Reprogramming adult human hepatocytes into liver progenitors with unlimited self-renewal, efficient differentiation and transplantation capacities

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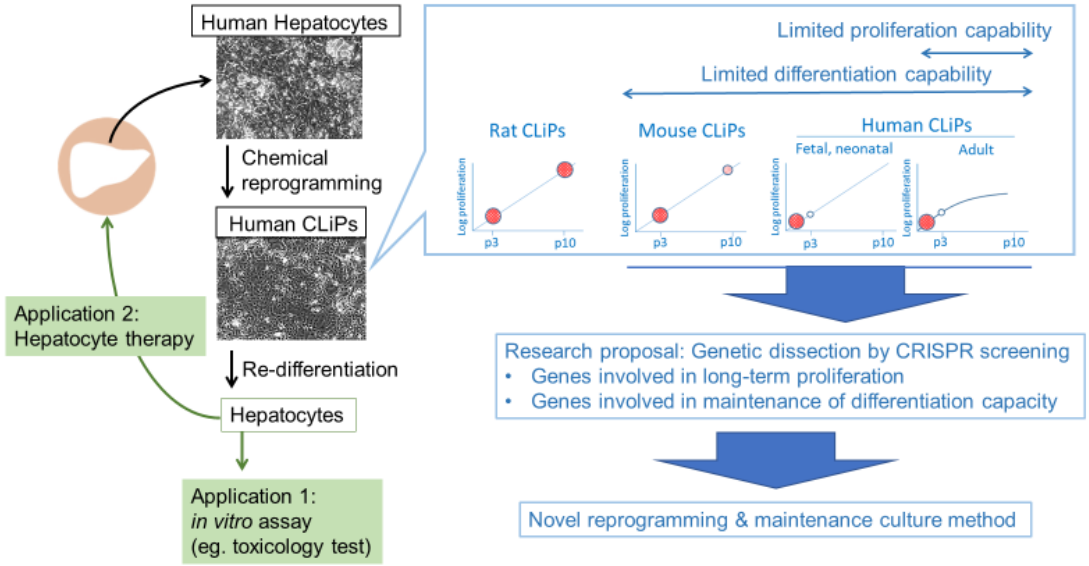
Chronic or large acute liver diseases often require liver transplantation for cure; however, the shortage of liver donor is the major issue. As an alternative to whole liver transplantation, hepatocyte transplantation therapy has been proposed but the supply of large-scale high-quality hepatocytes has yet to be solved. Our research group aims to solve this issue by using chemically reprogrammed hepatocyte progenitors, which has been recently reported using rat hepatocytes. Progenitors derived from adult human hepatocytes were successfully generated and capable of proliferating and re-differentiating into hepatocyte; however, the progenitors rapidly lost both abilities. In this project, we employ a CRISPR-based forward genetic screening approach to genetically dissect gene/pathways involved in proliferation and differentiation of hepatocyte progenitors, and establish a culture method that supports long-term proliferation of human liver progenitors with a differentiation capability. Our research not only brings hepatocyte-based therapy closer to the clinic but also provides a more reliable hepatocyte source for in vitro use.



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