Calcium Phosphate/Mesoporous Silica Bone Cement Containing Osteogenic Growth Peptide

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By overlayering cell sheets on resected tissue as a vascular bed, we have attempted to fabricate artificial cardiac tissues in a bioreactor. However, upon the fabrication of these tissues, oxygen supply to the tissue was assumed to be insufficient, because culture medium used for *in vitro* culture dissolves a lower amount of oxygen than blood. Therefore, this study attempted to supply a sufficient amount of oxygen to the vascular bed by using oxygen carriers. The activity of the vascular bed was assessed by an ATP-dependent luciferin-luciferase luminescence imaging system.

A resected section of femoral tissue with a connectable artery and vein was put onto a tissue culture chamber and served as a vascular bed. The vascular bed was then perfused in a custom-made bioreactor. This study used perfluorocarbon (PFC) emulsion, which is an effective oxygen carrier. Oxygenated PFC with luciferin-containing culture medium was continuously infused into the vascular bed from the artery side. The amount of ATP production was observed as a metabolic activity index by measuring bioluminescence imaging (BLI) signal intensity.

Without PFC-perfusion, the oxygen level decreased gradually as observed by the decrease of BLI signal intensity; however, BLI signal intensity in the vascular bed increased with oxygenated PFC-perfusion. The increased intensity of BLI was found to be greater than that of the control medium-perfusion, indicating that the metabolic activity and ATP production of the vascular bed increased by supplying oxygen from the oxygen carrier.

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Hyaluronic Acid Down-regulates Interferon Signalling in an Injured Bovine Intervertebral Disc

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Low back pain is a major cause of disability for people between 20 and 50 years old that imposes a serious socio-economic burden. Therefore, the current focus of regenerative medicine is on identifying molecular markers for designing specific therapeutics. Previously, we have identified the anti-proliferative IFIT3 and IGFBP3 as downstream targets of the inflammatory cytokine IFNα2b signalling pathway in the human annulus fibrosus (AF). In this study, injection of hyaluronic acid (HA) hydrogel was hypothesized to have an anti-inflammatory effect on this signalling pathway using the bovine disc as a model system. Inflamed bovine organ culture was used to test the anti-inflammatory effect of HA hydrogel on the IFNα2b signalling pathway and the downstream targets, IFIT3 and IGFBP3. Discs harvested from seven young calves were cultured for three days with or without 100 U/ml IFNα2b. Experiments included intact disc, injured disc, injured disc treated with a cross-linked HA hydrogel, injured disc treated with IFNα2b, and injured disc treated with IFNα2b and HA hydrogel. PCR analysis was carried out to check the gene expression of IFNα2b signalling molecules in extracted AF cells. Additionally, immunohistochemistry was used for protein expression. Relative gene expression data was statistically analyzed with one way Anova, where $p < 0.05$ were considered significant. The results showed that HA significantly down-regulates IFNα2b receptors, STAT1/2, JAK1, IFIT3 and IGFBP3. Protein expression analysis also confirmed the PCR results. Hence, it was concluded that HA plays an anti-inflammatory role in the IFNα2b signalling pathway resulting in down-regulation of anti-proliferative IFIT3 and IGFBP3.

Early Detection Of Structural Abnormalities and Cytoplasmic Accumulation of TDP-43 in Tissue-Engineered Skins Derived from ALS Patients

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Amyotrophic lateral sclerosis (ALS) is a fatal adult-onset disease characterized by the selective degeneration of motor neurons (MNs) in the central nervous system (CNS). Current diagnosis of ALS is based on clinical assessment of related symptoms which appear late in the disease course after degeneration of a significant number of MNs. As a result, the identification and development of disease-modifying therapies is difficult. Novel strategies for early diagnosis of ALS, to monitor disease progression and to assess response to existing and future treatments, are urgently needed.

Due to the common embryonic origin of both skin and neural tissues, many neurological disorders, including ALS, are accompanied by skin changes that often precede the apparition of neurological symptoms. We have developed a unique tissue-engineered skin model (TES) derived from symptomatic, sporadic and familial ALS patients as well as pre-symptomatic FALS patients carrying a known pathological DNA mutation. TES were generated from isolated keratinocytes and fibroblasts and analyzed using different biochemical, immunohistological and molecular methods. Our ALS-TES presents a number of striking structural and molecular features, uniquely seen in patients-derived TES, including extracellular matrix (ECM) disorganization and cytoplasmic TDP-43 inclusions, a pathological signature found in the majority of ALS cases in the affected regions of the CNS.

Consequently, our ALS-TES could represent a renewable source of human tissue to better understand the physiopathological mechanisms underlying ALS, facilitate the identification of disease biomarkers for early diagnosis and disease monitoring, as well as provide a unique tool for the development of drug screening assays.

Calcium Phosphate/Mesoporous Silica Bone Cement Containing Osteogenic Growth Peptide

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Calcium phosphate (CaP) cements have been widely investigated as bone graft substitutes due to its excellent self-setting ability, biocompatibility and osteoconductivity. In additional, mesoporous materials have also been studied for application in medical devices due to their large surface area, which is capable of loading numerous biological molecules. This study aimed the development of bone cement based on CaP and mesoporous silica (mSi) functionalized with synthetic peptide, osteogenic growth peptide (OGP). The mSi-based particles were prepared by sol-gel process. After adsorption of OGP into mSi particles, the cement was prepared in a suitable liquid-to-powder ratio: mSi-OGP, β-tricalcium phosphate, monocalcium phosphate monohydrate and solution PEG400. The surface area and porosity of the mSi were characterized by adsorption-desorption of Nitrogen (BET) and transmission electronic microscopy (TEM). Compressive strength (CS) of the cement was evaluated after the periods of 1 and 7 days soaking in simulated body fluid (SBF). The release profile *in vitro* of OGP peptide from cement in SBF was monitored by fluorescence spectroscopy. BET patterns confirmed the porosity of the silica particles. TEM images showed the hexagonal arrangement of mesopores. CS revealed an increase in strength after 7 days (1.95 ± 0.20 to 2.81 ± 0.45 MPa). After this period, a fracture of the cement can be observed by scanning electronic microscopy. The release profile of OGP peptide showed that the peptide content was not released until 7 days. According to results, the CaP/mSi cement containing OGP peptide can be a potential material for bone graft substitutes.

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