

STATE OF THE SCIENCE: EVALUATING EPIGENETIC CHANGES SUBCOMMITTEE

Mission

The goal of this Subcommittee was to design and execute a workshop to enhance the scientific knowledge base regarding epigenetics and the possible relationship between epigenetic changes and transgenerational effects. The workshop program was aimed to provide participants with a general overview of the current state of the field to enhance an understanding of what one needs to know prior to thinking about incorporating an “epigenetic evaluation” into safety assessments.

2009 Participants

BASF Corporation

Bristol-Myers Squibb Company

Duke University

ExxonMobil Biomedical Sciences, Inc.

Federal Institute for Drugs and Medical Devices (BfArM)

Merck & Co., Inc.

Michigan State University

US Environmental Protection Agency

US Food and Drug Administration

US National Institute of Environmental Health
Sciences

University of Aarhus (Denmark)

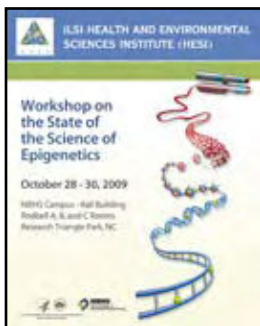
STATE OF THE SCIENCE: EVALUATING EPIGENETIC CHANGES SUBCOMMITTEE

MISSION

The mission of the HESI State of the Science: Evaluating Epigenetic Changes Subcommittee is to design and execute a public workshop focused on enhancing the scientific knowledge base regarding epigenetics and the possible relationship between epigenetic changes and transgenerational effects.

2009 ACTIVITIES AND ACCOMPLISHMENTS

HESI, with co-sponsorship from the NIEHS, hosted a successful workshop on October 28–30, 2009, at the NIEHS site in Research Triangle Park, North Carolina. The workshop, “State of the Science: Evaluating Epigenetic Changes,” drew nearly 100 participants and provided a general overview of the current state of the field and emphasized discussions around what one needs to know before thinking about incorporating an “epigenetic evaluation” into safety assessments. Workshop speakers included representatives from industry, academia, and government from the United States and Europe. A key feature of the workshop was an extended open discussion session on day three of the meeting. During this session, speakers and attendees addressed questions of appropriate model systems, endpoints, and techniques for evaluating epigenetic effects.



In addition, they considered when/if it would be appropriate to incorporate epigenetics into the regulatory process and what knowledge gaps might need to be addressed before such incorporation. Although perspectives varied, most of the participants concurred that epigenetic techniques can offer unique insights into alterations to the genome. However, they cautioned that the current complexities in the techniques and interpretation of these data would likely pose significant challenges to routine incorporation in a risk assessment paradigm.

FUTURE ACTIVITIES

As of December 2009, a manuscript that captures the participants’ perspectives on the questions outlined above was in preparation and is anticipated to be submitted to *Toxicological Sciences* in early 2010.

2009 WORKSHOP STEERING COMMITTEE

- Dr. Karen Augustine, Bristol-Myers Squibb Company (Program Co-Chair)
 - Dr. Jay Goodman, Michigan State University (Program Co-Chair)
 - Dr. Herman Autrup, University of Aarhus, Denmark
 - Dr. Ammie Bachman, ExxonMobil Biomedical Sciences Inc.
 - Dr. Michael Bolger, US Food and Drug Administration
 - Dr. Adriana Doi, BASF Corporation
 - Dr. Jerry Heindel, US National Institute of Environmental Health Sciences
 - Dr. Randy Jirtle, Duke University
 - Dr. Klaus Olejniczak, Federal Institute for Drugs and Medical Devices, Germany
 - Ms. Syril Pettit, ILSI Health and Environmental Sciences Institute
 - Dr. Chunhua Qin, Merck & Co. Inc.
 - Dr. John Rogers, US Environmental Protection Agency
 - Dr. Rick Storer, Merck & Co. Inc.
- HESI Scientific Program Manager:** Syril D. Pettit, MEM, E-mail: spettit@hesiglobal.org



Committee Presentations and Data Resources

January 19, 2009: Evaluating Epigenetic Changes Subcommittee Presentation.
"State of the Science: Evaluating Epigenetic Changes." Presented at the 2009 HESI Annual Meeting.
Tucson, Arizona. Presentation by Dr. Jay Goodman, Michigan State University.

