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Associate professor (Univ. Bordeaux –CHU Bordeaux) Associate researcher, team biofabrication and bioprinting BioTis (U1026)



Research Interests:

Biofabrication, Laser assisted Bioprinting

During my PhD at the University of Toulouse, I worked on osteogenesis imperfecta and sphingomyelinase. I have been appointed as associate professor at the University of Bordeaux . Since 2011 I joined the Tissue Engineering Assisted by Laser in BioTis as associate researcher.

Within the unit, as co-leader of the group "and Biofabrication and bioprinting », our research focuses nowadays on the creation of bone and vascular structures in 3 dimensions by bioprinting assisted by laser.

My early research in the U1026 has been to develop a printable biomaterial. Choosing a composite of collagen hydrogel and alginate has set up a model for the pulp regeneration in dentistry, this work resulted in a publication in the International Journal of Endodontics (Dec 2015). Subsequently, I worked on the isolation, differentiation and bioimpression assisted laser endothelial progenitor cells co-culture cells and mesenchymal stem both from the pulp for bone regeneration,

To my knowledge in photonics and to better understand the physical aspects of laser interaction / biological tissues, I realized an one-year internship at mobility CELIA on the development of a new needleless injection strategy assisted by intense laser. During this internship, I acquired optical skills that allowed me to participate in the design of a new fully automated fire station used in the field of femtoseconds laser bioimpression within the U1026 . The prototype produced by Alphanov is currently used by the company Poietis. I have also filed a patent on the use of laser for removal of fractured surgical instruments.

Vascularization in tissue engineering is a crucial theme for which I considered using a process of bioassembly to produce cellularized microfibers based on my previous expertise in hydrogel and co-cultures. The goal is to create a module within microvascular bone microfiber module capable of

connecting in vivo vasculature and thus allow potential implantation of larger volume substitutes. This method has been patented and received the support of Aquitaine Science Transfer for 18 months of maturation by a technician.

In the same vein, optimization of vascularization is under progress but this time using the bioprinting assisted by laser, hydrogels and co-culture, I supervised a student in MSc whose work focused on the laser assisted bioprinting of mesenchymal stem cells and endothelial cells in co-culture for the creation of pseudo capillary network.

Recent advances in the field of tissue engineering, bio-manufacturing is currently exponential progression, including the manufacture of scaffolds for rapid prototyping. These can be custom-made with internal and external controlled architecture. The manufacturing process, the resolution of the resulting parts and materials used are varied, but these new methods of manufacturing scaffolds fail to overcome the limits related to the mass macro porous materials or the problem of limited cells seeding due in the absence of diffusion of nutrients and oxygen. Thus, despite the progress made by rapid prototyping, it has not solved the seeding limits of scaffolds in tissue engineering because the spatial organization of the elements (scaffolds - cells - biomolecules) is not always under control.

The Bordeaux Consortium for Regenerative Medicine has allowed funding for a collaborative project on multimodal biomanufacturing of prevascularized substitutes for the regeneration of hematopoietic nests from human iPS cells. This project proposes, based on preliminary results to promote a multimodal approach biomanufacturing for the production of tissue-engineered products. The substitutes will be generated by successive layers with a bioprinter by extrusion whose funding was obtained from the BxCRM. The biomaterial retained to this day is the composite of collagen hydrogel and alginate previously developed within the U1026 and functionalized with the U869. When biomanufacturing process, cellularized microfibers will be incorporated to reproduce vascularization finally induced stem cells (U869) will be organized in the biomaterial using Laser assisted bioprinting to optimize interaction between cells and material. Ultimately, the use of a femtosecond laser will connect the different structures and solve the limits set forth above.

If these multimodal approaches will allow the in vitro creation of substitutes, another approach developed in the laboratory based on the bioprinting in vivo and in situ to guide bone regeneration. We have recently submitted a funding application for a project in the field of biomanufacturing applied to bone and skin regeneration in vivo and in situ with Poietis. The main objective will be the design, development and production of a third generation of laser bioprinter for tissue regeneration in vivo and in situ to demonstrate the effectiveness of the approach based on bioprinting for the treatment of losses bone and skin tissue.

