Development of Liver Assist Device Using Hypoimmunogenic Hepatocyte System

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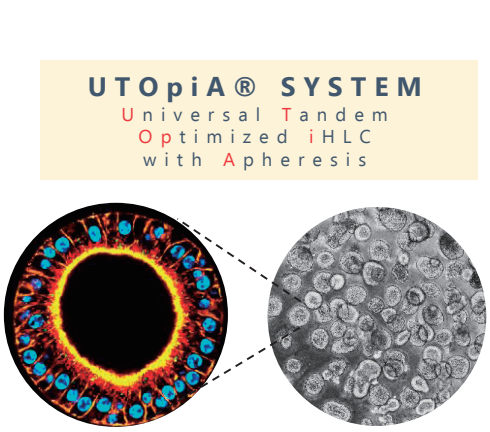
Project Outline

Acute-on-chronic Liver Failure (ACLF) is a disease in which a patient with cirrhosis or other chronic liver failure develops due to some trigger such as infection, gastrointestinal hemorrhage, or heavy alcohol consumption, leading to a precipitous state of liver dysfunction within 28 days. ACLF is characterized by systemic inflammatory response syndrome (SIRS) and multiple organ failure and is a critical disease with a mortality rate of over 80% for ACLF Grade 3, the most severe form. However, there exists no effective treatment other than liver transplantation at present, and many patients' lives cannot be saved.

In this project, we are developing an extracorporeal circulatory system (UTOpiASystem) for liver function assistance by incorporating liver organoids (iHLC: induced Hepatocyte-Like Cells) derived from Low immunogenic induced pluripotent stem cells (iPSCs) into the system for such serious liver diseases, based on the liver organoid technology obtained in our previous research (Figure 1). The UTOpiAsystem is a unique extracorporeal circulation system that consists of a granulocyte and monocyte adsorption apheresis (GMA) column, which traps neutrophils and inflammatory cytokines released in excess due to inflammation, and an iHLCcolumn, which is capable of supplementing proteins secreted by the liver and removing toxins such as ammonia and bilirubin. Successful development of this product would provide a new treatment option other than liver transplantation for patients with severe liver failure.



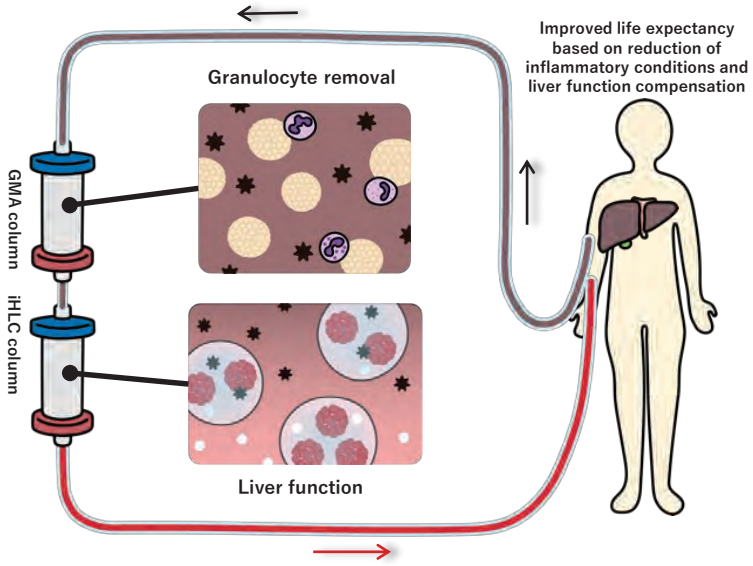


Figure 1: iPSC derived Liver Organoids technologies
Cell Metab, 2019; Cell, 2022

【Results of research to date and future plans for development】

When ACLF model rats were treated with UTOpiAfor 2 hours, a significant improvement in survival rate was observed compared to the group that was not treated with UTOpiAor the group that was treated with each column alone. We are currently working to scale up the manufacturing process of liver organoids for clinical application and to establish a technology to produce columns of a size that can be used for patients. After establishing the manufacturing method and conducting non-clinical safety studies, we aim to begin clinical studies to confirm safety and tolerability within two to three years.

Target disease: ACLF, Acute Liver Failure, Post Hepatectomy Liver Failure, Severe Alcoholic Hepatitis
Patent information: PCT filed
Technology features: Non-clinical POC obtained using ACLF model rats
Markets and challenges in development: Large market expected due to the global increase in liver failure patients. Scale-up of manufacturing is the challenge.
Desired corporate collaboration: Joint research with Yokohama City University Venture KanzoBiomedicines, Inc.