



Hugo Oliveira, Ph.D.
Post Doc , BioTis (U1026)

Coordinator of Tissue Engineering and Biofabrication,
Bordeaux Consortium for Tissue Engineering (BxCRM).



Research Interests:

I have, during my scientific pathway, placed myself at the interface of Biology and Chemistry and this conscious effort relates to my personal vision that therapeutic approaches for tissue regeneration need the import from different fields, with different languages and specifications. In this sense, I have established a scientific pathway focused on the development of nano-sized structures for drug delivery and diagnostic purposes, and gained expertise in the fabrication and modification of biomaterials to attain specific functions in regard to distinct applications: peripheral neuropathies, cancer diagnostics and treatment, and bone regeneration. The last years this last thematic has been the focus of my research, where I have participated in different aspects of bone regeneration approaches.

Bone tissue engineering

Presently, one of the main limitations of current scaffolds for bone tissue regeneration is their lack of vascularization, compromising the growth and viability of these regenerated tissues. Therefore, the development of new cell-based strategies and materials able to induce vascularization is a key issue. Our work focuses on the three following strategies for the improvement of angiogenesis and osteogenesis:

A) The impact of cellular co-culture and their interplay: Previous studies, from BioTis, have shown that the co-culture of human progenitor-derived endothelial cells and human mesenchymal stem cells within a 3D macroporous polysaccharide-based scaffold promoted osteogenesis. More recently, we have investigated the role of pannexins in the mediation of these cell-to-cell contacts and their impact on osteogenesis. In addition, we have shown that by using the total fraction of human bone marrow cells (hWBMCs) we could improve osteogenesis and angiogenesis, within the

same polymeric matrix, without the need of cell selection and amplification of the mesenchymal stem cells and microvascular endothelial cells contained in the human bone marrow.

B) The impact of the design of the biomaterial for promoting angiogenesis and osteogenesis:

One important strategy in tissue regeneration consists in the development of smart tailored scaffolds able to signal and stimulate progenitor cells for colonization and activation of their natural behavior, resulting in the formation of new healthy living tissue.

In this context, the European project (nAngiofrac, Euronanomed FP7) deals with nanostructured materials that can promote angiogenesis and regeneration in the case of non-consolidated bone fractures. This project, which includes 5 partners (academic and clinical; www.nangiofrac.org), focus on the development of PLA based materials, containing CaP glass ceramics, consisting on biodegradable and bioactive nanostructured scaffolds that ensure the correct calcium release to activate the angiogenic cascade and promote tissue repair in a well defined application: pseudarthrosis, a pathological condition highly dependent on vascularization.

C) Sensory nervous system - a new target for bone regeneration strategies: Bone is a mineralized living tissue, equally vascularized and innervated and the impact of these different actors has been a point of focus. The importance of angiogenesis in bone regeneration process has developed a robust body of literature and has been considered to play a pivotal role in new bone formation. Among the other actors, the role of the nervous system in bone tissue has received less attention and for some time considered as secondary. The existence of nerve fibers entering and leaving the bone has been described, where a number of histological studies showed the existence of neuropeptides of sensory, sympathetic and glutaminergic neuron types.

Recent work has shown that sensory neurons play an important role in bone development, mass accrual and regeneration. However, the direct or indirect effect of sensorial nervous system on bone tissue remains unknown.

In this sense, a deeper understanding on the impact of the sensory nervous system for regenerative purposes opens a new field in bone therapy. The understanding of this intricate cellular interplay, considering soluble factor secretion within the three dimensional and time dependent bone regeneration process, will allow new insights on novel bone regeneration strategies. With this aim we develop new platforms, based on microfluidics, to study the communication between sensory neurons and bone cells. Also, we focus on the development of novel biomaterials, based on elastin like polypeptides (ELPs) with the aim to tune peripheral nerve integration within a 3D environment.

Keywords/expertise:

- Biomaterials
- Bone tissue engineering
- Cell communication
- Co-culture systems
- Controlled drug delivery
- Nanoparticle active targeting
- Gene delivery
- Bioengineering
- Regenerative Medicine
- Histology
- Microfluidics

Selected publications:

1. Oliveira H, Catros S, Boiziau C, Siadous R, Marti-Munoz J, Bareille R, Rey S, Castano O, Planell J, Amédée J, Engel E. "The proangiogenic potential of a novel calcium releasing biomaterial: Impact on cell recruitment.", *Acta Biomaterialia*, 2016, 29 : 435–445.
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3. Guerrero J, Oliveira H, Catros S, Siadous R, Derkaoui SM, Bareille R, Letourneur D, Amédée J. "The Use of Total Human Bone Marrow Fraction in a Direct Three-Dimensional Expansion Approach for Bone Tissue Engineering Applications: Focus on Angiogenesis and Osteogenesis." *Tissue Engineering part A*, 2015, 21(5-6):861-74.
4. Oliveira H, Thevenot J, Garanger E, Ibarboure E, Calvo P, Aviles P, Guillen MJ, Lecommandoux S. "Nano-encapsulation of plitidepsin: *in vivo* pharmacokinetics, biodistribution and efficacy in a renal xenograft tumor model", *Pharmaceutical Research*, 31(4):983, 2014.
5. Pourtau L, Oliveira H, Thevenot J, Wan Y, Brisson AR, Sandre O, Miraux S, Thiaudiere E, Lecommandoux S. "Antibody-functionalized magnetic polymersomes: *in vivo* targeting and imaging of bone metastases using high resolution MRI." *Advanced Healthcare Materials*, 2, 11 (1420–1424), 2013.
6. Oliveira H, Pérez-Andrés E, Thevenot J, Sandre O, Berra E, Lecommandoux S. "Magnetic field triggered drug release from polymersomes for cancer therapeutics." *Journal Controlled Release*, 10;169(3):165-70, 2013.
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9. Oliveira H, Pires LR, Fernandez R, Martins MCL, Simões S, Pêgo AP, "Chitosan-based gene delivery vectors targeted to the peripheral nervous system", *J Biomed Mater Res - A*, 2010.
10. Oliveira H, Fernandez R, Pires LR, Martins MCL, Simões S, Barbosa MA, Pêgo AP "Targeted gene delivery into peripheral sensorial neurons mediated by self-assembled vectors composed of poly(ethylene imine) and tetanus toxin fragment c", *Journal Controlled Release* 2010; 143: 350-8.

Awards:

Young Scientist Award at the 9th World Biomaterials Congress, June 2012, Chengdu, China.

Education:

2005-2010	PhD in Biomedical Engineering	Faculdade de Engenharia da U. Porto Instituto de Engenharia Biomédica (INEB), Porto (AP Pêgo)
2009	Internship (3 months)	Johannes Kepler Universität Linz, Austria (Pr. P. Hinterdorfer)
2005	Laboratory animal certificate (FELASA)	Porto, Portugal
2004	M.Sc. in Endocrinology	Universiteit Utrecht, The Netherlands (Pr. J. Bogerd)
2000-2004	B.Sc. in Biochemistry	U. Beira Interior, Portugal

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Scopus: <http://www.scopus.com/authid/detail.uri?authorId=47461672900>