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

In this year, we aimed to explore the allogeneic transplantation of iPS cells derived liver organoid in cynomolgus monkeys with ACLF or ALF. First of all, we reprogrammed monkey peripheral blood mononuclear cells into iPS cells using the auto-erasable Sendai virus vector and identified the cellular characteristics of monkey iPS cells in vitro. Based on the experience on human iPS differentiation, we have optimized the protocols and differentiated monkey iPS cells into hepatic endoderm, endothelial progenitor cells and mesenchymal progenitor cells. By co-culturing these three progenitor cells in a three-dimensional microwell culture plate, we successfully generated monkey iPS cells derived liver organoid. By transplantation of monkey iPS cells derived liver organoid in ACLF mice, we found these organoids could engraft in mice. Moreover, we also established an ACLF model with cynomolgus monkeys. After 12 weeks of intraperitoneal injection of Thioacetamide, 75% of monkeys developed mild liver fibrosis, and 25% developed severe liver fibrosis.