VIRTUAL FALL MEETING

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Tuesday, December 1, 2020
Thursday, December 3, 2020

Agenda

Virtual Fall Meeting 2020

DAY 1: 1 December

11:00-11:05 am EST	**Welcome and Opening Remarks** Dr. Hungyun Lin, President NESOT https://aim-hq.webex.com/aim-hq/onstage/g.php?MTID=ebea1a675fb30f051b049507aeb43fc90 Event number: 172 437 8714 Event password: SoT2020 Call-in toll-free number (US/Canada)1-866-469-3239 Call-in toll number (US/Canada) +1-650-429-3300
11:05-12:00	**Graduate Student Oral Presentation**
12:00-1:30	**Student and Postdoctoral Poster Session** https://us02web.zoom.us/j/88292697434?pwd=bDRha0JGOURrOFh2T0tLSU5MM2Fvdz09 Meeting ID: 882 9269 7434 Passcode: 585965

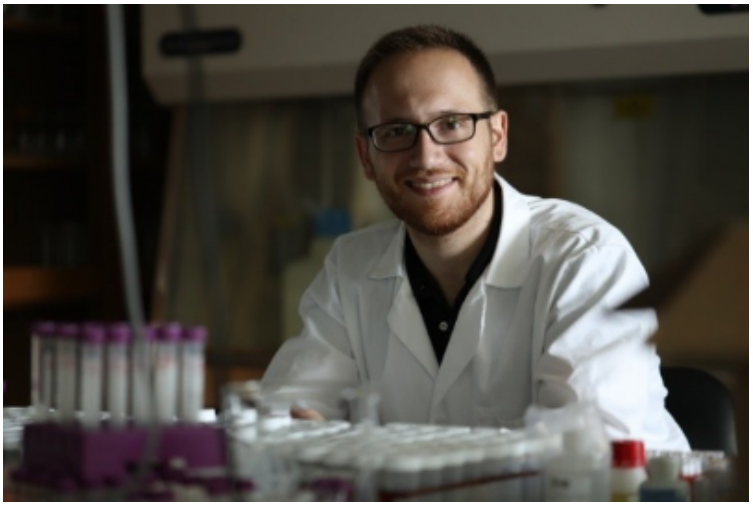
DAY 2: 3 December

11:00 am EST	**Welcome and Opening Remarks** Dr. Hungyun Lin, President NESOT https://aim-hq.webex.com/aim-hq/onstage/g.php?MTID=e64a377d59772bb7a9c70aab62d97064a Event number: 172 296 6423 Event password: SoT2020 Call-in toll-free number (US/Canada)1-866-469-3239 Call-in toll number (US/Canada) +1-650-429-3300
11:05-12:00	**Keynote Presentation** **Dr. Elias Oziolor, Principle Computational Toxicologist, Pfizer**
12:00-1:00	**Expert Panel and Breakout Sessions** https://us02web.zoom.us/j/84842543327?pwd=MXZ6aWg5dDhtK245SEpDQ2lhM2pZZz09 Meeting ID: 848 4254 3327 Passcode: 210421
1:00-1:15	**Awards Ceremony** https://aim-hq.webex.com/aim-hq/onstage/g.php?MTID=e64a377d59772bb7a9c70aab62d97064a Event number: 172 296 6423 Event password: SoT2020

KEYNOTE PRESENTATION

Dr. Elias Oziolor (Principle Computational Toxicologist, Pfizer)

"COMPUTATIONAL TOXICOLOGY IN DRUG DEVELOPMENT"



Biographical Sketch: Elias Oziolor graduated with a bachelor's degree in Biology and Biochemistry from DePauw University in 2012. He then continued to a Ph.D. at Baylor University, where he explored the mechanism and evolutionary history of adaptive resistance to chronic industrial contaminants in the Gulf killifish in the Houston Ship Channel. He extended his research in a postdoctoral fellowship at University of California at Davis to understand the genomic impacts underlying population collapse of Pacific Herring in Prince William Sound following the Exxon-Valdez oil spill. Currently, Elias is a computational toxicologist in Drug Safety Research and Development at Pfizer. His work employs computational and statistical approaches to understanding mechanisms of toxicity and improving translatability between preclinical and clinical studies.

