Release Technology of Cell Recruitment Molecules to Induce In Situ Tissue Regeneration Therapy

Yasuhiko Tabata
Laboratory of Biomaterials, Department of Regeneration Science and Engineering
Institute for Frontier Life and Medical Sciences, Kyoto University
53 Kawara-cho Shogoin, Sakyo-ku, Kyoto 606-8507, JAPAN

A new therapeutic trial based on the natural-healing potential of body itself to induce tissues regeneration and repairing, has been recently expected. To realize this tissue regenerative therapy, there are two approaches of cell transplantation and tissue engineering. For the first cell approach, it is necessary for an enhanced therapeutic efficacy to improve the in vivo viability and functions of cells transplanted. On the other hand, the basic idea of tissue engineering is to enhance the proliferation and differentiation abilities of cells for tissue regeneration. To this end, it is of prime importance to develop a biomaterial technology or methodology to give cells a local environment for their ability enhancement. For example, if a cell scaffold or a key bio-signaling molecule is supplied to the right place at the right time period or concentration by the release technology of biomaterials, the body system initiates to physiologically function, resulting in the natural induction of cell-based tissue regeneration. The tissue engineering technology also enables cells to improve their in vivo viability and functions, promoting the therapeutic efficacy of cell transplantation.

With the recent scientific development of stem cell biology, various molecules which have an ability to enable cells to accelerate their recruitment in vivo to the site necessary, have been available for cell-based tissue regeneration therapy. If the cell recruitment molecule can be supplied to the site to be regenerated by the release technology, it is highly expected that the molecule enhanced the recruitment of key cells at the site, resulting in promoted cell-induced tissue regeneration and repairing thereat. We have explored biodegradable hydrogels for the controlled release of biologically active stromal cell-derived factor (SDF)-1 of cell recruitment ability. When implanted subcutaneously into the mice

back, the hydrogel incorporating SDF-1 enhanced SDF-1-induced angiogenesis around the site of hydrogel implanted to a significantly high extent compared with the injection of SDF-1 solution. The number of cells with the SDF-1 receptor increased around the hydrogel implanted, in remarked contrast to that of SDF-1 solution. It is possible that the controlled release of SDF-1 enabled angiogenic cells to accelerate their recruitment, resulting in a cell-induced in situ angiogenesis. Such a cell-based tissue regeneration by making use of cell recruitment molecule was further promoted by combining with the controlled release technology of growth factors. For example, the controlled release of a cell recruitment molecule can enhance the in vivo recruitment of stem cells, followed by the local functional activation of cells recruited by another drug released, which results in an enhance cell-based tissue regeneration. In situ tissue regeneration through the functional activation of cells originally present in the body by utilizing the release technology of biomaterials is a new and promising therapeutic strategy of regenerative medicine.