ICCVAM Public Forum Update

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Objective

Provide an update on ERDC’s activities related to alternative methods for toxicology testing for the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) Public Forum.
Activities that support ICCVAM

• Participating in ICCVAM Acute Toxicity Working Group (ATWG), Read Across Working Group (RAWG), In Vitro to In Vivo Extrapolation Working Group (IVIVE-WG).

• Co-chairing ICCVAM Ecotoxicology Working Group (Eco-WG).

• Participating in the Tri-Services Toxicology Consortium (TSTC)
  o Includes representatives from relevant DoD Organizations
  o Share knowledge, collaborate on projects, implement best practices, promote 3Rs

• Participating on activities that support the development of predictive approaches such as the Adverse Outcome Pathway framework.
Adverse Outcome Pathways

- Members of the AOP-Knowledge Base group
- Members of the OECD Extended Advisory Group for Molecular Screening and Toxicogenomics (EAGMST)
- Founding members, and members of the Society for the Advancement of Adverse Outcome Pathways (SAAOP)
- Developing AOPs and AOP Networks
- Developing computational predictive tools.
AOP-Xplorer

Tool to Visualize Adverse Outcome Pathway Networks

Visualize Adverse Outcome Pathway Networks

With AOPXplorer, you can visualize AOP Networks (AOPNs) from the US Army Engineer Research and Development Center’s AOPN repository. AOPXplorer is part of the [http://aopkb.org/ AOP-KB project].

See your data on an AOP network.

See for yourself what’s going on. By harnessing the power of Cytoscape, we enable you to paint your data on the AOPNs from our repository. You can also make your own AOPNs in Cytoscape (nothing special to do -- just make a pathway in Cytoscape).

Get Involved

If you have an AOPN that you want to share with us, drop us a note at our AOPN issue tracker or send me an email.
Development of AOP Networks

STEP 1
Selection of chemicals
- Exposure related DB
  - BPR (132)
  - OSHA (134)
- Toxicity related DB
  - IRIS (54)
  - eChemPortal (440)

STEP 2
AOP206 related ToxCast Assay
- PPARγ (4)
- ATF4 (3)
- TGFβ (3)
- NF-κB (3)
- EMT (3)
- Inflammation (10)
- Angiogenesis (10)
- Tox21
  - BSS KEK
  - BSS KF3CT
  - BSS LPS
  - BSS GARMIC

STEP 3
Deep learning model
- Pre-processing
- Modeling dataset
- Multilayer perceptron classification model

STEP 4
- Tested in ToxCast
  - Potential chemicals for AOP206 from ToxCast
- Not tested in ToxCast
  - Potential chemicals for AOP206 from deep learning model

STEP 5
Identification of Potential chemicals for validation of AOP206

Level of Organization
- PPARγ dependent lung fibrosis
  - Inactivation of PPARγ
  - Activation of TGF-β
  - Inflammation
    - EMT
      - Collagen deposit
    - Lung fibrosis

Macromolecular

Cell/Tissue

Organ/Organ System

Development of AOP Networks

Developing approaches for the use of qAOPs for hazard assessment

Hazard Screening

• Use the zebrafish embryo to understand the potential hazard of chemicals and mixtures, including field samples for environmental monitoring.

• Use of the zebrafish embryo and the water flea *Daphnia magna* to understand the potential hazard of nanoparticles and engineered nanomaterials.
DoD Roadmap for Rapid Hazard Assessment

• DoD wide initiative to develop a DoD Strategic Roadmap to promote the use of New Approach Methodologies in Rapid Chemical Hazard Assessment
  o US Department of Defense
  o US Department of the Army
  o US Department of the Air Force
  o US Department of the Navy

• As DoD is composed of a range of organizations with multiple user needs, regulatory drivers, and application areas, a coordinated DoD strategy is needed to support technical development, policy development and implementation of emerging chemical hazard assessment methods, approaches, tools, and frameworks.

• Work in close collaboration with ICCVAM partners and NICEATM.