CARTILAGINOUS MATRIX COMPONENTS PRODUCTION IN THE *IN VIVO* 'CELL-SCAFFOLD' CONSTRUCT

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ABSTRACT

Articular cartilage has the potential to be regenerated via tissue engineering strategy. This approach aims to improve the available cartilage degenerative related treatment modalities. With the utilisation of the tissue engineering principles, the engineered cartilage tissue was formed in the *in vitro* three-dimensional (3D) culture and evaluated in the *in vivo* ectopic implantation setting. The cultured chondrocytes at passage-1 were transfected with SRY (Sex Determining Region Y)-box9 (*SOX9*) and Telomerase Reverse Transcriptase (*TERT*) genes. The cells were grouped into 1) *SOX9*/*TERT*-transfected chondrocytes, and 2) non-transfected chondrocytes (NTC). The NTC serves as a control. A total of 1×10^5 cells were seeded into the porous poly(lactic-*co*-glycolic) acid (PLGA) with and without fibrin scaffolds. The formed *in vitro* "cell-scaffold" construct were cultured for three weeks. The constructs were subcutaneously implanted at the dorsum of the athymic mice for two and four weeks. The evaluation includes macroscopic observation as well as histological analyses to detect sulphated glycosaminoglycan (sGAG) and proteoglycan productions. The *in vivo* construct's morphology has the appearance that resembles cartilage. Regardless of cells and scaffold groups, the *in vivo* constructs at week-4 were firmer than the constructs at week-2 confirmed thru simple palpation using forceps. The construct's rigidity supported by the extracellular matrix distribution in the construct. The presence of sGAG can be visualised in all *in vivo* constructs. However, the proteoglycan can be seen only at the pericellular matrix region of the week-4 *SOX9*/*TERT*-PLGA/fibrin construct. The presence of these two extracellular matrix components indicates ongoing cartilaginous tissue development. The overall findings showed that the *SOX9*/*TERT*-PLGA/fibrin construct has the potential to be developed into functional cartilage tissue. The information retrieved from this study gives some insight into the translational endeavours to manoeuvring laboratory-grown engineered tissues to tangible impact in the future clinical application.

Keywords: Articular Cartilage, Chondrocytes, *In Vivo*, Tissue Engineering, Gene Transfer

Acknowledgement: The authors thanked the Kulliyyah of Allied Health Sciences, IIUM Kuantan Campus and the Ministry of Energy, Science, Technology, Environment and Climate Change (MESTECC) or formerly known as the Ministry of Science, Technology and Innovation (MOSTI) for providing ScienceFund (SF14-012-0062).