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Abstract

Building Implantable Human Liver Tissue from Pluripotent Stem Cells †

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Abstract: Liver disease is an escalating global health issue. While liver transplantation is an effective mode of therapy, patient mortality has increased due to the shortage of donor organs. Therefore, developing renewable sources of human liver tissue is attractive. Pluripotent stem cell-derived liver tissue represents a potential alternative to cadaver derived hepatocytes and whole organ transplant. At present, two-dimensional differentiation procedures deliver tissue lacking certain functions and phenotypic instability. Efforts to overcome these limiting factors have led to the building of three-dimensional (3D) cellular aggregates. Although enabling for the field, their widespread application and adoption is limited due to the reliance on variable biological components. Our study focus on developing 3D liver tissue under defined conditions. We demonstrate that 3D derived tissue can be generated at scale and implanted underneath the skin of mice. Excitingly, implanted human tissue provides support to mice with metabolic liver disease. This includes immunocompetent recipients. In addition to their clinical application, in vitro generated 3D tissues have important roles to perform in developing safe and efficacious medicines to treat human diseases. We demonstrate that stem cell derived 3D liver tissue exhibits liver cell phenotype for over one year in culture, providing an attractive resource for long-term disease modelling and screening studies. In conclusion, stem cell derived liver tissue has great potential for in vitro and in vivo endeavours. Our most recent advances will be presented at the meeting.

Keywords: hESC; iPSC; liver; hepatocyte; endothelial cell; tissue engineering

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Conflicts of Interest: David Hay is a founder, director and shareholder in Stimuliver ApS and Stemnovate Limited.

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