nanogels by temperature-induced self-assembly[3]. Such nanocarriers possess hydrophobic cores, offering the possibility of hydrophobic molecule encapsulation, and hydrophilic shells, allowing to control their biological behaviour and targeting ability. Notably, the characteristics of these nanosystems, such as their critical aggregationtemperature (CAT) and their loading capacity, can be tuned by varying several parameters, especially the cloud point temperature (T_{cp}) of the grafted co- or terpolymer and its chemical composition. The choice of the monomersfor the synthesis of the thermosensitive co- or terpolymer thus represents a major stake in this project to obtain nanogels that can be formed at room temperature and that can encapsulate a large amount of boron-rich compounds. In this work, the hydrophobic monomer diacetone acrylamide (DAAM) possessing a ketone moiety allowing nanogels crosslinking [4] , dimethylacrylamide (DMA) and *n*-butylacrylate (BA) were selected for the synthesis of well-defined thermosensitive terpolymers. After selecting the terpolymer with optimal chemical composition, we successfully prepared nanogels as theranostic platforms for BNCT. These nanocarriers based on HA and Hep could be formed at room temperature and loaded with a fluorescent boron cluster consisting of a BODIPY derivative modified with BSH. *In vitro* biological experiments showed that the nanogels could be efficientlytaken up by U87-MG et U251-MG cancer cells without adverse effect on them. Furthermore, preliminary BNCT experiments conducted with a neutron beam on tumor-containing chicken eggs that had been treated with our ^{10}B rich nanocarriers showed inhibition of the tumor growth.



Strategy for the targeted delivery of ^{10}B into tumor cells for BNCT

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P12: INGENIERIE TISSULAIRE POUR LA RECONSTRUCTION MAMMAIRE A L'AIDE DE TRICOTSBIORESORBABLES EN PLA/PCL

Mélanie Dhayer[1], Stéphanie Brun[1], Salim Dekiouk[1,3], Vivien Barral[2], Christine Campagne[2], NicolasGermain[1,3], Philippe Marchetti[1,3]

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Keywords : Prothèse, reconstruction mammaire, polymères biorésorbables

ABSTRACT

Le cancer du sein est le cancer le plus fréquent chez la femme et représente 16 % de tous les cancers féminins. Actuellement, le traitement de référence est la mastectomie. Toutefois, peu de femmes (~ 20%) bénéficient d'une reconstruction mammaire. Cela souligne la nécessité de développer de nouvelles prothèses plus adaptées qui pourraient être implantées directement lors de la mastectomie et limiterait ainsi le nombre d'opérations. A cette fin, le projet européen interreg 'Mat(t)isse' est né afin de fournir une solution innovante aux chirurgiens. Cette prothèse doit répondre à plusieurs critères : (i) être biocompatible, (ii) être biorésorbable et (iii) permettre la croissance du lambeau graisseux sans toutefois favoriser la fibrose. Pour cela, le développement d'un biomatériau textile multi-filaments a été développé puis mise en œuvre sous forme de tricot.

Après un criblage de différents thermoplastiques, le poly-(D,L-lactide) (PLA) et la polycaprolactone (PCL) ont été sélectionnés afin que les tricots soient rigides, possèdent une cinétique de dégradation et une stabilité dimensionnelle compatible pour une implantation. Les tricots ont été produit avec différents ratios de PLA/PCL : PLA_{100}, $PLA_{90}PCL_{10}$ et PLA_{70}/PCL_{30} grâce à une extrudeuse bi-vis corotative puis par filage en voie fondue de 80 filaments de $\varnothing$ ~ 20-35 µm chacun.

Par la suite, la biocompatibilité des tricots PLA/PCL a été testée dans une étude préliminaire (Fig. 1).

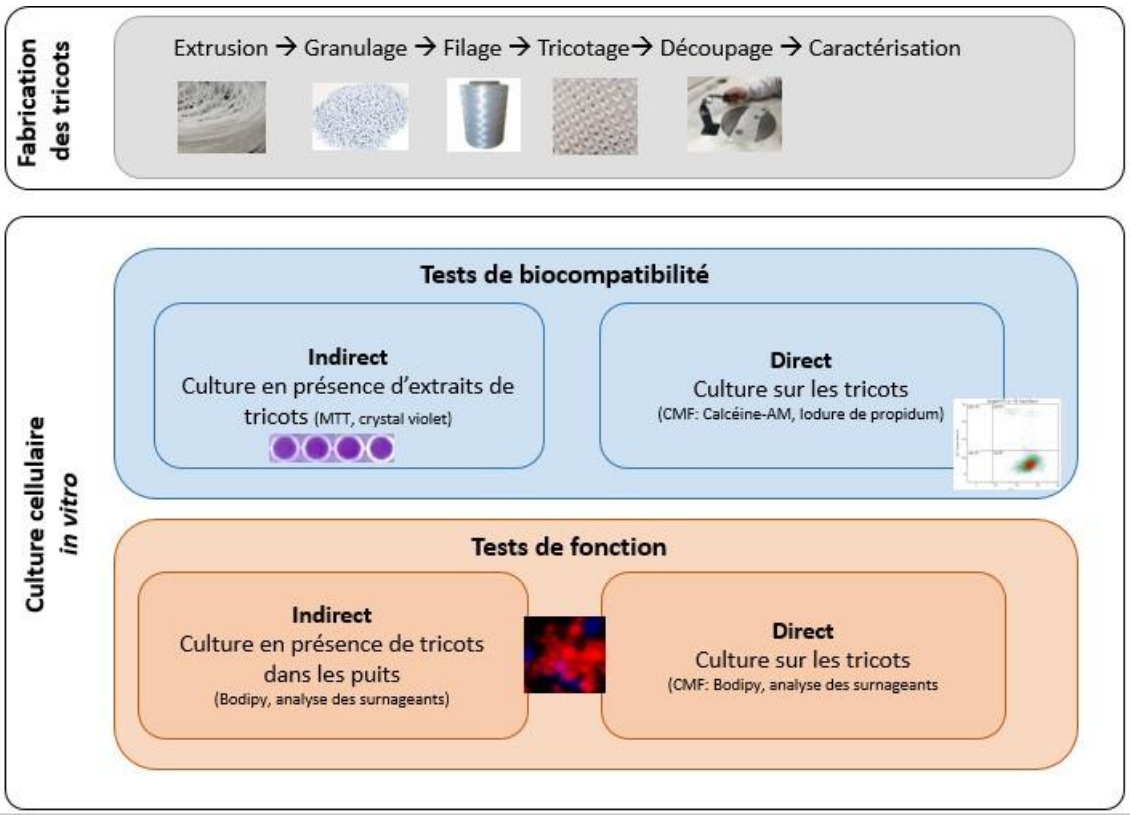

Figure 1: Plan d'expérience

Des cellules du lignage adipocytaire (D1 ORL UVA, 3T3-L1) ont été placées en contact direct ou indirect avec les tricots et différents paramètres ont été suivis tels que la viabilité et la prolifération (Indirect : crystal violet, MTT ; Direct : Calceine-AM, Iodure de propidium) sans révéler de toxicité importante et de différence en fonction de la composition des tricots. Dans un second temps, la différenciation adipocytaire a été étudiée en microscopie à fluorescence (Hoechst, Bodipy 493, Iodure de propidium) couplée à l'analyse du surnageant (pH, glucose, lactate, triglycérides) montrant la capacité des cellules à se différencier en présence des supports en PLA/PCL.

Cette étude montre des résultats prometteurs pour le domaine de l'ingénierie tissulaire, avec une capacité significative du support textile à permettre la prolifération et la différenciation en adipocytes.

