EDITORIAL

Current research trends on arsenic toxicology

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Arsenic, a compound with a long history as a toxicant (Bolt 2012, 2013), continues to be a major public health issue in a number of countries worldwide (Golka et al. 2010; Martinez et al. 2011). As far as exposure is concerned, the most important matter of current publications is drinking water pollution (Maity et al. 2012; Deb et al. 2012; Guha Mazumder et al. 2012; Marchiset-Ferlay et al. 2012; Chen et al. 2012; Kumasaka et al. 2013). Another contemporary issue coming into focus is environmental contamination from (former) mining activities (Coelho et al. 2012; Li et al. 2012; Chakraborti et al. 2012) and from waste deposits (Moreno-Santini et al. 2012).

Mechanistically, adverse health effects result from processes such as induction of oxidative stress, alterations of DNA methylation, histone modification, mRNA expression, and others (Martinez et al. 2011). There is an intensive further development at present, which is reflected in current publication activities, also affecting this journal.

Therefore, the present issue of Archives of Toxicology again presents some outstanding examples for different aspects of arsenic-induced toxicity mechanisms.

One focal point of research is metabolism of arsenic compounds (Bolt and Stewart 2010). A review by Watanabe and Hirano (2013) addresses the requirements for As^{3+} methylation and the role of glutathione in this process. The As^{3+} species is highly reactive with thiols in general (Chang et al. 2012). This reaction is competitive to the oxidation of As^{3+}–As^{5+}, the latter being less toxic than As^{3+}. The As–glutathione conjugate stability is seen as an important factor in the overall toxicity of arsenicals.

As stressed in a previous Editorial (Bolt 2012), combination effects between As and other toxicants are an upcoming research issue, mainly driven by practical environmental situations. Thus, in Bangladesh well water, combinations of As and Fe are found, and Fe may act synergistically on distinct signalling pathways, as now shown by Kumasaka et al. (2013). The authors demonstrate that this situation is improved by remediation of the water using a low-cost and high-performance absorbent.

From the standpoint of mechanistic toxicology, a most important research focus related to arsenic is on carcinogenic pathways. Oxidative stress and apoptotic mechanisms appear to play a major role (Bolt and Hengstler 2011). Just recently this year, Sinha et al. (2013) presented a review collecting evidence that the cellular redox state and associated complications are closely associated with Nrf2 and its different molecular responses. In relation to As-mediated urothelial cancer, Liu et al. (2013) discuss the downstream effects on signalling pathways of oxidative stress. Specifically related to skin cancer, Jiang et al. (2013) point to the epithelial–mesenchymal transition (EMT) acquisition of cancer stem cell (CSC)-like properties as essential steps in the initiation of human skin cancers. They present arguments that EMT, with acquisition of a CSC-like phenotype mediated by IKKβ/IκBα/RelA signal pathway via Snail, contributes to As-induced skin carcinogenicity. In addition, Pastoret et al. (2013) discuss a role of As-induced downregulation of HNF1α and HNF4α in cancer development.

Apart from being a highly relevant environmental pollutant, As has a long history of medical use. Today, arsenic trioxide is a most effective drug for treatment of acute promyelocytic leukaemia (APL). Also, this aspect is covered in the present issue of Archives of Toxicology. Xu et al. (2013) point to the mechanism underlying HL-60 cell resistance to As^{3+} and point to the implication of the

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multidrug resistance protein MRP1. Yu et al. (2013) investigate the effect of the antioxidant resveratrol on As^{3+}-induced nephrotoxicity and suggest that resveratrol may be used in post-remission therapy of APL after treatment with As^{3+}, in order to prevent nephrotoxicity.

In total, the current issue of Archives of Toxicology again presents a number of highly topical and timely aspects of arsenic, which is a scientifically and practically important research field in toxicology.

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