Clinical application of human iPS cell-derived regenerated cardiomyocytes for the treatment of severe congestive heart failure

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Abstract: 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 used human HLA haplotype homo-iPS cells, which matches to approximately 20% of the Japanese population, to generate ventricular cardiomyocytes. We performed transcriptome of the metabolic enzymes and fluxome analysis using ^{13}glucose and ^{13}lactic acid on both ES/iPS cells and cardiomyocytes, and found that their metabolic pathways were completely different. Moreover, amino acid consumption analysis and metabolome analysis revealed that glutamine is another important energy source for the iPS cells. Based on these findings, we could purify the cardiomyocytes with more than 99% purity. The transplanted cardiomyocytes did not make teratoma formation in immuno-deficient NOG mice skin and heart. We transplanted the aggregate (spheroid) cardiomyocytes using our newly developed device. The transplanted cardiomyocytes could survive in the heart for the long period, showed physiological cell hypertrophy after transplantation, and could improve cardiac function due to myocardial infarction. We are now planning to examine the first in human clinical trial to transplant the human regenerated cardiomyocytes to the patients with HLA-6 class matched dilated cardiomyopathy in the near future.