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P13: MECHANICAL CHARACTERIZATION OF A ROTATING BIOREACTOR FOR TISSUE ENGINEERING

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Keywords : rotating bioreactor; tissue engineering; fluid mechanics

ABSTRACT

Biological scaffolds composed of extracellular matrix (ECM) derived from decellularized tissue are increasingly used in regenerative medicine [1]. Esophageal tissue engineering is a promising approach tocreate an esophageal substitute and improve clinical results in diseased esophageal treatment and surgery. Therefore, the need has arisen to develop decellularization techniques in order to obtain a clinical grade esophageal extracellular matrix. Decellularization should preserve the general structure and the biomechanical properties of the organ. Preservation of native ECM structure is essential to createa biocompatible scaffold that can be used for further cell seeding, differentiation and proliferation. In thisstudy, decellularized scaffolds are prepared from pig esophagus using mild detergents, acids, and enzymes to remove animal cells, with the objective to provide scaffolds for recellularization with human stem cells, thus producing a new human esophagus [2]. For this purpose, a flow perfusion bioreactor is used: the rotary cell culture system (RCCS), commercially available from Synthecon (Houston, TX) [3]. This device allows liquid flow within the tubular esophagus, as well as a mechanical rotation in and around the tissue in two successive closed chambers. The aim of this paper is to provide an experimental and theoretical mechanical characterization of this flow device, in order to determine: i) the velocity fields, pressures, shear stresses in the fluid without suspended cells, ii) the forces that act on a suspended cell and determine its motion.

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P15: DESIGN OF DEGRADABLE STAR-SHAPED COPOLYMERS FOR THE CONCEPTION OF BIORESORBABLEANTI-INFLAMMATORY PATCHS

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Keywords: resorbable networks, medical device

ABSTRACT

Degradable copolymers, such as elastomers and hydrogels, are largely spread among biomedical applications owing to their potentials for use in medical devices, like surgical patchs, or as drug deliverysystems, like subcutaneous therapeutic depot[1,2]. However, standard linear prepolymers present some limitations: difficulty to modulate and reach the adequate properties due to their low molecular weight, limited functionality leading to low crosslinking efficiencies if no toxic photoinitiators are used.

To overcome these limitations, our team recently designed eight-armed polyether-polyester star block copolymers, composed of eight-arm poly(ethylene glycol) core and poly(lactide) or poly(caprolactone) side arms. These copolymers exhibited a significant interest, since it is possible to obtain either elastomer or hydrogel by adjusting the polyether-polyester ratio[3,4]. Moreover, once the polymers have been synthesized by ring opening polymerization, the chain ends can be functionalized either with (meth)acrylic groups[5] to allow UV cross-linking or with bioadhesive groups to promote bioadhesion.

These copolymers are currently developed to produce a biodegradable self-rolled/self-unrolled multi- layer patch that could be applied locally by colonoscopy without surgical intervention to treat alterations of colonic tissue induced by radiotherapy. This patch will act as a dressing loaded with anti- inflammatory molecules that could protect and heal the ulcerated area. One major objective is to design the patch so that i) it facilitates the placement into the colon by surgeons under a rolled shape and ii) it then self-unrolls and adheres to the ulcerated zone to permit a targeted unidirectional release toward tissues.

Figure 1. Multi-layer structure model and prototype of self-rolled patch

In this communication, the methodology to build the patch will be presented. In more details, the synthesis of the polymers and the preparation of the bi-layered construct (figure 1) and its cross-linking under UV irradiation will be described. The mechanical properties of each layer and of the patch will be discussed. Evaluation of the patch ability to self-rolling[6] due to the different swelling behaviours of the two layers, the biodegradation properties and the loading capacities with drugs will be presented.

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P18: INTER-DONOR VARIABILITY EVALUATION OF HUMANCELL-ASSEMBLED EXTRACELLULAR MATRICES

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Keywords : Cell-Assembled Extracellular Matrix; Inter-Donor Variability; Human Fibroblast

ABSTRACT

Many laboratories have developed tissue-engineered approaches based on the ability of mesenchymal cells to assemble in vitro their endogenously-secreted extracellular matrix. However, patient-to-patient variability of this cell-assembled extracellular matrix (CAM) production can be a hurdle for clinical applications. This study aimed to evaluate this variability as well as parameters that drive CAM production. To this end, human CAM sheets were produced using different primary dermal fibroblast populations obtained from 21 donors/patients requiring arteriovenous shunt.

Results demonstrated that the strength, the thickness, and the hydroxyproline content of the CAM sheets varied between donors by 33% (coefficient of variation), 19%, and 24%, respectively. Another objective was to characterize the CAM matrisome to better understand its relation with the CAM properties. The CAM sheet strength showed moderate and strong positive correlations with the CAM thickness and hydroxyproline quantity, respectively. A detailed CAM matrisome characterization was performed by mass spectrometry and confirmed the inter-donor variability in term of CAM protein composition. Data also revealed that the CAM strength correlates with collagen alpha-1(I) chain abundance. The CAM thickness showed strong correlations with fibrillin-1, dermatopontin, and peroxidasin, which are involved in collagen fibril formation and stabilization. In addition, the CAM hydroxyproline quantity intensely correlated with proteoglycans (e.g. decorin) and ECM regulators (e.g. serpin H1) involved in collagen fibril biosynthesis.

Finally, this study formally evaluates the CAM inter-donor variability in a clinical manufacturing context. Furthermore, the detailed CAM composition characterization identified molecular predictor of the CAM properties and possible targets for improving CAM strength.

P19: SUIVIE NON INTRUSIF DU RYTHME CARDIAQUE AU TRAVERS DES DEFORMATIONS D'UN POLYMERE : CARACTERISATION DE LA MOUSSE POLYURETHANE

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Mots de passe : Ballistocardiographie, modélisation numérique, polymère, hyper élasticité,viscoélasticité

Résumé :

D'après l'Organisme Mondial de la Santé, les maladies cardio-vasculaires sont les premières causes de mortalité dans le monde. La surveillance domestique, la rapidité et la précision des mesures de l'activité cardiaque sont des approches de prévention qui aideraient à réduire le taux de mortalité de la population mondiale. La ballistocardiographie (BCG) est la mesure des forces balistiques générées par le cœur.

Cette technologie est implémentée dans un dispositif médical utilisant une mousse de polyuréthane et un capteur afin de rendre non-intrusif la mesure du rythme cardiaque. La caractérisation de la mousse est l'une des étapes clé pour l'étude de ce dispositif.

La mousse polyuréthane présente un comportement différent en fonction du niveau de déformation, du type de sollicitation (statique, quasi-statique et dynamique) et de la durée de la sollicitation. Deux types d'essais ont été réalisés afin d'étudier son comportement mécanique : un essai de compression pour l'aspect élastique et un essai de relaxation pour l'aspect visqueux.

La mousse polyuréthanne présente en compression un comportement élastique sous forme d'une hystérésis pouvant être segmenté, en chargement, en trois régions. Les trois régions peuvent être modélisées par une droite.

Avec l'hypothèse de sollicitation quasi-statique, un modèle élastique linéaire est un choix à considérer en petites déformations. Pour des grandes déformations, les modèles élastiques linéaires ne sont plus assez précis, seuls les modèles hyper élastiques sont à privilégier. Le modèle hyper élastique choisi est celui d'Ogden à deux paramètres. L'aspect visqueux sera modélisé uniquement par un modèle visco-élastique utilisant les paramètres de Prony. Le choix du nombre de paramètres de ces modèles est un compromis ente précision et complexité.

Ces lois de comportement identifiées seront implémentées dans le logiciel de simulation « Ansys ». La mousse est représentée par un cube de 10 cm de côté. Pour de petites déformations, ce cube est sollicité par une force linéaire. Pour de grandes déformations, le cube sera comprimé jusqu'à 10% de déformation.

La validation se fera par confrontation avec les essais expérimentaux. Pour de petites déformations, le modèle d'élasticité linéaire et le modèle hyper élastique ont une précision de l'ordre de 10^{-3}. Pour les plusgrandes déformations, le modèle hyper élastique choisi est assez précis avec une précision de l'ordre de 10^{-7}

. La précision du comportement visqueux quant à lui sera de l'ordre de 0,7. La précision sera définiecomme étant la somme des distances entre les points de mesure expérimentale et numérique.