Keywords/expertise:

- Laser-Assisted Bioprinting
- Biofabrication
- Tissue-engineering
- · Human cell culture
- Endothelial progenitors
- SCAPs
- Vascularization

- Regenerative Medicine
- Cell-based therapies
- Cell patterning
- Coculture
- Collagen
- Immunofluorescence

Selected publications:

1. In vitro assessment of a collagen/alginate composite scaffold for regenerative endodontics.

Devillard R, Rémy M, Kalisky J, Bourget JM, Kérourédan O, Siadous R, Bareille R, Amédée-Vilamitjana J, Chassande O, Fricain JC.

Int Endod J. 2015 Dec 9. doi: 10.1111/jej.12591. [Epub ahead of print]

PMID: 26650723

2 <u>Cell patterning by laser-assisted bioprinting.</u>

Devillard R, Pagès E, Correa MM, Kériquel V, Rémy M, Kalisky J, Ali M, Guillotin B, Guillemot F.

Methods Cell Biol. 2014;119:159-74. doi: 10.1016/B978-0-12-416742-1.00009-3.

PMID: 24439284

3. <u>Stress-induced sphingolipid signaling: role of type-2 neutral sphingomyelinase in murine cell apoptosis and proliferation.</u>

Devillard R, Galvani S, Thiers JC, Guenet JL, Hannun Y, Bielawski J, Nègre-Salvayre A, Salvayre R, Augé N.

PLoS One. 2010 Mar 23;5(3):e9826. doi: 10.1371/journal.pone.0009826.

PMID: 20352118

4. <u>Resveratrol inhibits the mTOR mitogenic signaling evoked by oxidized LDL in smooth muscle cells.</u> Brito PM, **Devillard R**, Nègre-Salvayre A, Almeida LM, Dinis TC, Salvayre R, Augé N.

Atherosclerosis. 2009 Jul;205(1):126-34. doi: 10.1016/j.atherosclerosis.2008.11.011. Epub 2008 Nov 24.

Patents:

Procédé de retrait d'un fragment solide et ancillaire associé.

Raphaël DEVILLARD, John LOPEZ, Florent DELOISON, Jean François PELI, Benoit Appert-Colin, Christophe Pierre, 2015

Procédés de fabrication de structures tridimensionnelles par moulage pour l'ingénierie tissulaire. Jérôme Kalisky, Raphaël Devillard 2014

Teaching Activities: Endodontics

Univ. de Bordeaux, UFR Sciences Odontologiques, Bordeaux, France

Clinical Activities: Endodontics

CHU de Bordeaux, Service d'Odontologie et de Santé Buccale, Bordeaux, France

Funding:

Aquitaine science Transfert Institut Français pour la Recherche Odontologique Bordeaux Consortium for Regenerative Medicine

Memberships:

CNEOC (Collège National des Enseignants en Odontologie Conservatrice), SFE (Société Française d'Endodontie)

Education:

2011 - Ph.D. in Cell Biology Univ. Toulouse

2006/2007 - M.Sc in Cell and disease physiopathology Univ. Toulouse

2005 - Doctor of Dental Medicine - Univ. Toulouse

Experience:

2010 – Associate professor U.F.R d'Odontologie, Université de Bordeaux C.H.U de Bordeaux Pôle d'Odontologie et de Santé buccale Groupe Hospitalier Pellegrin

2006/2010 – Assistant professor U.F.R d'Odontologie, Université de Bordeaux C.H.U de Bordeaux Pôle d'Odontologie et de Santé buccale Groupe Hospitalier Pellegrin

Links:

ReaserchGate: https://www.researchgate.net/profile/raphael_devillard

BxCRM: Bordeaux Consortium for Tissue Engineering: https://bcrm.u-bordeaux.fr