EPA
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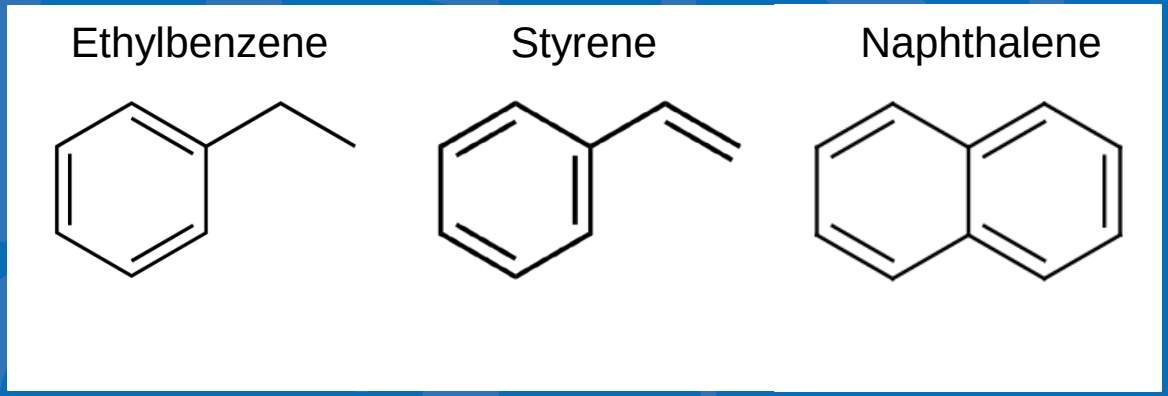
Mouse Lung Tumor Workshop: Session 4: Evidence for Cellular, Genetic, and Molecular Toxicity

Co-chairs: Gary Stoner and Nagu Keshava



Office of Research and Development
National Center for Environmental Assessment

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Introduction

Panelists:

David Eastmond, University of California

Andrew Kligerman, US EPA

Andrew Salmon, Cal EPA

Speakers:

Stephen Nesnow, Independent Consultant

David Eastmond, University of California

Brian Chorley, US EPA

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Session Goals

- Review the types of cellular, genetic, epigenetic, and molecular effects evident from exposure to the chemicals of interest.

- Understand the role of cellular and molecular/genetic evidence in the development of lung tumors (both in mice and human).

- Discuss how biological mechanisms on the three chemicals of interest (ethylbenzene, naphthalene, and styrene) lead to effects on the cellular and subcellular level, and the contribution of those effects on observable pathology.

- Review the evidence from the related chemicals (cumene, coumarin, fluensolfone) for any additional insights not available from studies on the chemicals of interest.

Agenda

12:30 pm	**Session Overview** Nagu Keshava and Gary Stoner
12:40 pm	**An Overview of the Genotoxicity of Aromatic Hydrocarbons and their Reactive Intermediates** Stephen Nesnow | *Independent Consultant*
1:00 pm	Guided discussion
1:10 pm	**Mouse Lung Carcinogens, Reactive Metabolites and Toxicity** David Eastmond | *University of California, Riverside*
1:30 pm	Guided discussion
1:40 pm	**Overview of New and Developing Omic Technologies: Assessing Molecular Toxicity and Disease Susceptibility**
2:00 pm	Guided discussion
2:10 pm	**Break**
2:25 pm	**Integration of Sessions 3 and 4** Gary Stoner | *Medical College of Wisconsin*
2:45 pm	Guided discussion
3:00 pm	**Session Summary Discussion**

Discussion Topics

1. Evidence for a role of genotoxicity/mutagenicity in the development of the specific mouse lung tumors being discussed in this workshop (e.g., mutational events, clastogenicity, other genotoxic mechanisms). Consider the role of metabolites and ROS to cause DNA damage and repair, as well as damage to other cellular organelles (cytotoxicity).

2. Epigenetics: (a) Potential for epigenetic mechanisms to play a role in the development of mouse lung tumors; (b) Evidence of epigenetic alterations due to chemical exposure leading to the formation of mouse lung tumors.

3. Relevance of more recent methods (e.g., Tox21 and Next Generation) to generate data on gene expression, toxicity pathways, and epigenetics that could inform the MOA for these mouse lung tumors.

4. Most in vivo genotoxicity data are for tissues other than the lung and in vitro data are difficult to relate to specific tissues. How do we consider these other (in vivo and in vitro) data?