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Part of Europa Biosite

Produktinformation

- Forschungsprodukte & Biochemikalien
- Zellkultur & Verbrauchsmaterial
- Diagnostik & molekulare Diagnostik
- Laborgeräte & Service

Weitere Information auf den folgenden Seiten!
See the following pages for more information!

Lieferung & Zahlungsart

siehe unsere Liefer- und Versandbedingungen

Zuschläge

- Mindermengenzuschlag
- Trockeneiszuschlag
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Corning® 3D Spheroid-qualified Primary Human Hepatocytes

CORNING

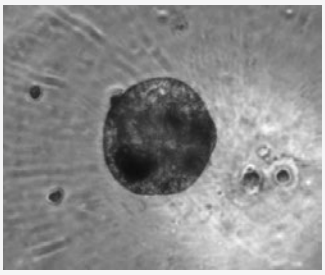
Under conventional 2D monolayer culture conditions, primary human hepatocytes (PHHs) rapidly lose their hepatic phenotypes and become unhealthy within several days. 3D liver spheroid culture has been shown to maintain the viability and functions of PHHs for several weeks (Bell, et al., 2016 and Lauschke, et al., 2016). Drug-induced liver injury (DILI) is a leading cause of drug development failures and post-marketing withdrawals. 3D PHH spheroids have been shown to significantly improve the sensitivity (2- to 3-fold) of *in vitro* hepatotoxicity assay in comparison to 2D PHH monolayer culture or spheroid cultures of hepatic cell lines such as HepaRG or stem cell-derived hepatocytes (Proctor, et al., 2017 and Bell, et al. 2017).

To support the increasing interest in applying the 3D liver spheroid model in drug discovery and development studies, Corning now offers 3D spheroid-qualified primary human hepatocytes (Cat. No. 454552) using Corning spheroid microplates (Cat. No. 4515 or 4520).

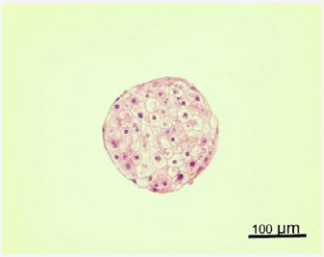
Features

- Optimized spheroid culture procedures
- PHH spheroid formation in 6 to 7 days; stable morphology, viability, and hepatic functions in long-term culture
- Increased sensitivity in 3D hepatotoxicity assays
- Capable of co-culture with other liver cell types (e.g., Kupffer cells)

Spheroid-qualified PHHs and Corning Spheroid Microplates



3D PHH Spheroid



H&E Staining of Day 8 PHH Spheroid (1,000 cells/spheroid)

Figure 1. Corning technologies to build a 3D PHH spheroid model. The bright field image and Haemotoxylin and Eosin (H&E) staining of a day 8 PHH spheroid are shown.

Size and Morphology of PHH Spheroids

We have developed an optimized protocol for establishing spheroid culture using 3D spheroid-qualified primary human hepatocytes (contact Customer Service to request the Corning® 3D Spheroid-qualified Primary Human Hepatocytes Instructions for Use Guide). PHHs form small cell clusters, larger cell aggregates, and then spheroids in 6 to 7 days (Figure 2). Once formed, PHH spheroids remain stable over 4 weeks as shown by morphology and size measurement.

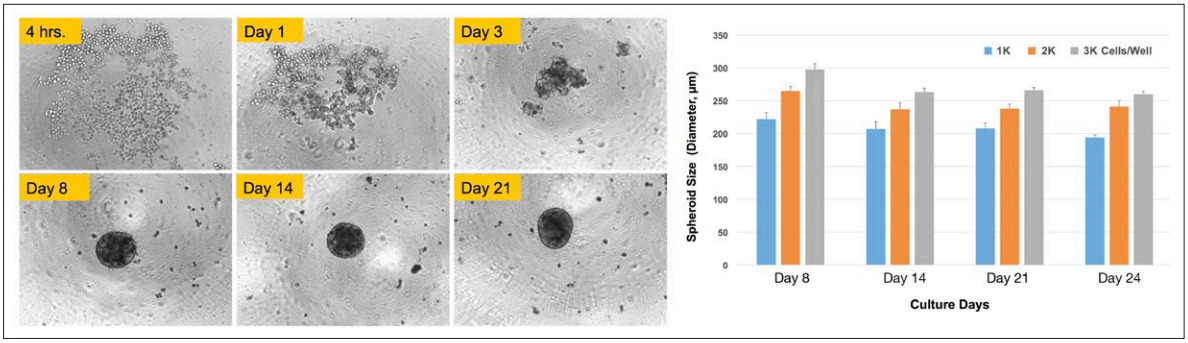


Figure 2. The size and morphology of PHH spheroids remain stable in long-term culture. Time course of spheroid culture (left, 1000 cells/well were seeded) shows the progression of cell aggregation and spheroid formation. 1,000, 2,000, and 3,000 cells/well were initially seeded, and spheroid sizes were measured over a 4-week culture (n = 12). Spheroid sizes correlate with the initial number of seeding cells (right).

