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Paper #4

Human Skin Stem Cells Successfully Used to Engineer Articular Cartilage.

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Summary:
Skin derived stem cells can be successfully used to engineer scaffold-less neo-cartilage grafts that can be used for management of chondral and osteochondral lesions

Abstract:
Introduction
Articular cartilage injuries have a major implication in quality of life of patients. Most of these lesions lead to cartilage degeneration and subsequent osteoarthritis. Tissue engineering represents one of the most promising biological solutions for chondral and osteochondral lesions. Engineered autografts can be generated in order to replace the injured tissue. The use of stem cells is of paramount importance due to donor morbidity and unavailability of healthy cartilage. Recently, stem cells isolated from the dermis layer of the skin were differentiated towards chondrocytes. The purpose of this study was to use human dermis isolated skin stem cells to engineer functional neocartilage tissue with properties comparable to native cartilage.

Methods
Human stem cells were isolated from the dermis layer of the skin using the rapid adherence and microsphere formation techniques. Stem cells were identified using the fluoroscopy markers CD44, CD105, and CD271. Subsequently, they were grown in culture media that induced differentiation of stem cells towards chondrocytes. 60 million cells were seeded in non-adherent surface of 2% agarose wells without the use of scaffold to form fifteen (15) engineered neo-cartilage constructs (4 million cells per neo-cartilage construct). Tissue engineered constructs from human chondrocytes seeded with the same seeding density were used as control. All constructs were grown for 4 weeks in chondrogenic culture media. Total collagen content, collagen II and glycosaminoglycans were measured at the end of the culture period. Compressive and tensile properties of neo-cartilage tissue of both groups were evaluated using confined compression creep test and tensile testing using the Instron machine. The assessments were made by researchers that were blinded to the groups.

Results
Neo-cartilage tissue created from dermis stem cells had macroscopic appearance similar to that of native articular cartilage. Immunohistochemistry showed no difference in the amount of collagen II between the stem cell and chondrocyte control. Collagen, and glycosaminoglycan content was 1.3±0.6%/WW and 0.4±0.1%/WW respectively in stem cell constructs. Ultimate Tensile Strength (UTS) and Young's modulus were 0.7±0.1MPa and 1.2±0.2MPa for skin stem cell constructs and 0.6±0.1MPa and 0.9±0.2MPa for chondrocyte constructs (p=0.01 and p=0.003) respectively. Compressive instantaneous and relaxation Moduli were 138±14kPa and 24±4kPa for skin stem cells and 146±21kPa and 27±7kPa for chondrocytes (p=0.23 and p=0.16). Aggregate Modulus was 88±9kPa that was no significantly different to control values (85±11kPa, p=042).

Conclusions
Skin derived stem cells can be successfully used to engineer articular cartilage grafts that could be used for management of chondral and osteochondral lesions. Engineered neo-cartilage from human skin stem cells exhibited

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significant mechanical integrity and biochemical content.