Damien Le Nihouannen, Ph.D.
Associate Professor in Physiologie (MCU, University of Bordeaux)

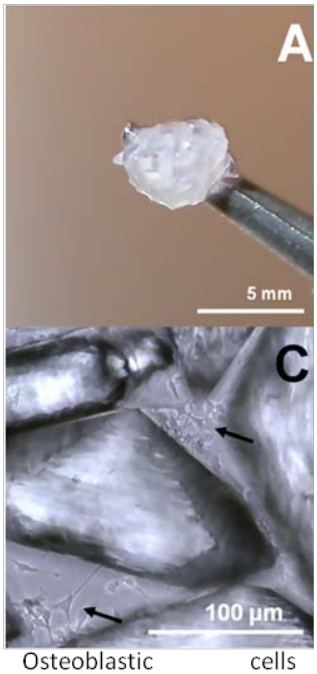
Coordinator of the Biomaterials and Medical Devices (BiDiM) Master program

Research Interests:

My broad interest lies in enhancing the bone healing process after a trauma or a bone related surgery. Naturally, my research will primarily focus on bone biology and on biomaterials. Both of these areas are highly linked jointly considered in order to develop the most appropriate treatments for skeletal diseases. As a result, while their strengths present obvious application to bone tissue engineering, there are also highly relevant for developing new approaches to treat osteoporosis, osteoarthritis and others bone related diseases. My research focuses on 1) the evaluation in vitro and in vivo of new generation of biomaterials to accelerate the bone healing process and reduce the time required to recover patient mobility, 2) the role of osteoclast metabolism and activity on bone formation remodelling and 3) the investigative of osteoclast – osteoblast interactions to reveal significant mechanisms in the field of bone physiology and regeneration.

While the most commonly used synthetic bone filler materials are calcium phosphates, modification of their formulation and the addition of components can improve the bone healing process occurring after their implantation. In fact, for an optimal tissue reconstruction with a biomaterial it is important to simulate the biological sequence of tissue healing and regeneration. For this purpose the release of molecules/drugs controlled both in a spatial and temporal manner is critical. Among the different molecules I am currently evaluating, the best candidates that will be loaded into new biomaterials to stimulate the bone remodelling process in a specific area.

I believe that an optimal stimulation of the bone turnover process by activation osteoclastic cells will lead to a closer physiological regeneration of



Osteoblastic cells cultured on newberyite matrices. (from: F. Tamimi et al.; Acta Biomaterialia 7 (2011) 2678–2685)

the tissue. In fact, the first step of bone healing process is the formation of osteoclastic cells. During the following steps of the bone remodelling process, bone formation is coupled to bone resorption. During the last decade, extensive work has been carried out to describe how osteoblasts regulate osteoclasts. However, the opposite signals and mediators of this process are yet to be identified. I have developed an original in vitro model to study the crosstalk between osteoblasts and osteoclasts. I intent to apply my results to optimize the bone healing process after biomaterials implantation as previously described. It is expected that the new biomaterial will not only recruit functional osteoclasts, but also induce the formation of osteoblasts and further improve its own osteointegration.

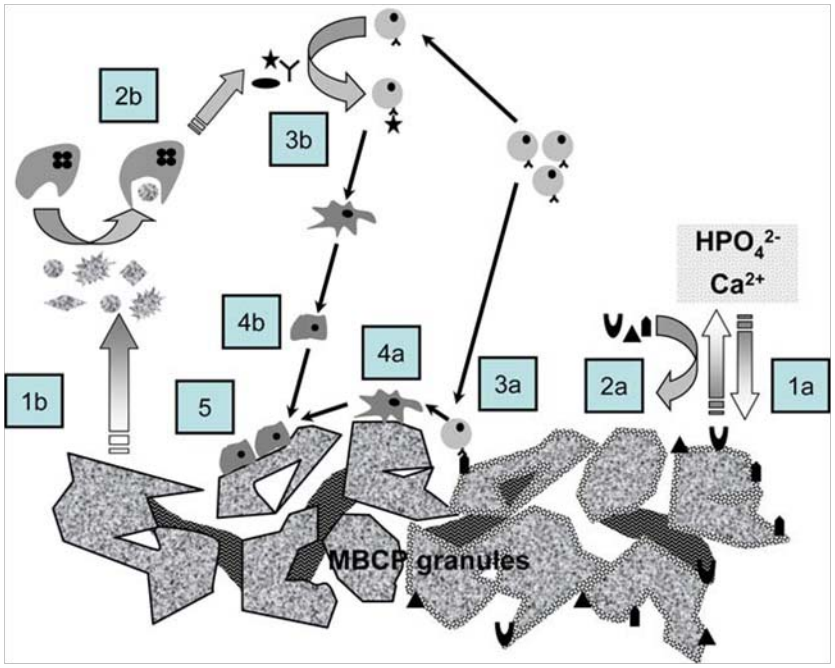


Diagram of possible mechanisms for material induced osteogenesis. Following implantation, the CaP granules partly dissolved (1a) and a biological apatite precipitated on to the surface of the MBCP concentrating endogenous bone growth factors (2a). Circulating stem cells were recruited by this surface (3a) and differentiated into osteoprogenitors (4a). Microparticles detached from the micro-porous surface of MBCP (1b) and phagocytized by macrophages, which released inflammatory cytokines (2b). The inflammatory cytokines stimulated circulating stem cells (3b) to differentiate into osteoprogenitors (4b). Osteoblastic cells aligned and produced bone extracellular matrix on the MBCP (5). (from : D. Le Nihouannen et la. J Mater Sci: Mater Med (2008) 19:667–675)

