



EMERGING SCIENCE FOR ENVIRONMENTAL HEALTH DECISIONS

AGENDA

● Use of Emerging Science and Technologies to Explore Epigenetic Mechanisms Underlying the Developmental Basis for Disease

JULY 30-31, 2009 ■ WASHINGTON, DC

THURSDAY, 8:30-5:00, FRIDAY, 8:30-NOON ■ KECK BUILDING, 500 FIFTH STREET, NW

Traditionally, chemical-mediated DNA sequence changes (for example, mutation, deletion) have been areas of great concern for their potential to cause heritable and irreversible effects that can contribute to cancer and other diseases. Scientists have now uncovered the potential for heritable changes affecting gene expression that are not associated with underlying sequence changes in DNA. These mechanisms may include DNA methylation, chromatin structure changes, and others. Some evidence in animals, including humans, indicates that these modifications, like those in DNA sequence, are heritable and may even transmit transgenerationally.

WHAT ARE THE HEALTH IMPLICATIONS of these so-called “epigenetic” changes? Mutagenic chemicals receive much attention, with a number of testing procedures available to screen chemicals for their potential to cause mutations. However, there are no analogous

screening tests for epigenetic effects. Science has yet to determine whether screening tests or transgenerational animal bioassays are needed to detect such effects, and if they are, what specifically they would look for. Are humans more sensitive to such impacts during particular developmental periods? How much agreement is there about the importance of such effects? How much morbidity and mortality might they account for? Are they reversible? Does available science tell us whether these effects occur in humans or whether they persist transgenerationally in humans?

THE MEETING WILL PRESENT concepts about epigenetic mechanisms and effects, explore the current regulatory paradigm for handling implicated chemicals, and identify areas of scientific controversy. The objective is to gain understanding of what research is most needed to inform public-health decision-makers about chemicals that cause epigenetic effects. The meeting will include regulatory perspectives and information dissemination to the broader public and clinicians, and will focus on the following:

- observations that raise concern about epigenetic changes
- existing, emerging, and yet-unidentified tools for screening chemicals for such effects
- the most pressing needs for research to improve the state of the science
- implications for risk practitioners and regulatory decision-makers
- strategies for communicating emerging conclusions to the public

MORE FORUMS IN 2009

- Computational Toxicology:
From Data to Analyses to Applications
September 21-22, 2009, Washington, DC
- The Exposome: A Powerful Approach for Evaluating
Environmental Effects on Chronic Diseases
December 8-9, 2009, Washington, DC

Visit the committee's website <http://nas-sites.org/emergingscience> to learn more about this activity. Follow the “Subscribe for Updates” link to receive updates on follow-up from this meeting, announcements about related committee activities, and newsletters.

THURSDAY, JULY 30

8:30 **Opening Remarks.** *Linda S. Birnbaum, Ph.D., D.A.B.T., A.T.S., Director of the National Institute of Environmental Health Sciences and the National Toxicology Program*

8:40 **Introduction to the Standing Committee and Objectives of Today's Meeting.** *William Farland, Ph.D.—Colorado State University*

EMERGING SCIENCE

8:50 **Epigenetics Overview.** *Richard Meehan, Ph.D.—Medical Research Council Human Genetics Unit*

EMERGING PATHWAYS

What Are the Bases of Concern for Epigenetic Changes that May Lead to Latent Effects?

This session will review epigenetic changes in humans, their persistence, and animal models that illustrate the concept. Topics include exposure periods and morbidity/mortality. (5 to 10 minutes for Q&A after each presentation)

9:50 **Epigenetics in Cancer.** *Karl Kelsey, M.D., MOH—Brown University*

10:30 **Epigenetic Markers for Transplacental Exposure to Airborne Polycyclic Aromatic Hydrocarbons and Childhood Asthma.** *Wan-Yee Tang, Ph.D.—University of Cincinnati*

11:10 Break

11:25 **The Early Life Environment and the Epigenome.** *Moshe Szyf, Ph.D.—McGill University*

12:05 **Nickel Carcinogenesis and Cell Culture Models as Proof of Concept.** *Max Costa, Ph.D.—New York University Medical Center*

12:45 Lunch—On Your Own (cafeteria is on 3rd floor)

EMERGING TOOLS: ARE THERE APPROACHES FOR DEVELOPING SCREENING TOOLS TO IDENTIFY CHEMICALS THAT CAUSE THESE EFFECTS?

