Letter to the Editor Regarding the Article by Dheeman et al., 2014

ARTICLE *in* CHEMICAL RESEARCH IN TOXICOLOGY · NOVEMBER 2014

Impact Factor: 3.53 · DOI: 10.1021/tx5004358 · Source: PubMed

1 AUTHOR:

Hua Naranmandura
Zhejiang University
48 PUBLICATIONS **800** CITATIONS

Chemical Research in Toxicology

Letters to the Editor

pubs.acs.org/crt

Letter to the Editor Regarding the Article by Dheeman et al., 2014

To the Editor: I would like to focus your attention on some major concerns that I have found while reading the article *Pathway of Human AS3MT Arsenic Methylation* by Dheeman et al. (10.1021/tx500313k).

The current article has suggested the production of trivalent methylated arsenicals as a result of oxidation and reduction of arsenic in protein bound form. Here, the authors have also highlighted the two previously proposed mechanisms of arsenic metabolism suggested by Challenger in 1945[1] and Hirano's group in 2005.[2] However, the authors overlooked a third metabolic pathway proposed by Suzuki's group in 2006,[3] which suggested a similar metabolic pathway for arsenic as that presented in the current article. Originally, the pathway given by Challenger[1] proposed the oxidative methylation of arsenic in which pentavalent arsenic species were suggested to be intermediates rather than end products of arsenic biotransformation. On the other hand, Hirano's group suggested that arsenic involves arsenic−glutathione complexes (but not in protein-binding forms), with glutathione being a compulsory constituent of arsenic methylation through arsenic methyltransferase. The arsenic−glutathione complexes were considered to be undergoing methylation without being oxidized.[2]

However, most recently, Suzuki's group (2006)[3] proposed the latest pathway for arsenic metabolism in which they indicated that arsenic can bind to soluble and insoluble proteins and found that arsenic can bind to cysteinyl residues on proteins to produce mono- and dimethylated methylation arsenicals through methylation. This work clearly explicated that inorganic arsenic is metabolized in the body bound to proteins in a trivalent form during successive reductive methylation by AS3MT in the presence of glutathione and that pentavalent arsenic metabolites are the end products of arsenic metabolism.[3] Moreover, the three arsenic metabolism pathways have also been recently discussed in detail in work by our group as well as by Dr. Cullen.[3−5]

Although the findings of the current article reflect the views of the findings by Suzuki's group, the authors did not confer as they should have regarding their work. Instead, they provide a new pathway of arsenic metabolism, which, in fact, was already suggested in 2006 by Suzuki.[3]

Hua Naranmandura

Department of Toxicology, School of Medicine and Public Health, Zhejiang University, Hangzhou 310058, China

REFERENCES

(1) Challenger, F. (1945) Biological methylation. *Chem. Rev. 36*, 315−361.

(2) Hayakawa, T., Kobayashi, Y., Cui, X., and Hirano, S. (2005) A new metabolic pathway of arsenite: arsenic−glutathione complexes are substrates for human arsenic methyltransferase Cyt19. *Arch. Toxicol. 79*, 183−191.

(3) Naranmandura, H., Suzuki, N., and Suzuki, K. T. (2006) Trivalent arsenicals are bound to proteins during reductive methylation. *Chem. Res. Toxicol. 19*, 1010−1018.

(4) Cullen, W. R. (2014) Chemical mechanism of arsenic biomethylation. *Chem. Res. Toxicol. 27*, 457−461.

(5) Rehman, K., and Naranmandura, H. (2012) Arsenic metabolism and thioarsenicals. *Metallomics 4*, 881−892.

Published: November 10, 2014

dx.doi.org/10.1021/tx5004358 | *Chem. Res. Toxicol.* 2014, 27, 2011−2011