Technology Offer

Long-term expansion of human hepatocytes
Wnt-surrogate and Hippo pathway-modulated hepatocyte organoid expansion
Ref.-No.: 1305-6671-IKF

This technology presents a platform for long-term expansion of 3D organoids from adult human hepatocytes that preserve polarity, bile canaliculi and mature metabolic functions, enabling scalable DMPK/tox screening, and disease modelling.

Background
Human primary hepatocytes are the gold standard for toxicology, metabolism, and disease modeling, yet they rapidly lose polarity and function ex vivo and are difficult to expand at scale. Rodent models and hepatoma lines poorly predict human responses, while iPSC-derived hepatocytes remain immature and lack mature bile canaliculi networks. Prior organoid systems expanded biliary or fetal/embryonic cells or yielded short-lived, poorly polarized hepatocyte-like cells, limiting functional assays and throughput. A robust method enabling long-term expansion of adult primary human hepatocytes that preserves apical–basal polarity, bile canaliculi formation, and mature metabolic functions would unlock reliable toxicology, pharmacology, and cell therapy workflows.

Technology
Researchers from the Max-Planck-Institute of Molecular Cell Biology and Genetics in Dresden have developed long-term expandable human primary hepatocyte organoids from patient-tissue which maintain the expression, metabolic function and polarization of human hepatocytes in vitro. Expansion is achieved in extracellular matrix using an expansion medium comprising a Wnt activator and an inhibitor of the Hippo pathway, explicitly omitting nicotinamide to boost organoid formation and longevity. The approach sustains weeks to months proliferation, maintains polarity and bile canaliculi, and supports differentiation with adult like CYP activity and albumin secretion across multiple donors. The grown organoids retain patient-to-patient variation in culture showing expression of genes susceptible for liver infection or metabolic alterations in a patient specific manner.

Advantages
- Preserves hepatocyte polarity and bile canaliculi during expansion
- Long-term proliferation from adult human donors (serial passages, months)
- Mature hepatic functions after differentiation (CYP activity, albumin)
- Scalable ECM-embedded 3D organoid workflow, donor-agnostic conditions

Applications include high-throughput DMPK and tox screens, disease modeling, biobanking of donor-specific hepatocytes, and upstream manufacturing for cell therapy research. We are seeking partners for licensing or collaboration to adapt and further develop this technology for broader clinical, pharmaceutical, and research applications.

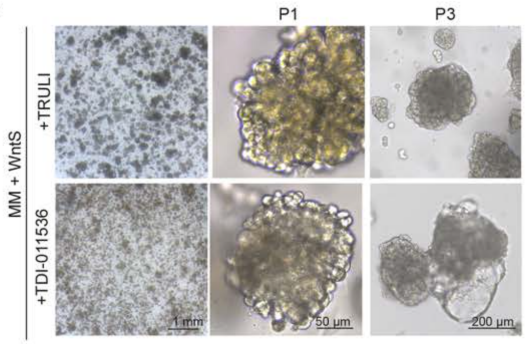

Figure 1 Long-term expansion of human adult hepatocytes as hepatocyte organoids is achieved by culturing hepatocytes in hepatoblast organoid culture medium (MM) with WNT surrogate (WntS) and LATS1/2 inhibitor (TRULI, TDI).

Publication
Yuan, Lei *et al.*; Human assembloids recapitulate periportal liver tissue in vitro (Nature, 2025); https://doi.org/10.1038/s41586-025-09884-1

Patent Information
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