A regulated equilibrium between osteoclasts and osteoblast activities is required for bone homeostasis. However, an impairment of this balance mainly leads to an excess of bone resorption like in the cases of osteolytic lesions or osteoporosis. Aging, joint diseases and cancer metastasis are the main causes of this kind of deregulations. However, other diseases like diabetes also show abnormal bone metabolism and are linked to a dysfunction of osteoclastic cells. Another part of my future work will focus on the metabolic activities of osteoclasts. I am specifically interested in the effects of the cell metabolism precursors on the osteoclast formation, differentiation and activity. I conduct this work to describe the correlation between these specific syndromes and the regulation of osteoclastic cells to ultimately improve treatment for patients suffering from bone degenerative diseases.stage renal disease patients with durability of up to 3 years.

Keywords/expertise:

- Bone tissue/physiologie
- bone cell
- osteoclasts
- Cell-material interaction
- In vitro studies
- Biomaterials
- Calcium phosphate material
- Bone tissue engineering
- Regenerative Medicine
- Bone related diseases
- osteointegration
- Bone regeneration
- Electron microscopy
- Image analysis

Selected publications:

1- Marelli B., Le Nihouannen D., Hacking SA., Tran S., Li J., Murshed M., Doillon CJ., Ghezzi CE., Zhang YL., Nazhat SN., Barralet JE. : Newly identified interfibrillar collagen crosslinking suppresses cell proliferation and remodelling. Biomaterials (2015) Jun;54:126-35.

2- Fong JE., Le Nihouannen D., Tiedemann K., Sadvakassova G., Barralet JE., Komarova SV. : Moderate excess of pyruvate augments osteoclastogenesis. Biol Open. (2013) Mar 22;2(4):387-95.

3- Tamimi F., Comeau P., Le Nihouannen D., Zhang YL., Bassett DC., Khalili S., Gbureck U., Tran SD., Komarova SV., Barralet JE.: Perfluorodecalin and bone regeneration. Eur Cell Materials (2013) Jan 2;25:22-36.

4- Tamimi F., Le Nihouannen D., Eimar H., Sheikh Z., Komarova SV., Barralet JE.: The effect of autoclaving on the physical and biological properties of dicalcium phosphate dihydrate bioceramics: brushite vs. monetite. Acta Biomaterialia (2012) Aug;8(8):3161-9.

5- Tamimi F., Le Nihouannen D., Bassett DC., Ibasco S., Gbureck U., Knowles J., Wright A., Flynn A., Komarova SV., Barralet JE.: Biocompatibility of magnesium phosphate minerals and their stability under physiological conditions. Acta Biomaterialia (2011) Jun;7(6):2678-85.

6- Fong JE., Le Nihouannen D., Komarova SV.: Tumor-supportive and osteoclastogenic changes induced by breast cancer-derived factors are reversed by inhibition of {gamma}-secretase (2010). Journal of Biological Chemistry 285(41):31427-34.

7- Le Nihouannen D., Barralet JE., Fong JE, Komarova SV.: Ascorbic acid accelerates osteoclast formation and death (2009). Bone 46:1336–1343.

8- Ibasco S., Tamimi F., Meszaros R., Le Nihouannen D., Harvey E., Barralet JE: Magnesium sputtered titanium for the formation of bioactive coatings (2009). Acta Biomaterialia Jul;5(6):2338-47.

9- Tamimi F., Kumarasami B., Doillon C., Gbureck U., Le Nihouannen D., Cabarcos EL., Barralet JE.: Brushite-collagen composites for bone regeneration (2008). Acta Biomaterialia Sep;4(5):1315-21.

10- Le Nihouannen D., Komarova SV., Gbureck U., Barralet JE.: Bioactivity of bone resorptive factor loaded on osteoconductive matrices: stability post-dehydration (2008). Eur J Pharm Biopharm. 70(3):813-8.

11- Le Nihouannen D., Hacking SA., Gbureck U., Komarova SV., Barralet JE.: The use of RANKL-coated brushite cement to stimulate bone remodelling (2008). Biomaterials 29(22):3253-9.

