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EDITORIAL

Highlight report: epoxide hydrolases—protection from reactive compounds and risk of cardiovascular disease

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Recently, El-Sherbeni and El-Kadi (2014) from the University of Alberta, Edmonton, Canada, have published a comprehensive review article on epoxide hydrolases in the Archives of Toxicology. It is well known that microsomal epoxide hydrolases are protective against carcinogenic epoxides (Decker et al. 2009; Arand et al. 2003; Oesch et al. 2001; Hengstler et al. 1998). On the other hand, soluble epoxide hydrolase mediates transformation of endogenous fatty acid epoxides to dihydrodiols (El-Sherbeni and El-Kadi 2014). This may disturb cellular homeostasis, since some fatty acid epoxides have cytoprotective effects, while the corresponding dihydrodiols become cytotoxic. Together, this created an overall picture where inhibition of microsomal epoxide hydrolases is detrimental, while inhibition of soluble epoxide hydrolases may be beneficial under certain circumstances.

In their critical review, El-Sherbeni and El-Kadi illustrate that this is a too simplified view, particularly because of an overlap of substrate selectivity and consequently physiological functions of cytosolic and microsomal epoxide hydrolases. The strength of the present review is its comprehensive overview over substrates, inhibitors, inducers and physiological functions of both enzymes.

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Drug metabolism represents a cutting edge topic in toxicology with a particular focus on toxification versus detoxification of xenobiotics (Oesch et al. 2014; Rodriguez-Mateos et al. 2014; Dohnal et al. 2014), contribution of drug metabolism to oxidative stress (Xiao et al. 2014; Møller et al. 2014; Wu et al. 2014), and regulation of metabolic activity (Juricek et al. 2014; Bitter et al. 2014; Lim et al. 2014; Braeuning 2014). Moreover, recent research focuses on integrating metabolic pathways into mathematical models in order to predict the metabolic capacity of tissues and organs under physiological and disease conditions (Drasdo et al. 2014a, b; Schliess et al. 2014; Hoehme et al. 2010).

Finally, compromised xenobiotic metabolism represents one of the major problems in alternative methods and in vitro systems (Godoy et al. 2009, 2013, 2015; Pfeiffer et al. 2015; Heise et al. 2012; Ghallab 2013, 2014a, b; Stewart 2010). The present review of El-Sherbeni and El-Kadi represents a must-read for anyone interested in these fields of research.

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