EMERGING SCIENCE FOR ENVIRONMENTAL HEALTH DECISIONS

AGENDA

Stem Cell Models for Environmental Health

JUNE 3–4, 2010 ■ WASHINGTON, DC

THURSDAY, 8:30–5:30, FRIDAY, 8:30–12:30* ■ KECK BUILDING, 500 FIFTH STREET, NW

Stem cells have received much attention due to their potential therapeutic applications. However, their anticipated value as research tools may be even greater. Why? Stem cells have the special property of being able to differentiate into different cell types. This property enables them to be used to model aspects of human biology that have been largely inaccessible to study by other means. A few examples include prenatal developmental processes, cell types that are difficult to maintain in the laboratory, and gene-environment interactions.

How can human stem cells become important tools for making environmental health decisions? Stem cell technologies are rapidly evolving. Several emerging or postulated uses relevant to environmental health include:

- ***Modeling developmental processes.*** Under the right conditions, stem cells can recapitulate the normal developmental processes that occur before birth. Therefore, these models can be used to study the effects of many factors, including environmental chemicals, on the pathways that generate mature cells.
- ***Studying many types of cells in vitro.*** Stem cell models can be used to study the effects of environmental chemicals in a cell, tissue, or organ systems. The human body is made up of over 200 cell types, many of which are difficult or impossible to grow in the laboratory. Stem cells can differentiate into some of the more elusive cell types or be engineered to form more complex structures such as tissues and organs that are composed of multiple cell types.
- ***Elucidating genetic and environmental contributions to disease.*** Scientists are using stem cells from individuals with a wide array of diseases to study interactions among genetic, epigenetic, and environmental factors. This approach is amenable to illnesses or disease in which the genetic contribution is known (e.g., cystic fibrosis) and other disorders with complex or unknown causes (e.g., cancer and autism).

This meeting will foster a synergetic exploration of ways in which these powerful cell-based tools can be used to better understand the effects of environmental chemicals and other xenobiotics on human health. Toxicologists and environmental health regulators will learn about the most powerful stem cell models, with particular emphasis on human systems, that could be used to make environmental health decisions. Stem cell biologists will learn more about the critical questions plaguing environmental health scientists, to which these novel cell-based tools may be applied.

* On Friday, June 4, the committee and liaisons will meet following the forum.

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Register at http://nas-sites.org/emergingscience

AGENDA

THURSDAY, JUNE 3, 2010; KECK 100

8:30 **Introduction and Welcome—William Farland†,** *Colorado State University*, **Leslie Reinlib,** *NIEHS*

8:40 **Opening Remarks—Susan Fisher†,** *University of California, San Francisco*

Session 1: The Basic Biology of Stem Cells

The goal of this session is to understand the model systems and the types of data that they generate. How faithfully do in vitro stem cell models mimic the analogous in vivo processes? What are the strengths and weaknesses of stem cell models? How can stem cell models be improved (e.g., co-culture strategies, 2-d vs. 3-d models)? What lessons can we learn from epigenetic issues with iPS cells?

8:55 **The Nature of Adult and Embryonic Stem Cells and What We Can Learn From Them—R. Michael Roberts,** *University of Missouri*

9:30 **Human Embryonic Stem Cells (Derivation Approaches, Propagation, Differentiation)—Jane Lebkowski,** *Geron Corporation*

10:05 **Induced Pluripotent Stem Cells (Inducing Pluripotency, Basic Properties, Disease-Specific Lines)—M. William Lensch,** *Harvard University*

10:35 **Discussion: Moderated by Susan Fisher†,** *University of California, San Francisco*

11:00 **Break**

Session 2: Stem Cell Science in the Regulatory World

How can stem cell biologists and toxicologists synergize their efforts? How could new partnerships that bridge scientific and regulatory fields benefit everyone? (sessions include 5 minutes of Q&A for each speaker)

11:15 **Toxicology: A Springboard for Stem Cell Scientists?—Roger Pedersen,** *University of Cambridge*

11:45 **Stem Cells in an Early Screening Context for Drug Development/Discovery—William Pennie,** *Pfizer*

12:15 **Human Embryonic Stem Cell Systems: A Platform for Regulatory Decision Making? Are Stem Cells an Answer to Some of the Challenges in Toxicology and Regulatory Decision Making?—Tracey Woodruff,** *University of California, San Francisco*

