PRODUCT BULLETIN
ADME/Tox

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by life technologies™

Hepatic Co-cultures

Powerful new *in vitro* tools for modeling the liver

- Cryopreserved Kupffer cells available for your convenience
- Model normal and inflamed liver states—make your own custom ratios
- Evaluate cytokine-mediated toxicity

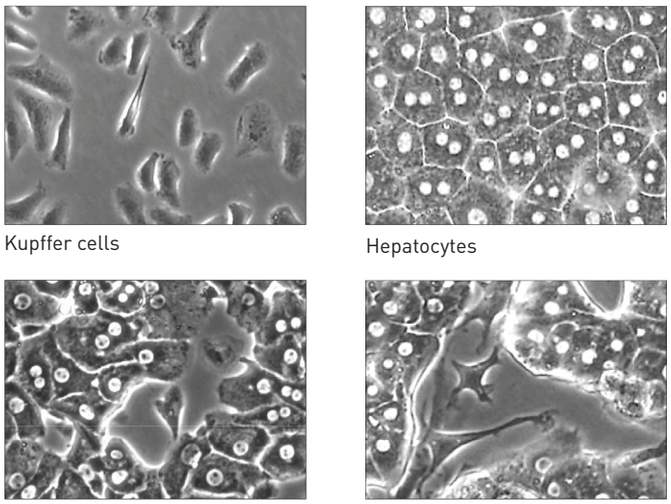

Figure 1. Model normal and inflamed liver states. These models enable researchers to study the interactions between hepatocytes and Kupffer cells during liver inflammation.

Our hepatic co-cultures are powerful new *in vitro* tools for modeling the liver. (Figure 1) Hepatocyte monocultures have served as the standard *in vitro* model for ADME/Tox-related research, including metabolism and drug–drug interactions. However, research is demonstrating that monocultures of hepatocytes alone are not predictive of certain physiological conditions.

Growing evidence shows that under both normal and pathological conditions, many hepatocyte functions are regulated by substances released from neighboring nonparenchymal cells (NPC). These cells, particularly Kupffer cells, play an important role in the modulation of xenobiotic metabolism in the liver. Studies indicate that co-culture of hepatocytes with NPCs would better represent both normal liver physiology and disease states.

- Kupffer cells play an active role in the remodeling and maintenance of liver extracellular matrix
- Kupffer cells secrete potent mediators of the inflammatory response that controls liver inflammation
- Kupffer cell cytokine mediators control hepatocyte metabolic rates through direct interactions with phase I and phase II enzymes

Evaluate cytokine-mediated P450 inhibition

Kupffer cell and hepatocyte co-cultures can self-assemble within 72 hr of treatment with pro-inflammatory cytokines or lipopolysaccharide (LPS), and the Kupffer cells, in the presence of hepatocytes, can effectively modulate P450 expression in neighboring hepatocytes. IL-6 is significantly up-regulated in co-cultures at 72 hr, as compared to in Kupffer cells alone. This suggests that Kupffer cells and hepatocytes self-assemble and the co-culture functions in a more physiologically relevant way (Figures 2 and 3). This is further demonstrated in rat co-cultures, in which evidence of CYP3A and CYP1A2 activity modulation is seen (Figure 4).

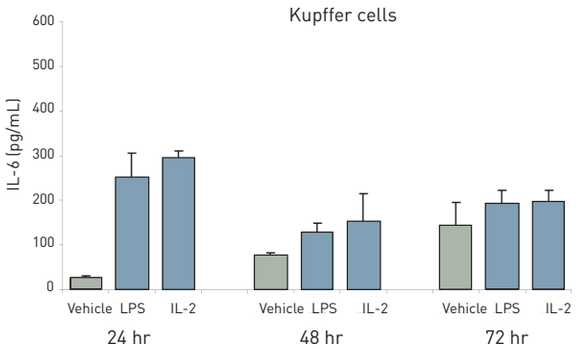

Figure 2. IL-6 production in Kupffer cells after LPS and IL-2 stimulation for 24, 48, and 72 hr. As expected, following activation with LPS, IL-6 production is significantly up-regulated at 24 hr and then it progressively decreases, suggesting desensitization of Kupffer cells to chronic stimulation with LPS.

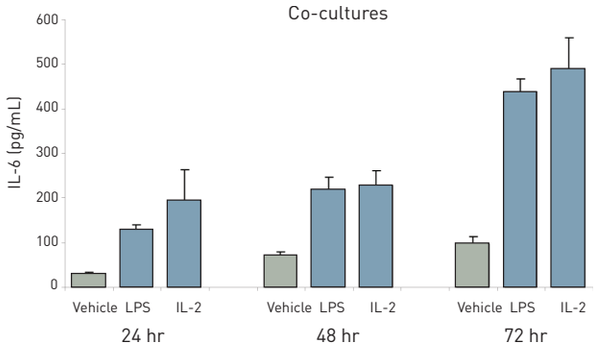

Figure 3. IL-6 production in Kupffer cells and hepatocyte co-cultures after LPS and IL-2 stimulation for 24, 48, and 72 hr. Note that IL-6 is significantly up-regulated in co-cultures at all time points. This suggests cellular self-assembly between Kupffer cells and hepatocytes that synergistically allows the cells to function together during resolution of inflammation.

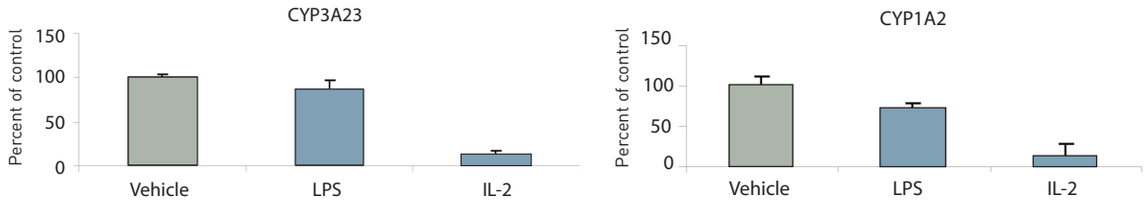

Figure 4. Modulation of CYP3A23 and CYP1A2 enzyme activities in co-cultures after LPS and IL-2 stimulation for 72 hr. Note the nearly 80% decrease in CYP3A23 and CYP1A2 levels after IL-2 treatment.

Ordering information

Product	Size	Cat. No.
Rat Cryopreserved Kupffer Cells	1 million viable cells	RTKCCS
Cryopreserved Rat Hepatocytes, Plateable	4—8 million cells	RTCP10

Printed in the USA. **CO23120 0611**

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