CENTENNIAL SPEED TALKS

Session 4
Engineering a sustainable future: in vitro toxicity testing (alternatives to animal models)
Thursday, April 8 at noon

Using liver models generated from human induced pluripotent stem cells for evaluating maternal, fetal, and child health outcomes
Celeste Carberry (PhD, 2024) – Advisor: Julia Rager

Abstract: hiPSC-derived hepatocytes may be used to fill the current research gap surrounding the impact of prenatal/perinatal chemical exposures on liver-related maternal, fetal, and child health outcomes.

About Celeste: Hi, my name is Celeste and I am a first-year PhD student studying toxicology with a special interest in how exposures to environmental chemicals impact maternal and child health outcomes. Fun fact: When I am not in lab, I enjoy painting and digital illustration.

In Vitro High-Throughput Screening of Chemically Induced Oxidative Stress Using Human Hepatocyte Models
Nancy Carolina Urbano (2022) – Advisor: William Gwinn

Abstract: Oxidative stress is thought to be critical in the pathogenesis of many diseases including inflammation and cancer and is one of IARC's Key Characteristics of Carcinogens. In vitro high-throughput screening approaches are needed to characterize the potential of chemicals to induce oxidative stress. In this study, chemical-induced cytotoxicity and oxidative stress were evaluated and compared in vitro across 3 human hepatocyte culture models. This evaluation focused on a set of chemicals which were previously tested by the NTP, mostly in 2-yr bioassays, and thus have established in vivo toxicity data in mice and rats. This set included chemicals that were carcinogenic and non-carcinogenic to the liver. 2D-HepaRG cells, 3D-HepaRG spheroids, or 3D-primary human hepatocyte (PHH) spheroids were exposed to 9 doses of chemical (or vehicle control) in a high-throughput (384-well plate) format for 96 hr at 37°C. Culture media containing chemical was replaced with fresh media/chemical after 48 hr of exposure. Cell viability and oxidative stress were measured after 96 hr of exposure using the CellTiter (ATP)-Glo and reactive oxygen species (ROS)-Glo assays, respectively. Menadione and ginseng were used as the positive and negative controls, respectively. ROS/ATP ratios were calculated. BPAF, milk thistle extract, and triclosan induced oxidative stress (increased ROS/ATP) in all 3 culture models; whereas PFOA induced oxidative stress only in the 3D culture models. TBBPA induced oxidative stress only in the 3D HepaRG model. These in vitro human hepatocyte culture models have the potential to be used for high-throughput screening of chemical-induced oxidative stress. Discrepancies with regards to in vivo vs. in vitro chemical-induced hepatotoxic effects may be attributable to species-specific differences (human vs. mice/rat).

About Nancy: I graduated with a B.S. in Environmental Science from St. Mary's University. Currently I am trainee at the National Toxicology Program at the National Institute of Environmental Health Sciences. My research focuses on predictive toxicology and screening. I enjoy writing for the Environmental Factor

and Women in Toxicology, painting and fostering through independent animal rescue.

A Clustered Cytokine Approach Identifies Immune Cell Communicators are Modified in E-Cigarette Users and Cigarette Smokers across Multiple Compartments of the Body
Alexis Payton (MS, 2021) – Advisor: Julia Rager

Abstract: We investigated if clustered cytokines would be more representative of immune system interactions, therefore providing a more robust assessment of toxicological injury resulting from e-cigarette or cigarette exposure.

About Alexis: I have been performing computational toxicology research with Dr. Rager for over two years and enjoy leveraging data science to do so. I eat peanut butter and jelly just about every day. I aspire to be a Data Scientist to help address public health questions.