P21: TRIPLE-HELICAL PEPTIDES FOR CARTILAGE TISSUE ENGINEERING

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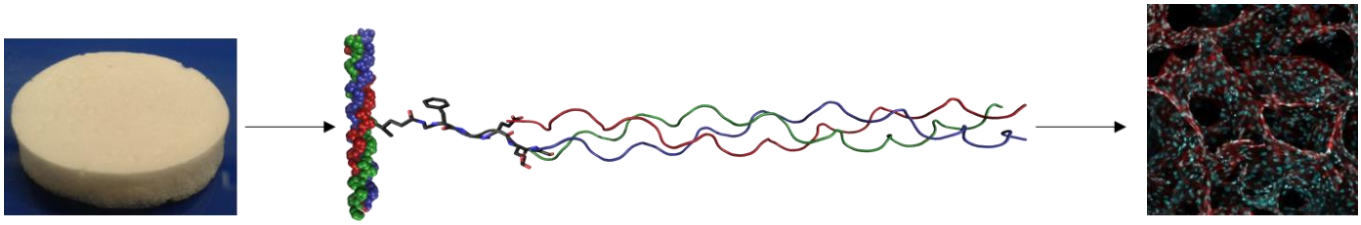
Keywords : Collagen ; Triple-helical peptide ; Biomaterial functionalization

ABSTRACT
The development of cell-laden biomaterials to repair damaged tissues represents a major challenge in regenerative medicine. Collagen, the main constituent of the extracellular matrix (ECM), naturally provides a structural and biological support for cells, and is frequently advocated as a prominent material for tissue engineering. The mechanical properties and stability of collagen-based biomaterials can be improved by covalently crosslinking collagen chains, most often using carbodiimides. However, this chemical treatment involves amino acid residues in the collagen sequence that are naturally engaged in the recognition of cellular collagen-binding receptors, such as the α1β1, α2β1, α10β1 and α11β1 integrins or the discoidin domain receptors (DDRs) 1 and 2. This results in a loss of cell-biomaterial interactions, leading to impaired cellular function, adhesion and viability.

To restore biological cues naturally provided by collagen, carbodiimide-crosslinked collagen biomaterials have been functionalized with triple helical peptides (THPs). THPs are composed of a series of triplets, with a glycine every three residues, that adopt the triple-helix structure of native collagen and can replicate binding sites of the collagen sequence. Active sequences include GFOGER and GLOGEN (binding to the α1β1, α2β1, α10β1 and α11β1 integrins) or GPRGQOGVMGFO (binding to DDRs, Secreted Protein Acidic and Rich in Cysteine (SPARC) and von Willebrand Factor (vWF)).

THPs were covalently grafted to collagen biomaterials upon UV exposure through the Diazirine photoreactive group. This functionalization led to the recovery of cell survival, proliferation and function in carbodiimide-crosslinked collagen films and 3D scaffolds. THPs notably supported endothelial cell survival over 10 days, cardiomyocyte coordinated contraction and embryonic stem cell-derived cardiac cell maturation, highlighting their strong potential in heart tissue engineering.



We now aim to transpose this technology to cartilage regenerative medicine. We are currently investigating the influence of THPs on mesenchymal stem cell (MSC) behavior, focusing on conditions driving their differentiation into chondrocytes. THPs that favor chondrogenesis and cartilage ECM production by mature chondrocytes will be grafted on collagen biomaterials to yield an engineered cartilage tissue. This project will contribute to our fundamental understanding of the role of collagen-binding receptors in MSC response and will establish new methodologies to repair damaged cartilage, using THP-derived biomaterials as gels to fill in cracks or as 3D scaffolds to be implanted on cartilage focal lesion.

P22: CONCEPTION OF PHOTOPOLYMERISABLE, DEGRADABLE AND BIOACTIVE POLYMERIC INK FOR MENISCUS REGENERATION

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Keywords: Photopolymerisation, Poly(acid)-lactide, peptides, 3D printing, Tissue regeneration

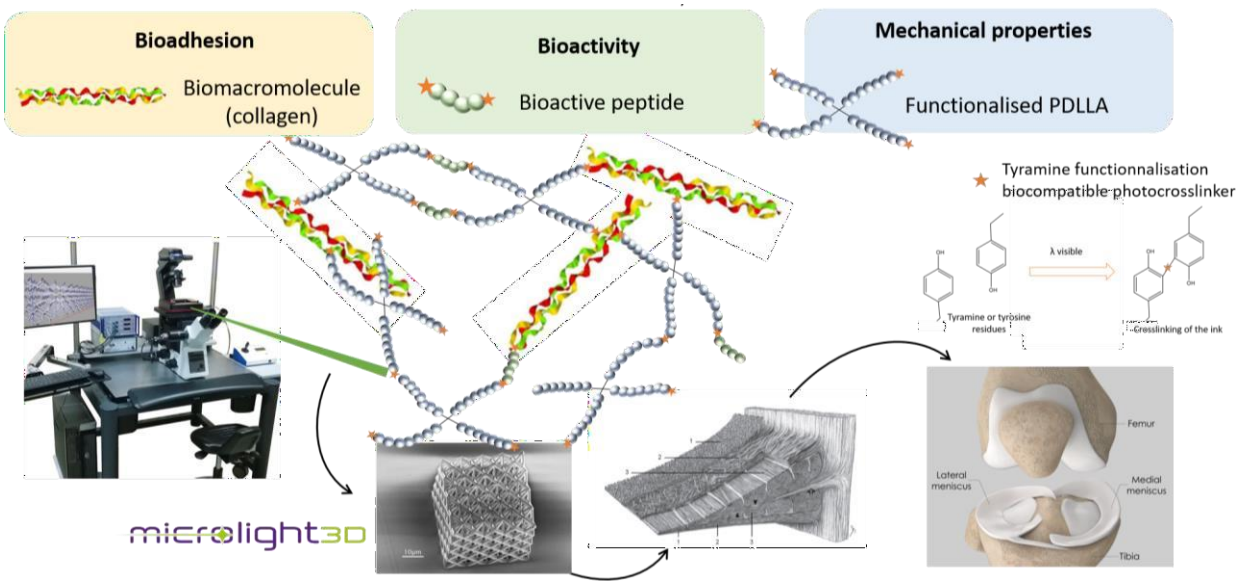
ABSTRACT

Nowadays, 3D printing techniques are giving rise to new processing strategies. Photopolymerisation offers new advances with high-definition techniques like 2 photon polymerisation (2PP), which allows photo-triggered crosslink with micro to nanometric resolution. CAD-customized implants are plebiscited for repairing complex default especially in physiogically microstrutured tissues like meniscus. However, for this tissue a good balance with both mechanical and bioactive properties need to be found. Indeed, if various polymeric inks exist, very few of them has shown good properties concerning both tissue regeneration and shear/compression strength. Therefore, biocompatible inks should be conceived to fit closely physiological properties in order to finally meet clinical requirements.

The aim of this project is to develop a new biocompatible, photo-triggered and degradable polymer-based ink. Poly (D,L-lactic acid) is a well-known polymer, widely used in biomaterials field as a biodegradable material which has shown great biocompatibility. In order to make this polymer photopolymerizable, a biocompatible photocrosslinker, tyramine, was grafted on both extremities of polymer chains.

Subsequently, peptides were synthesized to provide bioactive properties directed toward meniscus regeneration to the polymeric matrix and thereafter incorporated into the ink. Biomacromolecules such as collagen will be added to the ink in order to create a suitable environment to enhance cell migration and proliferation.

In this poster, we present the synthesis of a 4-arm PDLLA star synthesis and its functionalization with tyramine through PNC pathway. We also present 2PP technique and the preliminary tests in order to verify photocrosslinking related to functionalization percentage.



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P23: DESIGN OF COMPOSITE HYDROGELS FOR EXTRUSION BIOPRINTING: MOLECULAR INTERACTIONS, RHEOLOGICAL BEHAVIOR AND PRINTABILITY

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Keywords : Composite hydrogel, bioprinting, rheology

Bioinks for extrusion bioprinting consist of a cell population suspended in a biopolymer solution or a weakly crosslinked hydrogel.[1] In order to be properly extruded in a well-defined 3D objects, bioinks must possess an adequate rheological behavior. More precisely, the polymer matrix of the ink should display (i) shear thinning properties, (ii) a yielding behavior and (iii) a rapid recovery of their viscosity post printing.[2] Such properties are seldom achieved with simple biopolymer solutions.[3]

To address this issue, nanoparticles (NPs) have been recently introduced in bioink formulations. By interacting with the polymer chains in the ink, NPs have been found to induce shear-thinning and yielding behaviors in polymer-based bioinks thereby improving their printability.[4] However, there is no systematic understanding of the link between the NP/polymer interactions, the resulting rheological properties and the ultimate printabilityof the system.

