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Summary

A NEW APPROACH TO LIVER DISEASES THROUGH REGENERATIVE STRATEGY: CLIP-DERIVED HEPATO-BILIARY SHEETS AND EVALUATION OF THEIR STRUCTURE AND FUNCTION IN A RODENT MODEL

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Hepatobiliary

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A novel hepato-biliary sheet incorporating chemically induced liver progenitor cell-derived bile ducts demonstrates improved hepatic function and sustained albumin production compared to conventional hepatocyte sheets in a mouse liver failure model.

KEY POINTS

- The hepato-biliary sheet combines mature rat hepatocytes with biliary drainage structures derived from chemically induced liver progenitor cells (CLiPs), addressing the lack of bile drainage in conventional hepatocyte sheets that may cause liver damage from bile stasis.
- In vitro, hepato-biliary sheets showed significantly higher CYP3A4 activity (139.3±59.9 vs 75.4±47.1 LUM/hr, p<0.0001) and albumin production (1.5±0.5×10^4 vs 1.1±0.1×10^4 ng/day, p=0.005) compared to conventional hepatocyte sheets.
- In a mouse liver failure model created by Retrorsine administration and 70% hepatectomy, hepato-biliary sheet transplantation resulted in higher rat albumin concentrations at 7 days (9.5×10^5 vs 5.8×10^5 ng/mL, P<0.05) and 28 days (1.1×10^6 vs 3.2×10^5 ng/mL, P<0.05) compared to conventional hepatocyte sheet transplantation.
- Transplanted hepato-biliary sheets maintained bile duct-like structures (CK7-positive), adjacent mature hepatocytes (ALB-positive), and incorporated host-derived vascular components (CD34-positive) with confirmed cell viability for at least 1 month.
- This work may inform researchers developing cell-based regenerative therapies for liver disease, particularly those addressing limitations of current hepatocyte transplantation approaches.

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