**Final Report**

**(MC CIG grant 294154 EOBoTE)**

**Scientific results:**

Bone diseases like osteoporosis and osteoarthritis are affecting an increasing number of people worldwide. Despite the good clinical results of synthetic materials in these indications and their advantages over bone autograft, their lack of biological properties is still a major drawback. Recent studies highlight the importance both of the vascularisation and the communication between cells to build efficient tissue engineering strategies. The EOBoTE project aims to establish a link between two major cellular actors of the bone physiology: the osteoclastic bone resorbing cells and the blood vessel (or endothelial cells), in order to go give a more accurate sketch of the difference process involved in bone regeneration.

Working only with human cells, we were able to isolate, to culture and to differentiate the human monocular cells from cord blood into both osteoclasts (OC) and endothelial cells (PDEC). Our aim was to examine the interactions between endothelial cells and osteoclastic cells, either isolated or co-cultured with osteoprogenitor cells, to determine both the role and the modulation process of the vasculature during bone remodeling. As no co-cultures system between human osteoclastic cells and human endothelial cells were described in the literature and our first goal was to set up an optimal cell culture medium to realize such co-cultures.

We establish a new cell culture protocol and we found that “elderly” (or “late”) endothelial cells significantly inhibited osteoclast differentiation while “young” (or “early”) ones did not exhibit any effect on osteoclastic cells. This result showed that bone remodeling process depends on cell interactions and that regulating factors are differently expressed by the same cell across ages.

Based on these results and together with the expertise of the lab on cell communication, we decided to establish a new and unique co-culture model including three cell types, namely osteoblastic, endothelial and osteoclastic cells. We succeeded on this task and we are now analyzing the behavior of the three cells type in this model.

Our promising results show that cell cultures of several different bone cell types are possible. However, our model lacks the main bone cell type, namely osteocytes. The next major step of the study will be to culture these cells in the same environment and to study their behavior. Such model would be valuable both for fundamental research to dissect bone cell communication patterns but also in applied research to understand the global mechanism of molecules on communicated cells. In a bone tissue engineering point of view, this studies will open new opportunities in the development of more efficient strategies/approaches.

**Project Management:**

The opportunity of starting my career with a Marie Curie Carrier Integration Grant gave me one of the best opportunities to start both research and teaching activities in the University of Bordeaux. First, getting this fund allowed me to start a project as an independent researcher, not only as a co applicant. I was also able to recruit a Master student, PhD student in dentistry and to hire a research assistant. The three direct consequences were, 1) an opportunity to present results of this work during international congresses 2) together with initiating new collaborations and 3) to get recently, as co-applicant, a regional starting grant. Finally, considering another part of my career, this grant positively helped me to get, two year ago, a permanent position as associate professor in physiology and to be nominated as person in charge of a 2 years Master course in Biomaterials and Medical Devices.

Working in the laboratory INSERM U1026 (http://www.u1026.u-bordeaux2.fr/) as an independent research and promoting my research activities was essentially due to the Marie Curie grant. Regarding the research part of the re-integration, I am an independent researcher being part of a research group leads by Joelle Amédée and working on new bone tissue engineering strategies with two share research associate. Unfortunately, I was not able to hire any post doctoral or PhD student due to the lack of fund that compels me to work with only 2 Master students and one PhD student in dentistry. To confirm the success of my re-integration, I was nominated, in January 2013, as head teacher of a 2 years Master course in Biomaterials and Medical Devices (<http://www.u-bordeaux.fr/formation/PRMABS_142/master-professionnel-mention-biologie-sante-specialite-biomateriaux-et-dispositif-medicaux>). Similarly, a year ago I was nominated at the scientific board of the SFBTM (French Society for the Biology of Mineralized Tissues). Taking together, I am creating a growing network around the field of biomaterial and medical devices mainly targeted to bone diseases and I try and get together researchers from public laboratories and company leaders to initiate new projects linked on the topic of bone regeneration. From one of this collaboration, one project, still related to the close relationship between osteoclastic cells and endothelial cells, namely [“operating data of the skeletal system to understand the regulation of the exchange factor FGD1 by the TFG-ß in endothelial aortic cells”) was submitted to a regional research group (SFR TECSAN) and was granted (15k€) in July 2013 for a period of one year. This grant is a starting grant that will be used as fundament for a national research grant project (ANR, 3 years, 200k€) that was submitted in october 2014. I plan to use this grant both to consolidate the collaboration with the co-applicant (Dr. Elisabeth Genot), to get PhD. and/or postdoctoral students and to continue with the next step of the EOBoTE project.

**Scientific conferences:**

- Aussel A., Thebaud N., Amédée J., Le Nihouannen D.: Réalisation de cocultures pour analyser l’interaction cellules endothéliales/ostéoclastes (oral communication). 15ème Journées Françaises de biologie des tissus minéralisés (2013).

- Aussel A., Thebaud N., Bareille R., Amédée J., Le Nihouannen D.: Coculture system to analyse osteoclast and endothelial cell communication (poster). The scientific day of the Federal Structure Research (FSR) “Technologies for Health” (2013).

- Gremare A., Aussel A., Bareille R., Guerrero J., Amédée J., Le Nihouannen D.: Mise au point et Validation d’un système pour étudier la communication entre les cellules du tissue osseux. 16ème Journées Françaises de biologie des tissus minéralisés (2014). Price for the best oral presentation.

- Gremare A., Aussel A., Bareille R., Guerrero J., Amédée J., Le Nihouannen D.: Development of an original model to investigate cell communication in bone tissue engineering. The scientific day of the Federal Structure Research (FSR) “Technologies for Health” (2014).

- Gremare A., Aussel A., Bareille R., Guerrero J., Amédée J., Le Nihouannen D.: Development of an original model to investigate cell communication in bone tissue engineering (oral communication). The 26th European Conference on Biomaterials (2014).

**Additional publication (unable to upload on the REA website):**

- 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.

- Gremare A., Aussel A., Thebaud N., Bareille R., Guerrero J., Amédée J., Le Nihouannen D.:

A unique cell culture model to study the communication between human osteoclastic, osteoblastic and endothelial cells. PlosOne. In preparation (2015)