has also been demonstrated both in vitro and in vivo in a large animal study.It was also shown that the quality of the repair tissue at 6 month achieved by NCs was statistically superior to AC controls.

In summary, the scientific knowledge generated in those pre-clinical research projects supports the compatibility and efficacy of NC for articular cartilage repair.

NANOCOMPOSITE SCAFFOLDS FOR NOSE2KNEE APPLICATION

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Due to the poor self-repair capacity, most severe chondral and osteochondral lesions are source of progressive pain and disability, limiting joint motion and quality of life. The major challenge in the regeneration of large osteochondral lesions is the rapid restoration of the joint function after treatment. The integration between the newly formed bone and cartilage at the interface and with the host tissues is paramount for the success of the regenerative treatment. Tissue engineering strategies involving perfusion bioreactors, offer the potential to improve the intimate integration between bone and cartilage layer during the culture, before implantation. Biphasic scaffolds with appropriate microstructure and gradient composition are crucial not only to physically and chemically guide cell response and tissue growth during the culture, but also to promote the formation of a well integrated osteochondral interface.

The developed material is a bi-layer scaffold comprising type I collagen isolated from the equine tendon for the cartilage component and type I collagen biomineralized with bioactive Magnesium-doped hydroxyapatite (Mg- HA) nano-crystals for the bone component. The use of natural materials was selected to enhance biological interaction with the host tissue. Crosslinking reaction was optimized to improve adhesion between layers and the resistance to the perfusion of culture medium in bioreactor. A peel test was performed to quantify the adhesion force between the two interconnected layers. The results obtained (4.1 ± 1.2N) showed better integration in comparison with other bilayer collagen hydroxyapatite scaffolds.

The morphological and microstructural analysis of the scaffold was performed by SEM. Cartilage layer possesses a sponge-like structure with well-defined, uniform, interconnected macropores. Freeze drying process was optimized to replicate

the vertical orientation of collagen fibers. The biomineralized layer shows a highly fibrous structure with well interconnected pores with diameters up to 600 micron. Chemical characterization was performed to verify the composition and quantify the percentage of the inorganic mineral content.

The biomaterial was shaped in disks of 2.5cm of diameter and appeared to be suitable for culture of nasal chondrocytes for 5 weeks in perfusion bioreactor. Preliminary experiments showed the potential of the engineered graft for mimimally invasive treatment of osteochondral lesions.

PRECLINICAL ANIMAL MODEL – NOVEL TECHNOLOGY FOR ARTICULAR CARTILAGE REPAIR

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Nasal chondrocytes could be viable alternative for ACI in human patients. Before using it in clinical settings, it is necessary to test this hypothesis on translational (large animal) model.

Designed model was chronic, full-thickness cartilage defect placed on lateral and medial femoral condyles in sheep. The protocol included two surgical procedures. First procedure was to create two partial-thickness defects, 4 mm in diameter on the lateral and medial femoral condyle with a standard mosaicplasty instruments used in human orthopaedic surgery. Biopsy of nasal septum cartilage was also performed with skin biopsy puncher, 8 mm in diameter. Cartilage samples from both origins were used for production of autologous tissue grafts. Chondrocytes were isolated, seeded on biphasic collagen-hydroxiapatite scaffolds, and cultured in automated bioreactor for 5 weeks. Engineered tissue was then implanted in condyle defects during second procedure. First, 4 mm partial-thickness defects were converted to osteochondral defects 6,5 mm in diameter and 5 mm deep. Then engineered cartilage tissue was implanted. There were four study groups. Autologous tissue grafts, engineered from scaffold and nasal septum chondrocytes were implanted