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CONTROL ID: 2005227

PRESENTATION TYPE: Symposium

Secondary Pres Type - Proposal:

IAT/ITS Designation: Innovations in Toxicological Sciences (ITS)

CURRENT ENDORSERS: Neurotoxicology Specialty Section | Reproductive and Developmental Toxicology Specialty Section | In Vitro and Alternative Methods Specialty Section

TITLE: MICROPHYSIOLOGICAL MODELS OF THE DEVELOPING NERVOUS SYSTEM: BIOLOGICALLY-DRIVEN ASSEMBLY INSPIRED BY EMBRYOLOGY AND TRANSLATED TO HUMAN DEVELOPMENTAL TOXICOLOGY

ABSTRACT BODY: Recent advances using human stem cells and other cells that can be ushered through differentiation and developmental maturation offer an unprecedented opportunity to develop predictive systems for toxicological assessment. The use of human cells is an advantage because there is no need to extrapolate across species, but even so, there may be the requirement that different cell types interact in a three dimensional (3D) relationship in order to provide prediction of the intact human. For example, in the developing nervous system, multiple cell types including neurons, astrocytes and oligodendrocytes interact in the presence of growth factors, cytokines and other hormones to function within a 3D spatial configuration that can reflect normal biological functioning in a predictive manner. The purpose of this symposium is to take a close look at the novel approaches being applied for biologically-driven assembly, in which exploiting the capacity of an embryo to build tissues and organs from scratch, and the multicellular response dynamics in biologically-driven assembly are facilitating 'human-on-a-chip' microsystems and other cellular-complex culture models. The target audience will be those interested in the technology and application of cellular-complex culture models and human microphysiological systems in general, and newer applications of these approaches for evaluating developmental neurotoxicity.

The first speaker will address the progress that has been made concerning how the cellular microenvironment dictates tissue morphogenesis and the importance of 3D cellular architecture in cellular function. The second speaker will the use a 3D in vitro model that consists of neurospheres (clusters of primary neural progenitor cells) to identify signaling pathways that contribute to exogenously-induced developmental neurotoxicity. To maximize the predictive capacity of these model systems, they should reflect an appropriate disease state and developmental stage. Our third speaker will describe microphysiological systems that combine different human pluripotent stem cell (hPSC) derived cell types in a specific 3D configuration of mini-organoids to study complex cellular networks and disease models for drug development, toxicology and medicine. To reproduce the desired outcome, standard procedures need to be developed and widely agreed upon concerning positive and negative test agents, dose-response characterization and reproducibility. Our fourth speaker will address the requirement for quantitative outcome measures that are essential to the overall success of the organotypic culture approach in order for it to be predictive of the human situation. Standard approaches will be outlined with the use of positive and negative test agents to allow confirmation of the reproducibility of these in vitro test systems in different laboratory environments.

Chair Name: Thomas B. Knudsen

Chair Affiliation: US EPA/NCCT

Chair Email: knudsen.thomas@epa.gov

Co-Chair Name: William Slikker, Jr.

Co-Chair Affiliation: US FDA/NCTR

Co-Chair Email: william.slikker@fda.hhs.gov

CHAIR/PRESENTER INFORMATION:

Name: Thomas B. Knudsen, PhD
Affiliation: National Center Computational Toxicology, US EPA, Research Triangle Park, NC, 27711, United States;
City: Research Triangle Park
State: NC
Country: United States
Phone: 919-541-9776
Fax: (none)
E-mail: knudsen.thomas@epa.gov

Member Type: SOT Member
Funding: No SOT Funding Needed
Presentation Title: Session Introduction
Presentation Description: Brief introduction to the technology and goal of the symposium.