ATP Levels and Albumin Secretion of PHH Spheroids in Long-term Culture

Using 3D spheroid-qualified PHHs, consistent and stable morphology of spheroids has been observed in long-term culture. Viability (ATP measurement) and albumin secretion from PHH spheroids also remain stable for at least 4 weeks in culture (Figure 3).

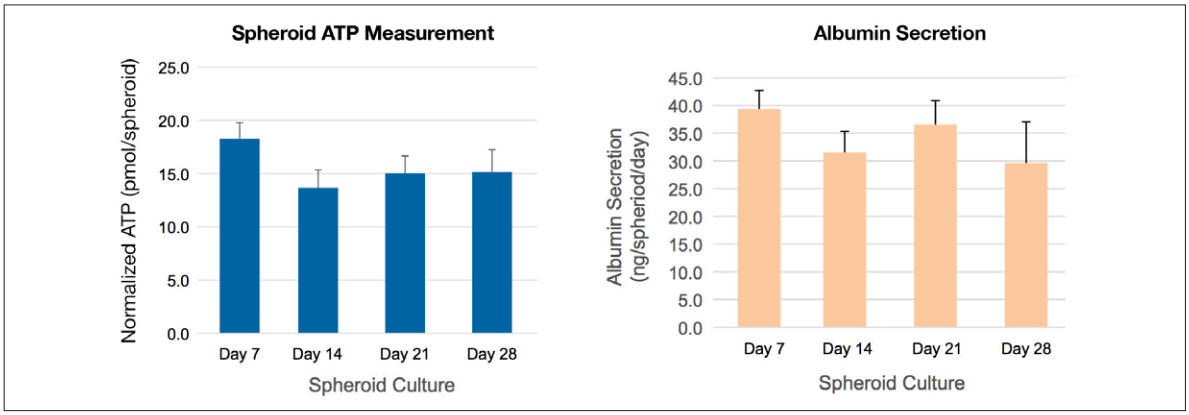


Figure 3. Viability and albumin secretion of PHH spheroids remain stable over a 4-week culture. Time course of spheroid culture (1,000 cells/well were seeded) shows the ATP levels per spheroid with bioluminescent ATP assay. Albumin secretion was measured by ELISA assays using culture supernatant samples.

Use of 3D PHH Spheroids for High Content Imaging-based Mechanistic Toxicity Assay

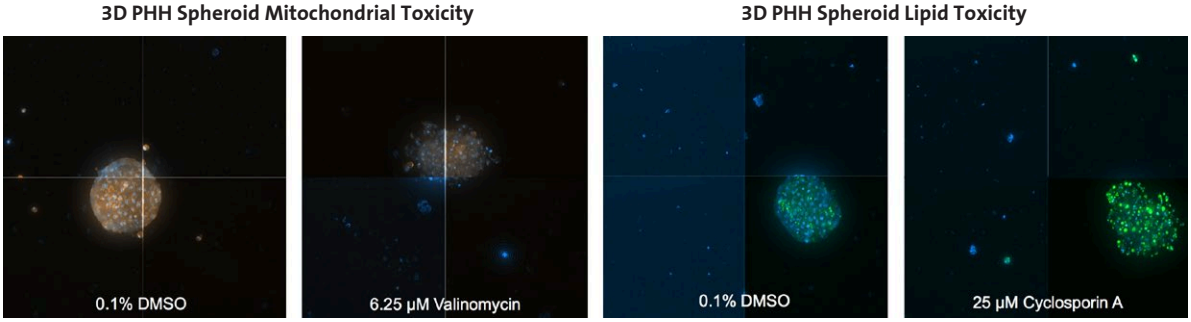


Figure 4. 3D PHH spheroids can be used for high content imaging-based mitochondrial toxicity or lipid toxicity assays. PHH spheroids exposed to 6.25 µM Valinomycin showed a diminished signal from MitoTracker® Orange stain, and PHH spheroids exposed to 25 µM Cyclosporin A showed an increased lipid accumulation as shown with HCS LipidTOX™ Green stain.

