Development of Muscle Tissue Engineering Technology for End-Stage Heart Disease Therapy

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Cardiac transplantation is a definitive therapy for the majority of patients with end-stage heart failure. However, the cardiac transplantation is currently limited by increasing shortage of donor hearts. Even if transplantation is successful, it is necessary for the patients to permanently take immunosuppressive medicine that causes various side effects. The situation undoubtedly deteriorates the quality of patient life.

Regenerative medicine is one of the promising ways to provide an ideal therapy for patients, since it is based on the idea that tissue regeneration is achieved by use of their own cells, including stem cells and/or precursor or blastic cells. Indeed, the isolation and characterization of the stem or blastic cells are fundamentally important for tissue regeneration. However, most of the cells cannot always expect their proliferation and differentiation, including tissue regeneration, unless an environment suitable for regeneration induction is provided together with the cells.

Tissue engineering is a key technology to create this environment, so-called artificial extracellular matrix, which allows stem or blastic cells isolated from a patient to regenerate tissues and organs of patient own. The artificial extracellular matrix is fabricated into a porous three dimensional structure as a physical support for cell in cell proliferation and differentiation or morphogenesis for tissue regeneration, functions as a reservoir of an extracellular signal protein, such as a growth factor, which can stimulates cell proliferation and differentiation, and is degraded in harmonization with tissue regeneration. In this research, we investigate the artificial extracellular matrix suitable for muscle regeneration based on these requirements and utilize this muscle tissue engineering technology for cardiac muscle regeneration of the animal models with end-stage heart failure. This technology will enable only patient cells to achieve creation of cardiac muscle without cardiac transplantation.

This project is undertaken to establish the following key technologies to realize muscle tissue engineering, aiming at improvement in quality of life for the patients with end-stage heart failure without cardiac transplantation.

<Basic technologies of muscle tissue engineering>

- 1) Isolation and characterization of muscle cells and creation of their artificial extracellular matrix suitable for muscle cell proliferation and differentiation
- 2) Ectopic muscle regeneration in vivo based on the artificial extracellular matrix technology
- Establishment of animal models with end-stage heart failure and therapeutic experiments with the animals based on ectopic muscle regeneration technology.

