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Human liver organoids an in-vitro drug discovery model

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Background: The liver has a remarkable ability to regenerate to repair tissue damage; in severe liver injury hepatic progenitor cells (HPCs) are activated differentiating into both hepatocytes and cholangiocytes.

Objectives: Our aims are to produce a physiologically relevant human liver organoids from HPCs and to scale-up their production to be utilized in disease modelling and drug testing.

Methods: Immunohistochemistry, q-RTPCR, FACS, WB, SEM and functional assays were used to identify, isolate and characterize HPCs and differentiated cell populations.

Results and Conclusion: EpCAM+ cells revealed the ability to expand forming liver organoids, expressing stem cell and hepatic lineage markers (CD133, CD24, Lgr5, TROP2, EpCAM, CK19 and HNF4α) with the potential to differentiate into Hepatocytes and Cholangiocytes. Hepatocyte differentiation resulted in the loss of progenitor cell marker expression while the expression of differentiated hepatocyte- specific genes increased.

Differentiated organoids showed low albumin expression compared to primary human hepatocytes; suggesting that the differentiation arisen from a limited population of cells or the organoids- derived hepatocytes were not fully mature.

FACS sorting using a combination of specific markers (EPCAM, CD133 and CD24) produced a more homogeneous cell population that differentiated effectively into hepatocytes compared to EpCAM+ cells.

Repopulation of acellular liver scaffolds with human HPCs resulted in more mature (physiologically relevant) hepatocytes with synthetic functionality.