ILSI Health and Environmental Sciences Institute (HESI)

E.I. Subcommittee on State of the Science: Evaluating Epigenetic Changes

January 2009

Co-Chairs: Dr. Jay Goodman, Michigan State University
Dr. Karen Augustine, BMS
Staff: Syril Pettit



H E S I



Mission and Goal

H E S I

MISSION:

- To design and execute a **public workshop** focused on enhancing the scientific knowledge base regarding epigenetics and the possible relationship between epigenetic changes and transgenerational effects.

GOAL: .

- The **goal** of the workshop is to gain an understanding of what we need to know prior to thinking about incorporating an “epigenetic evaluation” into safety assessments.



Project Progress Timeline

- **August 2007:** Selected by EISC to be pursued as a workshop, facilitated by SOT's Contemporary Concepts in Toxicology (CCT)
- **Sept 2007:** Steering team formulated
- **Dec 2007:** HESI submits proposal for CCT sponsorship of Hemangiosarcoma workshop
- **Oct '07 – Feb '08:** Workshop agenda, overview document, budget (w/SOT staff input), and submission letter prepared per available SOT CCT guidance
- **February '08-** HESI Hemangiosarcoma Workshop accepted for CCT sponsorship
- **March '08 –** Epigenetics Workshop materials submitted to SOT.



Project Progress Timeline

H E S I

- **April '08– Sept '08** – SOT promise of feedback on submission 'soon', indications that CCT process undergoing revision/formalization, mixed messages about viability of 2 HESI CCTs in one year.
- **Oct '08:** CCT committee asks HESI to resubmit under new guidelines, offers no timelines for decision process, suggests HESI proposal may be disadvantaged.
- **Oct '08:** HESI EISC authorizes Subcommittee to proceed with workshop plans but **WITHOUT** pursuing CCT sponsorship
- **Dec '08:** HESI-SOT CCT Hemangiosarcoma Workshop Held



Project Progress Timeline

H E S I

- Nov '08 to Present:
 - Steering Team informed of revised charter
 - Agenda re-examined and speakers specified
 - Outreach for potential venues/co-sponsors completed
 - NIEHS in RTP
 - Georgetown U
- Program and site selection to be finalized in 1Q '09 and workshop anticipated by end of '09.



Steering Team

Dr. Chunhua Qin – Merck

Dr. Herman Autrup - U. Aarhus

Dr. Adriana Doi- BASF

Dr. Klaus Olejniczak - EISC Sci Advisor to Committee - Fed.
Institute for Drugs and Medical Devices

John Rogers - EPA

Randy Jirtle - Duke University

Michael Bolger – FDA

Ammie Bachman - ExxonMobil

Jerry Heindel- NIEHS

Jay Goodman- MSU (Co-Chair)

Karen Augustine - BMS (Co-Chair)

Rick Storer - Merck



Exc erpted Agenda

I. State of the science of epigenetics

A. Where is the field? Why this workshop?

B. Epigenetics 101

C. Epigenetics in Development – background information

II. What constitutes Epigenetic changes?

I. Normal variability and adaptive changes

II. Transgenerational changes

III. Adverse effects

III. Research in Epigenetics

I. Development

II. Disease

III. Application to safety assessment

IV. Measuring Epigenetic Changes (techniques and interpretations)

V. Panel Discussion



Anticipated Outcomes

- **White paper to be generated to summarize workshop presentations and discussions, and the consensus reached regarding the goals of the workshop**
- **Recommendations from workshop could be circled back to EISC for consideration as potential new topics**