Highlight report: xenobiotic-metabolizing enzymes in skin models

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Recently, Franz Oesch and colleagues have published a comprehensive review about the xenobiotic-metabolizing activity in skin of rat, mouse, pig, guinea pig, man, and human skin models (Oesch et al. 2014). Since the skin is constantly exposed to different xenobiotics, its xenobiotic-metabolizing activity is of high relevance. The use of human skin is limited for ethical and practical reasons. Therefore, non-human skin and in vitro skin models are frequently applied (Oesch et al. 2014). The authors give a comprehensive overview over possibilities and limitations of the most frequently applied in vitro systems used in skin toxicology. Some critical key messages are as follows:

- For xenobiotic metabolism relevant for dermal absorption, the pig skin most closely resembles the human skin compared to the other analyzed species. Similarly, for studies of skin irritation, the pig skin represents an adequate model for humans.
- Moreover, some reconstructed human skin models are reasonably close to primary human skin.
- However, currently available skin models have a too low barrier function to correctly estimate dermal absorption.
- With respect to genotoxicity and sensitization, activating metabolism has not yet been sufficiently studied to come to final conclusions.

In vitro systems of skin metabolism and absorption represent a cutting-edge topic in toxicology (Manwaring et al.

2015; Jacquilleot et al. 2015; Crane et al. 2015; Gegotek and Skrzydlewska 2015; Manevski et al. 2015; Wiegand et al. 2014). As for other in vitro systems, e.g., for liver (Reif et al. 2015; Godoy et al. 2013, 2015; Watzek et al. 2013; Schug et al. 2013; Fang et al. 2014; Grinberg et al. 2014), kidney (Sanchez-Niño et al. 2014; Fujiki et al. 2014, 2013), and neuronal system (Balmer et al. 2014; Zimmer et al. 2014; Krug et al. 2013; Waldmann et al. 2014), it is important to know the metabolizing capacity in relation to the in vivo situation. A model that represents the human situation in all aspects will possibly never be accomplished (Ghallab 2013, 2014a, b; Stewart 2010). One limitation is that it is extremely difficult to sufficiently maintain all critical biochemical factors of the in vivo microenvironment, when cells are isolated from an organism and transferred to artificial culture conditions (Godoy et al. 2009, 2010a, b; Godoy 2011). Therefore, Oesch et al. (2014) have chosen a reasonable strategy in this complex situation: Carefully scrutinize the properties of the available in vitro systems to allow an informed decision about endpoints which can be reliably studied because of sufficient similarity to the human in vivo situation.

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