Abstract Template

Title: Effects of genetic diversity on carcinogen metabolism.

Name(s) of Authors and Co-authors: Gunnar Boysen[1,2] Jessica H. Hartman,[3] Grover P. Miller,[3] Lance M. Hallberg,[4,5] Bill T. Ameredes,[5]

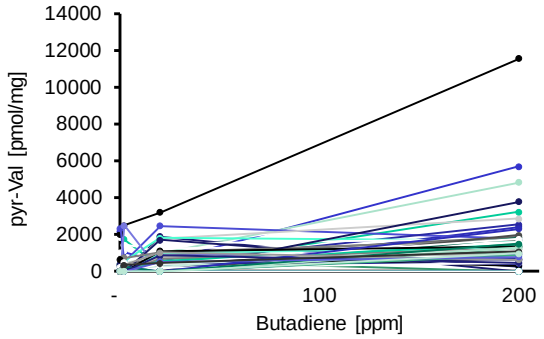
Affiliations:
[1]Environmental and Occupational Health, [2]The Winthrop P. Rockefeller Cancer Institute, [3]Biochemistry and Molecular Biology, University of Arkansas for Medical Sciences, and [4]Department of Preventive Medicine and Community Health, [5]Pharmacology and Toxicology, University of Texas Medical Branch

Keywords: Genetic diversity, carcinogen metabolism, 1,3-Butadine

I. Abstract Body (up to 250 words)

Individual cancer susceptibility varies between regional, racial, and cultural groups, and it is commonly assumed that, in addition to chemical exposure and genetic background, lifestyle, e.g. diet selection, significantly modifies individual susceptibility. To simulate a polymorphic human population we combined the 'collaborative cross[1] of mice, genetically designed to represent a complete intermixed mouse population covering all possible genotypes with the 1,3-butadiene (BD) carcinogenesis model[2–4] to determine the variability in cancer susceptibility derived from genetic diversity. BD metabolism was assess using BD-derived protein adducts as biomarkers. The variability in formation of N-terminal valine adducts was highest at the lower exposures. For individual exposure groups, CYP2e1 activities initially decreased and then increased with exposures. Together, these results provide evidence for an up to 13.25-fold variation in CYP2E1 activity based solely on genetic diversity. Formation of HB-Val and THB-Val poorly correlate with CYP2E1 activity. In contrast, there seem to be relationship with CYP2E1 and *pyr*-Val formation. CC strains can be grouped based on their dose response for *pyr*-Val formation which can be linear or saturates at exposures above 2 ppm BD (figure 1). In conclusion large inter-individual difference can be attribute to genetic diversity, questioning current the safety testing in sing animal strains.

Figure 1: Dose Response of *pyr*-Val in Collaborative Cross Mice



II.

III. Reference:

1. Liu, Y., Xiong, S., Sun, W. & Zou, F. Joint Analysis of Strain and Parent-of-Origin Effects for Recombinant Inbred Intercrosses Generated from Multiparent Populations with the Collaborative Cross as an Example. *G3 (Bethesda).* (2017). doi:10.1534/g3.117.300483
2. Swenberg, J. A., **Boysen, G.**, Georgieva, N., Bird, M. G. & Lewis, R. J. Future directions in butadiene risk assessment and the role of cross-species internal dosimetry. *Chem. Biol. Interact.* (2007). doi:10.1016/j.cbi.2007.01.012
3. Georgieva, N. I. N. I. *et al.* Quantitative analysis of N-terminal valine peptide adducts specific for 1,2-epoxy-3-butene. *Chem. Biol. Interact.* **166,** 219–225 (2007).
4. Georgieva, N. I., **Boysen, G.**, Bordeerat, N., Walker, V. E. & Swenberg, J. A. Exposure-response of 1,2:3,4-diepoxybutane-specific N-terminal valine adducts in mice and rats after inhalation exposure to 1,3-butadiene. *Toxicol. Sci.* **115,** 322–329 (2010).

Biography:

Dr. Boysen obtained his PhD in 2002 from the University of Kaiserslautern, Germany for research done at the University of Minnesota Cancer Center. After a post-doc at The University of North Carolina at Chapel Hill he joined the faculty at University of Arkansas for Medical Sciences where he is now Associate professor for Environmental and Occupational Health. He has published more than 50+ papers in reputed journals and has been serving on several review panels.

IV. Presenting author details



Full Name : Gunnar Boysen
Contact number : +1 (501) 526 4956
Email-id(s) : gboysen@uams.edu