Herein, we address this question in two distinct parts. Firstly, by characterizing the rheology of synthetic polymer solutions (Pluronic) and submitting them to printing experiments, we precisely quantified, for the first time, the rheological parameters (shear thinning coefficients and yield stress values) to be targeted in order to ensure an adequate printability.

Secondly, by performing rheology and printing experiments on composite systems in which biopolymers and NPs interact in different ways, we described the effect of specific molecular interactions on the rheology and printability of composite systems. For that, hyaluronic acid (HA) was used as biopolymers in combination with silica nanoparticles (SiNPs). HA was selected for its biocompatibility, biodegradability and its previous use in bioink formulations[4] while SiNPs were chosen because their surface chemistry can be modified so as to tune their interaction with HA.[5] Different formulations of the composite systems were prepared upon varying structural (SiNP size, chain length, concentration) and chemical (negatively and positively charged SiNP surface) parameters. The result of rheological analysis showed that the nature and the extent of the polymer/NP interaction greatly influence the rheology of composite systems. Drawing a parallel with the first part of this work, we demonstrated that weak NP/Polymer interactions (electrostatic, hydrogen bond) were not sufficient to reach the targeted rheological parameters for adequate printing.

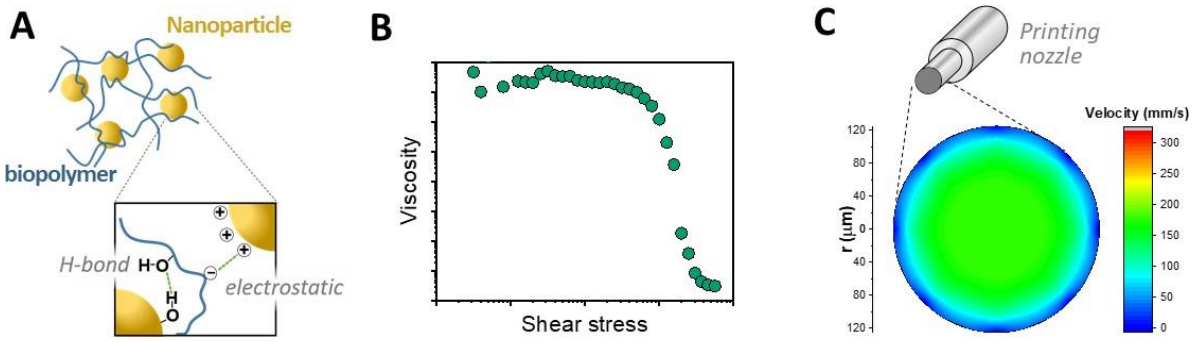

Figure 1: Establishing the link between NP/Polymer interactions and the rheological behavior and printability of composite hydrogels. (A) Scheme of molecular interactions in composite hydrogels. (B) typical shear stress sweep rheology experimentto determine the yield stress. (C) Flow profile of material with adapted rheology for extrusion printing.

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P26: CHITOSAN-FIBRONECTIN HYDROGEL FOR APPLICATION IN TISSUE ENGINEERING

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Key words: hydrogel, chitosan, fibronectin

ABSTRACT

Among the different strategies developed in regenerative medicine, the use of cellularized hydrogels emerges as one promising solution. 3D hydrogel polymeric network must be adapted to favor a correct cell behavior and to provide an appropriate remodelable environment to produce a new extracellular matrix (ECM). Thus, hydrogel needs specific mechanical properties and appropriate biological cues(1). Chitosan (CS), a natural polysaccharide, has been extensively studied as a component of hydrogels applied in tissue engineering. Nevertheless, CS lacks binding sites for cell adhesion therefore the addition of biological signals is necessary. Fibronectin (Fn) is an ECM dimeric glycoprotein and the principal molecule involved in cell adhesion, migration and differentiation(2). It has been shown that the covalent addition of Fn using 1-ethyl-3-(3 [dimethylamino]propyl) (EDC) and N- hydroxysulfosuccinimide (sulfo-NHS) ameliorates cell adhesion and proliferation at the surface of CS membranes(3).Moreover, the presence of Fn increases biological and specific mechanical rigidity in polyelectrolyte-based thin films(4). Herein, a novel formulation of CS/Fn hydrogels was developed using EDC/sulfo-NHS as cross-linking agents. This technique was investigated to provide biological cues and improve the viscoelastic properties of the hydrogel. CS and Fn solutions were mixed at a monomer molar ratio of 1:100 (Fn:CS) by stirring. EDC/sulfo-NHS solution was added to the mixture and crosslinking was attended by stirring for

4h at room temperature, then for 20h at 4°C. Hydrogel without Fn was also prepared. Samples were characterized by FTIR and rheology. For cell culture, samples were prepared in sterile conditions and rinsed with phosphate-buffered saline (PBS). Cell behavior was evaluated using pre-osteoblast cells (MC3T3-E1). Cell adhesion and proliferation were observed by confocal microscopy after incubation of 24h and 72h.Homogeneous and transparent CS/Fn hydrogels were obtained. FTIR spectra revealed an increase in amide I peak in hydrogels, but no differences between hydrogels with or without Fn. Rheology demonstrated elastic and stable hydrogels. However, Fn did not affect the viscoelastic behavior in hydrogels. After 24h of incubation, cell adhesion was observed only in CS/Fn hydrogels (Fig.1a) (spread morphology with a high quantity of actin fibers in cell cytoskeleton). Cell proliferation was also observed only in CS/Fn hydrogels after 72h ofincubation (Fig.1b).

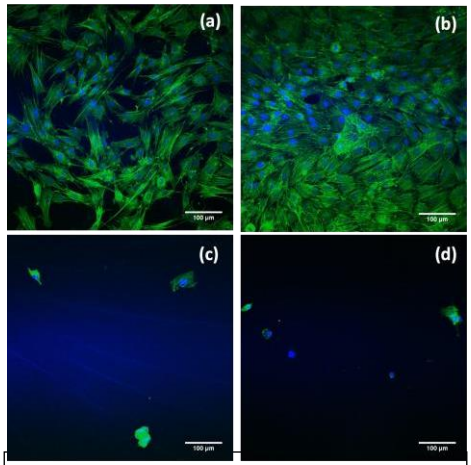

Fig. 1. MC3T3-E1 cells on CS/Fn hydrogels (Fn covalent binding): (a) 24 h and (b) 72 h of incubation. MC3T3-E1 cells on hydrogels without Fn: (c) 24 h and (d) 72 h of incubation

In conclusion, CS/Fn hydrogels demonstrated the need of biological cues (Fn) to promote cell adhesion and proliferation. The addition of Fn did not modify the viscoelastic behavior of the hydrogels. Further analyses are needed to better understand the chemical reaction involved in hydrogel formation.

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P28: ETUDE DE L'ADHERENCE DE STAPHYLOCOCCUS AUREUS SUR DIVERSES SURFACES LIEES AU CONTEXTE OSSEUX

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Mots clefs : adhérence, *Staphylococcus aureus*, os, prothèses, phosphate de calcium

RÉSUMÉ DES TRAVAUX

Les infections bactériennes sur matériaux et plus particulièrement sur prothèses ostéoarticulaires sont décrites comme ayant des origines variées (hématogène, contiguë ou exogène lors de la pose de l'implant). L'espèce majoritairement impliquée est *Staphylococcus aureus.* Ces infections sont complexes du fait de la capacité des bactéries à adhérer sur le matériau et à former un biofilm résistant aux traitements antibiotiques.

Dans cette étude, nous nous sommes intéressés au comportement de l'espèce bactérienne *Staphylococcus aureus* [deux souches sensibles à la méthicilline (SASM) : CIP 53.154 et SH1000, et une souche résistante à la méthicilline (SARM) : USA300] sur plusieurs surfaces : le phosphate de calcium (CaP – utiliser pour le revêtement prothétique notamment), le collagène (protéine majoritaire dans le tissu osseux) et la fibronectine (parmi les premières protéines à adhérées au matériel prothétique) recouvrant du titane pour mimer la surface d'une prothèse implantée.

