PEPH webinar highlights alternative testing methods

By Audrey Pinto

Promoting the discovery and application of novel test models for environmental health research is a core objective of the NIEHS strategic plan.

The NIEHS Partnerships for Environmental Public Health (PEPH) sponsored a webinar Jan. 23 highlighting the Institute's commitment to develop, apply, and validate cutting-edge scientific methods aimed at ensuring human and animal health, while protecting the environment. Efforts include in-house research by NIEHS and NTP scientists; collaborations with agency partners to advance predictive toxicology and alternative testing; and grant awards.

The two presenters - Elizabeth Maull, Ph.D., of the NTP Biomolecular Screening Branch, and Kristie Willett, Ph.D.,
(http://home.olemiss.edu/~kwillett/)
an NIEHS-funded grantee with the Environmental Toxicology Research Program
(http://www.pharmacy.olemiss.edu/etrp/index.html)
at the University of Mississippi School of Pharmacy - described their group's efforts to foster and promote scientifically sound alternative test methods.

Maull is an NTP toxicologist in the Biomolecular Screening Branch, the NTP lead group for Tox21, and a NICEATM administrator. (Photo courtesy of Steve McCaw)

Willett is a professor of pharmacology with research interests that include using fish models to study mechanisms of polycyclic aromatic hydrocarbon toxicity. (Photo courtesy of Ole Miss Communications)

Advancing, promoting, and validating the discovery of innovative test models

Maull introduced webinar attendees to the unique role the NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) and the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) play in promoting the acceptance of innovative test methods by both the federal government and the global community.

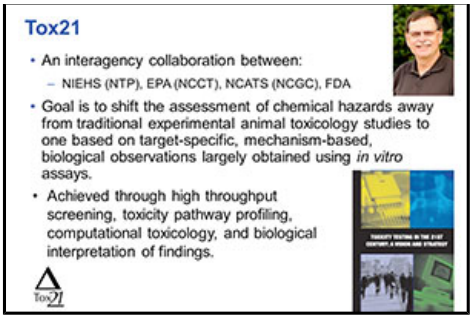
Linked Video

Watch a European Union video released in January on the science behind development of 21st century safety testing using alternative methods (11:23)

Using what the groups call the 3Rs, Maull explained, "[The mission is to] facilitate interagency and international collaboration to promote the development, regulatory acceptance, and use of alternative tests that encourage the reduction, refinement, or replacement of animal test methods."

Maull pointed to Tox21,
(http://ntp.niehs.nih.gov/?objectid=05F80E15-F1F6-975E-77DDEDBDF3B941CD)
now beginning Phase III, as a successful partnership among four federal agencies - NIEHS/NTP, the National Center for Advancing Translational Sciences, the U.S. Environmental Protection Agency, and the U.S. Food and Drug Administration - to promote the emerging field of predictive toxicology. The consortium is using alternative methods including high-throughput screening assays - *in silico* models; lower-organism model systems, such as zebrafish and *Caenorhabditis elegans*; and investigating 3-D tissue models; as well as the so-called organs on a chip. The goal of this partnership is to evaluate and prioritize approximately 10,000 chemicals of toxicological concern.

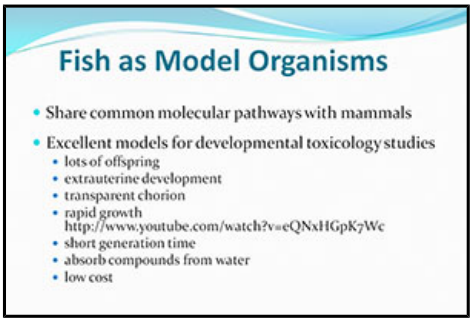
While great strides have been made in the design and application of new testing models, Maull said, "There is an ongoing need for an evolving definition of 'validation' that should be responsive to new technologies and ongoing paradigm shifts in toxicity testing."



With Tox21, the emphasis in toxicology is evolving from descriptions of pathological outcomes to prediction of the potential effects of chemicals on the biochemical pathways. (Photo courtesy of Elizabeth Maull)

Zebrafish - a model organism for tracking the fetal origins of human diseases

Willett is a passionate proponent of the contribution and utility of research with zebrafish (*Danio rerio*) as a model organism. She opened her presentation by highlighting the advantages of using zebrafish for testing the effects of environmental toxicants. Willett pointed out that because scientists have extensive information on the genomic, developmental, and reproductive biology of zebrafish, they are invaluable to the global scientific community in providing answers to the origins and causes of human diseases, including cancer and neurological diseases.



As Willett explained, fish offer several important advantages over other animal models, including a 48-hour window of embryo development that parallels mammal development in a fraction of the time. (Photo courtesy of Kristine Willett)

Linked Video

Watch a short video on the advantages of using zebrafish to study human disease (02:56)

As she explained, "Not only do zebrafish share common molecular pathways and diseases with mammals, which make them ideal for developmental toxicological studies, they also possess a very unique characteristic - their extrauterine development is transparent, so that researchers can watch the progress of a disease from an environmental exposure while it's happening." To highlight this unique feature, Willett used her research findings on dietary benzo(*a*)pyrene exposure as a case study, to show the adverse developmental effects on body shape of multiple generations of offspring.

In summary, Willett said, "Because zebrafish produce large numbers of offspring that develop rapidly, researchers now have a test model that can evaluate the impact of toxicological exposures on multigenerational and transgenerational offspring in a matter of months instead of years."

(Audrey Pinto, Ph.D. is technical editor for the NIEHS journal Environmental Health Perspectives.)

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