ABSTRACT SUBMISSION

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Evaluation of an osteogenic hMSC-secreted extracellular matrix as a platform for BMP-2 delivery

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ABSTRACT

Owing to its numerous biological and mechanical properties, cell-derived extracellular matrices (ECM) have recently received considerable interest for tissue engineering applications. Indeed, this rich meshwork of macromolecules not only contains biological cues for cell behavior, but is also a reservoir for growth factors. Therefore, they may provide a therapeutic platform for delivering exogenous binding growth factors to damaged tissues.
Bone morphogenetic protein-2 (BMP-2) is a highly potent osteoinductive growth factor involved in the early stage of bone formation making this molecule one of the most prevalent growth factors used clinically for bone tissue regeneration. Physiologically, BMP-2 bioavailability and activity are tightly regulated by binding to ECM components. In addition, literature data reported an affinity between BMP-2 and calcium phosphate minerals. In this context, we hypothesized that a mineralized ECM may present a great potential as efficient carriers for BMP-2. The purpose of this study was, therefore, to assess and to compare the efficacy of an ECM derived from osteogenic differentiated human bone marrow-derived multipotent stromal cells (hMSC) with an ECM derived from undifferentiated hMSCs on BMP-2 retention and its resultant effect on bone formation (Figure 1).
ECMs were produced by hMSC cultured in either osteogenic (ECM-OS(+)) or in standard culture medium (ECM-OS(-)), respectively, for 21 days and then decellularized using a TritonX100/NH_4OH solution. Both ECMs bind and retain BMP-2 at a similar extent (~50%). By using C2C12 cells and an alkaline phosphatase assay, the biological activity of BMP2 bound into ECM-OS(+)(prepared either in fresh or freeze-dried conditions) were 2-fold higher than the one obtained in ECM-OS(-).
In order to determine the osteogenic potential of the constructs, polycaprolactone 3D scaffolds were coated with each ECM, loaded with fluorescent labelled-BMP-2 ($BMP\text{-}2^{DL800}$) and subcutaneously implanted in mice for 8 weeks. In vivo monitoring of the bone formation by µ-CT revealed that the amount of newly formed bone increased during the 2-3 first weeks and then reached a plateau; the induced bone tissue in ECM-OS(+) was higher (1.4-fold) than in

ECM-OS(-). In vivo kinetic releases of BMP-2^{DL800} from the scaffolds indicated BMP-2 retention half-times of 9, 5 and 3 days for ECM-OS(+), ECM-OS(-) and bare scaffolds, respectively.

In conclusion, our results provide evidence that an ECM produced by hMSCs can be used as a delivery vehicle for BMP-2. More interestingly, the osteoinductive performance properties of the BMP-2 contained in ECMs derived from osteogenic differentiated hMSC was enhanced compared to a control ECM.

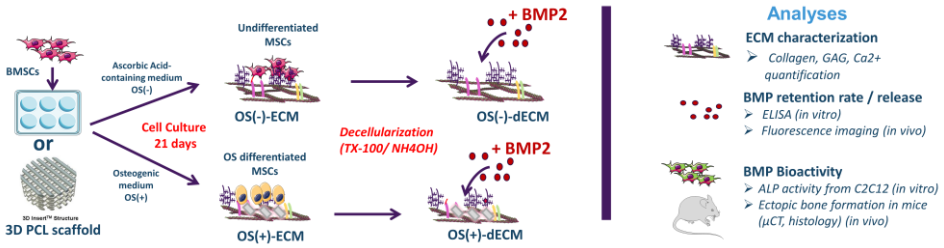

Figure 1 : Experimental plan of the project