ABSTRACT SUBMISSION

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The IEIK13 self-sssembling peptide hydrogel is efficient to repair osteochondral defects in a non-human primate model

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ABSTRACT

INTRODUCTION: *In vivo* evaluation of tissue engineered-cartilage is an indispensable step before human application. Most animal models differ in biomechanical functions and/or physiological responses from human, limiting our ability to extrapolate data to clinical practice. The non-human primate (NHP) model overcomes many of these limitations. In the present study, autologous chondrocytes were amplified and combined with a new self-assembling peptide (IEIK13 hydrogel) or a biomaterial already used in other medical applications (fibrin hydrogel), in the presence of chondrogenic factors. We investigated the capacity of the cartilage gels to repair osteochondral defects created in the knee joint of *Cynomolgus* monkey.

METHODS: During a first surgery, articular chondrocytes were isolated from cartilage biopsies (3.5 mm diameter) sampled from femoral condyles of three adult animals. Cells were amplified for 14 days with FGF-2 and insulin (cocktail FI) then re-differentiated for 21 days in IEIK13 or fibrin in the presence of BMP-2, insulin and triiodothyronine T3 (cocktail BIT). During a second surgery, cell-loaded or acellular hydrogels were implanted within osteochondral defects originally created at the biopsy zones. For a given animal, each joint was treated with a specific hydrogel (IEIK13 or fibrin). Animals were implanted for 3 months. Implant integration was evaluated by micro-computed tomography (µ-CT) and immunohistological analyses.

RESULTS: NHP articular chondrocytes were responsive to FI/BIT concentrations already used in clinical trial with auricular chondrocytes to treat nasal deformities. *In vitro* analyses (real-time PCR, Western-blotting and immunohistochemistry) revealed that NHP chondrocytes were able to reconstruct a cartilage matrix in IEIK13 and fibrin hydrogels. Cartilage gels were successfully implanted, all animals showed normal mobility through the study without medical complication or sign of distress. The µ-CT analysis allowed the follow-up of the hydrogel-based implants (figure 1A) which appeared well integrated into the cartilage defects (figure 1B). Histological analyses are in progress and will determine more precisely the nature/quality of the reconstructed cartilage using IEIK13 or fibrin hydrogel.

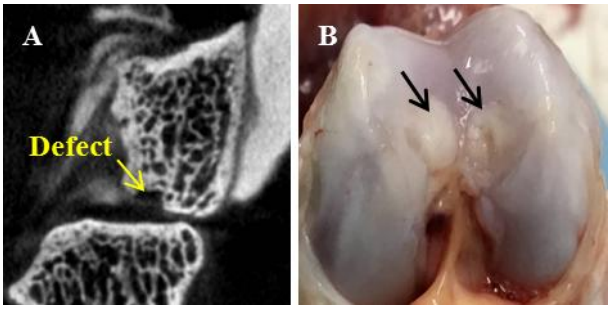

Figure 1: (A) maintenance of the hydrogel-based implant prevents penetration of the contrast agent within the defect. (B) Macroscopical

aspect of implanted defects (arrows) at the end of the study.

DISCUSSION & CONCLUSION: These results demonstrate the value of a combined approach using autologous chondrocytes, selected soluble factors (available under drug forms) and IEIK13 hydrogel to repair articular cartilage by tissue engineering technique. Firstly, our *in vitro* study shows that the FI/BIT cocktail is efficient to stimulate cartilaginous matrix synthesis by NHP articular chondrocytes, as previously shown with human articular chondrocytes. Secondly, our *in vivo* study shows that NHP is a relevant animal model for challenging articular cartilage repair by using tissue engineering. Interestingly and in contrast to natural material-based hydrogels, IEIK13 offers advantages such as low risks of biological pathogen transmission and homogeneous batches in production.