International Symposium on Alternatives Assessment

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Deputy Director, NIEHS
Principal Investigator
National Institute of Environmental Health Sciences

- NOT in Bethesda area
  - Research Triangle Park, NC
- Wide variety of programs supporting our mission of environmental health:
  - National Toxicology Program
  - Intramural laboratories
  - Extramural funding programs

- Funding from 3 Congressional Committees
  - Health – Regular NIH appropriation
  - Interior - Superfund Research Program and Worker Training
  - Energy - Worker Training Program
The mission of the National Institute of Environmental Health Sciences is to discover how the environment affects people in order to promote healthier lives.

The vision of the National Institute of Environmental Health Sciences is to provide global leadership for innovative research that improves public health by preventing disease and disability.
NIEHS Strategic Plan 2018-2013

- Advancing Environmental Health Science
- Promoting Translation: Data to Knowledge to Action
- Enhancing EHS through Stewardship and Support

http://www.niehs.nih.gov/strategicplan
Addressing Individual Susceptibility
What is the NIH All of Us Research Program?

The All of Us Research Program is a historic, longitudinal effort to gather data from one million or more people living in the United States to accelerate research and improve health. By taking into account individual differences in lifestyle, socioeconomics, environment, and biology, researchers will uncover paths toward delivering precision medicine – or individualized prevention, treatment, and care – for all of us.

“All of Us is among the most ambitious research efforts that our nation has undertaken!”

NIH Director Francis Collins, M.D., Ph.D.
Diversity Among Inbred Strains: Acetaminophen Toxicity

Mouse strains

Threadgill and colleagues
UNC, JAX NCSU, NIEHS
Differential Host Response to Toxic Exposure: Benzene Clearance

French et al., EHP, 2014
Using Mice as a “Model” for Human Exposures

Inbred Strain
(C57BL/6J)
(B6C3F1)

Not equal to

Genetically Diverse Human Population
“Modeling” Reference Human Populations with Reference Populations of Mice

Genetically Diverse Mouse Population

Equal to

Genetically Diverse Human Population
Diversity Outcross (DO): Complementary Resource Produced from Collaborative Cross Lines

- 8 way advanced intercross
- Continuously breeding “outbred” colony—each mouse different
- “Controlled” genetic complexity
- Enhanced mapping resolution

Churchill, Threadgill, Pardo-Manuel de Villena, and colleagues
Change in %MN-RET before and after exposure

Bringing Genetic Heterogeneity into Tox21: “In Vitro Genetic Studies”

Reference population of Mouse Lines (Human in the future)

ES Derivation from Blastocysts

iPS reprogramming

Reference population of ES/iPS Cell Lines
“In Vitro Genetic” Studies

Reference population of ES/iPS Cell Lines from the CC/DO

High Content Cell-based Screening

Transcriptomics
Proteomics
Metabolomics
Automated Time Resolved Cardiomyocyte Beating Assay

- EBs produced in 384 well format
- Astemizole (antihistimine) txt
- Video processed to digitize motion.
- Regions of Interest (ROI) isolate beating regions
- Fully automated 384w format assay, label-free, non-invasive.

Ted Choi and colleagues
predictive biology, inc. www.predictivebio.com
Thank you!

NIEHS Strategic Plan Website
http://www.niehs.nih.gov/strategicplan