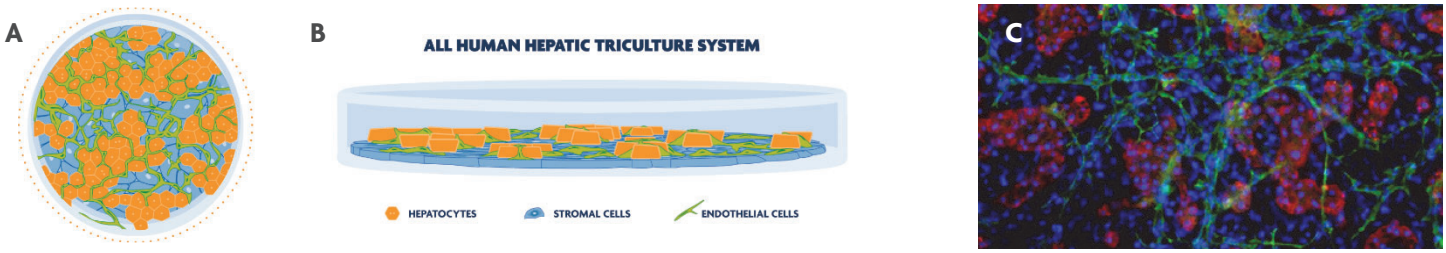
TruVIVO®

All-Human 2D+ Hepatic System

TruVivo is an all-human 2D+ hepatic system that combines primary human hepatocytes (PHHs) with primary human feeder cells (FCs) resulting in a human-relevant, reliable, and simplistic *in vitro* platform for compound testing.



A schematic representation of TruVivo showing (A) the top view of self-assembled hepatocyte colonies, (B) the side view of hepatocyte colonies integrated among the mixed feeder cell layer, and (C) a representative confocal laser microscopy image of TruVivo (blue: nuclei [DAPI], green: endothelial cells [CD31], red: hepatocytes [albumin]) revealing self-assembled hepatocyte colonies that mimic the microarchitecture of the human liver.

TruRELEVANCE

TruVivo is an **all-human 2D+ hepatic system that addresses the limitations of other traditional methods** by maintaining the morphological and functional properties of hepatocytes over several weeks. TruVivo can be established from a broad spectrum of donors, including prevalent disease states.

TruRELIABILITY

Hepatic Model	Limitation(s)	TruVivo Solution
Animal	Marked species differences versus human *in vivo*	All human cells; no species differences
Mono- and sandwich culture (MC and SC)	Short- to mid-term loss of hepatic morphology and functionality	Maintains hepatic morphology and functionality over prolonged periods up to 31 days
Isolated human hepatocytes in suspension (SHH)	Relatively short incubation time (≤ 6 h), limiting accurate evaluation of slowly metabolized compounds	Suitable to determine metabolic profiles and clearance of low-turnover compounds
Traditional Co-culture or Tri-Culture	Combine hepatocytes with one or more different types of non-human FCs	All-human FCs

TruVivo **is an easy-to-use platform that delivers equivalent or better performance** for predicting drug- and chemical-induced hepatotoxicity or metabolic clearance compared to other methods[1-10]

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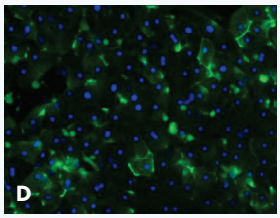
TruRELIABILITY

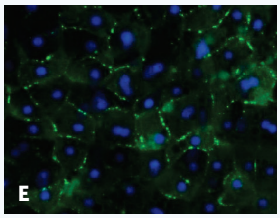
1. Maintains viability and native hepatocellular morphology over several weeks:[1-4]

a. PHHs in TruVivo formed extensive anastomosing networks of bile canaliculi with both tight and gap junctions and can maintain hepatocyte morphology for 42 days *in vitro* with no collagen or Matrigel overlay (Figures D-H).[1-3]

