GENETIC TOXICOLOGY AT THE CROSSROADS: From Qualitative Hazard Evaluation to Quantitative Risk Assessment

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HESI GTTC Workshop
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Four Decades of Genetic Toxicology

• Primarily used to identify potential carcinogens.

• A qualitative hazard identification tool.

• Little emphasis on quantitative assessment of dose-response data.

• Not considered to be an apical endpoint to drive risk assessment.
Evolution of a New Paradigm

- Growing interest in responses at lower, relevant exposure levels.
- Identification of threshold responses (NOGELs) and point of departure (PoD) metrics.
- Use quantitative data to drive risk assessment/risk management decisions.
ILSI- HESI
Genetic Toxicology Technical Committee (GTTC)

• An international tri-partite (academia, industry, and the government) collaborative initiative.

• Provides a forum for international experts in the field.

• Facilitates consensus building on contentious issues.

• Identifies resources to undertake high impact projects.
Genetic Toxicology Technical Committee Mission

- Improve scientific basis of the interpretation of results,
- Develop follow-up strategies to determine the relevance of test results,
- Provide a framework for a risk-based assessment of test results,
- Promote integration new/innovative techniques/scientific knowledge.
## 2014 GTTC Membership & Leadership

**Co-Chairs:**

Jan van Benthem, RIVM; Stefan Pfuhrler, P&G; Veronique Thybaud, Sanofi

### Industry Participation

- Abbott Laboratories
- AstraZeneca
- Bayer Healthcare Pharma
- BioReliance
- Boehringer Ingelheim GmbH
- Bristol-Myers Squibb
- Celgene
- Covance
- Dow Chemical
- GlaxoSmithKline
- Hoffmann-La Roche Inc.
- Janssen Pharma
- Litron Laboratories
- L'Oreal
- Novartis
- Pfizer Inc.
- Procter & Gamble
- Sanofi
- Servier
- Takeda

### Government / Research Institution Participation

- Federal Institute for Drugs and Medical Devices (BfArM, Germany)
- Health Canada
- National Institute for Public Health and the Environment (RIVM, NL)
- National Institute of Health Sciences (Japan)
- National Institutes of Environmental Health Sciences
- U.S. Department of Agriculture
- U.S. Environmental Protection Agency
- U.S. Food and Drug Administration

### Consultant Participation

- Bhaskar Gollapudi - Exponent
- David Kirkland Genetox Consulting
- Jim MacGregor Toxicology Consulting Services
- Errol Zeiger Consulting

### Academic Participation

- Aarhus University
- Leiden University Medical Center
- Swansea University
- St. George's University of London
- University of California, Riverside
Workshop Objectives

• Examination of biological processes dealing with low dose exposures to genotoxic stressors.

• Approaches to extrapolate dose metric across test systems, in vitro to in vivo, and from experimental models to humans.

• Methodologies to identify PoDs/thresholds and their use in risk assessment/management decisions.
Plenary Lecture

PK and PD Tools for DNA-Damage Pathways: Modeling Dose Metrics and DNA-Repair Processes

By
Dr. Melvin Andersen
The Hamner Institutes
Research Triangle Park, NC, USA.