

Post-Doc, BIOTIS U1026

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RESEARCH INTERESTS: BONE TISSUE ENGINEERING

The effective reconstruction of large bone segments remains a major unsolved problem in the clinical field, evident in cases of severe trauma, cancer treatment and reconstructive surgery. Most of the bone biomaterials have been shown to be insufficient to achieve efficient bone repair, for large and complex bone defects when the vasculature and the nerve fibers of the host bed tissue are damaged, after radiotherapy for example. In this respect, despite a significant progress in the field of bone tissue engineering, the lack of attention to the vascular and mostly the nervous networks within bone substitutes could be one of the main reasons for the delayed or impaired recovery of bone defects. Conscious of the complexity and heterogeneity of the bone tissue, new and innovative horizons towards other key players in bone regeneration, especially nerve fibers, are expected. An increasing body of physiological, experimental and clinical data supports the role of the nervous system in skeletal development, bone turnover and fracture healing. In order to understand the impact of the nervous system in bone biology, my research is divided into different approaches:

A) Evaluation of neuro-osteovascular interactions using microfluidic devices.

The understanding of this intricate cellular interplay will allow new insights on novel bone regeneration strategies. The aim is to study the communication between sensory neurons and bone cells to guide and support angiogenesis, osteogenesis and innervation *in vitro*. A collaboration with the Laboratory of the Future (LOF, UMR5258) has allowed us to produce microfluidic systems for cell cocultures able to physically separate SNs from other cells, while permitting cellular communication through neurites emission. Using these devices, neuro-osteogenic, neurovascular and neuro-osteovascular interplay can be evaluated and molecules that orchestrate the functions of each cell type can be identified.

B) Development of a cell-free and growth-factor free implant capable of inducing vascularization and innervation to bone tissue engineering.

The aim is to design natural polymeric functionalized matrix as 3D microenvironment for supporting SNs, ECs and MSCs recruitment and their functions. In collaboration with the Laboratory of Organic Polymer Chemistry (LCPO, UMR5629), we have already designed and produced a new biodegradable elastin-like polypeptide-derived matrix. The main difficulty in such development is to integrate within a same matrix, multiple cell/tissue types that require different micro-environments, in terms of stiffness, roughness, micro-/macro-porosities, and mechanical properties. In such context, there are limited studies that have developed innervated bone implants. However, none of them was designed for supporting the coupling of bone formation, vascularization and innervation at the same time.

KEY WORDS :

Cell communication	Regenerative Medicine
Stem cells	Innervation
Bone biology	Angiogenesis
Mesenchymal stem cells	Hydrogel
Endothelial cells	Biomaterials
Bone tissue engineering	Microfluidics
Bioengineering	Sensory neurons

EDUCATION

2016 - today : Post-doc at Laboratory BIOTIS Inserm U1026, Bordeaux, France.

2012 - 2016: PhD Student at Laboratory of Stem Cells and Tissue Engineering, Universidade Luterana do Brasil (ULBRA), Canoas – Brazil.

2009 - 2011: Master Student at Laboratory of Immunogenetics, Universidade Federal do Rio Grande do Sul (UFRGS), Porto Alegre – Brazil.

2004 - 2008: Biological Sciences - Universidade Federal do Rio Grande do Sul (UFRGS), Porto Alegre – Brazil.

TEACHING AND STUDENT SUPERVISION

- Lecturer at Technical School Cristo Redentor (2012 – 2014)
- Lectures as guest:
 - Lutheran University of Brazil for Medicine and Biomedicine Courses (2012-2016)
 - University of Bordeaux for Master degree (2019)
 - Bordeaux's National Superior School for Technology of Biomolecules (ENSTBB) for Chemistry and Bioengineering Courses (2019)
 - University Paris Diderot for Master degree (2019)
- Scientific and Research Advising os students at BIOTIS and LACET (since 2013)
 - 2 PhD students (co-advising)
 - 3 Master 2 students
 - 3 Master 1 students
 - 2 License students

FUNDINGS

2019-2021: SPARK Bordeaux – University of Bordeaux

Leader: Bruno PAIVA DOS SANTOS, co-leader : Bertrand GARBAY.

Project VIBI « Innovative matrix for a vascularized and innervated bone engineered implant ». Collaboration between U1026 et U5629.

