

Use of Microsomal Epoxide Hydrolase (mEH) and NADP(H) Quinone Oxido-reductase Null Mice to Evaluate the Role of Specific Metabolic and Detoxification Steps in Altering Benzene Induced Toxicity

Leslie Recio. *CIIT Centers for Health Research.*

The activity of the enzyme systems involved in the activation and detoxication reactions of benzene metabolism are likely genetic determinants of individual-to-individual variability and risk in response to the toxic effects of benzene. Since NQO1 and mEH have significant roles in the metabolism of benzene, deficiencies in these enzymes will likely have an impact on the metabolism of benzene. In humans, deficiency in mEH is associated with an increased risk of colon and hepatocellular cancer and chronic pulmonary obstructive disease, while NQO1 deficiency is associated with an increased risk of benzene poisoning and adult and childhood leukemia. We hypothesize that humans deficient in NQO1 or mEH are at an increased risk of adverse health outcomes following exposure to benzene. To test this hypothesis, animal models that lack either NQO1 or mEH were used to define the role of these specific enzymes in mediating the pathogenicity, hematotoxicity, and genotoxicity of inhaled benzene. These studies have helped define the role of NQO1 and mEH as genetic determinants of benzene toxicity and assess the relevance of the genetic status of NQO1 and mEH as biomarkers of human genetic susceptibility.

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Presentation(s):

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