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Research Interests:

Effects of alcohol consumption on bone

My first interest was to characterize the effects of chronic alcohol consumption on bone. The effects are well known on the liver and the brain, but it is not well known that chronic heavy alcohol consumption can lead to secondary osteoporosis. I devoted my PhD to compare different alcohol doses regarding to their effects on trabecular and cortical bone, on bone mineral density and bone remodeling. The results of our analyses were that chronic heavy alcohol consumption in the rat, leads to loss of cortical and trabecular bone, in correlation with the dose ingested. We decided to analyze the mechanism further and we did different experiments with bright field and transmission electron microscopy to observe the osteocytes, since these cells are the most abundant in bone (90-95%). We were surprised to observe higher osteocyte apoptosis with heavy alcohol consumption, and also more lipid droplets in the osteocytes and bone marrow. We found a correlation between the amount of lipid droplets in the cells and their apoptosis.

Role of osteocytes in the bone response to loading / unloading

After my PhD in Orléans, France, I had the privilege to do a post-doctoral fellowship with Dr Lynda Bonewald, in Kansas City, MO, USA. Dr Lynda Bonewald has been leading the research on osteocyte for the past 20 years. In her lab, my work was devoted to characterize the role of beta-catenin in osteocyte in the bone response to unloading. To this end, we deleted 1 allele of beta-catenin in the osteocytes (2 alleles is lethal) using the Dmp1-Cre model and suspended male and female mice, control and cKO for 4 weeks. We first found an effect of stress in the males that was translated by a decrease in some bone parameters. Second, we found a difference in the response to unloading between males and females. While the females cKO were able to lose cortical and trabecular bone

with unloading similar to the control mice, the males cKO did not lose any more bone with unloading. However these mice already had a bone phenotype compared to their controls. It then appeared that beta-catenin has different function in the skeleton in males and females.

My second project was to characterize a new Cre model to target gene deletion or recombination in osteocytes, using the Sost ERT2 Cre promoter. We crossed these mice with reporter mice (td tomato) which express a fluorescent red protein in the cells where DNA recombination occurs. I was able to track where and when there was DNA recombination in this model, using tamoxifen injections to activate the Cre (ERT2 system). This second project is still being worked on in Dr Bonewald's lab.

Role of osteocytes in bone regeneration

I obtained my Assistant Professor position in November 2015, in the U1026 Inserm Unit (BioTis) in Bordeaux, France. This research lab is devoted to bone regeneration and vascularization. My position was created to reinforce the *in vivo* team testing the implants and scaffold in pathological animal models, to be closer to the patients that need bone bioengineered products. I am particularly interested in the role of osteocyte in bone regeneration. In fact, this cell is the orchestrator of bone remodeling and can act on both the osteoblasts and the osteoclasts, to regulate bone formation and resorption respectively. The osteocytes also have the capacity to be a mechanosensor, which mean they can "feel" when we do exercise or go in space, and this increase or decrease of mechanical load is translated to the other cells as a biological signal to adapt bone mass to its environment (bone gain or bone loss). To date, the role of the osteocytes in bone regeneration is not well known.

Keywords/expertise:

- Small animal models
- *In vivo* loading, unloading
- Treadmill training
- Injections fluorochromes, anesthetics, tamoxifen
- Histology
- Histomorphometry
- MicroCT analysis
- 3-point bending test
- Epifluorescence microscopy
- Confocal microscopy
- Synchrotron imaging
- Plastic, paraffin and OCT embedding
- Microtome, cryostat sectioning
- TRAP, H&E staining
- ELISA assays
- PCR, qPCR analysis
- Transgenic animal production
- Genotyping
- Sexing pups
- Dissection
- Cre/Lox model

Selected publications:

Effect of the alcohol consumption on osteocyte cell processes: a molecular imaging study. Maurel DB, Benaitreau D, Jaffré C, Toumi H, Portier H, Uzbekov R, Pichon C, Benhamou CL, Lespessailles E, Pallu S. *J Cell Mol Med*. 2014 Aug; 18(8):1680-93.

Centrosome fine ultrastructure of the osteocyte mechanosensitive primary cilium. Uzbekov RE, Maurel DB, Aveline PC, Pallu S, Benhamou CL, Rochefort GY. *Microsc Microanal*. 2012 Dec; 18(6):1430-41.

Synchrotron ultraviolet microspectroscopy on rat cortical bone: involvement of tyrosine and tryptophan in the osteocyte and its environment. Pallu S, Rochefort GY, Jaffré C, Refregiers M, Maurel DB, Benaitreau D, Lespessailles E, Jamme F, Chappard C, Benhamou CL. *PLoS One*. 2012; 7(8):e43930.

Chronic and intermittent exposure to alcohol vapors: a new model of alcohol-induced osteopenia in the rat. Maurel DB, Jaffré C, O'Brien ES, Tournier CC, Houchi H, Benhamou CL, Naassila M. Alcohol Clin Exp Res. 2013 Jan; 37 Suppl 1:E216-20.

Osteocyte apoptosis and lipid infiltration as mechanisms of alcohol-induced bone loss. Maurel DB, Pallu S, Jaffré C, Fazzalari NL, Boisseau N, Uzbekov R, Benhamou CL, Rochefort GY. Alcohol Alcohol. 2012 Jul-Aug; 47(4):413-22.

Alcohol and bone: review of dose effects and mechanisms. Maurel DB, Boisseau N, Benhamou CL, Jaffré C. Osteoporos Int. 2012 Jan; 23(1):1-16.

Low bone accrual is associated with osteocyte apoptosis in alcohol-induced osteopenia. Maurel DB, Jaffré C, Rochefort GY, Aveline PC, Boisseau N, Uzbekov R, Gosset D, Pichon C, Fazzalari NL, Pallu S, Benhamou CL. Bone. 2011 Sep; 49(3):543-52.

Teaching Activities:

I teach physiology in the Pharmaceutical Sciences Department. Our role is to explain how the different big functions work (Respiratory, Cardiovascular, Reflexes and Movements, Central Nervous System and Emotions, Immune System, Inflammation and Pain, Digestion and Reproduction) and illustrate these classes with practical labs on pathologies related to these systems and show the students some tests to assess the vital functions, as it is done with the patients.

Education:

2012-2015	Post-doctoral fellowship	University of Missouri at Kansas City (UMKC) Kansas City, MO, USA
2008-2011	Ph.D. in Bone Physiology	Université Orléans, Orléans, France Laboratoire INSERM U658
2007	Internship (5 months)	Sport Center University of Montréal (CEPSUM) Montréal, Canada
2007	M.Sc. in Perf, Rehabilitation and Handicap Engineering	Université de Poitiers, Poitiers, France
2005	Exchange program (1 year)	California State University of Bakersfield (CSUB) Bakersfield, CA, USA
2005	B.Sc. in Exercise Science	Université Orléans, Orléans, France