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Cell sheet-based tissue engineering fabrication of functional 3-D tissues

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We have developed novel technology "cell sheet-based tissue engineering", which has realized cell-dense tissue fabrication without any scaffolds. Confluently, cultured cells are harvested as contiguous cell sheets from temperature-responsive culture surfaces only by lowering temperature. Cell sheets are directly transplanted onto damaged tissues or stacked into multi-layer constructs of various types of tissues. For fabricating pulsatile myocardial tissues, stacked cardiomyocyte sheets simultaneously beat in macroscopic view both *in vitro* and *in vivo* and revealed characteristic structures of native heart tissue. Multi-step transplantation of triple-layer cell sheets has overcome the scale-up limitation and finally, 10-time transplantations have realized about 1 mm-thick functional myocardial tissues. Next challenge is *in vitro* fabrication of functionally vascularized myocardial tissues. To imitate in vivo environment, we have tried to make media-perfused microvascular beds in vitro and transplant layered rat cardiac cell sheets over the beds. Culture media was perfused by using novel bioreactors, and then triple-layer rat cardiac cell sheets co-cultured with endothelial cells were put on the vascular beds. Interestingly, capillaries were regenerated between the cardiac cell sheets and the vascular beds. Blood perfusion analyses clearly demonstrated that red blood cells passed through the capillaries and reached into the cardiac tissues. These data indicated the possibility of *in vitro* perfusable blood vessel formation and further development of bioengineered 3-D thick tissues with functional vascular network. Cell sheet-based tissue engineering has enormous potential for regenerative medicine and 3-D tissue models.

Biography

Tatsuya Shimizu is a professor of Institute of Advanced Biomedical Engineering and Science, Tokyo Women's Medical University. He graduated from Faculty of Medicine, the University of Tokyo and got medical doctor (M.D.) in 1992. After two-year clinical training, He made a specialty of cardiovascular medicine including catheterization and got Ph.D in 1999. After that, He moved to ABMES of TWMU and have developed myocardial tissue engineering research based on "cell sheet technology". His recent work is especially concentrated on neovascularization in 3-D tissue to reconstruct more functional tissue.

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