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EDITORIAL

Highlight report: toxicology of copper

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Recently, Gaetke and colleagues from Kentucky University published a review about the toxicological relevance and mechanisms of copper (Gaetke et al. 2014). Copper is an essential trace element that is associated with the prosthetic groups of numerous enzymes and participates in key redox reactions (MacPherson and Murphy 2007; Bento et al. 2006; Klinman et al. 1991). Well-known examples are cytochrome C oxidase, which catalyzes an essential step in cellular respiration, superoxide dismutase that detoxifies the free radical superoxide, and dopamine-beta-hydroxylase, which is involved in catecholamine biosynthesis (Gaetke et al. 2014). In addition, ceruloplasmin (ferroxidase I), the main copper-carrying protein in the blood, transports copper to the sites of erythropoiesis and is involved in iron metabolism (Gaetke et al. 2014). Furthermore, copper plays a key role in the formation of myelin that covers neurons (Herring and Konradi 2011). The review of Gaetke and colleagues summarizes the main sources of human exposure to copper, discusses the control factors of copper status and homeostasis and finally focuses on the mechanisms of copper toxicity (Gaetke et al. 2014). Although copper can be found in almost all tissues, the highest concentrations occur in brain and liver (Turnlund et al. 1998). Therefore, it is not surprising that neurodegenerative diseases and disturbed liver functions, including fibrosis, are consequences of compromised copper homeostasis (Pal 2014; Stys et al. 2012; Zheng and Monnot 2012; Tiffany-Castiglioni et al. 2011; Fanni et al. 2014; Rivera-Mancía et al. 2010; Aigner et al. 2015) via different possible mechanisms. For instance, excess of copper in the liver has been shown to alter lipid metabolism and also to activate sphingomyelinase, leading to release of the pro-apoptotic signal ceramide (Engle 2011; Gaetke et al. 2014). However, it remains to be studied, whether these changes represent primary events caused by copper or whether they are consequences of copper-induced oxidative stress (Gaetke et al. 2014). Currently neurotoxicity (Balmer et al. 2014; Zimmer et al. 2014; Krug et al. 2013; Leist et al. 2013; Krause et al. 2013), hepatotoxicity (Campos et al. 2014; Liu et al. 2014; Godoy et al. 2009, 2013, 2015; Schyschka et al. 2013; Schliess et al. 2014; Grinberg et al. 2014; Ghallab 2013, 2014a, b) and control mechanisms of oxidative stress (Møller et al. 2014; Lim et al. 2014; Finazzi and Arosio 2014; Wu et al. 2014; Toledo et al. 2014; Li Volti et al. 2006) represent cutting-edge topics in toxicology. The present review of Gaetke and colleagues is particularly interesting for everyone involved in these fields of research.

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