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Name: William L. Murphy, PhD
Affiliation: Biomedical Engineering and Orthopedics, University of Wisconsin, Madison, WI, United States;
City: Madison
State: WI
Country: United States
Phone: 608-265-9978
Fax: (none)
E-mail: wlmurphy@wisc.edu

Member Type: Non-member
Funding: SOT Full Funding Requested
Presentation Title: Engineered microphysiological systems for cell-based predictive models of developmental neurotoxicity and teratogenicity
Presentation Description: The cellular microenvironment dictates tissue morphogenesis. ECM, proteins, growth factors, steroids, hormones, small molecule agonists/antagonists, shear flow, mechanical strain, synthetic compound libraries, mineral ions and electromagnetic fields have diverse functions in maintaining 3D cellular architectures during signaling. Biologically-inspired engineering approaches to generate organotypic micro-tissues for drug and toxicity screening can lead to novel biomaterials to define the stem cell microenvironment for biologically driven synthetic arrays for neurodevelopment.

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Name: Ellen Fritsche, PhD
Affiliation: Sphere Models and Risk Assessment Group, IUF-- Leibniz Research Institute for Environmental Medicine, Dusseldorf, Germany;
City: Dusseldorf
State: (none)
Country: Germany
Phone: +49-211-3389217
Fax: (none)
E-mail: ellen.fritsche@uni-dusseldorf.de

Member Type: SOT Member
Funding: No SOT Funding Needed
Presentation Title: Probing signaling pathways in developmental neurotoxicity with human 3D neurospheroids
Presentation Description: Identification of signaling pathways which contribute to exogenously-induced developmental neurotoxicity. This research addresses a 3D in vitro model which consists of neurospheres, clusters of primary neural progenitor cells. Pathways include AhR, thyroid hormone receptor and Nrf2

signaling. Knowledge of toxicity pathways feed into the application of such a system for toxicity testing. High content image analysis is established to increase the image-based experimental throughput.

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Name: Thomas Hartung, MD, PhD
Affiliation: CAAT, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, United States;
City: Baltimore
State: MD
Country: United States
Phone: 39 3486 614006
Fax: 41 0223 1603
E-mail: thartung@jhsph.edu

Member Type: SOT Member
Funding: No SOT Funding Needed
Presentation Title: Biological and medical applications of a brain-on-a-chip
Presentation Description: With limited understanding of the complexity of brain development, simple in vitro systems do not represent form and function of the brain. Moreover, the difficulty of studying interactions between human genetics and environmental factors leads to lack of knowledge about the events that induce neurological diseases. Microphysiological systems that combine different hPSC-derived cell types in a specific 3D configuration into mini-organoids to generate a human-on-a-chip could enable studies of complex cellular networks and disease models for drug development, toxicology and medicine.

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Name: Robert E. Chapin
Affiliation: Developmental and Reproductive Toxicology, Pfizer, Inc, Groton, CT, United States;
City: Groton
State: CT
Country: United States
Phone: 860-441-0571
Fax: (none)
E-mail: robert.e.chapin@pfizer.com

Member Type: SOT Member
Funding: No SOT Funding Needed
Presentation Title: Standards and minimum requirements for validation of complex organotypic culture model systems
Presentation Description: Quantitative outcome measures are essential to the overall success of the organotypic culture approach, and they should reflect the human condition and be relevant to improving the practice of evidence-based medicine and regulation. Most of these quantitative measures should reproduce the normal functioning of the tissue in situ and be consistent with a mechanistic understanding. The model systems will need to reflect an appropriate disease state or developmental stage in order to provide a valid prediction. Additional features to be considered include relevant chemical exposure, dose-response characterization and the influence of varying the developmental stage of selected cells. And to reproduce the desired outcome, standard procedures will need to be developed and widely agreed upon. Multi-center trials with positive and negative test agents will be necessary to confirm the reproducibility in different laboratory environments.

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Name: William Slikker, Jr, PhD, ATS
Affiliation: National Center for Toxicological Research, US FDA, Jefferson, AR, United States;
City: Jefferson
State: AZ
Country: United States

Phone: (870) 543-7517
Fax: (870) 543-7576
E-mail: william.slikker@fda.hhs.gov

Member Type: SOT Member
Funding: No SOT Funding Needed
Presentation Title: Session Wrap-up
Presentation Description: Brief closing to synopsize main points across all four talks..
