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HESI APPLICATION OF GENOMICS TO MECHANISM-BASED RISK ASSESSMENT TECHNICAL COMMITTEE

FALL 2013 SYMPOSIUM ON "ADVANCES IN ASSESSING ADVERSE EPIGENETIC EFFECTS OF DRUGS AND CHEMICALS"

NOVEMBER 18TH 2013
WASHINGTON, DC

Abstract

Epigenetics, which represents mechanisms that control gene expression in a potentially heritable way without modification of the DNA sequence, is a rapidly developing area of research with relevance to stem cell differentiation, developmental processes, cancer and other diseases. Several mechanisms, including DNA methylation, histone modifications, and regulatory noncoding RNAs, appear to influence gene expression in an epigenetic manner. Epigenetic alterations can be induced by exposure to environmental chemicals or as side effects of drugs and thus have implications for human health. In addition, drugs that target specific epigenetic mechanisms are being developed to treat human disease, including several that have been approved for use.

New technological advances have led to recent and rapid progress in the characterization and mapping of epigenetic changes. However, there are significant knowledge gaps in understanding the relevance of such changes for toxicological safety assessment that requires further investigation with respect to the science, including potential model systems, endpoints and the most relevant techniques that could be employed.

The HESI Technical Committee on the Application of Genomics to Mechanism-based Risk Assessment, whose mission is to develop a scientific basis for application of genomic methodologies to mechanism-based risk assessment, is hosting a workshop on epigenetics and its potential implication for toxicology. This topic was the subject of a HESI-sponsored workshop in 2009 on the state of the science of epigenetics. A conclusion from the meeting was that "a great deal still needs to be learned prior to being able to rationally incorporate epigenetic evaluation into safety assessment." The 2013 workshop will review the current status of different areas of epigenetics research, provide an overview of available methods, and then use case studies to expand on topics with potential relevance for toxicological assessment. The goal is to obtain an up-to-date overview on epigenetic processes with probable toxicological implications, and to identify specific questions/issues that would be of interest for HESI to pursue further, perhaps in the form of new scientific research projects organized by HESI and supported by members of the Genomics Committee.

DRAFT
7 October 2013

DRAFT PROGRAM OUTLINE

Morning Sessions: Introduction to Epigenetic Research Areas and Methods for Assessment

9:00-9:15AM **Welcome & Opening Remarks**
- **Heidrun Ellinger, Bayer Pharma AG & Karol Thompson, US FDA**

9:15-10:00AM **Keynote lecture**
- **Igor Koturbash, University of Arkansas for Medical Sciences**

10:00-10:45AM **Advances in methods for assessing epigenomic modifications**
- **Richard Meehan, Medical Research Council, UK**

10:45-11:00AM ***Break***

11:00-11:45AM **Epigenomics - Impact for Drug Safety Sciences**
- **Jonathan Moggs, Novartis**

11:45-12:15PM **Liabilities associated with epigenetics targeting drugs**
- **Kaushik Datta, Celgene**

12:15-1:00PM ***Lunch***

Afternoon Sessions: Advances in Assessing Adverse Epigenetic Effects of Drugs and Chemicals - Case Studies and Model Systems

1:00-1:45PM **Multigenerational epigenetic adaptation of wound repair and regeneration mechanisms in response to toxic liver damage**
- **Derek Mann, Newcastle University**

1:45-2:30PM **Model Systems: Stem Cells as a model system for detecting epigenetic alterations**
- **Renee A. Reijo Pera, Stanford School of Medicine**

2:30-2:45PM ***Break***

2:45-3:30PM **Epigenetics in Product Safety Assessment**
- **Reza Rasoulpour, Dow Chemical**

3:30-4:15PM **Model Systems: NTP/NIEHS Mouse Methylome Research Project**
- **Jef French, NIEHS**

4:15-5:15PM **Panel Discussion**