

Meeting on mammalian transgenerational inheritance fosters collaboration

By Jacqueline Powell

The NIEHS Division of Extramural Research and Training (DERT) hosted the Transgenerational Inheritance in Mammals after Environmental Exposure (TIME) grantee meeting Feb. 12-13. [Lisa Helbling Chadwick, Ph.D.](#), health scientist administrator in the NIEHS Genes, Environment, and Health Branch, organized the gathering of twenty experts in the field.

With predictions for severe winter weather on the day of the meeting, Chadwick and colleagues made a prudent decision to circumvent transportation-related issues by moving the meeting site from the NIEHS Rodbell auditorium to a nearby hotel, where many of the attendees were staying. While the weather created some hardships for visitors and prevented several of the presenters from traveling to the meeting, each enjoyed an opportunity to learn about others' research and present their own work through teleconferencing.

Along with NIEHS-funded researchers, scientists with the NIEHS Division of Intramural Research and Division of the National Toxicology Program attended in person and by phone, signifying the high level of interest in this topic and program across all parts of the Institute's research community.

The TIME program is focused on how adverse consequences of environmental toxicant exposure can be transmitted from one generation to the next, ultimately affecting multiple generations beyond the original insult. These adverse effects of environmental exposure can occur through transgenerational inheritance, which refers to heritable changes in gene activity that are typically introduced by epigenetic modifications.

Aligning transgenerational research with the NIEHS strategic plan

"The program is getting off to a much better start than the meetings are," said [Gwen Collman, Ph.D.](#), DERT director, referring to cancellation of the original meeting because of the government shutdown in October 2013. "We hope not to have you [in North Carolina] longer than you intend to stay."



A graphic for the TIME grantee meeting illustrates the concept of transgenerational inheritance, as exposures in utero (Fo) may affect offspring in succeeding generations.



*Chadwick is also involved in other NIEHS research initiatives related to transgenerational inheritance, including *Developmental Origins of Health and Disease*, *Environmental Epigenetics*, and the *NIH Roadmap Epigenomics Program*. (Photo courtesy of Steve McCaw)*

Collman then emphasized how research being conducted on transgenerational inheritance is linked to understanding how environmental factors influence individual susceptibility to chronic complex diseases across the lifespan, a priority for NIEHS-sponsored environmental health research as articulated in the Institute's strategic plan.

"One of the key goals of the meeting is to try and identify opportunities for collaboration among groups so that we can maximize the amount of information we can get from these [multigenerational animal] studies," said Chadwick. Other goals for the meeting included having discussions on optimizing study designs and coordinating outreach activities to explain the emerging concept of transgenerational inheritance to the scientific community and lay public.

Highlighting divergent approaches to transgenerational inheritance

The conference began with a talk by Marisa Bartolomei, Ph.D., professor of cell and developmental biology at the Perelman School of Medicine at the University of Pennsylvania, on the transgenerational effects of bisphenol A (BPA), a known endocrine disruptor. This research is providing insight into mechanisms that may be explored in humans.

Another presentation led by Alvaro Puga Ph.D., professor at University of Cincinnati (UC) College of Medicine, described a cross-disciplinary approach to investigate the transgenerational effects of exposure to polychlorinated biphenyls (PCBs). Collaborating with neurobiologist Charles Vorhees, Ph.D., professor at the Cincinnati Children's Hospital Medical Center, and cardiologist Jack Rubenstein M.D., assistant professor at UC College of Medicine, they were able to examine the effect of PCB exposure on DNA methylation, neurophysiology, and cardiovascular function.

The research presented at the meeting examined exposure to a variety of endocrine disrupting chemicals including BPA, tributyltin, diesel exhaust particles, phthalates, and polychlorinated biphenyls. The array of endpoints being examined was also impressive, including assessments of DNA methylation status, body weight, glucose regulation, immune cell function, learning, and cardiac function. Given the wide array of exposure paradigms and endpoints presented, it is clear that collaborations between investigators have great potential to advance the field.

(Former NIEHS postdoctoral fellow Jacqueline Powell, Ph.D., is a writer and analyst with Education and Training Systems International.)



In her remarks, Collman pointed to goal 2 in the NIEHS strategic plan, which involves support of research into understanding individual susceptibility to environmental exposures across the human lifespan. Research has clearly established the effects of early life exposure, she said, but a question remains for researchers - "Do they persist through future generations?" (Photo courtesy of Steve McCaw)

Mapping the transgenerational effects of environmental exposures

In addition to the presentations by Bartolmei, Puga, Vorhees, and Rubenstein that opened and closed the information-packed morning session, representatives from other transgenerational inheritance projects presented their preliminary findings.

- David Crews, Ph.D., spoke by phone about work he and Andrea Gore, Ph.D., are directing on "Ancestral Exposures/Modern Responses to EDCs [Endocrine Disrupting Compounds]" at the University of Texas at Austin.
- University of Rochester graduate student Lisbeth Boule outlined research conducted by her group, led by Paige Lawrence, Ph.D., exploring "Transgenerational Exposures as Modifiers of Host Defense Against Infection."
- Harvard School of Public Health researcher Lester Kobzik, M.D., described his work on "Transgenerational Susceptibility to Asthma From Air Pollution Exposure" in collaboration with Alexey Fedulov, M.D., Ph.D.
- Massachusetts General Hospital physician-scientist Toshihiro Shioda, M.D., Ph.D., reported on his collaboration with University of California, Irvine researcher Bruce Blumberg, Ph.D., on "Transgenerational Inheritance of Prenatal Obesogen Exposure."
- Speaking by phone from her office at the University of California, San Francisco, Diana Laird, Ph.D., outlined her group's work on "Assessing Transgenerational Effects of Phthalates on Primordial Germ Cells."

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