Abstract: The study of toxicology is rapidly expanding and becoming more relevant across the world. This includes the impact of a highly urbanized locations on environmental and human health, the push to produce safer chemicals and pharmaceuticals and do this faster and more effectively, and the evaluation of the residual damage of contaminated environments over time. The ability of toxicologists to leverage the latest technologies in sequencing, high-throughput screening and available databases is becoming crucial for gleaning insight into the inner works of new chemical modalities. In this keynote, I will highlight the importance of computational methods on improving the scope of toxicological insight and driving the automation of current work. I will cover some of the best ways to acquire and master computational skills quickly, while learning to apply them to relevant projects.

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Expert Panelists

Address: https://us02web.zoom.us/j/84842543327?pwd=MXZ6aWg5dDhtK245SEpDQ2lhM2pZZz09
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Expert	Organization	Role	Sector
Sarah Campion	Pfizer, Inc.	Senior Principal Scientist	Industry
Robert Casillas	Latham BioPharm Group	Nonclinical & Animal Health Consulting, Reserve Colonel in the Army	Consulting
Erin Hines	EPA	Biologist, Principal investigator, Reproductive Toxicology	Government
Vivek Kadambi	Blueprint Medicines	Senior Vice President	Industry
Swetha Rudraiah	University of Saint Joseph	Assistant Professor	Academia
Jessica Sapiro	Takeda	Scientist II Toxicology	Industry
Andrew Sonderfan	Nonclinical Strategies LLC	Senior Consultant	Consulting
Dan Spade	Brown University	Assistant Professor	Academia
Matthew Taylor	DuPont	Associate Environmental, Health and Safety Product Stewardship Manager	Industry

Graduate Student Presentations

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Regulators turned renegade: BDE-47, BPS, and TBBPA permanently alter mouse pituitary transcriptome and endocrine feedback when exposed developmentally.

Joshua P Mogus* and Alexander Suvorov
Department of Environmental Health Sciences, School of Public Health and Health Sciences, University of Massachusetts, Amherst, MA, USA

Environmental contaminants are ubiquitous, and many structurally different chemicals are known to be endocrine disrupting chemicals (EDCs). When exposed in critical stages of development, these chemicals can alter normal hormone signaling and lead to permanent changes in gene expression leading to endocrine disease. Many EDCs have been studied for their direct effects on endocrine organ development and function. However, few studies address how EDCs can deter endocrine feedback regulation at the level of the pituitary, where disturbances may offset hormone control for the whole body. Here we evaluate the long-term expression changes in mouse pituitary to BDE-47, BPS, and TBBPA, three EDCs routinely found in the human exposome. Pregnant CD-1 mice were treated daily with environmentally relevant doses of individual EDCs from pregnancy day eight to the end of nursing. Pituitaries were collected from offspring at the age of 20 weeks and analyzed for global gene expression via RNA sequencing. Bioinformatic analysis showed that developmental exposure of BDE-47 suppressed adult pituitary thyroid hormone signaling pathways as well as TGF-β and Wnt/β-catenin pathways. BPS treatment reduced activity of gonadal axis signaling hormones and growth hormone expression, while TBBPA reduced amino acid and oxidative phosphorylation function. Importantly, BPS and BDE-47 had convergent disruption of innate and adaptive immune cell signaling, inhibition of NF-kB pathways, and reduction of intracellular signal transduction molecules associated with G-protein – coupled receptors. This study reveals both unique and shared disruption of three structurally different EDCs on long term pituitary function and endocrine feedback regulation.

