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Project Title	New treatment strategy in acute on chronic liver failure using iPS cell derived liver organoids
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Report

The generation of transplantable organs is a promising and challenging therapy to meet the critical shortage of donor organs. We previously developed liver organoids (LOs) from human pluripotent stem cells (iPSCs), and transplantation of these LOs helped alleviate liver fibrosis in injury models. To promote the clinical translation for treating liver diseases, we launched a preclinical experiment using a non-human primate cirrhosis model to evaluate the potential therapeutic effects of allograft transplantation of LOs. Based on our advanced protocols, we successfully differentiated cynomolgus macaques iPSCs into endoderm, mesenchymal progenitors, and endothelial progenitors. By co-culturing these three progenitor cells, we reconstructed cynomolgus macaques derived LOs that could gradually mature in vitro. We then fused LOs on a cell culture insert that matured into fetal-like liver tissues with positively staining fetal hepatic markers. Moreover, we optimized the dose of TAA to establish a severe fibrosis model with cynomolgus macaques. Transplantation of fused cynomolgus macaques LOs partially alleviated liver fibrosis in vivo, including the declined serum hyaluronic acid and type IV-Collagen 7S and attenuated level of tissue fibrosis. Furthermore, we established a platform to generate my-liver organoids from cynomolgus macaques and hoped to develop an autologous transplantation therapy for liver fibrosis and acute on chronic liver failure.