1:40 **Overview of Current Tools and Approaches Used to Demonstrate Epigenetic Effects.** *John Grealley, M.B., B.Ch., Ph.D.—Albert Einstein College of Medicine*

2:10 **Speaker Identification of Additional Tools and Approaches.** *Costa, Kelsey, Meehan, Szyf, Tang*

2:30 Development of Screening Tools

*Panelists: Trevor Archer, Ph.D.—National Institute of Environmental Health Sciences; Kim Boekelheide, M.D., Ph.D.—Brown University; Michele Cleary, Ph.D.—Merck & Co., Inc.; David Dix, Ph.D.—Environmental Protection Agency; and *William Farland, Ph.D.—Colorado State University*

How do we start evaluating which stressors cause epigenetic effects—what are some thoughtful, rapid screening approaches?

1. Can existing tools be used to broadly screen chemicals for epigenetic effects?
2. What potential for scale-up do current and emerging tools offer?
3. What are the technological and research hurdles to developing new tools?

3:30 Break

IMPROVING THE STATE OF THE SCIENCE: QUESTIONS ABOUT EPIGENETIC EFFECTS OF CHEMICALS

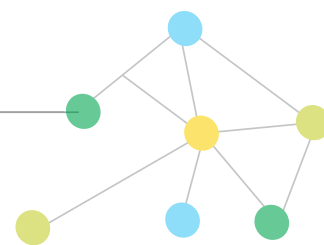
3:45 Knowledge Gaps and How to Address Them

*Panelists: Boekelheide; *Thomas Gasiewicz, Ph.D.—University of Rochester; L. Earl Gray Jr., Ph.D.—Environmental Protection Agency; Igor Pogribny, Ph.D.—Food and Drug Administration; Costa, Kelsey, Grealley, Meehan, Szyf, Tang*

1. What assumptions about the science need to be critically evaluated? What research is needed to address these questions?
2. How do we know which changes cause effects of concern and which are only associated?
3. Are there sensitive life stages? Do transgenerational effects result only from exposures during particular life stages?
4. Does the demonstration of epigenetic effects suggest alternative explanations for understanding how some chemicals cause toxicity?
5. How should dose-response principles be addressed?
6. Are we sure these effects are important? Do we need more research to determine this?
7. Can current lines of research be improved to make them more useful for regulators?

4:45 Summary of Day 1

5:00 Adjourn for the Day



REGULATORY AND COMMUNICATION IMPLICATIONS

8:30 Regulatory and Communication Implications Discussion

Panelists: Steven Bradbury, Ph.D.—Environmental Protection Agency; George Daston, Ph.D.—Procter & Gamble; Lynn Goldman, M.D.—Johns Hopkins University; Christopher Portier, Ph.D.—National Institute of Environmental Health Sciences; Rebecca Renner—freelance science writer; and William Slikker Jr., Ph.D.—Food and Drug Administration; Gray

1. What value do epigenetic effects have for prioritizing and categorizing chemicals for hazard identification?
2. What are the implications of identifying compounds that cause transgenerational effects for practitioners, now and in the future?

3. Will effective regulation be based on screening tools, or do animal models that look for transgenerational effects need to be developed?
4. What would identification of chemicals that cause effects mean for regulators? Does this fit into current paradigms or would a paradigm shift be needed?
5. Can markers be identified and, if so, how does this translate into lifestyle changes—individual decision making—for disease prevention?
6. What questions are important to the public, and how do we determine this? What would be effective strategies for engaging the public, and when should this happen?

11:30 **Summary of Meeting.** *William Farland*

12:00 **Adjourn**

At the request of the National Institute for Environmental Health Sciences, the National Academies formed the *Standing Committee on Use of Emerging Science for Environmental Health Decisions* to facilitate communication among government, industry, environmental groups, and the academic community about scientific advances that may be used in the identification, quantification, and control of environmental impacts on human health.