PHH Liver Spheroids Have Increased Sensitivity for Hepatotoxicity Screening

When the same lot of PHHs were tested in hepatotoxicity assays measuring ATP, an increased sensitivity (2- to 3-fold) of 3D PHH spheroids to DILI compounds was shown in comparison to 2D monolayer cultures (Figure 5). A comprehensive hepatotoxicity study with 100 DILI and control compounds with detailed 3D hepatotoxicity assay protocols can be found in the Corning application note *3D Liver Spheroids Demonstrate Increased Sensitivity to Drug-induced Liver Injury in Comparison to 2D PHH Monolayer Culture* (CLS-AN-514).

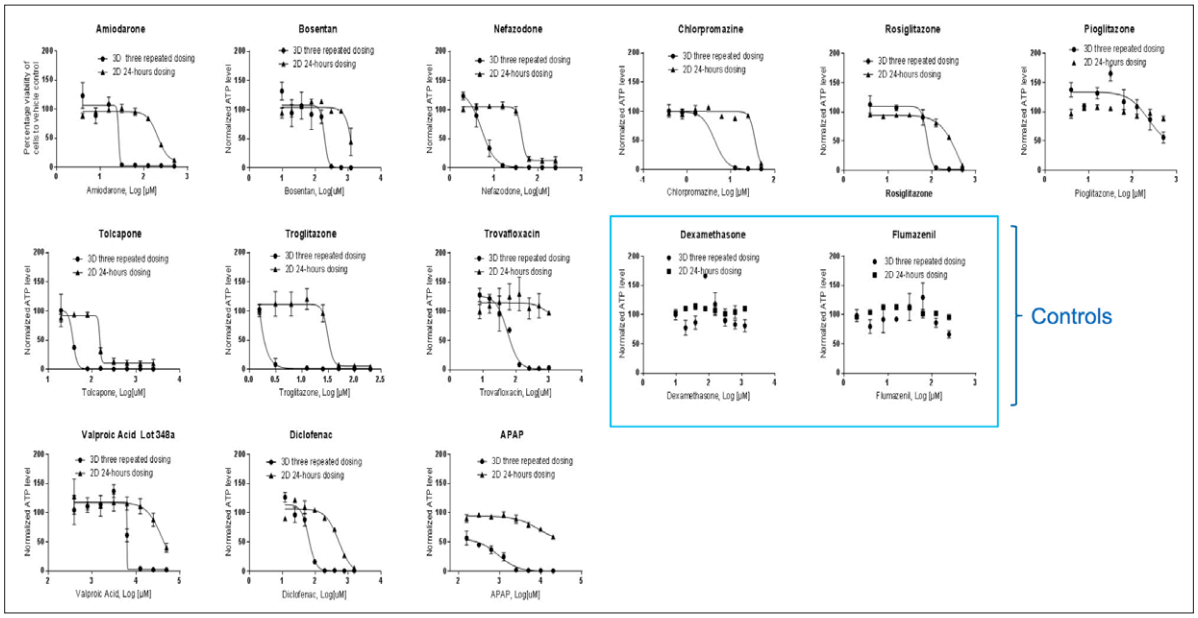


Figure 5. PHH spheroids have increased sensitivity for liver toxicity screening.

3D Spheroid-qualified PHH for Co-culture Liver Spheroids with Kupffer Cells

3D spheroid-qualified PHHs can be used to set up co-culture liver spheroids with Kupffer cells, which can recapitulate the liver inflammatory responses *in vitro*. When challenged with bacterial endotoxin lipopolysaccharides (LPS), IL6 secretion was detected in co-culture liver spheroids (Figure 6). Trovafloxacin, a model compound for immune-mediated liver toxicity was used to treat PHH spheroid and co-culture spheroids, with or without LPS co-treatment (Figure 7). Co-culture liver spheroids showed increased sensitivity compared to PHH spheroids.