Antimicrobial agent cetylpyridinium chloride interferes with phosphatidylinositol 4,5-bisphosphate-protein interactions in influenza infection fibroblast model and in mast cells

Prakash Raut, Sasha Weller*, Bright Obeng, Bailey West, Christian Potts, Suraj Sangroula, Marissa Kinney, Jack Burnell, Dr. Julie Gosse and Dr. Samuel Hess
*presenter and co-first author
University of Maine, Orono, ME 04469

The COVID-19 pandemic raises significance for a potential influenza therapeutic compound, cetylpyridinium chloride (CPC), a positively-charged quaternary ammonium antibacterial agent. Recent studies indicate that CPC may alleviate influenza infection, and CPC is currently in clinical trials to assess its effects on severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) morbidity. However, there is a dearth of information regarding the mechanism of how CPC might affect virus-host interaction or immune cell function. Previous studies showed the importance of clustering of influenza viral protein hemagglutinin (HA) and interaction of HA with of negatively-charged mammalian lipid phosphatidylinositol 4,5-bisphosphate

(PIP2), for influenza infection. Here we present super-resolution microscopy data indicating that CPC (at non-cytotoxic doses, 5-10 μM) reduces HA density and number of HA molecules per cluster within the NIH-3T3 fibroblast plasma membrane, while also destabilizing clusters of PIP2, which is also a key player in immune cell signaling. Furthermore, we have found that CPC interferes with membrane localization of three different PIP2-binding proteins: along with HA, myristoylated alanine-rich C-kinase substrate (MARCKS) and Pleckstrin homology domain in both mammalian fibroblasts and mast cells. This disruption of PIP2 is correlated with inhibition of mast cell function, beginning at 1 μM CPC. Nanoscale co-localization of HA with PIP2, in the plasma membrane, is drastically reduced by CPC, offering a mechanism underlying CPC disruption of influenza. Acquired results inform safe CPC dosage levels in OTC products but also potential pharmacological use of this drug as an influenza therapeutic to reduce global deaths from viral disease.

A lipid formulation-based approach for overcoming cisplatin- resistance in triple negative breast cancer.

Nandini Gandhi*1, Shail Modi1, Terrick Andey1
1- Department of Pharmaceutical Sciences, MCPHS University, MA, 01608.

Cisplatin, a platinum-based antineoplastic drug is widely used in the treatment of various cancers. Tumor resistance, as well variability in patient response to cisplatin in the triple-negative breast cancer (TNBC) subtype limits its clinical use and long-term efficacy. This study proposes a formulation-based approach to improving therapeutic outcomes with cisplatin using a self-emulsifying drug delivery system (SEDDS). Cisplatin-SEDDS formulations (Cis-SEDDS) were prepared and characterized according to particle size, polydispersity, and zeta potential. SEDDS were optimized using pseudo-ternary phase diagrams to facilitate self-emulsification of Labrafac PG, Labrasol, and Gelucire 44/14, without and with Compritol (Cis-SEDDS 1) and (Cis-SEDDS 2) respectively in water. MDA-MB-468 TNBC cells were treated with dilutions of cisplatin solution and Cis-SEDDS for 48 h. Cell viability was investigated using resazurin dye assay and results presented as average cell viability±SEM. Stable emulsification was achieved for both formulation types with up to 60% (w/w) oil phase for at least 10 days. SEDDS ranged in size, PDI, and surface charge from 174 – 221 nm, 0.153 – 0.207, and -6.87 – -7.29 mV, respectively. Average cell viability was decreased across dilutions by Cis-SEDDS 1 (94%) and Cis-SEDDS 2 (90%), compared to cisplatin solution (99%). At 10 μM, significant inhibition of cell viability was observed for Cis-SEDDS 2 (85%) compared to Cis-SEDDS 1 (94%) and cisplatin solution (92%). Cis-SEDDS 2 significantly inhibited MDA-MB-468 cell viability, potentially through the sustained-release of cisplatin by Compritol. A SEDDS formulation approach may be useful in enhancing the anticancer effects of chemotherapeutics such as cisplatin and rescuing from tumor resistance.

