



National Institute of Environmental Health Sciences
Your Environment. Your Health.



National Toxicology Program
U.S. Department of Health and Human Services

International Symposium on Alternatives Assessment

Rick Woychik, Ph.D.

Deputy Director, NIEHS

Principal Investigator



The National Institute of Environmental Health Sciences



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?



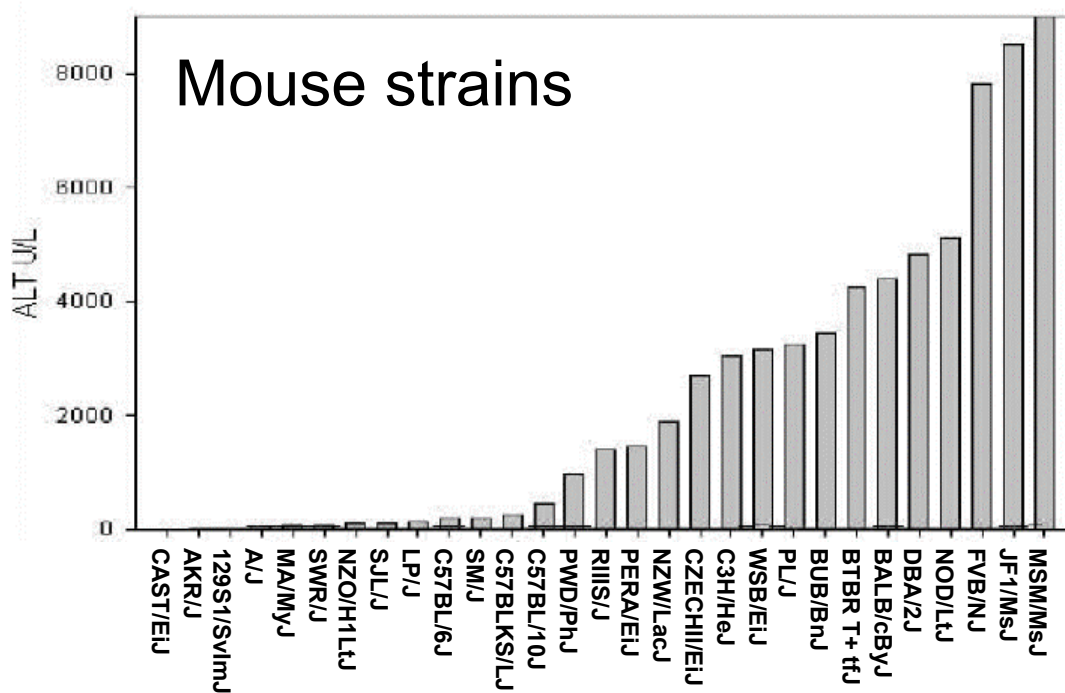
The *All of Us* Research Program is a historic, longitudinal effort to **gather data from one million or more people** living in the United States to accelerate research and improve health. By **taking into account individual differences in lifestyle, socioeconomics, environment, and biology**, researchers 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!”

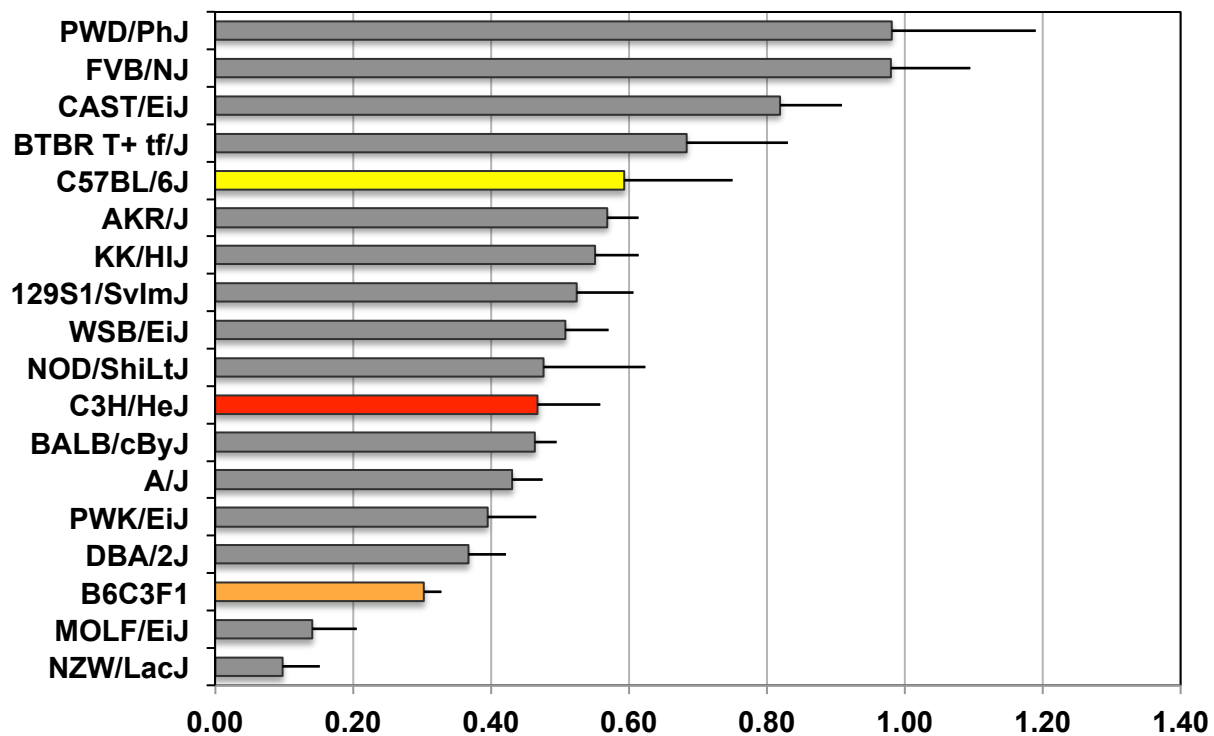
NIH Director Francis Collins, M.D., Ph.D.