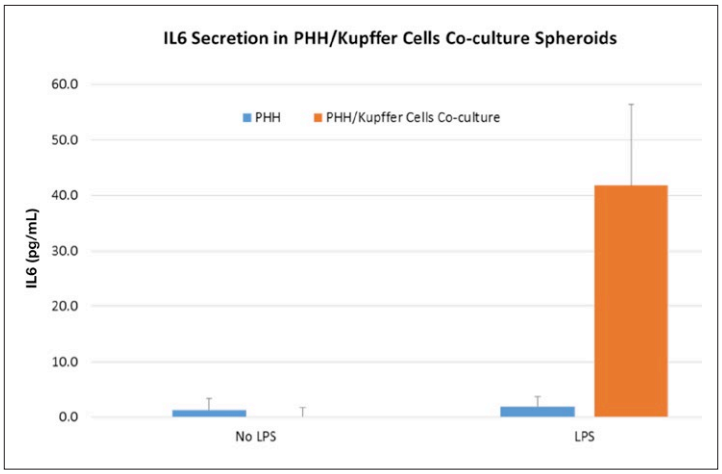
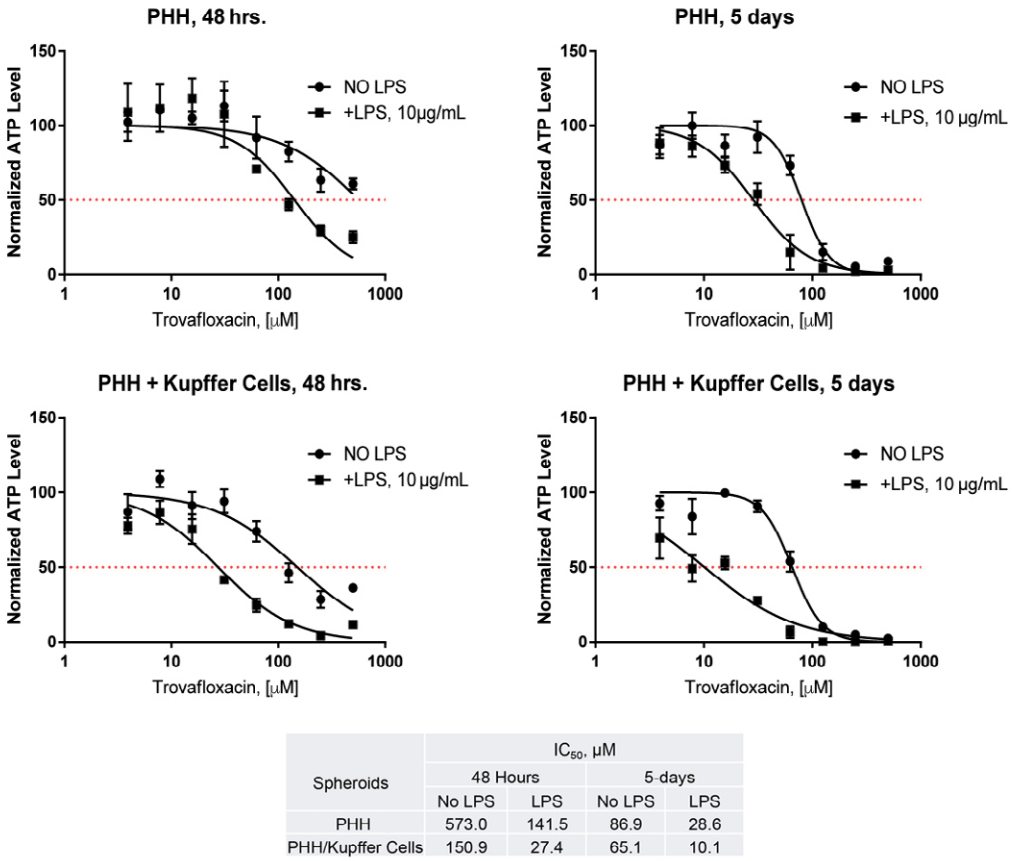


Figure 6. Day 7 PHH spheroids or co-culture spheroids were treated with LPS at 10 µg/mL for 48 hours and culture supernatants were collected for IL6 ELISA assay.



Spheroids	IC_{50}, µM			
	48 Hours		5-days	
	No LPS	LPS	No LPS	LPS
PHH	573.0	141.5	86.9	28.6
PHH/Kupffer Cells	150.9	27.4	65.1	10.1

Figure 7. Co-culture liver spheroids made from Corning 3D spheroid-qualified PHHs and Kupffer cells were shown to detect immune-mediated hepatotoxicity upon treatment with Trovafloxacin and LPS.

Ordering Information

Corning® 3D Spheroid-qualified Primary Human Hepatocytes (PHHs)

Cat. No.	Description	Qty.
454552	Spheroid-qualified	≥2 million cells/vial

Corning Spheroid Microplates

Cat. No.	Description	Sterile	Qty/Pk	Qty/Cs
4515	96-well, black/clear round bottom, with lid, Ultra-Low Attachment surface	Yes	1	5
4520	96-well, black/clear round bottom, with lid, Ultra-Low Attachment surface	Yes	10	50

For more specific information on claims, visit the Certificates page at **www.corning.com/lifesciences**.

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