

New Technologies - Bioengineering II

Bioengineered human liver for transplantation

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To establish clinically reliable bioengineered organ graft, we have been investigated a tissue engineering approach “decellularized organ scaffold” by discarding viable cells from native tissues, in which a large number of different cell types can be repopulated and maintained. The aim of our study was to generate native tissue derived organ scaffold for the development of liver regenerative therapy, with primary porcine derived cells or human iPS derived cells. De/recellularization protocols such as organ harvest, de/recellularization and transplantation were standardized to establish pre-clinical large animal model that represented liver injury and fibrosis under immune-suppressed condition. Especially, the procedure for introduction of a large number of different cell types into the expected location of the parenchymal/non-parenchymal space was critical and was finally established by using pressure monitoring system. In addition, angiography after transplantation of the liver graft revealed the continuous blood flow throughout the graft from surgically connected portal vein through inferior vena cava. Interestingly, the histological analysis of the tissues from the liver graft in 30 days after the implantation revealed that not only sufficient angiogenesis spread through the graft but also bile production and accumulation from the repopulated porcine primary hepatocytes. Finally, a large number of human iPS derived hepatic progenitor cells and endothelial cells as well as human iPS derived hepatic organoids were introduced into the porcine scaffold and successfully transplanted into the porcine body. The liver graft with iPS derived cells were evaluated 7 days after the surgery, which showed clusters of hepatocyte like cells with hepatic markers and human ALB in the serum of a recipient pigs. The result provides definitive evidence for the feasibility of engineering human-scale transplantable liver grafts for clinical applications, though further study is required to show a long-term efficacy.