Special Issue: Positioning of Tissue Engineering in Regenerative Medicine

Brief Review

Positioning of Tissue Engineering in Regenerative Medicine

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As the third choice of advanced medical therapy following reconstruction surgery and organ transplantation, a new therapeutic trial based on the natural-healing potential of body itself to induce tissues regeneration and repairing, has been recently expected. The natural-healing potential is basically governed by the inherent potentials of cells for proliferation and differentiation. To realize this tissue regeneration therapy, there are two practical approaches of cell therapy and tissue engineering. The idea of tissue engineering is to artificially create a local environment which enables cells to enhance their proliferation and differentiation, resulting in cell-induced tissue regeneration. For this purpose, biomaterials are being used as the cell scaffold and delivery carrier of growth factors. The cell scaffold gives cells a good platform to assist their proliferation and differentiation. If a key growth factor is supplied to the right place at the right time period and concentration, it is no doubt that the body system will initiate to physiologically function, resulting in the natural induction of tissue regeneration. One practically possible way to enhance the *in vivo* therapeutic efficacy of growth factor with in vivo short half-life period is to make use of drug delivery system (DDS) technology. The controlled release of growth factors succeeds in the growth factor-induced regeneration and repairing of various tissues. The release system can be combined with cells or/and the cell scaffold to promote the therapeutic efficacy of tissue regeneration.

Biomaterial is defined as material which is used in the living body as well as contacting with biological components, including cells, proteins, nucleic acids, saccharides, and bacteria or viruses. The representative research areas well known are medical devices or artificial organs and DDS. However, biomaterials are not limited to the two areas. So far, biomaterials have been performed in the research direction to develop materials which are bio-inert, cell friendly or do not induce inflammation responses. Nowadays, however, the research direction is changed to the development of biomaterials which actively act on the living body to regulate the biological functions of cells or are subsequently integrated into the living system. One of

the representative research areas is regenerative medicine. Cell scaffolds, the DDS of growth factors, gene transfection reagents, and cell culture systems are designed and created by making use of biomaterials technology to enhance the cells potentials of proliferation and differentiation, resulting in the achievement of cell-based tissue regeneration. Taken together, tissue engineering is positioned as one new research area of biomaterial technology to regulate cell potentials which are necessary and indispensable to realize regenerative medicine based on natural-healing potentials.

Considering cell therapy, the therapeutic efficacy is not always as high as one expects although the cells transplanted are biologically active under *in vitro* conditions before the transplantation. This implies that the *in vivo* cell environment around the site to be transplanted is not good to allow cells to survive and maintain their biological functions. To tackle the problem of *in vivo* cell conditions, it is practically necessary to design the *in vivo* environment for cells transplanted. For example, the cell scaffold and growth factors modified with DDS are combined upon transplanting cells. The tissue engineering technology will provide cells with a good environment to increase their survival rate and consequently enhance their biological functions. Or cells are genetically engineered by gene transfection reagents for their functional activation and transplanted to enhance the *in vivo* therapeutic efficacy. Tissue engineering technology with biomaterials is important and useful to promote the activity of cells for regeneration therapy. The tissue engineering technology of cell scaffold and DDS-modified growth factors is also a good research tool for cell biology. The results obtained by the researches improve the biological states and the efficiency of cells proliferation and differentiation, which can be applied for drug discovery.

If the cell potential of tissue regeneration can be activated *in vivo* by using suitable biomaterials in an appropriate manner, the cell-based tissue regeneration can be achieved to treat diseases, which is regeneration therapy. When the cell potential is controlled by biomaterials technology *in vitro*, cell biology can be developed. Additionally, the research and development of drug discovery with cells potentially controlled are also advanced. This regeneration research of cell biology and drug discovery scientifically supports the regeneration therapy of next generation. Balanced development of both the regeneration therapy and regeneration research is necessary to realize regenerative medicine for efficient disease treatment, which is the strong expectation of patients.

It is my great pleasure to have this opportunity to serve as a guest editor of this special issue of "Tissue Engineering". In this issue, leading researchers in the field of tissue engineering are selected from all over the world to write reviews including the recent activities and new original papers. The first review is about recent advance for regeneration of cornea by regenerative medicine, given by Dr Gilson Khang at Department of PolymerNano Science & Technology, Chonbuk National University, Korea. Dr Antonios G. Mikos at Department of Bioengineering, Rice University, US provides a mini-review for leveraging synthetic biology for tissue engineering applications. Dr Liu Wei at Department of Plastic and Reconstructive Surgery, Shanghai Jiao Tong University, School of Medicine, China overviews fibrous scaffolds for tissue engineering. In addition to the reviews, three original papers are provided. Dr Manuela E. Gomes at 3B's Research Group — Biomaterials, Biodegradables and Biominetics, University of Minho, Portugal summarizes platelet lysate membranes as autologous templates for tissue engineering applications. Dr Asahi Tomitaka at Department of Biomaterials, Institute for Frontier Medical Sciences, Kyoto University describes the recent data about preparation of biodegradable iron oxide nanoparticles with gelatin for magnetic resonance imaging. Dr Masaya Yamamoto at Department of Biomaterials, Institute for Frontier Medical Sciences, Kyoto University reports a new finding on the ultrastructure of bone tissue ectopically regenerated by biodegradable hydrogels incorporating bone morphogenetic protein 2.

As mentioned above, the approach of regenerative medicine composes of cell transplantation and tissue engineering. However, there seems to be admiration that cell transplantation is the same as regenerative medicine. I never claim that this is wrong. The cell transplantation is one of the powerful approaches to realize regeneration therapy, because stem cells with high potentials can be obtained and used in clinic at present. However, it should be noted that tissue engineering-based regeneration therapy is also clinically achieved to treat patients. I am happy if readers could understand the recent development of biomaterials and tissue engineering technology which enabled cells to promote their biological functions for regenerative medicine, by reading through this special issue

of Tissue Engineering. I hope that substantial collaborations between cell biology and tissue engineering are essential to achieve the further research and development of regenerative medicine.

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