Listing of Posters

Recordings of posters can be accessed at this website: https://www.pulse-community.org/nesot

The poster session will be hosted as a series of breakout rooms for discussions between the authors and conference attendees.

https://us02web.zoom.us/j/88292697434?pwd=bDRha0JGOURrOFh2T0tLSU5MM2Fvdz09

Meeting ID: 882 9269 7434
Passcode: 585965

#	Undergraduate Student Posters
1	**Role of Nfe2 during inner ear development and the oxidative stress response of larval zebrafish (Danio rerio)** Hannah Neiditz1*, Ana Verma1, Larissa M. Williams2, Josef G. Trapani1 1Amherst College, Amherst, MA 2Bates College, Lewiston, ME
2	**Disease Categories Associated with Pathways and Genes Highly Sensitive to Chemical Exposure** Victoria Salemme*, Alexander Suvorov University of Massachusetts Amherst, Department of Environmental Health Sciences

#	Graduate Student Posters
3	**Repurposing Small Drug Molecules for Tissue Regeneration: Vascular Development** Dominic Alfano*, Philippe Recalt, Sama Abdulmalik, Sangamesh G. Kumbar, Swetha Rudraiah Department of Pharmaceutical Sciences, University of Saint Joseph, West Hartford, CT Department of Orthopedic Surgery, University of Connecticut Health, Farmington, CT
4	**Effects of racetam nootropic/anti-seizure drugs on DHFR and ACHE enzymatic activity in zebrafish (Danio rerio) embryos** Sam Arami*, Jung Ho Kim*, and Paul V. Kaplita, Department of Pharmaceutical Sciences, MCPHS University, Worcester, MA 01608
5	**Synergy in gene expression affected by chemicals and COVID-19** Olatunbosun Arowolo*, Alexander Suvorov Department of Environmental Health Sciences, University of Massachusetts, Amherst
6	**Daily Variation of Air Pollutants Near an Elevated Highway System in Syracuse, NY** Coleman, Shelby S (1)*, Mirowsky, Jaime E (1), Zhang, Jianshun (2), and Kong, Meng(2) (1) SUNY ESF, 1 Forestry Dr, Syracuse, NY 132101 (2) Syracuse University, 900 S Crouse Ave, Syracuse, NY 132442
7	**Increased expression of TIMP4/MAOA and associated proteins implicated in the severity of COVID-19 symptoms in older patients** Jeihun Kuack MCPHS University

8	**Iron promotes cardiac doxorubicin retention and toxicity through downregulation of the efflux transporter ABCB8** Archita Venugopal Menon*, Jonghan Kim
9	**PBMC cells derived from COVID-19 patients: Circadian Rhythm, Phosphatidylinositol signaling and Cytokine Storm** Shail Modi*1, Hoeyeon Lee1, George Acquaah-Mensaah1 1-Department of Pharmaceutical Sciences, MCPHS University, MA, 01608
10	**Antimicrobial Agent Cetylpyridinium Chloride Inhibits Immune Mast Cell Function** Bright Obeng*, Bailey E. West, Marissa S. Kinney, Christian M. Potts, Suraj Sangroula, Sasha R. Weller, Alan Y. Baez, Julie A. Gosse Department of Molecular and Biomedical Sciences, University of Maine, Orono, ME 04469, USA
11	**Effects of Multiwalled Carbon Nanotubes on Immune Cells in a Hepatocyte co-culture Setup In Vitro** Philippe Recalt*, Dominic Alfano, Rosalie Bordett, Sangamesh G. Kumbar, Swetha Rudraiah Department of Pharmaceutical Sciences, University of Saint Joseph, West Hartford, CT Department of Orthopedic Surgery, University of Connecticut Health, Farmington, CT

#	**Postdoc Posters**
12	**4-hydroxynonenal inhibits pyroptosis by blocking inflammasome activation and gasdermin D pore formation in macrophages** Chia George Hsu*, Mark Sowden, Bradford C. Berk Department of Medicine, Aab Cardiovascular Research Institute, University of Rochester School of Medicine and Dentistry, Rochester, NY, USA

NESOT Officers 2020-2021

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