Clinical application of huma iPS cells for cardiovascular Medicine

Keiichi Fukuda

Department of Cardiology, Keio University School of Medicine

Although heart transplantation can drastically improve the survival, shortage of the donor heart is a serious problem. The regenerative medicine of the failing heart had been long awaited. To address this question, we had developed novel methods to induce human iPS cells from circulating human T lymphocytes using Sendai virus containing Yamanaka 4 factors. We had screened the factor that were expressed in future heart forming area of the early mouse embryo, found several growth factors and cytokines that can induce cardiomyocytes differentiation and proliferation, and applied them to human iPS cells. We performed transcriptome of the metabolic enzymes and fluxome analysis using $^{13}$glucose and $^{13}$lactic acid on ES/iPS cells and cardiomyocytes, and found that their metabolic pathways were completely different. Based on these findings, we purified cardiomyocytes using glucose-free lactate-supplemented medium. Purity of the cardiomyocytes was $>99\%$, and they did not make teratoma formation. The transplanted cardiomyocytes using our technique can survive in the heart with more than $90\%$, and can show physiological growth after transplantation. We expect the combination of these techniques can achieve future heart regeneration. We also developed human disease model cardiomyocytes using human iPS cells from the patients with long QT syndrome and other hereditary heart disease. These disease model cardiomyocytes represented the phenotype of the disease, and might be helpful for drug screening and pathophysiological analysis.