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EDITORIAL

Highlight report: biomarkers of acetaminophen-induced liver injury

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A comprehensive review about translational biomarkers of acetaminophen-induced acute liver damage has been published in our journal (Beger et al. 2015). Currently, diagnosis of APAP overdose is still based on the analysis of acetaminophen (APAP) levels in blood (Rumack et al. 1981) and on the elevation of the liver enzyme alanine aminotransferase (Zyoud et al. 2012). Analysis of APAP and alanine aminotransferase (ALT) in blood serves as a basis of decision making by clinicians, for example, whether the antidote *N*-acetylcysteine should be administered (Beger et al. 2015). However, a limitation of the use of APAP and ALT in clinical routine is that interpretation of these makers depends on the knowledge of the exact time of intoxication, because both APAP and ALT in blood are strongly time dependent (Beger et al. 2015). Therefore, the identification of novel biomarkers of APAP intoxication, which can be interpreted independently from the time point of overdose, or even in a setting of long-term exposure to APAP, still represents a cutting-edge topic. In their review Beger et al. (2015) discuss the discovery and validation process of new biomarkers with the following key messages:

- Acylcarnitines represent a promising development, because they occur earlier in human blood after APAP intoxication than the conventional diagnostic marker ALT and is back to near normal when ALT reaches it maximum. Therefore, acylcarnitines inform about the early phase of an acute intoxication. Acylcarnitines represent fatty acid metabolites that are transported into the mitochondria for beta-oxidation (Beger et al. 2015). Since oxidative stress of mitochondria represents an early step in APAP-induced hepatotoxicity (Godoy et al. 2013), the increase in blood acylcarnitines represents a mechanistically well-understood biomarker.
- MiR-122 is one of the dominating miRNAs of the liver (Beger et al. 2015). It represents approximately 75 % of total liver miRNAs. Several studies have shown a transient increase after APAP intoxication in animal models; however, clinical research is required to learn whether miRNAs give additional information over the conventional biomarker ALT.
- Bile acids as biomarkers of APAP-induced liver damage represent a further promising field of research. Particularly, total bile acids, glycochenodeoxycholic acid and taurochenodeoxycholic acid represent intensively studied candidate biomarkers.

Research on the molecular mechanisms of acetaminophen toxicity still represents a cutting-edge topic in our journal (Lancaster et al. 2015; Hwang et al. 2014; Sjogren et al. 2014; McGill et al. 2014; Schyschka et al. 2013; Singh et al. 2013). Moreover, large efforts are undertaken to establish in vitro systems for hepatotoxicity testing (Ramaiahgari et al. 2014; Grinberg et al. 2014; Tolosa et al. 2013; Hewitt et al. 2007; Godoy et al. 2015; Schug et al. 2013) and elucidating mechanisms of hepatotoxicity (Rodrigues et al. 2013; Ghallab 2014a, b; Reif 2014a, b; Godoy 2011). Besides its clinical relevance, the translational biomarkers discussed in the review of Beger et al. (2015) are also of high interest for scientists optimizing in vitro systems for hepatotoxicity testing.

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