Diversity Among Inbred Strains: Acetaminophen Toxicity



Threadgill and colleagues
UNC, JAX NCSU, NIEHS

Differential Host Response to Toxic Exposure: Benzene Clearance





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



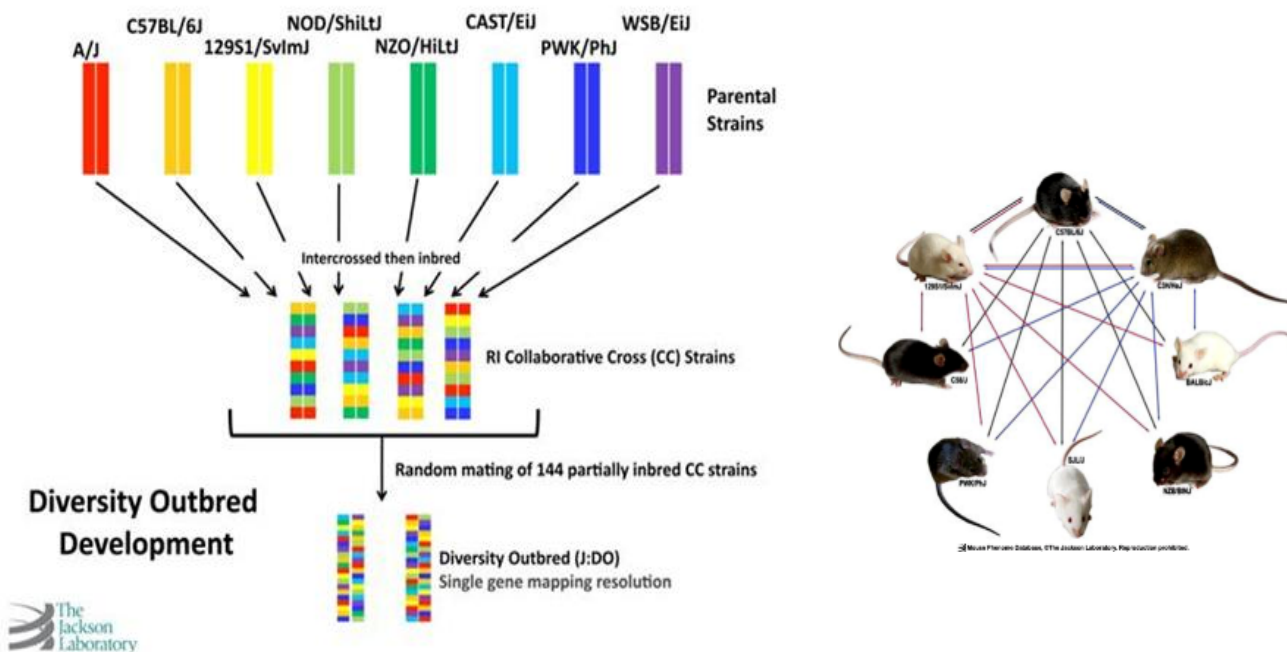
Genetically Diverse
Mouse Population

Equal to



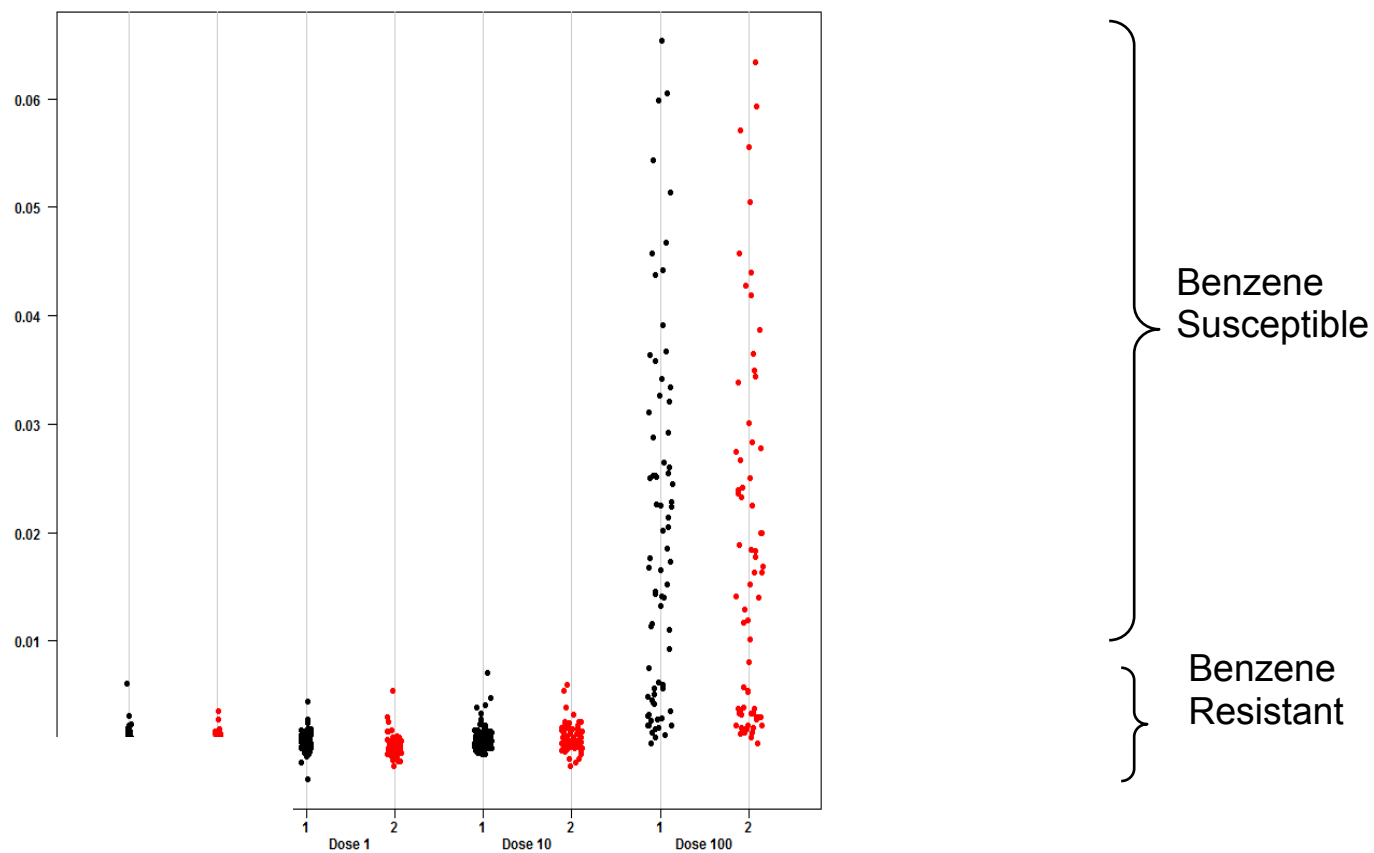
Genetically Diverse
Human Population

Diversity Outcross (DO): Complementary Resource Produced from Collaborative Cross Lines



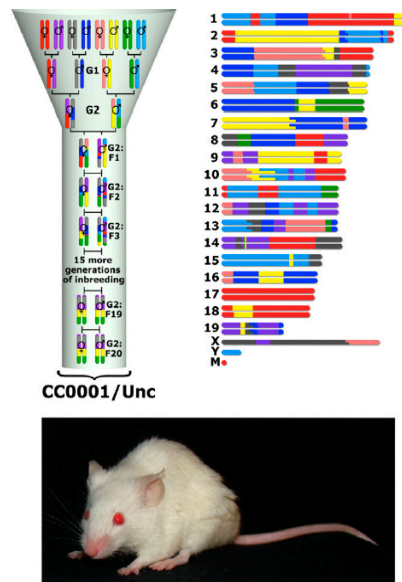
- **8 way advanced intercross**
 - **Continuously breeding “outbred” colony—each mouse different**
 - **“Controlled” genetic complexity**
 - **Enhanced mapping resolution**
- Churchill, Threadgill, Pardo-Manuel deVillena, and colleagues