12- Le Nihouannen D., Saffarzadeh A., Gauthier O., Moreau F., Pilet P., Spaethe R., Layrolle P., Daculsi G.: Bone tissue formation in muscles of sheep induced by a biphasic calcium phosphate ceramic and fibrin glue composite (2008). Journal of Materials Science: Materials in Medicine 19(2):667-75.

13- Le Nihouannen D., Duval L., Lecomte A, Julien M, Guicheux J., Daculsi, G., Layrolle P.: Interactions of total bone marrow cells with increasing quantities of macroporous calcium phosphate ceramic granules (2007). Journal of Materials Science: Materials in Medicine 18(10):1983-90.

14- Le Nihouannen D., Saffarzadeh A., Aguado E., Goyenvalle E., Gauthier O., Moreau F., Pilet P., Spaethe R., Daculsi G., Layrolle P.: Osteogenic properties of calcium phosphate ceramics and fibrin glue based composites (2007). Journal of Materials Science: Materials in Medicine 18(2):225-35.

15- Le Nihouannen D., Goyenvalle E., Aguado E., Pilet P.,Bilban M, Daculsi G., Layrolle P.: Hybrid

composites made of calcium phosphate granules, fibrin glue and bone marrow for skeletal repair (2007). Journal of Biomedical Material Research:Part A 81(2):399-408.

16- Le Nihouannen D., Le Guéhennec L., Rouillon T., Pilet P., Bilban M., Layrolle P., Daculsi G.: Microarchitecture of composite associating calcium-phosphate granule and fibrin glue for bone tissue engineering (2006). Biomaterials 27(13):2716-22.

17- Le Nihouannen D., Gauthier O., Saffarzadeh A., Delplace S., Pilet P., Daculsi G., Layrolle P.: Bone formation induced by granular biphasic calcium phosphate porous ceramic in muscles of sheep (2006). Bone 36(6):1086-93.

Patents:

1- Barralet JE, Le Nihouannen D, Komarova SV. New drug delivery system combining calcium phosphate cement and bioactive molecule. US Patent (WO/2008/128342) - Publication Date: 30.10.2008 - Licensed 2009.

Teaching Activities:

2012 - Coordinator of the Biomaterials and Medical Devices (BiDiM) Master program
2010 - Assistante Professor in Physiology (Université de Bordeaux, France)

Clinical Activities:

Funding:

2013 - 2014 - 15,000 € - SFR TECSAN Starting Grant (co-applicant)
2011 - 2014 - 75,000 € - Marie Curie Career Integration Grant
2008 - 2011 - 90,000 CAD - Bourse Postdoctorale – FRSQ, Canada.
2008 - 2010 - 40,000 CAD - Bourse Postdoctorale – CAN, Canada.
2006 - 2008 - 36,000 CAD - Bourse Postdoctoral – « CIHR Strategic Training Program in Skeletal Health Research », Université de McGill, Canada.
2002 - 2005 - 36,000 CAD - Bourse de thèse « Atlanthèse », France.

Memberships:

European Orthopedic Research Society
American Society for Bone and Mineral Research
Canadian Arthritis Network
Canadian Chapter Controlled Release Society
Canadian Society for Biomaterials
Society for Biomaterials
Société française de Biologie des Tissus minéralisés

Awards:

2010 Prix de la meilleure communication affichée (Réunion annuelle du RSBO).
2009 Prix de la meilleure communication orale (27eme « Canadian Biomaterials Society Meeting »).
2008 Prix de la meilleure communication orale (1er « McGill Musculoskeletal Symposium »).

2005 Prix de la meilleure communication orale (Forum des doctorants de l'école doctorale de Chimie-Biologie de Nantes)

Education:

2006-2010	Inership (4 years)	McGill University, Montrel, Québec , Canada The Centre for Bone and Periodontal Research (Pr. J.E. Barralet, Pr. S.V. Komarova)
2002-2006	Ph.D. in Bone Tissue Engineering	Université de Nantes, France Laboratoire d'ingénierie ostéo-articulaire et dentaire (INSERM U791, Dr. G. Daculsi, Dr. Layrolle)
2000-02	M.Sc. in oral an osteo-articular biology, biomaterials and biofonctionalization	Universités de Paris V/VII, France
1997-2000	B.Sc. in Biology	Université de Nantes, France

Links:

Linkedin: https://www.linkedin.com/in/damien-le-nihouannen-53104636?trk=hp-identity-name

Viadéo: http://www.viadeo.com/p/002k9dugk0y7ywa/edit?viewType=main

ReaserchGate: http://www.viadeo.com/p/002k9dugk0y7ywa/edit?viewType=main

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

Master Biomatériaux et Dispositifs Médicaux (BiDiM): http://www.u-bordeaux.fr/formation/PRMABS_142/master-professionnel-mention-biologie-sante-specialite-biomateriaux-et-dispositif-medicaux

BIOMAT : The French association for the development of biomaterials, Tissue Engineering and Regenerative Medicine: http://www.biomat.fr