Dans un premier temps, nous avons observé jusqu'à 10 fois plus de bactéries adhérées par mm² sur le support CaP pour les souches SASM et 5 fois plus pour la souche SARM que sur les supports fibronectine et collagène. L'observation de ces conditions en microscopie électronique à balayage a révélé une morphologie normale des bactéries mais aussi une production de matrice dans certaines conditions, notamment pour la souche CIP 53.154.

Bien que les supports phosphocalciques restent des substrats privilégiés pour l'adhérence de *S. aureus*, la présence simultanée des trois types de supports entraîne un changement du comportement des souches CIP 53.154 et USA300, qui voient leur adhérence favorisée sur les supports collagène et fibronectine en présence du support CaP (4 à 5 fois plus de bactéries), alors que l'adhérence de SH1000 est diminuée de 5 fois sur le CaP en présence des deux autres supports.

Dans un second temps, nous avons observé que le niveau d'expression des gènes impliqués dans la formation de biofilm sur ces supports différaient entre les SASM et le SARM. La surexpression par les SASM, sur tous les types de surfaces, du gène *fnbpB* (codant pour une adhésine), et celle du gène *agrB* impliqué dans le *quorum sensing* sur le CaP pour le SARM soulignent la mise en place de systèmes différents dans les étapes d'adhérence.

En conclusion, l'adhérence de *S. aureus* sur les surfaces testées est souche-dépendante cependant les surfaces phosphocalciques restent des surfaces attrayantes pour cette espèce bactérienne et nécessitent d'adapter les stratégies antimicrobiennes lors de leur utilisation en clinique.

P29: PHOTOPOLYMERIZATION OF DEGRADABLE PEG-BASED HYDROGELS WITH ADJUSTABLE SWELLINGAND MECHANICAL PROPERTIES

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Keywords: hydrogel, degradable, mechanical properties

ABSTRACT

Poly(ethylene glycol) (PEG) hydrogels are used in a wide range of biomedical applications such as surgical glues and sealants, scaffolds for tissue engineering, vehicles for drug delivery and cell therapies [1]. Biomaterials based on the rapid photo-polymerization of PEG-diacrylate (PEGDA) have gained a lot of attention for the numerous possibilities they offer to build biocompatible functional systems [2]. In particular, degradable thiol-acrylate photopolymers can be synthetized from the mixed mode polymerization of a PEGDA chains with thiol cross-linkers [3]. Here we report the photo-initiated synthesis of PEG-based hydrogels with adjustable mechanical properties and swelling behavior. Our approach consisted in polymerizing PEGDA through a mixed mode step-chain growth mechanism in presence of mixtures of mono- and tetra-thiols. In a systematic study on model short PEGDA chains (Mn = 700 g/mol), we explored how hydrogel properties such as swelling ratio, degradation profile and mechanical strength can be finely adjusted by varying the thiol/acrylate functions ratio and the mono-/tetra-thiols ratio. We then applied this strategy to long chains of hydrolytically degradable poly(beta-thioester)s (from 2000 to 6000 g/mol) bearing acrylate end groups [4], [5]. This provided a way to enhance the biodegradability and the toughness of these PEG-based hydrogels, which are important features for biomedical applications. In particular, the bioadhesive performances of these gels were characterized by *ex vivo* tests on porcine liver tissues. This approach offers a simple way to fine tune the topology of PEG gels, insert functionalities and expand the scope of their applications.

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P30: ANIMAL BONE MATRICES PURIFICATION BASED ON MODIFIED SUPERCRITICAL CO_2 FLUID PROCESSES: BIOCHEMICAL CHARATERIZATIONS AND BONE TISSULAR REGENERATION CAPACITIES

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Keywords : Supercritical CO_2, bone matrix, xenogeneic source

ABSTRACT

The craniofacial area is prone to trauma or pathologies, often resulting in large bone damages, that cannot heal spontaneously. Their reconstruction is a real challenge and the gold standard surgical technique remains human bone grafting (autologous and allogenic). The increasing demand for bone grafting and the relative availability of autologous or allogenic materials are important driving forces of bone replacement research [1]. In this context, the use of alternative xenogeneic materials to repair human bone defects is a promising approach, with their natural structure and properties close to human bone. However, the risk of rejection due to immunogenic molecules – such as the alpha-Gal epitope [2] – is a major concern in animal bone transplantation to the human. To avoid immunogenicitywithout compromising biological and mechanical properties of the xenogeneic bone matrix, boneswere treated with the Supercrit® process. It is based on the delipidation of bone tissue by supercritical carbon dioxide, combined with a chemical oxidation of the residual proteins [3]. Supercrit® is already approved on human bone, showing complete viral inactivation and good preservation of bone properties [4]. The interest of transposing it to animal bone tissues is patent.

Our in vitro results show the efficiency of the Supercrit® process on animal bone. However, remaining traces of alpha-Gal epitope are evident on the treated bone, suggesting the need to improve the purification process. An optimized process, called Goxcrit, has been developed. It results in an important reduction of the quantity of solvent used, and therefore diminishes the potential toxicity of the chemicals on bone integrity and quality.

In vivo studies are currently in progress, the first one to analyze the tolerance of the treated biomaterials in subcutaneous mice ectopic sites; and the other one to assess their osteogenic capacity on bone regeneration in rat calvaria bone defect.

In vitro bone characterizations are conducted to complete our in vivo data. By comparingthermogravimetric analyses, scanning electron microscopy (SEM) images, and the biochemical composition of bones, the effectiveness of the Goxcrit process on animal bone has been demonstrated,with the added benefit of using less solvent.

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P31: HOW TO BUILD A BETTER TISSUE-ENGINEERED VASCULAR GRAFT WOVEN FROM CELL-ASSEMBLED EXTRACELLULAR MATRIX YARN?

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Key words: Vascular graft, weaving, cell-assembled extracellular matrix

ABSTRACT

INTRODUCTION: Vascular grafts are implanted daily, whether it is for leg and coronarybypasses or as arteriovenous shunts. Autologous blood vessels are the gold standard but havelimited availability while synthetic materials are prone to thrombosis, intimal hyperplasia andinfections. To overcome these limitations, our team produced a biological Tissue-Engineered Vascular Graft (TEVG) woven from yarn of Cell-Assembled Extracellular Matrix (CAM). This textile-based approach is very versatile because it gives fine control over the geometrical andmechanical properties of the TEVG. The goal of this study is to establish how changes in production parameters (e.g.: yarn count, yarn density, etc.) affect the properties of the TEVG(e.g.: mechanical properties, wall thickness, surface waviness, etc.).

METHODS: CAM sheets were produced by sheep skin fibroblasts seeded in 225 cm^2 flasks at passage 7 and cultured for 8 weeks in DMEM/F-12 with 10% FBS and 0.5 mM Na L-ascorbate.Threads were produced with a custom motorized device composed of rolling blades spaced atthe desired width (5 mm). Woven grafts were assembled on a circular loom and composed ofa series of longitudinal threads, called "warp", and a circumferential one that spirals along thelength of the vessel, the "weft". The latter was made of two 5 mm-wide threads twisted together at 5 $rev.cm^{-1}$. The first production parameter evaluated was the warp count (or number of longitudinal threads). Three warp counts were tested around a tube of 4.2 mm: 35,43 and 51 (n=3 TEVGs). Transmural permeability, compliance, suture retention strength and burst pressure were evaluated. Surface waviness, wall thickness and geometrical properties were assessed macroscopically and by X-ray microtomography.

RESULTS & DISCUSSION: Warp count had a significant effect on the overall properties of the TEVGs. A lower warp count resulted in TEVGs with thinner walls, that could be explained by the longitudinal threads spreading more along TEVG circumference. Consistent with a thinnerwall, a lower warp count led to TEVGs with lower strength. In addition to that, the surface profile was influenced by the warp count, which may have an impact on blood compatibility.

CONCLUSION: We demonstrated the influence of warp count on the geometrical and mechanical properties of a TEVG woven from CAM yarn. The investigation of the influence ofweft width and weft twisting is underway to improve our ability to control TEVG properties.

