

ABSTRACT SUBMISSION

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Boosting mesenchymal stem cells regenerative activities on biopolymers-calcium phosphate functionalized collagen membrane

Marie Dubus¹, Hassan Rammal¹, Halima Alem², Nicolae B. Bercu³, Isabelle Royaud², Fabienne Quilès⁴, Fouzia Boulmedais⁵, Sophie C. Gangloff¹, Cedric Mauprivez¹, Halima Kerdjoudj¹

1. EA 4691, Biomatériaux et Inflammation en Site Osseux (BIOS), SFR CAP Santé (FED 4231), Université de Reims Champagne Ardenne, 51100 Reims, France.

2. Université de Lorraine, UMR 7198 CNRS, Institut Jean Lamour, 54011 Nancy, France.

3. EA 4682, Laboratoire de Recherche en Nanoscience (LRN), Université de Reims Champagne-Ardenne, 51100 Reims, France.

4. CNRS, Laboratoire de Chimie Physique et Microbiologie pour les Matériaux et l'Environnement, LCPME, UMR 7564, Villers-lès-Nancy F-54600, France.

5. Université de Strasbourg, CNRS, Institut Charles Sadron, UPR22, 23 rue du Loess, BP 84047, 67034, Strasbourg Cedex 2, France.

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ABSTRACT

Alveolar bone resorption following tooth extraction or periodontal disease compromises the bone volume required to ensure stability of implant. Guided bone regeneration (GBR) is one of the most attractive technique for restoring oral bone defects, where an occlusive membrane is positioned over bone graft material, providing space maintenance enabling to seclude soft tissue infiltration and to promote bone regeneration. However, bone regeneration is in many cases impeded by a lack of an adequate tissue vascularization or by bacterial contamination. Using simultaneous spray coating of interacting species (SSCIS) process, a bone inspired coating made of calcium phosphate (CaP) / chitosan (CHI) / hyaluronic acid (HA) was built on one side of nanofibrous GBR collagen membrane.

Characterization of the built-up mineral, performed by scanning electron microscopy, infrared and Raman spectroscopies and high-resolution transmission electron microscopy, revealed the formation of carbonated apatite crystals embedded within an amorphous (brushite) matrix and polymeric film. Interestingly, dynamic mechanical analysis did not reveal an important increase of coated membrane stiffness compared to bare membrane. In addition to biocompatibility highlighted by a great proliferation of mesenchymal stem cells (MSCs) on coated membrane and by significant reduction of IL-1 β and TNF- α pro-inflammatory cytokines by human monocytes, we investigated the immunomodulatory properties of stem cells, critical in bone regeneration. MSCs paracrine evaluation in contact with coated membrane revealed a modest increase in interleukin (IL) -6 and 8 secretion (compared to bare membrane), as well as a low neutrophils recruitment (20 % *versus* positive control), confirming the neutral role of the coating. Furthermore, in addition to the secretion of osteoprotegerin, we observed a significant increase in angiogenic growth factors (b-FGF and VEGF) production, accompanied by an increase in endothelial cell recruitment (85 %). Functionalization of collagen membrane by CaP-CHI-HA showed an antibacterial effect, with a significant reduction in the number of alive and adhered *S. aureus* and *P. aeruginosa*, common pathogens responsible for bone infection. These significant data shed light on the potential regenerative application of CaP-CHI-HA bioinspired coating in providing a suitable environment for stem cell bone regeneration and an ideal strategy to prevent implant-associated infections.