

Report 62: A systematic evaluation of alternative model organisms for understanding the effect of environmental exposures on human development and health.

Convener: Antonio Planchart

Brief History: Currently, there are two favored approaches to understanding toxicity: in vitro, cell based models (low level) and in vivo rodent models (high level). However, the power of other comparative models, including vertebrate and invertebrate models, has not been adequately exploited to understand environmental health effects in humans despite their long and valued history in other scientific disciplines that have recognized their importance in understanding mechanisms that are fundamental to human biology, including development and disease. Embracing alternative models for toxicological studies can contribute to many aspects of environmental health research, including augmenting our understanding of critical stages during human development that lead to structural birth defects or set the stage for fetal origins of adult human diseases when perturbed by environmental exposures.

Discussion Highlights: It was acknowledged that a more systematic approach to developing and using alternative model organisms for use in environmental health studies would accelerate the pace of understanding the adverse outcomes on human development and health resulting from environmental exposures.

Recommendations:

- There is a real need to move away from treating model organism studies as purely ecological studies and instead focus on understanding why they are good proxies for understanding human biology. Other biological disciplines, (e.g., genetics, developmental biology, physiology) have long recognized the relevance and importance of multiple model organism systems in understanding the molecular bases of heredity, embryonic development and systems biology. There is much to be gained in the field of toxicology by embracing multiple model organisms to address specific questions related to the environment and its role in human development and health.
- There is a need to perform comprehensive evolutionary analyses among diverse model organisms (e.g., *C. elegans*, zebrafish, sea urchin, flies, *Daphnia*, Medaka, Tunicates) in order to determine the degree of biological pathway conservation and the degree to which these pathways are affected by environmental exposures. This knowledge will facilitate identifying the most cost-effective and efficient system in which to deploy strategies for:
 - Developing “green” chemicals that do not pose substantial teratological, developmental or adult health risks;
 - Evaluating which chemicals pose the greatest risk to human health, and establishing sound biological reasons to prevent their commercialization;
 - Understanding the biological outcomes of exposure to environmental stressors, toxins and toxicants;

- Evaluating the role of candidate genes/proteins in the mechanisms leading to toxic outcomes;
- Validating in vitro studies using in vivo systems that are cost-effective, genetically tractable, and result in rapid knowledge acquisition.
- Use of alternative models with rapid generation times can be valuable for understanding the role of parent-of-origin contributions (epigenetics) to the development biological risk factors leading to the onset of disease later in life.

Discussion Participants:

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