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GAROT	Charlotte	charlotte.garot@orange.fr	Jeune chercheur (thèse, Post-doc)	CNRS	CEA/IRIG/DS/BRM	Polymères et hydrogels;Ingénierie tissulaire;Interactions cellules-matériaux;Ingénierie de surface et fonctionnalisation;Fabrication additive;Interactions tissu-matériaux;Evaluation in vitro des biomatériaux;Evaluation in vivo des biomatériaux;Dispositifs médicaux;Evaluation clinique
GAUTHIER	Rémy	remy.gauthier@univ-lyon1.fr	Jeune chercheur (thèse, Post-doc)	UMR 5615 - CNRS UCBL	Laboratoire des Multimatériaux et Interfaces	Céramiques;Ingénierie tissulaire;Interactions cellules-matériaux;Diagnostic médical;Fabrication additive;Interactions tissu-matériaux;Evaluation in vitro des biomatériaux;Evaluation in vivo des biomatériaux
GOBIN	Maxime	gobin@brothier.com	Jeune chercheur (thèse, Post-doc)	CY Cergy Paris Université	ERRMECe	Délivrance de principes actifs;Ingénierie de surface et fonctionnalisation;Evaluation in vitro des biomatériaux
GORIN	Caroline	caroline.gorin@u-paris.fr	Chercheur, Industriel, Clinicien	Université de Paris	UR2496	Ingénierie tissulaire
GRIBOVA	Varvara	varvara.gribova@gmail.com	Jeune chercheur (thèse, Post-doc)	Inserm	Biomatériaux et Bioingénierie	Polymères et hydrogels;Ingénierie tissulaire;Délivrance de principes actifs;Ingénierie de surface et fonctionnalisation;Interactions tissu-matériaux;Evaluation in vitro des biomatériaux;Dispositifs médicaux
GRIVEAU	Louise	louise.griveau@gmai.com	Jeune chercheur (thèse, Post-doc)	CNRS UMR 5305	Laboratoire de Biologie tissulaire et ingénierie thérapeutique	Polymères et hydrogels;Ingénierie tissulaire;Interactions cellules-matériaux
GROSJEAN	Mathilde	mathilde.grosjean@umontpellier.fr	Jeune chercheur (thèse, Post-doc)	Université de Montpellier	Département Polymères pour la Santé et Biomatériaux (IBMM-UMR5247)	Polymères et hydrogels;Interactions cellules-matériaux;Délivrance de principes actifs;Interactions tissu-matériaux;Evaluation in vitro des biomatériaux;Dispositifs médicaux
GUICHEUX	jerome	jerome.guicheux@inserm.fr	Chercheur, Industriel, Clinicien	INSERM	INSERM-UN-ONIRIS UMR 1229-RMeS	Ingénierie tissulaire
GUIHARD	Pierre	pierre.guihard@univ-nantes.fr	Jeune chercheur (thèse, Post-doc)	Université de Nantes	RMeS - UMR1229	Ingénierie tissulaire
HADIDA	Mikhael	m.hadida@emse.fr	Jeune chercheur (thèse, Post-doc)	Mines Saint-Etienne	SAINBIOSE U1059	Ingénierie tissulaire;Fabrication additive;Interactions tissu-matériaux
HAMIDI	Salim	salim.hamidi.etu@univ-lille.fr	Jeune chercheur (thèse, Post-doc)	INSERM-Faculté de Medecine Lille	INSERM U 1008	Polymères et hydrogels;Céramiques;Matériaux composites;Ingénierie tissulaire;Interactions cellules-matériaux;Délivrance de principes actifs;Ingénierie de surface et fonctionnalisation;Diagnostic médical;Fabrication additive;Méthodes bio-inspirées;Interactions tissu-matériaux;Evaluation in vitro des biomatériaux;Evaluation in vivo des biomatériaux;Dispositifs médicaux;Evaluation clinique

HELARY	Christophe	christophe.helary@upmc.fr	Chercheur, Industriel, Clinicien	Sorbonne Université	Laboratoire de la Chimie de la Matière Condensée	Délivrance de principes actifs
HILDEBRAND	feng	feng.hildebrand@univ-lille.fr	Chercheur, Industriel, Clinicien	Univ Lille	INSERM U1008	Polymères et hydrogels;Ingénierie tissulaire;Interactions cellules-matériaux;Délivrance de principes actifs;Interactions tissu-matériaux;Evaluation in vitro des biomatériaux;Evaluation in vivo des biomatériaux
IANDOLO	Donata	donata.iandolo@emse.fr	Jeune chercheur (thèse, Post-doc)	EMSE	SAINBIOSE	Polymères et hydrogels;Matériaux composites;Ingénierie tissulaire;Interactions cellules-matériaux;Ingénierie de surface et fonctionnalisation;Diagnostic médical;Fabrication additive;Evaluation in vitro des biomatériaux;Dispositifs médicaux
JORDAO	Z. Amélia	amelia.jordao@lattice-medical.com	Jeune chercheur (thèse, Post-doc)	Lattice Medical	Canther UMR 1277 Inserm	Polymères et hydrogels;Ingénierie tissulaire;Interactions cellules-matériaux;Ingénierie de surface et fonctionnalisation;Fabrication additive;Interactions tissu-matériaux;Evaluation in vitro des biomatériaux;Evaluation in vivo des biomatériaux;Dispositifs médicaux;Evaluation clinique
KAWECKI	Fabien	fabien.kawecki@inserm.fr	Jeune chercheur (thèse, Post-doc)	Université de Bordeaux	INSERM U1026 BIOTIS	Ingénierie tissulaire
KERDJOUDJ	Halima	halima.kerdjoudj@univ-reims.fr	Chercheur, Industriel, Clinicien	URCA	EA4691 Bios	
KERIGNARD	Eloïse	e.kerignard@hubebi.com	Jeune chercheur (thèse, Post-doc)	UM-CNRS-ENSCM	IBMM	Polymères et hydrogels;Ingénierie tissulaire;Interactions cellules-matériaux;Délivrance de principes actifs;Ingénierie de surface et fonctionnalisation;Fabrication additive;Interactions tissu-matériaux;Evaluation in vitro des biomatériaux;Evaluation in vivo des biomatériaux
LAGNEAU	NATHAN	nathan.lagneau@etu.univ-nantes.fr	Jeune chercheur (thèse, Post-doc)	UNIVERSITE DE NANTES	RMeS U1229 - INSERM	Polymères et hydrogels
LE BAO	Chau	cbl007@bucknell.edu	Jeune chercheur (thèse, Post-doc)	Hopital Bichat	INSERM U1148 (LVTS)	
LE BIDEAU	Jean	jean.lebideau@cnrs-imn.fr	Chercheur, Industriel, Clinicien	Université de Nantes	Institut des Matériaux Jean Rouxel	Polymères et hydrogels;Matériaux composites;Ingénierie tissulaire;Délivrance de principes actifs;Interactions tissu-matériaux
LEMARIÉ	Lucas	lucas.lemarie@segula.fr	Jeune chercheur (thèse, Post-doc)	INSA Lyon	LBTI (Laboratoire de Biologie tissulaire et Ingénierie Thérapeutique ? UMR 5305 Intranet)	Polymères et hydrogels;Ingénierie tissulaire;Fabrication additive;Méthodes bio-inspirées;Interactions tissu-matériaux;Evaluation in vivo des biomatériaux
LEON-VALDIVIESO	Christopher Yusef	christopher-yusef.leon-valdivieso@umontpellier.fr	Jeune chercheur (thèse, Post-doc)	Université de Montpellier	Département Polymères pour la Santé et Biomatériaux (IBMM-UMR5247)	Polymères et hydrogels;Ingénierie tissulaire;Interactions cellules-matériaux;Evaluation in vitro des biomatériaux
LESIEUR	Romane	romane.lesieur.stag@chu-bordeaux.fr	Jeune chercheur (thèse, Post-doc)	BioTis (U1026)	CIC-IT	Ingénierie tissulaire
LETOURNEUR	Didier	didier.letourneur@inserm.fr	Chercheur, Industriel, Clinicien	INSERM - Université Sorbonne Paris Nord - Université de Paris	LVTS - INSERM U 1148	Polymères et hydrogels;Ingénierie tissulaire;Dispositifs médicaux

