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

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HESI GTTC Workshop
Lancaster, U.K

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ILSI Health and
Environmental Sciences
Institute

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 Pfuhler, 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.