ID No.	K2005	
Project Title	Generation of iPS-derived human hepatocytes in rat liver	
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Report		

In this project, we are going to establish a method for manufacturing a large-scale human iPS-derived hepatocytes (iPS-Heps) in model animals. In current, We have already generated severe combine immunodeficiency (SCID) rats by knockout of the *ll2rg* and *Rag2* genes in F344 rats by using CRISPR/Cas9 system. Furthermore, we have also generated the liver-specific *iCasp9* gene knockin in the F344 rats. The suicide *iCasp9* gene can regulate these rats' hepatocytes to apoptosis, therefor, we can proliferate human iPS-Heps in the rats' liver and harvest large-scale human hepatocytes without rat cells. The preliminary experiment of transplanting human hepatocytes into the SCID rats has already started in Kyushu University by Dr. Kazuki Takeishi.

At first, we planed to visit IMSUT and hold a conference with other members in March, 2020. However, due to the prevalence of COVID-19, the travel from America to Japan is very difficult, so the visit was canceled. Instead of this, we held a online meeting with all the project members in 19th, March. On the meeting, we had indepth communication about the current problems and the future plan with each other. All the members reached agreements in the subsequent task. After this meeting, we adjusted the protocol about the breeding of the SCID rats to ensure their survival and quality in different institutes. On the other hands, the optimization of proliferating human hepatocytes in SCID rats is continued in Kyushu University, by collaborating with Dr. Kazuki Takeishi. In the meantime, we have started to expend the liver-specific *iCasp9* gene knockin rats in IMSUT. By utilizing this model, we will establish the protocol of regulating the *iCasp9*-KI rats' hepatocytes to apoptosis and cross these rats with SCID rats for the proliferation of human iPS-Heps in future. To ensure our project progressing smoothly, we will have regular meeting to exchange information every month and visits for technology supports will be started after the outbreak of COVID-19.