L'HEUREUX	Nicolas	nicolas.lheureux@inserm.fr	Chercheur, Industriel, Clinicien	INSERM / Université de Bordeaux	BIOTIS - Laboratoire de Bioingénierie Tissulaire (UMR 1026)	Ingénierie tissulaire
LOGEART-AVRAMOGLOU	Delphine	delphine.logeart@cnrs.fr	Chercheur, Industriel, Clinicien	CNRS	B3OA UMR 7052	Ingénierie tissulaire;Interactions tissu-matériaux;Evaluation in vitro des biomatériaux;Evaluation in vivo des biomatériaux
LOPES CARDOSO FILHO	João Carlos	joao-carlos.lopes-cardoso-filho@univ-grenoble-alpes.fr	Jeune chercheur (thèse, Post-doc)	CEA	CEA IRIG Biosanté BRM	Ingénierie tissulaire;Interactions cellules-matériaux;Ingénierie de surface et fonctionnalisation;Méthodes bio-inspirées;Interactions tissu-matériaux;Evaluation in vitro des biomatériaux
LUTOMSKI	Didier	lutomski@univ-paris13.fr	Chercheur, Industriel, Clinicien	Université Sorbonne Paris Nord	URB2i - UR 4462	Polymères et hydrogels;Matériaux composites;Ingénierie tissulaire;Interactions cellules-matériaux;Méthodes bio-inspirées;Interactions tissu-matériaux;Evaluation in vitro des biomatériaux;Dispositifs médicaux
MAILLARD	Mathilde	mathilde.maillard@insa-lyon.fr	Jeune chercheur (thèse, Post-doc)	INSA de Lyon	MATEIS	Polymères et hydrogels;Céramiques;Ingénierie tissulaire;Diagnostic médical;Fabrication additive;Interactions tissu-matériaux;Evaluation in vitro des biomatériaux;Evaluation in vivo des biomatériaux;Dispositifs médicaux
MALCOR	Jean-Daniel	jean-daniel.malcor@ibcp.fr	Chercheur, Industriel, Clinicien	CNRS	Laboratoire de Biologie tissulaire et Ingénierie Thérapeutique ? UMR 5305	Ingénierie tissulaire;Interactions cellules-matériaux;Ingénierie de surface et fonctionnalisation;Evaluation in vitro des biomatériaux
MALLEIN-GERIN	Frédéric	f.mallein-gerin@ibcp.fr	Chercheur, Industriel, Clinicien	CNRS	Laboratoire de Biologie Tissulaire et Ingénierie thérapeutique CNRS UMR 5305	Ingénierie tissulaire
MARCHAT	David	marchat@emse.fr	Chercheur, Industriel, Clinicien	Ecole Mines Saint-Etienne	Sainbiose, INSERM U1059	Céramiques;Ingénierie tissulaire;Interactions cellules-matériaux;Interactions tissu-matériaux;Evaluation in vitro des biomatériaux;Evaluation in vivo des biomatériaux;Dispositifs médicaux;Evaluation clinique
MARTINIER	Isabelle	isabelle.martinier@sorbonne-universite.fr	Jeune chercheur (thèse, Post-doc)	Sorbonne Université	LCMCP	Polymères et hydrogels;Ingénierie tissulaire;Interactions cellules-matériaux;Méthodes bio-inspirées;Interactions tissu-matériaux;Evaluation in vitro des biomatériaux;Evaluation in vivo des biomatériaux;Dispositifs médicaux
MASSONIE	Mathilde	mathilde.massonie@gmail.com	Jeune chercheur (thèse, Post-doc)	Université de Montpellier	Département Polymères pour la Santé et Biomatériaux (IBMM-UMR5247)	Polymères et hydrogels;Ingénierie tissulaire;Interactions cellules-matériaux;Délivrance de principes actifs;Ingénierie de surface et fonctionnalisation;Fabrication additive;Méthodes bio-inspirées;Interactions tissu-matériaux;Evaluation in vitro des biomatériaux;Dispositifs médicaux
MATHIEU	Noëlle	noelle.mathieu@irsn.fr	Chercheur, Industriel, Clinicien	Institut de Radioprotection et de Surete Nucleaire	LRMED	Ingénierie tissulaire;Evaluation in vivo des biomatériaux
MATON	Mickaël	mickael.maton@univ-lille.fr	Chercheur, Industriel, Clinicien	Université de Lille	Inserm U1008, Groupe de Recherche sur les Biomatériaux	Evaluation in vitro des biomatériaux

M'BENGUE	Marie-Stella	marie-stella.m-bengue@univ-lille.fr	Jeune chercheur (thèse, Post-doc)	Université de Lille	INSERM U1008	Polymères et hydrogels;Fabrication additive;Evaluation in vitro des biomatériaux;Dispositifs médicaux
MICHEL	Raphaël	raphael.michel@cermav.cnrs.fr	Chercheur, Industriel, Clinicien	CNRS	CERMAV	Polymères et hydrogels;Matériaux composites;Ingénierie tissulaire;Interactions cellules-matériaux;Fabrication additive;Interactions tissu-matériaux;Evaluation in vitro des biomatériaux;Evaluation in vivo des biomatériaux;Dispositifs médicaux
MULLER	Quentin	quentin.muller@u-bordeaux.fr	Jeune chercheur (thèse, Post-doc)	InsermU1026	Bioingénierie Tissulaire (BioTis)	Polymères et hydrogels;Ingénierie tissulaire;Interactions cellules-matériaux;Evaluation in vitro des biomatériaux
NATIVEL	Fabien	fabien.nativel@univ-nantes.fr	Jeune chercheur (thèse, Post-doc)	INSERM UMR1229 RMeS	INSERM UMR1229 RMeS	Polymères et hydrogels;Ingénierie tissulaire;Interactions cellules-matériaux;Délivrance de principes actifs;Evaluation in vitro des biomatériaux;Evaluation in vivo des biomatériaux;Dispositifs médicaux;Evaluation clinique
ORIANNE	Borel	borelorianne@gmail.com	Master	Université de Paris	URP 2496 Laboratory Orofacial Pathologies, Imaging, and Biotherapies and Life Imaging Platform (PIV)	Ingénierie tissulaire;Fabrication additive
OUEDRAOGO	Sidzigui	christelle.charifa@gmail.com	Jeune chercheur (thèse, Post-doc)	Université de Haute Alsace	Institut de Sciences des Matériaux de Mulhouse	Polymères et hydrogels;Ingénierie tissulaire;Délivrance de principes actifs;Evaluation in vitro des biomatériaux;Dispositifs médicaux
PAIVA DOS SANTOS	Bruno	brnpaivas@gmail.com	Jeune chercheur (thèse, Post-doc)	Inserm	BIOTIS - U1026	Polymères et hydrogels;Céramiques;Matériaux composites;Ingénierie tissulaire;Interactions cellules-matériaux;Délivrance de principes actifs;Ingénierie de surface et fonctionnalisation;Diagnostic médical;Interactions tissu-matériaux;Evaluation in vitro des biomatériaux;Evaluation in vivo des biomatériaux;Dispositifs médicaux;Evaluation clinique
PALIERSE	Estelle	estelle.paliERSE@espci.fr	Jeune chercheur (thèse, Post-doc)	ESPCI Paris	Chimie Moléculaire, Macromoléculaire, et Matériaux (C3M)	Polymères et hydrogels;Céramiques;Ingénierie de surface et fonctionnalisation;Méthodes bio-inspirées;Interactions tissu-matériaux;Evaluation in vitro des biomatériaux;Evaluation in vivo des biomatériaux;Dispositifs médicaux
PALOMINO DURAND	Carla	cpalominodurand@gmail.com	Jeune chercheur (thèse, Post-doc)	CY Cergy Paris Université	ERRMECe	Polymères et hydrogels;Ingénierie tissulaire;Interactions cellules-matériaux;Délivrance de principes actifs;Evaluation in vitro des biomatériaux
PAPA	Steve	sp.papasteve@gmail.com	Jeune chercheur (thèse, Post-doc)	Université Jean Monnet	SAINBIOSE (LBTO) - U1059 INSERM	Métaux et alliages;Ingénierie tissulaire;Interactions cellules-matériaux;Ingénierie de surface et fonctionnalisation;Méthodes bio-inspirées;Interactions tissu-matériaux;Evaluation in vitro des biomatériaux;Dispositifs médicaux
PARISI	Cleo	clio.parisi@sorbonne-universite.fr	Jeune chercheur (thèse, Post-doc)	Sorbonne Université	Laboratoire de Chimie de la Matière Condensée de Paris (LCMCP)	Polymères et hydrogels;Ingénierie tissulaire;Interactions cellules-matériaux;Méthodes bio-inspirées;Evaluation in vitro des biomatériaux
PATT-LAFITTE	Guillaume	guillaume.lafitte@emse.fr	Jeune chercheur (thèse, Post-doc)	Ecole des Mines de Saint-Etienne	Centre Ingénierie Santé	Polymères et hydrogels;Matériaux composites;Ingénierie tissulaire
PAUTHE	Emmanuel	emmanuel.pauthe@u-cergy.fr	Chercheur, Industriel, Clinicien	CY Cergy-Paris Université	ERRMECe	Polymères et hydrogels;Céramiques;Métaux et alliages;Matériaux composites;Ingénierie tissulaire;Interactions cellules-

