Succeeded in revivification of the rat liver in hypoxia due to cardiac arrest

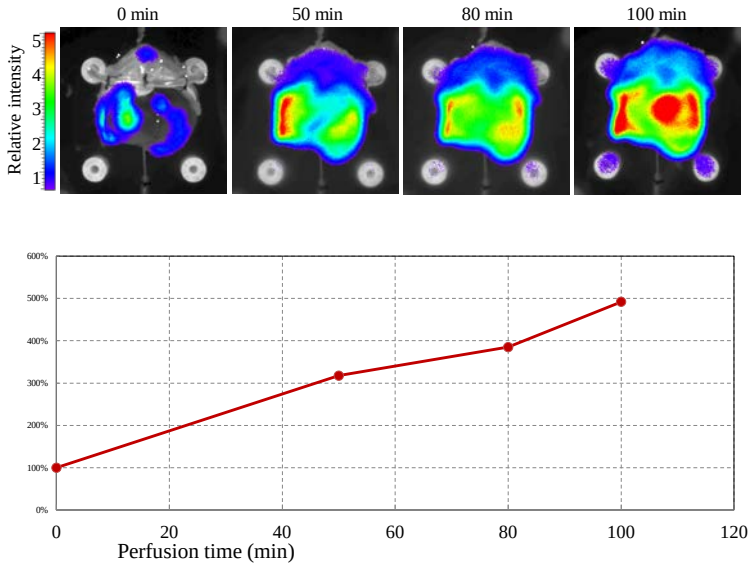
-It was made possible by using the Luciferase Transgenic Rat which enables the visibility of energy metabolism-

All the organs after the cardiac arrest are exposed to extreme hypoxia due to the bad circulation. There would be possibilities of converting inapplicable organs for transplantation to transplantable ones if we develop the technologies of cultivating for longer period of time the resected organs in hypoxia under proper conditions. Professor Eiji Kobayashi and Incorporated Administrative Agency RIKEN research center for multicellular system formation (Dr. Takashi Tsuji as a team leader) has been doing R&D for rat's liver perfusion system using rat model in vitro. They have found out the conditions for cultivation at a certain temperature through the perfusion cultivation of the Luciferase Transgenic Rats with visible function of energy metabolism developed by the Project Professor Eiji Kobayashi at the School of Medicine, Department of Regenerative Medicine Donation Scholarship at Keio University. This genetically modified rat is the one invented world-first by the Professor Eiji Kobayashi at Jichi Medical University (***Hakamata Y, et al. Transplantation 2006***). Luciferase gene has been integrated in the entire body and it enables to judge degree of organ recovery and regeneration thanks to the visibility of ATP amount in organs by adding light-emitting substrate; luciferin (***Sekine H, et al. Nature Communi 2013***).

The revivification of extracorporeal human liver in extreme hypoxia would greatly contribute to the improvement of disparate shortage of transplantable organs. The research results have been published in "***Scientific Reports***" dated on 22 April 2015.

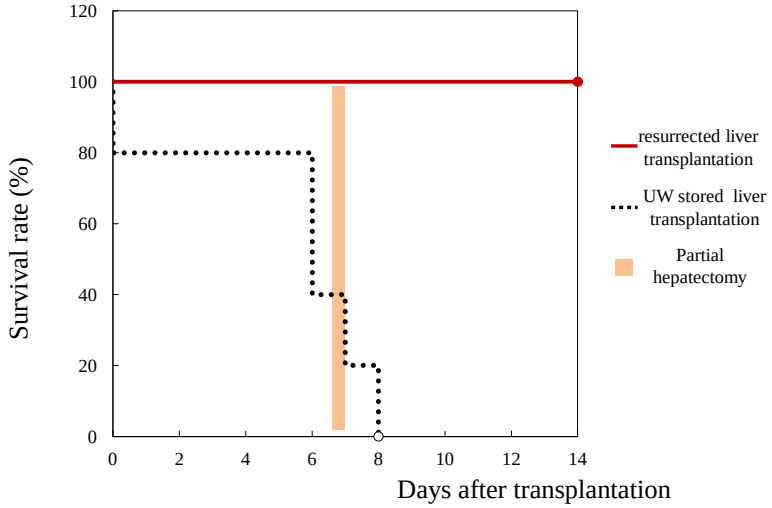
The research has started with setting up the sustainable conditions for preserving organ metabolism activities and has concluded in the fact that organ malfunctions are drastically suppressed by adding red corpuscle and keeping temperature at 22 degrees Celsius through the optimizations of oxygen carrier and storage temperature. Furthermore, the analysis of the effects on hepatocyte functionality by temperature has shown that storage under low temperature deeply restricts cell metabolism activities and closes metabolic pathway necessary for survival. On the other hand, the preservation at 22 degrees Celsius shows the energy output and it has been found that the temperature is enhanced to 37 degrees Celsius, the suspended proliferative activity and substance production are restarted. In the consequence the rat hepatocyte preserved for 24-hour perfusion added with red blood corpuscle under the temperature of 22 degrees Celsius, after the transplantation it has been found that it maintains albumin synthesis and hepatic regenerative competence.

Under the above conditions, the liver of Luciferase Transgenic Rat in warm ischemia for 90 minutes due to cardiac arrest has been cultured under perfusion for the purpose of revivification trial.



(Ishikawa J, et al. Scientific Reports 2015)

In order to further check the degree of organ recovery in ischemia, 100-minute perfusion under the same condition has been done and the liver bud was transplanted to other rat secondarily. The conventional organ preservation method (UW liquid in low temperature) leads the recipients to death within 3 days, on the contrary, it has been found that all the transplanted livers through the revivification by cultivation stay alive and also maintain albumin synthesis and hepatic regenerative competence.



(Ishikawa J, et al. Scientific Reports 2015)

It makes possible to maintain metabolism activity through adjusting metabolism by temperature control. It generates viability of organ revivification in extreme blood shortage.

Prof. Eiji Kobayashi at the lab room 7S4 in the Research Park Building in Keio University School of Medicine will set up a system he has invented to visualize energy metabolism and degree of regenerating organs and will further accelerate co-researches with top-notch teams both inside and outside the university through organizing a firm research driving force.