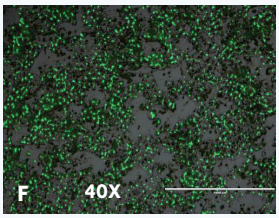
b. Cell viability is maintained over time in TruVivo, as indicated by a lactase dehydrogenase (LDH) viability assay with no media change for up to 7 days.[4]

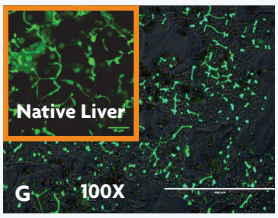


Tight Junction Marker: ZO-1

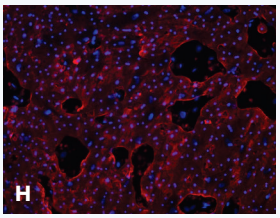


Gap Junction Marker: Cx-32





CDFDA fluorescent staining of bile canaliculi (Day 15)



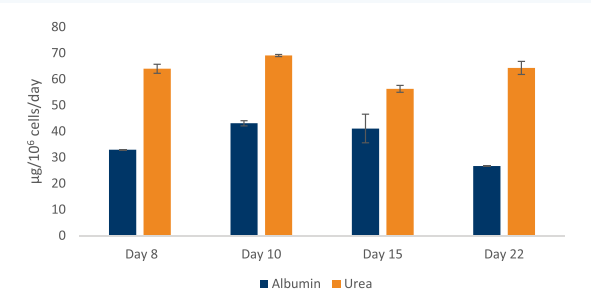
Ck-18 (red)

2. Sustains hepatocellular function and metabolic activity over time:[5]

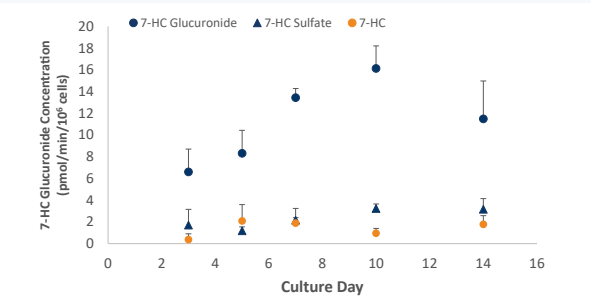
a. Significantly higher albumin synthesis and urea production compared to PHHs in the SC monoculture over a 4-week culture period (Figure I).[2,3]

b. TruVivo generated Phase I and II metabolites more extensively than SHH (Figure J).[6]

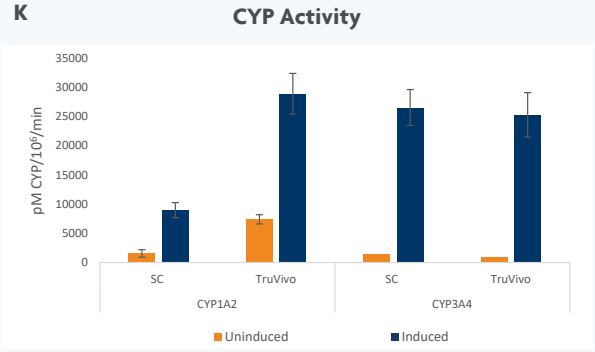
c. Hepatocytes in the 24- and 96-well formats maintained CYP and UGT activity, comparable to that of suspended hepatocytes, for as long as 31 days in culture (Figure K).[1,7]



TruVivo is able to maintain albumin and urea levels in PHHs over a 22 day culture period.[3]



Phase I and II metabolic pathways sustained in TruVivo over a 2-week period.[6]



CYP1A2 and CYP3A4 induction in TruVivo compared to SC monoculture on day 4.[1]

