A special issue about hepatotoxicity and hepatocyte in vitro systems

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In recent years, great advances in the development of hepatocyte in vitro systems have led to an improved understanding of the mechanisms of hepatotoxicity (Hewitt et al. 2007; Zellmer et al. 2010; Schug et al. 2013; Heise et al. 2012; Mielke et al. 2011). In this issue of the Archives of Toxicology, readers can enjoy one of the most comprehensive reviews ever published on the topic (Godoy et al. 2013). The more than 100-page compilation summarizes the current knowledge on liver function with particular emphasis on hepatotoxicity and addresses the development of adequate in vitro systems to study mechanisms of hepatotoxicity, metabolism, signaling, drug interactions, and clearance. The invited review, which is written by a consortium of outstanding experts in the field of liver physiology and toxicology, covers the following topics:

- Structure and cellular components of the liver, including non-parenchymal cells and zonal heterogeneity
- Regulatory genes and signaling pathways, including nuclear receptors
- Bile acid metabolism and transport
- Liver in vitro systems, including the isolated perfused liver, liver slices, isolated human hepatocytes, and co-cultures with non-parenchymal cells
- 3D liver models
- Recent developments in cryopreservation
- Mechanisms of hepatocyte dedifferentiation and novel anti-dedifferentiation strategies

- Alternative models to primary human hepatocytes, including cell lines and stem cell-derived hepatocytes
- Hepatocyte in vitro systems to study apoptosis and DILI
- Hepatocytes in toxicogenomics
- Mathematical modeling and systems biology in hepatocyte research

The article is supplemented by an electronic appendix with standard operating procedures of the most frequently applied in vitro systems. The individual sections contain a list of key questions and take home messages, which the reader can select accordingly.

In addition to the comprehensive review by Godoy et al., seven other contributions are presented in this special issue of the Archives of Toxicology:

- Based on in vitro metabolizing systems, the mechanisms of the human hepatotoxic drug fenclozic acid were studied (Rodrigues et al. 2013)
- Three- and two-dimensional culture systems were compared with acetaminophen-induced hepatotoxicity (Schyschka et al. 2013)
- The study of CYP induction in isolated mouse hepatocytes by vanadium (Abdelhamid et al. 2013)
- The key role of CTNNB1 in acetaminophen toxicity in mouse liver hepatoma cells (Singh et al. 2013)
- The study of combined effects of carcinogens in mouse liver (Kuroda et al. 2013)
- The study of toxicokinetics of acrylamide in primary rat hepatocytes (Watzek et al. 2013)
- The study of glucose homeostasis in rat liver (Zhang et al. 2013)

We hope that this special issue will provide readers with a clearer understanding of the complex field of hepatotoxicity.

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