A New Tox21 Strategic and Operational Plan

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The views expressed in this presentation are those of the presenter and do not necessarily reflect the views or policies of any of the Federal agencies represented.
Underlying Issues Facing Toxicology

Number of Chemicals / Combinations to Test

Human Relevance of Existing Tests

Lack of Data for Environmental Chemicals

- Modified from Judson et al., EHP 2010

Ethics Concerns

Economics
FORMATION AND RENEWAL OF U.S. TOX21 FEDERAL PARTNERSHIP

MEMORANDUM OF UNDERSTANDING
ON
High Throughput Screening, Toxicity Pathway Profiling, and Biological Interpretation of Findings

XI. APPROVAL
National Toxicology Program
Linda S. Birnbaum, Ph.D., DABT, ATS
Director
National Institute of Environmental Health Sciences
National Institutes of Health

National Center for Advancing Translational Sciences
Christopher P. Austin, M.D.
Director
National Center for Advancing Translational Sciences
National Institutes of Health

U.S. Environmental Protection Agency
Lukas O. Keddi
Acting Assistant Administrator
Office of Research and Development
U.S. Environmental Protection Agency

U.S. Food and Drug Administration
Susan T. Mayne, Ph.D.
Director
Center for Food Safety and Applied Nutrition
U.S. Food and Drug Administration

MOU Signed February, 2008; Revised July, 2010

5-11-15
Date

5/20/2015
Date

5/16/15
Date

5/27/15
Date
Toxicity Testing Data Generated by Tox21

*Total number of assays is ~70
Scientific, Public, and Regulatory Impact of Tox21

- Tox21 collaboration has published over 200 scientific peer-reviewed articles in over 56 journals
- Top 5 Tox21 publications cited an average of over 100 times (Web of Science)
- Tox21 mentioned in over 70 news articles, 13 blogs, 461 Twitter posts, and 8 Wikipedia articles (AltMetric, Aug, 2017)
  - National Academies of Science Reports (~80)
  - Publications Office of the European Union (~15)
  - European Food Safety Authority (~5)
  - World Health Organization (~5)
But, the Focus of Tox21 has been Predominantly on HTS
Need to Expand Vision to Move Toxicity Testing into 21st Century
The Challenge
Areas of Focus

1. Develop and deploy alternative test systems that are predictive of human toxicity and dose response
2. Address key technical limitations of current \textit{in vitro} test systems
3. Curate and characterize legacy \textit{in vivo} toxicity studies to serve as a resource for interpreting Tox21 data
4. Develop framework for efficient validation of Tox21 approaches
5. Refine and deploy \textit{in vitro} methods for characterizing pharmacokinetics to increase predictivity and reduce uncertainty
New Tox21 Structure

Tox21 Management Team

Cross Partner Project #1

Cross Partner Project #2

Cross Partner Project #3

Cross Partner Project #...

Infrastructure Team #1

Infrastructure Team #2

Infrastructure Team #3
New Tox21 Structure

Tox21 Management Team

- Cross Partner Project #1
- Cross Partner Project #2
- Cross Partner Project #3
- Cross Partner Project #...

Cross-Partner Projects
- Project charters
- 3 year terms
- Project leads from two or more partners
- Reviewed annually
Initial Infrastructure Teams and Example Cross Partner Projects

**Infrastructure Teams**
- Chemical Library Management
- Communications
- Assay Evaluation and Screening

**Cross-Partner Projects**
- *In Vitro* Disposition of Tox21 Chemicals
- Performance Based Validation of Tox21 Assays
- Development of a Reference Chemical Dataset for Interpretation of High-Throughput Transcriptomic Screening Data
- Incorporating Genetic Susceptibility into Developmental Neurotoxicity Screening
- Development of a High-Throughput Assay to Identify 5-α Reductase Inhibitors for Orthogonal Evaluation in an Androgen-dependent Human 3D Prostate Tissue
- Cell Line Selection for High-Throughput Transcriptomic Screening
- Predictive Modeling of Developmental Toxicity with Human Pluripotent Stem Cells
- Development of a High-Throughput Assay to Identify Acetylcholinesterase Inhibitors
Thank You for Your Attention!