ORGANOTYPIC CULTURE MODELS FOR PREDICTIVE TOXICOLOGY RESEARCH CENTERS

Background:
The U.S. Environmental Protection Agency (EPA), through its Science to Achieve Results (STAR) grant program, has funded 4 Research Centers to develop *in vitro* systems of cell cultures that replicate human biological interactions within complex tissues or organs. These models are called Organotypic Culture Models (OCMs), sometimes termed 'organs-on-a-chip'. When developed and evaluated, these OCMs will provide information needed to help predict toxicity due to chemical exposures. The OCMs will provide the biological understanding and data to help evaluate, improve and extend computational models currently being developed by EPA scientists.

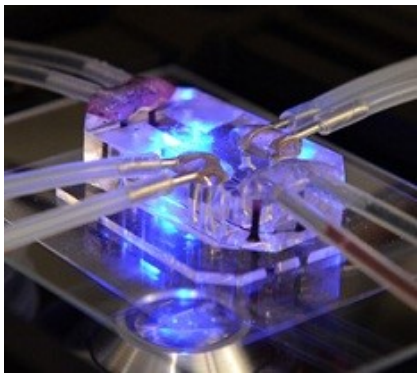
EPA provided research institutions up to $6 million each to develop OCMs for high-priority biological systems including the brain, liver, kidney, testis, breast tissue, heart and neurovascular systems. They are applying and evaluating these new modeling methods as platforms to screen for interactions of chemicals with key biological processes. This research will provide new insight about how tissues and organs function during chemical exposures.

The data will then be used to develop advanced models of how organs and tissues respond to these exposures. The developed models aim to replicate critical functions of tissues and organs such as metabolism, organization and communication of cells, providing researchers with insight into how tissues and organs grow and change over time.

The following Research Centers are taking advantage of innovations and advances in the fields of biology and medicine to transform the science of chemical safety evaluations:

University of Wisconsin, Madison
Award: $6,000,000
Project: *Human Model for Analysis of Pathways Center (H-MAPs)*

The Human Model for Analysis of Pathways Center is



based at the University of Wisconsin. The HMAP Center is researching innovative cellular modeling methods to develop broadly applicable tools for toxicity screening. OCMs are being developed for functions within the liver, brain, breast tissues, and neurovascular tissues.

Vanderbilt University
Award: $6,000,000
Project: *Vanderbilt-Pittsburgh Resource for Organotypic Models for Predictive Toxicology (VPROMPT)*

The VPROMPT Center is advancing alternative methods of chemical toxicity testing using three dimensional (3D) cultures of different types of cells binding with appropriate extracellular matrices to reduce

uncertainties regarding specific chemical exposures.

The 3D models of how cells behave and function will be used to more accurately simulate the biological response of liver, mammary gland, limb/joint formation, and fetal membrane tissues under different conditions and chemical stressors.

University of Washington
Award: $6,000,000
Project: *Predictive Toxicology Center for Organotypic Cultures and Assessment of AOPs for Engineered Nanomaterials*

This Center is developing innovative OCMs to evaluate the potential for cellular and organ toxicity following exposure to metal-based Engineered Nanomaterials (ENM) within an adverse outcome pathway (AOP) model. The Center aims to develop and apply OCMs for four target organs: lung, kidney, liver and testis. The University of Washington Center will examine life stage and genetic background as factors incorporated into the developed models.

Texas A&M University of
Award: $6,000,000
Project: *Cardiotoxicity Adverse Outcome Pathway: organotypic culture model and in vitro-to-in vivo extrapolation for high-throughput hazard, dose-response and variability assessments*

This Center will develop a cardiovascular OCM of disease for toxicity screening of environmental chemicals. They are using cardiac muscle cell models that reflect the diversity of humans, pilot in vitro to in vivo translation, and integrate and translate information from the first two projects. The long-term objective of the Center is to advance human health and environmental risk assessments and predictive toxicology by establishing and validating effective, accurate and fiscally responsible OCMs that can identify and characterize chemical exposures hazardous to the heart.

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Information about the Awards:
http://cfpub.epa.gov/ncer_abstracts/index.cfm/fuseaction/recipients.display/rfa_id/577

More Information on EPA's chemical safety for sustainability research
http://www.epa.gov/research/chemicalscience/

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