Design and Evaluation of ExO: An Ontology for Exposure Science

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Disclaimer. Although this work was reviewed by EPA and approved for presentation, it may not necessarily reflect official Agency policy.
“One side of the Hazard-Exposure equation continues to be refined while the other remains subject to crude characterization based largely on indirect estimates and default assumptions.”

Tox Sci 2009
Will fundamental knowledge of toxicity pathways improve understanding of real-world human-health risk?

• Assessing complex human-health risks requires that hazard, susceptibility, and exposure are all reliably characterized.

• Currently, balance of efforts to improve measuring hazard and exposure less than ideal.

• Accurate assessment of many environmental exposures remains an outstanding and largely unmet challenge in toxicology and risk assessment.

• To realize the NRC vision for toxicity testing, we face a critical need for advanced exposure science.

Adapted from Wild, 2005
Transforming Exposure Science for Toxicity Testing

New technologies must be applied to BOTH toxicology and exposure science if the ultimate goal of evaluating chemical safety is to be achieved.

- Systems exposure science
- Biologically-relevant exposure metrics
- Environmental informatics and advanced computational models

Cohen Hubal, Tox Sci, 2009
Systems Exposure Science: Exposure at All Levels of Biological Organization

![Diagram of Systems Exposure Science]

- **Stressor** → **Perturbation** → **Biological Receptor** → **Perturbation** → **Outcome**

- **Environmental Source**
  - Ambient Exposure
  - Personal Exposure

- **Internal Exposure (Tissue Dose)**
  - Dose to Cell
  - Dose of Stressor Molecules

- **Population** → **Individual** → **Tissue** → **Cell** → **Biological Molecules**

- **Disease Incidence/Prevalence**
- **Disease State** (Changes to Health Status)
- **Dynamic Tissue Changes** (Tissue Injury)
- **Dynamic Cell Changes** (Alteration in Cell Division, Cell Death)
- **Dynamic Changes in Intracellular Processes**

Figure 1

Cohen Hubal, JESEE, 2008
Exposure-Hazard Knowledge System

• Translation of HTP hazard information requires holistic risk assessment knowledge system
  – Include ontologies, databases, linkages
  – Facilitate computerized collection, organization, and retrieval of exposure, hazard, and susceptibility information

• Standardized exposure ontologies required to
  – Define relationships, allow automated reasoning, facilitate meta analyses
  – Develop biologically-relevant exposure metrics
  – Design \textit{in vitro} toxicity tests to measure environmentally-relevant hazard
  – Incorporate information on susceptibility and background exposures to individual and population-level risks
Pilot Curation of Exposure Data into Comparative Toxicogenomic Database

- Chemicals
  - chemical-gene interactions
  - chemical-disease relationships
- Genes
  - gene-disease relationships
- Diseases
  - Exposure Data (curated and public sources)

Functional annotations

Pathway data

Davis et al., 2011
Design and Evaluation of the Exposure Ontology: ExO

**Background:**
- Significant progress has been made in collecting and improving access to genomic, toxicology, and health data
- These information resources lack exposure data required to
  - translate molecular insights
  - elucidate environmental contributions to diseases
  - assess human health risks at the individual and population levels

**Objective:**
- ExO, that will facilitate centralization and integration of exposure data to inform understanding of environmental health
- ExO is intended to bridge the gap between exposure science and environmental health disciplines

**Vehicle:**
- Carolyn Mattingly, Mount Desert Island Biological Laboratory
- LRI seed funding, followed by NIEHS RO1
Objective

• Develop an exposure ontology consistent with those being used in toxicology and other health sciences to support annotation of the outcome of exposure of a receptor (human or ecological) to a stressor (chemical, biological, physical, psychosocial).

• Initially focus development on human exposure to chemicals

• Ultimately, provide domains that can be extended to encompass exposure data for the full range of receptors and stressors.
## Exposure Ontology Working Group

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Phases of Exposure Ontology Development

**Phase I**
- Initial pilot curation to identify major concepts

**Phase II**
- Model relationships among data concepts
- Expand test data set to evaluate extensibility of conceptual model and cross-reference existing ontologies
- Iterate data model refinement and curation

**Phase III**
- Full working group evaluation of draft ontology

**Phase IV**
- Disseminate exposure ontology for public feedback
“stressor interacts with a receptor via an exposure event resulting in an outcome”
Definitions of Central Concepts

- **Exposure Stressor** - An agent, stimulus, activity, or event that causes stress or tension on an organism (UMLS Cui:C0597530).

- **Exposure Receptor** - An entity (e.g., a human, human population, or a human organ) that receives a stimuli (e.g., environmental exposure).

- **Exposure Event** - Contact between a stressor and a receptor.
  - ("An exposure event is the act of subjecting someone or something to an influencing experience. E.g. exposure to cigarette smoke." [EFO:0000487])

- **Exposure Outcome** - Entity that results from the interaction between other entities (SBO:0000409)
Pilot Curation of Exposure Data into CTD

- **Exposure Stressor**
  - Chemicals
  - Chemical-gene interactions
  - Chemical-disease relationships

- **Exposure Event**
  - Time, Location
  - Receptor-disease relationships

- **Genes**
  - Gene-disease relationships

- **Diseases**
  - Gene-disease relationships

- **Receptor**
  - Chemical-receptor relationships

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**Functional Annotations**

**Pathway Data**

**CTD** advances understanding of the effects of environmental chemicals on human health.

**The Gene Ontology**

**Nature Precedings**: doi:10.1038/npre.2011.6321.1: Posted 1 Sep 2011
References