OTHER SCIENTIFIC RESPONSABILITIES

1. Member of the Young Scientists Committee of The French Society of Biomaterials since December 2019.

2. Member of the organizing committee of « Scientific Day of SFT Technologies for Health », June 2017, Pessac, France.

3. Member of the evaluation committee at « 19th Journées Françaises de Biologie des Tissus minéralise », Mai 2017, Lyon, France.

4. Invited reviewer for the following international journals since 2018: *Archives of Dermatological Research* (IF 2,309), *Molecular Biology Reports* (IF 2,107), *World Journal of Surgical Oncology* (IF 1,966), *Cell Cycle* (IF 3,259), *Biomacromolecules* (IF 5,667), *Theranostics* (IF 8,579), and *Biomaterials* (IF 10,317).

PATENTS

National Patents :

1. Hydrogel pour stimuler la neurotisation, l'osteogenèse et l'angiogenèse.

Inventers : Amedee J, Lecommandoux S, Oliveira H, Paiva dos Santos B, Garbay B, Garanger, E.

Registration number : 1851770, Publication number: FR3078261.

2. 3D bioprinting method for forming a cell specific tissue construct.

Inventeurs : Oliveira H, Paiva dos Santos B, Dussere N, Medina C, Stachowicz ML, Fracan JC.

Registration number : 1000497966, Publication number: EP20305640

International Patent :

1. Hydrogel for stimulating neurotization, osteogenesis and angiogenesis.

Inventeurs : Amedee J, Lecommandoux S, Oliveira H, Paiva dos Santos B, Garbay B, Garanger, E.
Registration number : PCT/EP2019/055075, Publication number: WO/2019/166594.

SELECTED PUBLICATIONS

1. Leroux A, Paiva dos Santos B, Leng J, Oliveira H, Amédée J. « Sensory neurons from dorsal root ganglia regulate endothelial cell function in extracellular matrix remodelling », *Cell Communication and Signaling*, 2020 Oct 19; 18:162. doi: 10.1186/s12964-020-00656-0.

2. dos Santos BP, Garbay B, Fenelon M, Rosselin M, Garanger E, Lecommandoux S, Oliveira H, Amédée J. « Development of a cell-free and growth factor-free hydrogel capable of inducing angiogenesis and innervation after subcutaneous implantation », *Acta Biomaterialia*, 2019 Nov ; 99:154-167. doi: 10.1016/j.actbio.2019.08.028.

3. Grémare A, Aussel A, Bareille R, Paiva dos Santos B, Amédée J, Thebaud NB, Le Nihouannen D, « A unique tri-culture model to study osteoblasts, osteoclasts and endothelial cells », *Tissue Engineering : Part C, Methods*, 2019 Jul;25(7):421-432. doi: 10.1089/ten.TEC.2018.0301.

4. dos Santos BP, Garbay B, Pasqua M, Chevron E, Chinoy ZS, Cullin C, Bathany K, Lecommandoux S, Amédée J, Oliveira H; Garanger E, « Production, purification and characterization of an elastin-like polypeptide containing the Ile-Lys-Val-Ala-Val (IKVAV) peptide for tissue engineering applications », *Journal of Biotechnology*, 2019 Jun 10;298:35-44. doi: 10.1016/j.jbiotec.2019.04.010.

5. Silva DI, Santos BP, Leng J, Oliveira H, Amédée J, « Dorsal root ganglion neurons regulate the transcriptional and translational programs of osteoblast differentiation in a microfluidic platform », *Cell Death & Disease*, 2017 Dec 13;8(12):3209.

6. Santos BP, da Costa Diesel LF, da Silva Meirelles L, Nardi NB, Camassola M, « Identification of suitable reference genes for quantitative gene expression analysis in rat adipose stromal cells induced to trilineage differentiation », *Gene*, 2016 Dec 15;594(2):211-219. doi: 10.1016/j.gene.2016.09.002.

7. Siqueira NM, Paiva B, Camassola M, Rosenthal-Kim EQ, Garcia KC, dos Santos FP, Soares RMD, « Gelatin and galactomannan-based scaffolds: Characterization and potential for tissue engineering applications », *Carbohydrate Polymers*, 2015 Nov 20;133:8-18. doi: 10.1016/j.carbpol.2015.06.039.

LINKS

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ResearchGate: [https://www.researchgate.net/profile/Bruno Paiva Dos Santos](https://www.researchgate.net/profile/Bruno_Paiva_Dos_Santos)

LinkedIn BIOMAT: <https://www.linkedin.com/groups/13768198/>