						matériaux;Délivrance de principes actifs;Ingénierie de surface et fonctionnalisation;Diagnostic médical;Fabrication additive;Méthodes bio-inspirées;Interactions tissu-matériaux;Evaluation in vitro des biomatériaux;Evaluation in vivo des biomatériaux;Dispositifs médicaux
PICART	Catherine	catherine.picart@cea.fr	Chercheur, Industriel, Clinicien	CEA/CNRS/UGA	EMR Biomimetism and Regenerative Medicine, Unité Inserm U1292 Biosanté	Polymères et hydrogels;Ingénierie tissulaire;Interactions cellules-matériaux;Interactions tissu-matériaux;Dispositifs médicaux
PIEUCHOT	Laurent	laurent.pieuchot@uha.fr	Chercheur, Industriel, Clinicien	CNRS	IS2M	Ingénierie tissulaire;Interactions cellules-matériaux;Ingénierie de surface et fonctionnalisation;Fabrication additive;Méthodes bio-inspirées;Interactions tissu-matériaux;Evaluation in vitro des biomatériaux;Evaluation in vivo des biomatériaux
PINESE	Coline	coline.pinese@umontpellier.fr	Chercheur, Industriel, Clinicien	Université de Montpellier-UFR pharmacie	DBA-IBMM	Polymères et hydrogels;Délivrance de principes actifs;Fabrication additive;Interactions tissu-matériaux;Dispositifs médicaux
POTART	Diane	potart.diane@gmail.com	Jeune chercheur (thèse, Post-doc)	BioTis U1026 - INSERM, Université de Bordeaux	BioTis U1026	Ingénierie tissulaire
QUINCEROT	Marie	marie.quincerot@ibcp.fr	Master	IBCP	LBTI	Polymères et hydrogels;Matériaux composites;Ingénierie tissulaire;Interactions cellules-matériaux;Délivrance de principes actifs;Diagnostic médical;Fabrication additive;Méthodes bio-inspirées;Interactions tissu-matériaux;Evaluation in vitro des biomatériaux;Evaluation in vivo des biomatériaux;Dispositifs médicaux;Evaluation clinique
RANGANATH	Sindhu	sindhu.kotogudda-ranganath@univ-lille.fr	Jeune chercheur (thèse, Post-doc)	University of lille	Inserm U1008	
RATHORE	Arvind	arvind.rathore@inserm.fr	Jeune chercheur (thèse, Post-doc)	INSERM	Inserm U1026 Biotis	Evaluation in vivo des biomatériaux
REFFUVEILLE	Fany	fany.reffuveille@univ-reims.fr	Chercheur, Industriel, Clinicien	Université de Reims Champagne Ardenne	Biomatériaux et Inflammation en site osseux EA 4691	Interactions cellules-matériaux;Interactions tissu-matériaux;Evaluation in vitro des biomatériaux;Evaluation in vivo des biomatériaux;Dispositifs médicaux
ROCHER	Lison	l.rocher@qub.ac.uk	Jeune chercheur (thèse, Post-doc)	Queen's University Belfast	Bioengineering Research Group	Polymères et hydrogels
ROQUART	Maïlie	mailie.roquart@espci.fr	Jeune chercheur (thèse, Post-doc)	Mines Paristech	Centre des Matériaux	Polymères et hydrogels;Ingénierie tissulaire;Interactions tissu-matériaux;Evaluation in vivo des biomatériaux;Dispositifs médicaux;Evaluation clinique
ROTA	Solène	solene.rota@gmail.com	Jeune chercheur (thèse, Post-doc)	CY Cergy Paris Université	ERRMECe	Céramiques;Ingénierie tissulaire;Dispositifs médicaux
ROUDIER	Gaëtan	gaetan.roudier@u-bordeaux.fr	Jeune chercheur (thèse, Post-doc)	Université de Bordeaux	BioTis - Inserm U1026	Ingénierie tissulaire
SAID	Moustoifa	moustoifa.said@univ-grenoble-alpes.fr	Jeune chercheur (thèse, Post-doc)	INSERM	Grenoble Institut Neurosciences U1216	Polymères et hydrogels
SENEPART	Oceane	oceane.senepart@sorbonne-universite.fr	Jeune chercheur (thèse, Post-doc)	Sorbonne Université	LCMCP	Ingénierie de surface et fonctionnalisation;Dispositifs médicaux

SICARD	ludovic	ludovic.sicard@aphp.fr	Jeune chercheur (thèse, Post-doc)	Université de PARIS	UR2496	Polymères et hydrogels;Ingénierie tissulaire;Délivrance de principes actifs;Evaluation in vivo des biomatériaux
SIGAUDO-ROUSSEL	Dominique	dominique.sigaudo@univ-lyon1.fr	Chercheur, Industriel, Clinicien	CNRS	LBTI	Polymères et hydrogels;Ingénierie tissulaire;Interactions cellules-matériaux;Délivrance de principes actifs;Ingénierie de surface et fonctionnalisation;Méthodes bio-inspirées;Interactions tissu-matériaux;Evaluation in vitro des biomatériaux;Evaluation in vivo des biomatériaux;Dispositifs médicaux;Evaluation clinique
SIMON-YARZA	Teresa	teresa.simon-yarza@inserm.fr	Chercheur, Industriel, Clinicien	INSERM U1148	LVTS	Polymères et hydrogels;Ingénierie tissulaire;Interactions cellules-matériaux;Ingénierie de surface et fonctionnalisation;Evaluation in vitro des biomatériaux;Evaluation in vivo des biomatériaux
SOHIER	Jerome	jerome.sohier@ibcp.fr	Chercheur, Industriel, Clinicien	CNRS	MATEIS UMR 5510	Polymères et hydrogels;Matériaux composites;Ingénierie tissulaire;Interactions cellules-matériaux;Délivrance de principes actifs;Evaluation in vitro des biomatériaux;Evaluation in vivo des biomatériaux
THORAVAL	Léa	lea.thoraval@univ-reims.fr	Jeune chercheur (thèse, Post-doc)	URCA	EA 4691 BIOS	Céramiques;Ingénierie tissulaire;Interactions cellules-matériaux;Interactions tissu-matériaux;Evaluation in vitro des biomatériaux;Evaluation in vivo des biomatériaux;Dispositifs médicaux
VELARD	Frédéric	frederic.velard@univ-reims.fr	Chercheur, Industriel, Clinicien	URCA	EA 4691 BIOS	Céramiques;Ingénierie tissulaire;Interactions cellules-matériaux;Interactions tissu-matériaux;Evaluation in vitro des biomatériaux;Evaluation in vivo des biomatériaux;Dispositifs médicaux
VERGNAUD	Florestan	florestan.vergnaud@sigma-clermont.fr	Jeune chercheur (thèse, Post-doc)	Clermont Auvergne INP	Institut de Chimie de Clermont-Ferrand	Céramiques;Matériaux composites;Fabrication additive;Evaluation in vitro des biomatériaux;Evaluation in vivo des biomatériaux
WEISS	Pierre	pierre.weiss@univ-nantes.fr	Chercheur, Industriel, Clinicien	UNIVERSITE DE NANTES	RMeS U1229	Polymères et hydrogels