【Grant-in-Aid for Scientific Research (S)】

Integrated Disciplines (Complex Systems)

Title of Project : Development of "4-dimensional scaffold system" that integrates signaling factors and 3-dimensional structural biomaterials

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Research Area : Complex Systems
Keyword : Regenerative medicine/Tissue engineering

【Purpose and Background of the Research】

Recent progress in stem cell biology helps elucidate signaling network for tissue and organ regeneration and also develop delivery system of signaling factors to target cells. In addition, emergence of 3D printer promotes control technology for 3D shape of scaffold materials. However, an individual element is insufficient to realize clinical regeneration; development of the interface that integrates both signaling factors and scaffold materials is essential.

This proposal attempts to develop high-performance hydrogel unit that retains signaling factors to enable their spatial placement and then degrades at desired timing to deliver the signaling factors to target cells. Such hydrogel system integrates signaling factors and scaffold materials to create "4D scaffold system" that controls differentiation and proliferation of local cells in time and space.

【Research Methods】

First, optimize signaling network for bone/cartilage regeneration and delivery of signaling factors in appropriate molality. Second, optimize the performance of scaffold materials for bone/cartilage by controlling 3D shape on various scales. Third, based on hydrogel design/fabrication method studied so far, develop new hydrogel unit that meets 5 demand characteristics for integrating interface of signaling factors and scaffold materials: ①Suppression of gel swelling in aqueous condition; ②Retention of mechanical strength in aqueous condition; ③Control of network size; ④Control of degradation in coordination with degradation; ⑤Biocompatibility. Then, prototype "4D scaffold system" that enables spatial and temporal control of cell differentiation and proliferation. Forth, implant the prototyped "4D scaffold system" into bone/ cartilage-defect model to test its performance and elucidate detailed mechanism of regeneration.

【Expected Research Achievements and Scientific Significance】

Integration of 3D shape control, signaling network for bone/cartilage regeneration, signal delivery system using high-performance hydrogel unit as an interface to create novel "4D scaffold system". By controlling both timing and 3D location of signal release, construct science and technology platform for precise regulation of differentiation and proliferation of local cells. In addition, using genome-wide analysis, investigate the mechanism of regeneration from molecular biology/epigenome viewpoint, study the interface of scaffold materials and living body, and obtain genome-level molecular basis for practical applications that guarantees efficacy and safety.

This proposal plans to create "4D scaffold system" using high-performance hydrogel unit that integrates scaffold materials and signaling factors and to provide proof of concept in bone and cartilage regeneration. This system may provide versatile science and technology platform for not only regeneration of other organs, but also prevention/diagnosis/treatment of various diseases.

【Publications Relevant to the Project】

Kondo S, Sakai S, Chung U, et al. Reliable hydrogel with mechanical 'fuse link' in an aqueous environment. Adv Mater 27:7407-7411, 2015.

Kanke K, Ohba S, Chung U, et al. Stepwise differentiation of pluripotent stem cells into osteoblasts using four small molecules under serum-free and feeder-free condition. Stem Cell Rep 2:751-760, 2014.

【Term of Project】 FY2016-2020

【Budget Allocation】 126,600 Thousand Yen

【Homepage Address and Other Contact Information】

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