ABSTRACT SUBMISSION

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Optimized and sterilized 3D biopolymer scaffold for cell therapy of soft tissues

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ABSTRACT

Biomaterial cell-based therapy holds great hope in the field of regenerative medicine including soft tissues. Cells delivery to the targeted organ via a 3D biomimetic scaffold present several advantages compared to direct cell injection, including cell retention on the injury site and improved viability and secretion. The success of such cell delivery strategy lies on the scaffold's design, as its biocompatibility and architecture influence may host's reaction and seeded cells fate.

Recently, CIRIMAT has developed a family of macroporous biopolymer 3D scaffolds based on a combination of polyelectrolyte complex of opposite charge formation and production processes. According to operating conditions, the resulting scaffolds presented various 3D architecture whose beneficial influence on cells fate and secretion properties has been demonstrated [1,2]. Based on alginate and chitosan, two well-known biocompatible polymers, the scaffolds exhibited an excellent biocompatibility and showed pro-angiogenic properties by itselves [3]. The challenge is now to optimize the scaffolds' architecture and physico-chemical properties according to the seeded cell type. In a first approach, bone marrow mesenchymal stem cells and macrophages have been chosen to explore the potentialities of seeded scaffolds on soft tissues repair and regeneration. *In vitro* experiments have permitted to determine the most promising scaffolds formulations according to cell type.

In view of a further clinical development, the validation of a sterilization technique, specifically adapted to porous materials of polysaccharidic nature, is of key importance. To that end, a pulsed electron beam based sterilization technique, developed by our industrial partner ITHPP, was tested and adapted in order to preserve scaffolds's architecture and mechanical properties. The impact of several ionizing doses, ranging from 5 to 20 kGy, on scaffolds' architecture was studied. Scaffolds' sensitivity to ionizing doses, according to their alginate/chitosan ratio, was particularly explored, in order to determine the best sterilization conditions, combining sterilization efficacy (validated according to European Pharmacopeia recommended conditions) and scaffolds preservation (demonstrated by TEM, X-ray tomography and evaluation of mechanical and swelling properties).

In vitro assays were achieved to study if the sterilized scaffolds still show positive effects on MSCs and macrophages viability to select the best sterilization conditions. *In vivo* assays are under way at the I2MC to determine cellularized scaffold effects *in vivo,* on damaged soft tissues, with regards to inflammation and angiogenesis during tissue regeneration.

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