12:45 **Lunch Break**

Session 3: Stem Cell Models for Assessing the Effects of Environmental Chemicals

1:45 **Stem Cell Models of Autism Spectrum Disorders: An Entree into Gene-Environment Interactions—Ricardo Dolmetsch,** *Stanford University*

2:25 **Use of Human Neuroprogenitor Cells to Screen Chemicals for the Potential to Cause Developmental Neurotoxicity—Tim Shafer,** *U.S. Environmental Protection Agency*

3:05 **Break**

3:20 **Adult Stem Cells and Breast Cancer—Zena Werb,** *University of California, San Francisco*

4:00 **Panel Discussion: Moderated by William Farland†,** *Colorado State University*

- What are typical sources of uncertainty in regulatory decision making and how might human stem cell systems help fill these gaps?
- What new types of questions/approaches do stem cell models enable regulators to ask?
- How can we use stem cell systems to better assess the complexity inherent in human biology?
- How might stem cell models reduce animal usage?

Discussants:

—**Deborah Hansen,** *U.S. Food and Drug Administration/National Center for Toxicological Research*

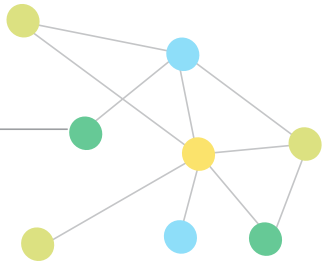
—**Stanley Barone,** *U.S. Environmental Protection Agency/National Center for Environmental Assessment*

—**Tom Knudsen,** *U.S. Environmental Protection Agency/National Center for Computational Toxicology*

—**David Jacobson-Kram,** *U.S. Food and Drug Administration/Center for Drug Evaluation and Research*

—**Richard McFarland,** *U.S. Food and Drug Administration/Center for Biologics Evaluation and Research*

4:45 **Discussion: Next Steps: Moderated by Helmut Zarbl†,** *Robert Wood Johnson Medical School*



5:25 **Day I Recap: George Daston†,** *Proctor & Gamble*

5:30 **Adjourn for the Day**

FRIDAY, JUNE 4, 2010

8:30 **Stem Cells as Tools for Environmental Science: A Vision—James Trosko,** *Michigan State University*

9:00 **Discussion: Moderated by William Farland†,** *Colorado State University*

Session 4: Exploring Environmental Effects on Stem Cells: What Might an NIEHS Program in This Area Look Like?

9:15 **Background and Charge for Impact of Environmental Factors on Stem Cells in Health and Disease—Les Reinlib,** *NIEHS*

9:30 **Roundtable Discussion:** Invited participants will discuss the future of stem cell research; the last 15 minutes will be available for audience questions.

Chair: Jose Russo, *Fox Chase Cancer Center*

Roundtable Participants:

Ricardo Dolmetsch, Roger Pederson, *Zena Werb, *Tim Shafer, *Tracey Woodruff, *Thomas Gasiewicz, George Daston†, Susan Fisher†, Max Wicha, *Helmut Zarbl†

*Asterisked participants are asked to propose visionary ideas for an NIEHS program to address questions and objectives below.

Roundtable Questions…

1. What directions should stem cell research take and what tools will be required?
2. What exposures should be examined?
3. Are there windows of susceptibility during which stem cells are vulnerable?
4. Is the exposure history of a stem cell an important variable that should be considered in designing experiments?

and Objectives…

5. Prioritize novel research directions at the genetic and molecular levels leading to understanding of the role of common exposures on stem, induced pluripotent (IPS), and multi-potent cells and the potential for disease and disorders. Identify 5–10 year expected outcomes.
6. Consider questions of subtle/latent responses to exposure or insult: mutations, epigenetics, cellular changes that might not become overtly phenotypic immediately
7. Identify gaps in exploration of exposure classes: pesticides, endocrine disruptors, as well as timing and dosage of exposure
8. Identify optimal research technologies and applications for future research directions: embryonic vs. adult pluripotent cells, culture vs. whole organism, systems approach

12:05 **Session 4 Recap: Les Reinlib,** *NIEHS*

12:15 **Adjourn**

12:30 **Committee and Liaison Meeting**

† indicates a member of the Standing Committee on Use of Emerging Science for Environmental Health Decisions

This meeting is being recorded for internet posting. Most presentations and recordings of discussions will be available online at http://dels.nas.edu/envirohealth, approximately two weeks after the meeting.

Visit the committee's website

http://dels.nas.edu/envirohealth

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.

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.