Change in %MN-RET before and after exposure



French, Churchill, Threadgill, Pardo-Manuel de Villena et al. EHP 2015

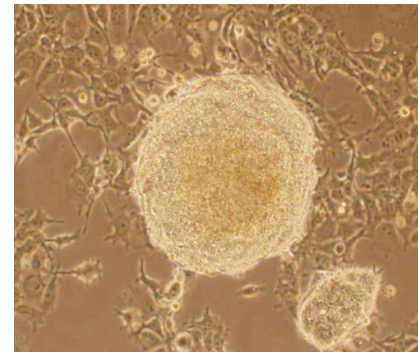
Bringing Genetic Heterogeneity into Tox21: “In Vitro Genetic Studies”



ES Derivation
from Blastocysts



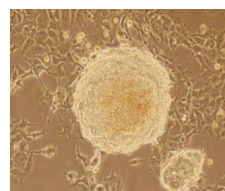
iPS
reprogramming



Reference
population of Mouse
Lines (Human in the
future)

Reference
population of ES/
iPS Cell Lines

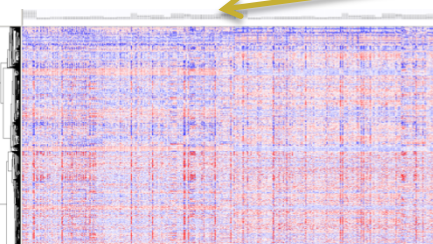
“In Vitro Genetic” Studies



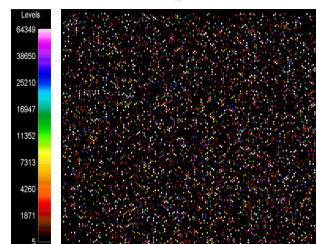
Reference population of ES/iPS Cell Lines from the CC/DO



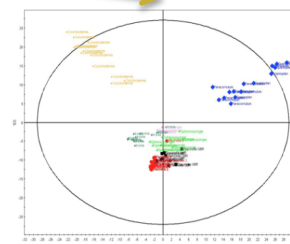
High Content Cell-based Screening



Transcriptomics

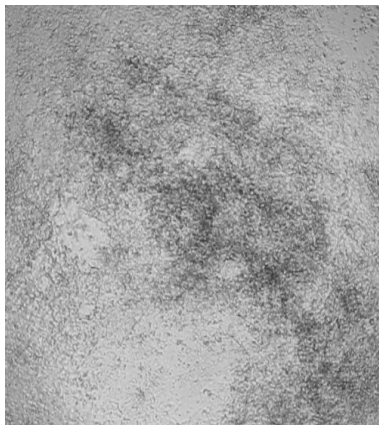


Proteomics

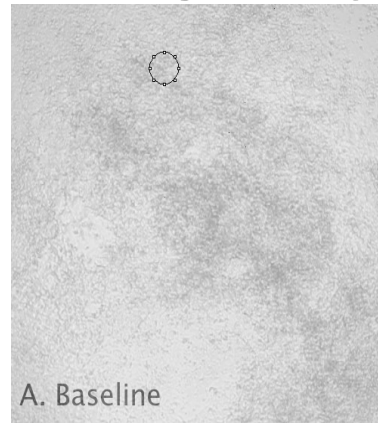


Metabolomics

Automated Time Resolved Cardiomyocyte Beating Assay



astemizole.brightfield
d

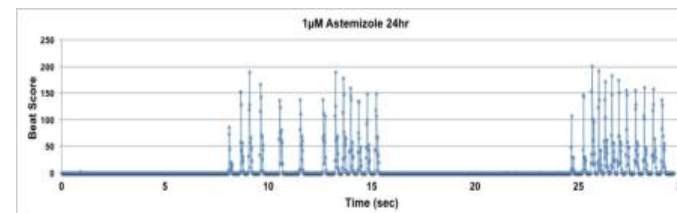
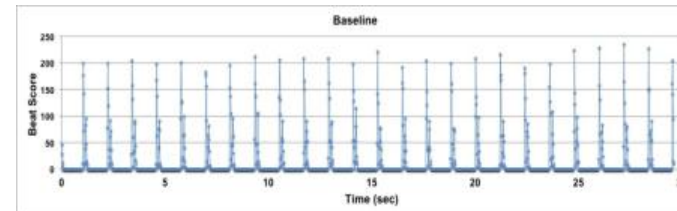


A. Baseline
astemizole.baseline



C. 1μM Astemizole 24hr
astemizole.24hr

- EBs produced in 384 well format
- Astemizole (antihistamine) 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

Thank you!



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

