

NOSE2KNEE – SCIENTIFIC RATIONALE FOR USE OF NASAL CHONDROCYTES IN ARTICULAR CARTILAGE REPAIR

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Articular cartilage injuries remain a clinical challenge and are known to double the incidence of degenerative joint disorders if left untreated. Current therapeutic options suffer from major drawbacks, such as defect-size limitations, long and complex rehabilitation times, donor-site morbidity and limited graft material. Even the more advanced cell-based therapies show highly variable clinical outcome and provide not entirely satisfactory treatment. Moreover, due to the use of articular chondrocytes (AC) their applicability for elder patients is limited, since the capacity of AC to redifferentiate and generate a functional matrix is limited, extremely donor dependent and is reduced with increasing donor age. The use of nasal chondrocytes (NC) could overcome these limitations.

Harvesting and donor site morbidity

In contrast to articular cartilage, harvesting of nasal cartilage, is less invasive and is performed under local anaesthesia leading to minimal donor site morbidity due to the fact that the donor site is easily accessible and not subjected to high levels of physical force.

Properties of Nasal Chondrocytes

The properties of NC are less age dependent than AC, they proliferate faster and have a higher and more reproducible capacity to generate functional cartilaginous tissues. In addition the contents of GAG and Collagen type II and, consequently, the mechanical properties are superior in tissues engineered from NC.

Compatibility of NC in a joint environment

In vitro experiments were conducted to study the response of NC to experimental conditions mimicking the mechanical and inflammatory joint environment. Although NC are not subjected to high mechanical forces in their native environment, they are capable to properly react to mechanical forces typical of joint loading. Furthermore, tissues generated from NC also showed a higher capacity to recover after a short exposure to IL-1. Molecular compatibility of NC to an articular environment

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 months 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 ($4.1 \pm 1.2\text{N}$) 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