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Guest editorial:

THE REDISCOVERY OF HepG2 CELLS FOR PREDICTION OF DRUG INDUCED LIVER INJURY (DILI)

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In the past HepG2 cells have been considered to show only little similarity to primary human hepatocytes (Godoy et al., 2013; Hewitt et al., 2007). However, recently it has become clear that the phenotype of HepG2 cells strongly depends on culture conditions. In a recent study, Ramaiahgari et al. (2014) cultivated HepG2 cells in spheroids. In this culture system the cells stopped proliferation and strongly upregulated phase I and phase II drug metabolizing enzymes and transporters (Ramaiahgari et al., 2014). Moreover, albumin and urea metabolizing enzymes were upregulated. This study shows that the potential of HepG2 cells may have been underestimated in the past. A critical aspect seems to be that they have to be kept in three dimensional culture systems.

Much effort has been invested in the establishment of hepatocyte culture systems that help to identify hepatotoxic compounds (Ilkavets, 2013; Abdelhamid et al., 2013; Vinken et al., 2013; Hasmall et al., 2001; Waterfield et al., 1998; Mennes et al., 1994; Krijt et al., 1993; Godoy et al., 2009; Adler et al., 2014; Maruf and O'Brien, 2014). In recent years HepG2 cells have become more and more popular for this purpose (Mostafavi-Pour et al., 2013; Shan et al., 2013; Krithika et al. 2013; Doricakova et al., 2013; Straser et al. 2011; Dias da Silva et al., 2013; Horinouchi et al., 2014; Wang et al., 2014). One reason for their frequent application may be that they are freely available in contrast to some other cell lines obtained from human liver tumors that are only commercially available. Another successful application of HepG2 cells is expression of human genes (Lahoz et al., 2013). The group of Castell and Gomez-Lechon have specialized in this field (Tolosa et al., 2012; Donato et al., 2010; 2008). Recently, five P450 enzymes have been expressed simultaneously in HepG2 cells resulting in a powerful test system for compounds that require metabolic activation (Tolosa et al., 2013). It is clear that primary human hepatocytes currently still represent the gold standard for hepatotoxicity testing (Hengstler et al., 2000; 2009; Hewitt et al., 2007). Future studies will have to show to which degree HepG2 based culture system can be used to predict hepatotoxic compounds in vitro.

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