

ORGANOTYPIC CULTURE MODELS FOR PREDICTIVE TOXICOLOGY RESEARCH CENTERS

Background:

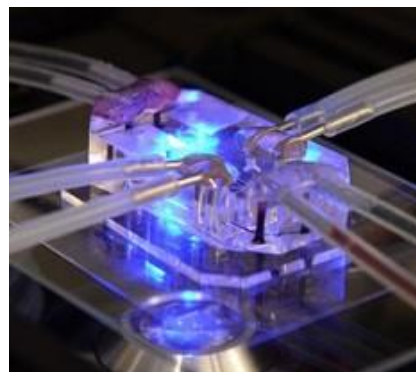
The U.S. Environmental Protection Agency (EPA), through its Science to Achieve Results (STAR) grant program, requested proposals to fund Research Centers to develop *in vitro* systems of cell cultures that will replicate human biological interactions within complex tissues or organs. These models are 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 developed OCMs will provide the biological understanding and data to help improve, evaluate and extend computational models currently being developed by EPA scientists.

EPA is providing 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 will apply and evaluate 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 computational models of how organs and tissues respond to chemicals. The developed computational models will ultimately be used to validate predictive models of human disease or response. The developed models aim to replicate critical functions of tissues and organs such as metabolism, organization and communication of cells within the tissue or organ, and how these tissues and organs grow and change over time.

This research takes advantage of innovations and advances in the fields of biology and medicine to transform the science of chemical safety evaluations. The grants will fund the following Research Centers:



University of Wisconsin, Madison

Award: \$6,000,000

Project: *Human Model for Analysis of Pathways Center (H-MAPs)*

The University of Wisconsin will establish the Human Model for Analysis of Pathways Center. The Center will research innovative cellular modeling methods to develop a broadly applicable set of tools for toxicity screening. OCMs will be developed for functions within the liver, brain, breast tissue with invasive ductal carcinoma (the most common type of breast cancer), and neurovascular tissue.

Vanderbilt University

Award: \$6,000,000

Project: *Vanderbilt-Pittsburgh Resource for Organotypic*

Models for Predictive Toxicology (VPROMPT)

This Center will advance alternative methods of chemical toxicity testing using OCMs – 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*

The overall goal of this Center is to develop 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

Center plans to examine life stage and genetic background as factors incorporated into the developed models.

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Information about the Awards:
<http://epa.gov/ncer/2013ocm>

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

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