Development of Hybrid Nanofibrous Matrices for Bone Regeneration

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Purpose of Study: Designing of materials with a composition mimicking the structure of bone matrix is one of the important strategies for successful regeneration of hard tissue (1,2). In this study, we report on the development of apatite-polymer hybrids into a novel nanofibrous structure, while mimicking the structure of bone extracellular matrix.

Methods: Biomimetic composition was designed to comprise apatite mineral phase and natural organic gelatin. Through the precipitation method of apatite nanocrystals within a gelatin sol, the initial hybridized sol was prepared to have appropriate viscosity and surface tension. In particular, the ratio of organic / inorganic amount was systematically varied in order to observe the effect of composition. The hybrid sol was freeze-dried and dissolved in an organic solvent to possess solution properties which are appropriate for the electrospinning process. Under controlled conditions, electrospinning was carried out to generate nanofiber form of the organic-inorganic hybrids. The electrospun nanofiber was further stabilized chemically, based on our previous experimental conditions (2). The phase and chemical structure of the hybrid nanofiber were analyzed with X-ray diffraction and Fourier-transform infrared spectroscopy, respectively. The morphology and internal structure of the nanofiber were characterized with scanning electron spectroscopy and transmission electron microscopy. For the biocompatibility test, the human osteoblastic cells were cultured on the nanofibrous matrices and initial cellular responses were observed, following previous protocols (2,3).

Results / Discussion: The hybrid matrices showed the evolution of only apatite mineral phase without creating other products, as confirmed by XRD and FTIR. In particular, the amount of apatite developed on the gelatin template increased according to the initial concentrations of the inorganic precursors, illustrating the occurrence of complete reaction between Ca- and P-precursors. Depending on the properties of the hybrid sol, such as concentration and composition, the morphology and diameter of the electrospun fiber varied significantly. As the mineral concentration increased, the fiber form was more difficult to generate. Instead, a large amount of bead was formed within the fiber matrices. Moreover, controlling the sol concentration was necessary to maintain the generation of fibers in case of hybrid sols. The generated fiber under controlled electrospinning conditions showed a continuous morphology with diameters of ~hundreds of nanometers (Fig. 1). The high resolution internal electron image of the fiber featured a typical hybrid structure, in other words, apatite nanocrystallines distributed well within the organic continuous matrix. Moreover, the apatite mineral phase revealed a typical evolution of electron diffraction pattern of apatite crystals. There observations correspond to the previous works performed on the biomimetic organic-templated apatite crystals as well as on the bone extracellular matrix. On the developed hybrid matrices, osteoblastic cells attached and grew actively with culturing period (Fig. 2, at day 2). Of particular importance, the osteoblastic activity of the cells, as assessed by the expression of alkaline phosphatase, was improved significantly when compared to that on the organic matrix equivalent or plastic culture dish, suggesting the potential of the hybrid nanofibrous matrix in the bone regeneration field. In order to confirm the osteogenic potential of our novel hybrid matrix, further in-depth study is currently underway, such as the assessments of bone-associated proteins using bone-marrow derived stem cells.

Conclusions: Hybrid nanofibers made up of organic matrix and inorganic apatite mineral were generated though novel biomimetic precipitation and electrospinning processes. Under controlled processing conditions, continuous nanofibers were obtained with diameters of hundreds of nanometers. The apatite ultrafine nanocrystals were homogeneously distributed within the gelatin matrix. The mineral composition within the hybrid fibrous matrices influenced the osteoblastic responses significantly with respect to the pure organic matrix.

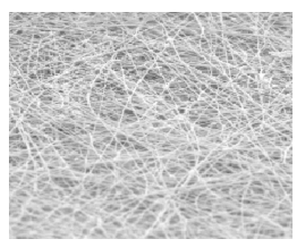

Fig. 1

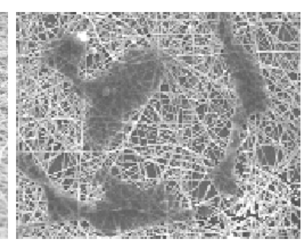

Fig. 2

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