Horizons and Challenges in Organotypic Culture Models for Predictive Toxicology

Saturday, March 11

9:00 AM – 5:00 PM

Baltimore Convention Center, Room 310

8:00 AM **Poster Set-ups** (in back of the hall)

9:00 AM **Welcome and Introduction**
Jeff Frithsen, EPA Chemical Safety for Sustainability Interim National Program Director

9:10 AM **Status of OCM-PT Co-Operatives with VTM Research**
Tom Knudsen, US EPA/NCCT

9:30 **Mammary Development and Breast Cancer**
Moderator: Jill Franzosa – US EPA/CSS

Mammary gland development is a complex process that advances from fetal through pubertal stages and pregnancy. Developmental exposures to some chemicals (e.g., EDs) can increase the risk of breast cancer and other disease outcomes that depend on the timing of exposure. Human studies are not able to demonstrate causal associations with EDs because exposures are not typically evaluated during critical windows of development. Microscale tissues (mammospheres) coupled with microfluidics provide novel research models to probe exposure-disease pathways in a human system.

- Dmitry Markov, PhD – Vanderbilt University [VPROMPT – mentor Lisa McCawley]
  Mammosphere bioreactor for Lifestage specific toxicology

- Megan Livingston (student) – U Wisconsin [HMAPS – mentor Dave Beebe]
  Synthetic hydrogels supporting 3D mammary duct morphogenesis

- Molly Morgan (student) – U Wisconsin [HMAPS – mentor Dave Beebe]
  Utilizing an adverse outcome pathway based approach to identify readouts and cellular components for an organotypic breast model

10:15 **Break**

10:30 **Novel Bioengineering Platforms for Developmental Toxicity**

Moderator: Sid Hunter – US EPA/NHEERL

Cells in developing tissues must integrate and respond to highly dynamic information in the form of metabolic intermediates, genetic signals, molecular gradients, and physical forces. Their perturbation by genetic errors and environmental factors (e.g., chemicals, intrauterine infection) may invoke malformations or preterm birth. Microscale tissues built from pluripotent human cells and coupled with microscale devices to impose morphogenetic constraints provide novel research models to probe cellular-biophysical interactions in spatially dynamic systems.

- Dave Belair, PhD – US EPA/NHEERL [USEPA – mentor Barbara Abbott]
  Engineering a human fusion-competent organotypic model of osteogenesis and morphogenetic fusion

- Brian Johnson, PhD – University of Wisconsin [HMAPs – mentor Dave Beebe]
  Engineering a human microfluidics platform for palate morphogenesis

- Pete Alexander, PhD – University of Pittsburgh [VPROMPT – mentor Rocky Tuan]
  Stage-specific OCMs to analyze teratogen-induced limb defects

- Morten Seirup (student) – University of Wisconsin [HMAPs – mentor Jamie Thomson]
  Spatial recovery of hepatocytes based on single cell-RNA seq profile

11:30 AM **Cardiovascular Development and Toxicity**

Moderator: Barbara Klieforth – US EPA/NCER

Cardiovascular development, physiology and vascular function are important considerations for assessing the toxicity of drugs and environmental chemicals. OCMs for these parameters offer new insights into the predictive modeling and mechanistic understanding of xenobiotics, including those affecting cardiac physiology and valvuloseptal morphogenesis. Microscale tissues built from pluripotent human cells and microscale devices that impose morphogenetic constraints including fluid-flow kinetics provide novel research models to investigate underlying pathways of toxicity.

- Fabian Grimm – Texas A&M [C-AOP – mentor Ivan Rusyn]
  Population-based cardiotoxicity assessment with human stem cell-derived OCMs

- Eric Nguyen, PhD – University of Wisconsin [HMAPs – mentor Nader Sheibani]
  Synthetic hydrogel matrices for assessing angiogenesis and vascular toxicity

- Kyle Grode, PhD – US EPA/NHEERL [USEPA – mentor Sid Hunter]
  Engineering a human endocardial OCM for assessing valvuloseptal development

- Julia Popp – Texas A&M [C-AOP - mentor David Threadgill]
  Embryoid body-based OCM for cardiotoxicity screening

12:30 Lunch Break, Poster viewing

1:45 PM **Paired Microphysiological Systems and Integrative Simulation**

Moderator: Tom Knudsen – US EPA/CSS

Microfluidics pairing of different OCM models provides an opportunity to incorporate complex issues in effects assessment, such as the role of systemic metabolism on target toxicity, the impact of microperfusion and physiologically realistic fluid budgets on toxicodynamics and cell signaling. This topic will cover progress and vision of human-based microphysiological systems paired with another organ for effects assessment of systemic (endocrine) signaling or local (paracrine) cytokine/growth factor signaling.

- Juan Gnecco, PhD – Vanderbilt University [VPROMPT – mentor Kevin Osteen]
  Instrumented Fetal Membrane-on-a-Chip (IFMOC) for human inflammatory pathways

- Kate Saili, PhD – USEPA/NCCT [USEPA – mentor Tom Knudsen]
  Classification model of blood-brain barrier development and toxicity

- Eli Weber, PhD - University of Washington [UWPTC – co-mentors Dave Eaton/Ed Kelly]
  An integrated liver-kidney platform for assessing Adverse Outcome Pathways (AOPs)

- Todd Zurlinden, PhD – USEPA/NCCT [USEPA – mentor Tom Knudsen]
  Agent based modeling of neurovascular unit development

- Todor Antonijevic, PhD [USEPA - mentor Imran Shah]
  Computational modeling of toxicological tipping points

3 - 5 PM **Attended Poster Session**