TruRELIABILITY

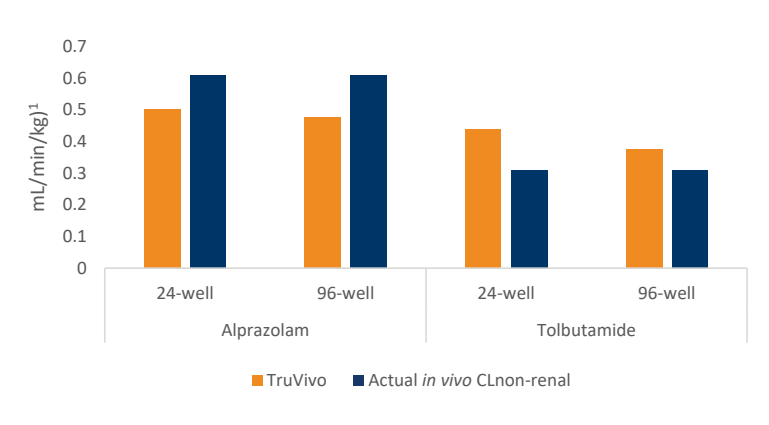
3. Suitable model for low-turnover compounds to predict *in vivo* metabolism:[4]

a. TruVivo determined metabolic profiles, clearance of low-turnover compounds, and enzyme induction from healthy and diseased tissues in both the 24- and 96-well formats.[4,6,8,9]

b. TruVivo predicted hepatic clearance (CL) of low-turnover compounds within 2-fold of actual *in vivo* non-renal CL values, in both 24- and 96-well formats (Figure L).[2,4]

c. TruVivo evaluated thyroid hormone perturbation (key and associated events) after exposure to known nuclear receptor agonists.[10]

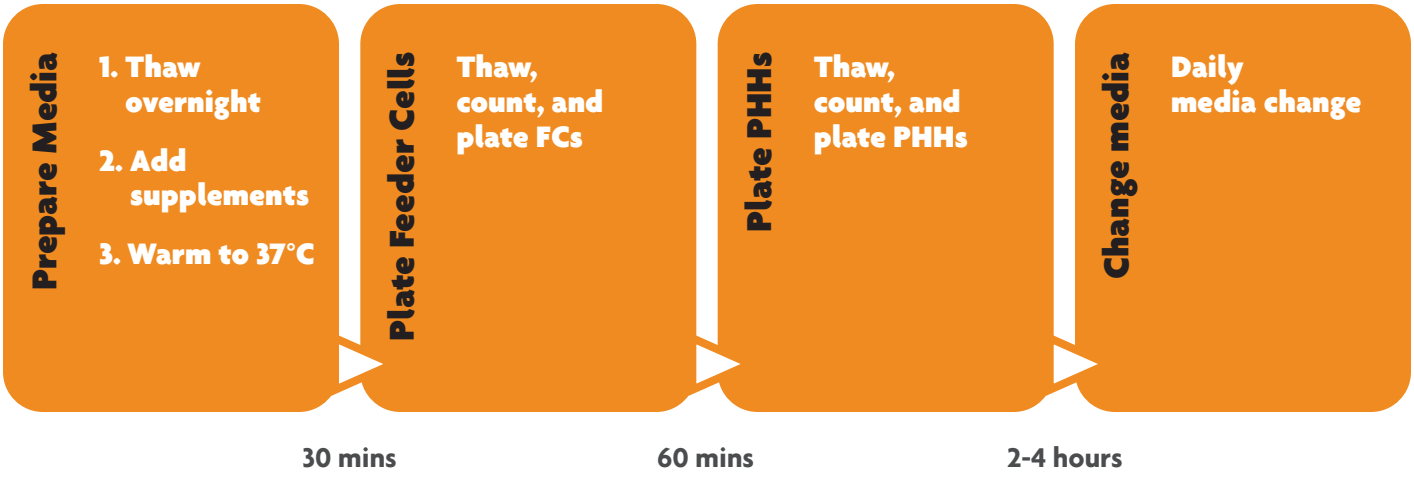
L



Comparison of predicted *in vitro* hepatic clearance values for alprazolam and tolbutamide to actual *in vivo* non-renal clearance.[4]

TruSIMPLICITY

The **2D+ system** offers the simplicity and flexibility of a 2D model with the robustness of a 3D model. It is a convenient, stable, and reproducible platform that can be set up in a matter of hours in any standard laboratory equipped for cell culture and is suitable for a wide range of applications.[8] This makes TruVivo a valuable tool for pharmacological and toxicological applications in drug development and risk assessment.



TruVIVO®

All-Human 2D+ Hepatic System

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