ABSTRACT SUBMISSION

To be submitted before Feb. 22nd, 2019 online at https://biomatsante.sciencesconf.org

Biomat – Materials for Health Congress – June 3-7 2019 – La Grande Motte, France

Development of a cell-free and growth factor-free hydrogel capable to induce angiogenesis and innervation after subcutaneous implantation

B. P. dos Santos[1], B. Garbay[2], E. Garanger[2], S. Lecommandoux[2], H. Oliveira[1], J. Amédée[1]

1. Bioingénierie Tissulaire (BioTis), Inserm U1026, Université de Bordeaux, Bordeaux, France

2. Laboratoire de Chimie des Polymères Organiques (LCPO), UMR 5629 CNRS, Bordeaux INP, Université de Bordeaux, Pessac, France

Type of contribution desired: ☒ **ORAL** ☐ **POSTER**

☐ Candidating to best presentation award for PhD students/young scientists* ?
(*PhD defense in 2018 or before the end of 2019".

Keywords : *IKVAV, osteogenesis, neurite outgrowth, elastin-like polypeptide*

ABSTRACT

Accumulating evidence has been revealing the importance of the sensory nervous system in the orchestration of bone turnover and repair [1]. The aim of this work is to develop a cell-free and growth-factor free hydrogel capable to promote innervation and angiogenesis in a bone regeneration context.

Hydrogels were produced using elastin-like polypeptides (ELPs) and different ratios of poly(ethylene glycol) (PEG), and the laminin-derived adhesion peptide IKVAV (or its scrambled VKAIV): ELP + (PEG); ELP + [low adhesion peptide] and ELP + [high adhesion peptide] and characterized by rheology, porosity and enzymatic degradation. Primary rat cell cultures: mesenchymal stromal cells (MSCs), endothelial cells (ECs) and sensory neurons (SNs) had metabolic activity, cellular behaviour and/or gene expression evaluated. Best *in vitro* performance composition was implanted subcutaneously in mice and the vascularization and innervation potential were assessed by histology and immunohistochemistry.

We produced ELP-based hydrogels with fine-tunable rheological properties, microporous structure, degradable and biocompatible *in vitro*. The [high IKVAV] composition had an important performance *in vitro* inducing: (i) in MSCs, gene upregulation of a panel of osteogenic markers; (ii) in ECs, upregulation of important a gene that trigger angiogenesis process; and (iii) in SNs, the formation of longer neurites. The [high IKVAV] composition and its scrambled were then implanted subcutaneously in mice. After histological analysis, hydrogels induced no signals of major inflammation. The surrounding region of the [high IKVAV] composition had higher vessel density relative to the scrambled after 26 days and the innervation process was detected only in IKVAV composition implantation after 11 and 26 days. The density and surface of neuronal structures also seem to increase over time.

The [high IKVAV] composition showed higher osteogenic, angiogenic and innervation potential *in vitro*. *In vivo*, hydrogels were not inflammatory and [high IKVAV] composition induced higher vascularization and innervation subcutaneously. [High IKVAV] composition has important features for biomedical applications, being a cell- and growth factors-free composite able to support vascularization and innervation *in vitro* and *in vivo* with a great potential to induce osteogenesis.

References : [1] Marrella A *et al.*, Mater Today (2018) 21:362-76, doi: 10.1016/j.mattod.2017.10.005