ABSTRACT NUMBER: 3575 **Poster Board Number:** P372

TITLE: Circulating Biomarkers of Neurotoxicity: Identifying Fluidic Endpoints Correlating with Central Nervous System Toxicity in a Rodent Model of Neurotoxicity

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ABSTRACT: Neurotoxicity has been linked to exposure to a number of common drugs and chemicals, yet efficient, predictive, and minimally-invasive methods to detect it are lacking. Fluid-based biomarkers such as those found in serum, plasma, urine, and cerebrospinal fluid (CSF) have great potential due to the relative ease of sampling, but at present, data on their expression and translation are lacking or inconsistent. Here, we present data on biomolecules that have some promise for detection and characterization of neurotoxicity induced by a single intraperitoneal injection of the known neurotoxic agent, trimethyltin (TMT). A single dose of TMT led to significant alterations in total oxidative stress markers, changes in lipid homeostasis, circulating interleukins and related factors, and markers of neuroinflammation. These findings provide an opportunity to explore the correlation of these fluid biomarkers with traditional neuropathology and magnetic resonance imaging (MRI) that serve to define TMT-induced neurotoxicity. Our data demonstrate a comprehensive correlation of TMT-induced neuropathology with several potential neurotoxicity biomarkers and MRI-based endpoints, findings suggestive of an involvement of specific pathways that can be assessed using peripheral fluids.

ABSTRACT NUMBER: 3576 **Poster Board Number:** P373

TITLE: An Evaluation of *In Silico* Predicted Neurotoxicity in Embryonic Rat Dorsal Root Ganglion (DRG) Cultures: Effects on Cytotoxicity, Neurite Length, and Neurophysiology

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KEYWORDS: Neurotoxicology; Toxicity; Acute; Predictive Toxicology

ABSTRACT: Numerous chemicals are proposed to produce non-receptor/ion-channel mediated neurotoxic responses through adverse interactions with intracellular proteins and macromolecules. These molecular initiating events may induce an adverse outcome pathway (AOP) that can hinder synaptic nerve terminal protein function and result in peripheral neuropathy. To test the Hard-Soft Acid and Base (HSAB) hypothesis which is based on the potential chemical bio-reactivity (electrophilicity) to cause a neuropathic effect, a test set of chemicals from the USEPA ToxCast database was evaluated *in vitro* in DRG cultures. Chemicals predicted to be neurotoxic were tested acutely, using a 3-tiered assessment of: 1. Cytotoxicity (% lactate dehydrogenase (%LDH) release); 2. Structural alteration (total neurite length per neuron via high content microscopy) and 3. DRG neurophysiology, as measured by mean firing rate (MFR), recorded on microelectrode arrays. DRG primary cultures were generated from

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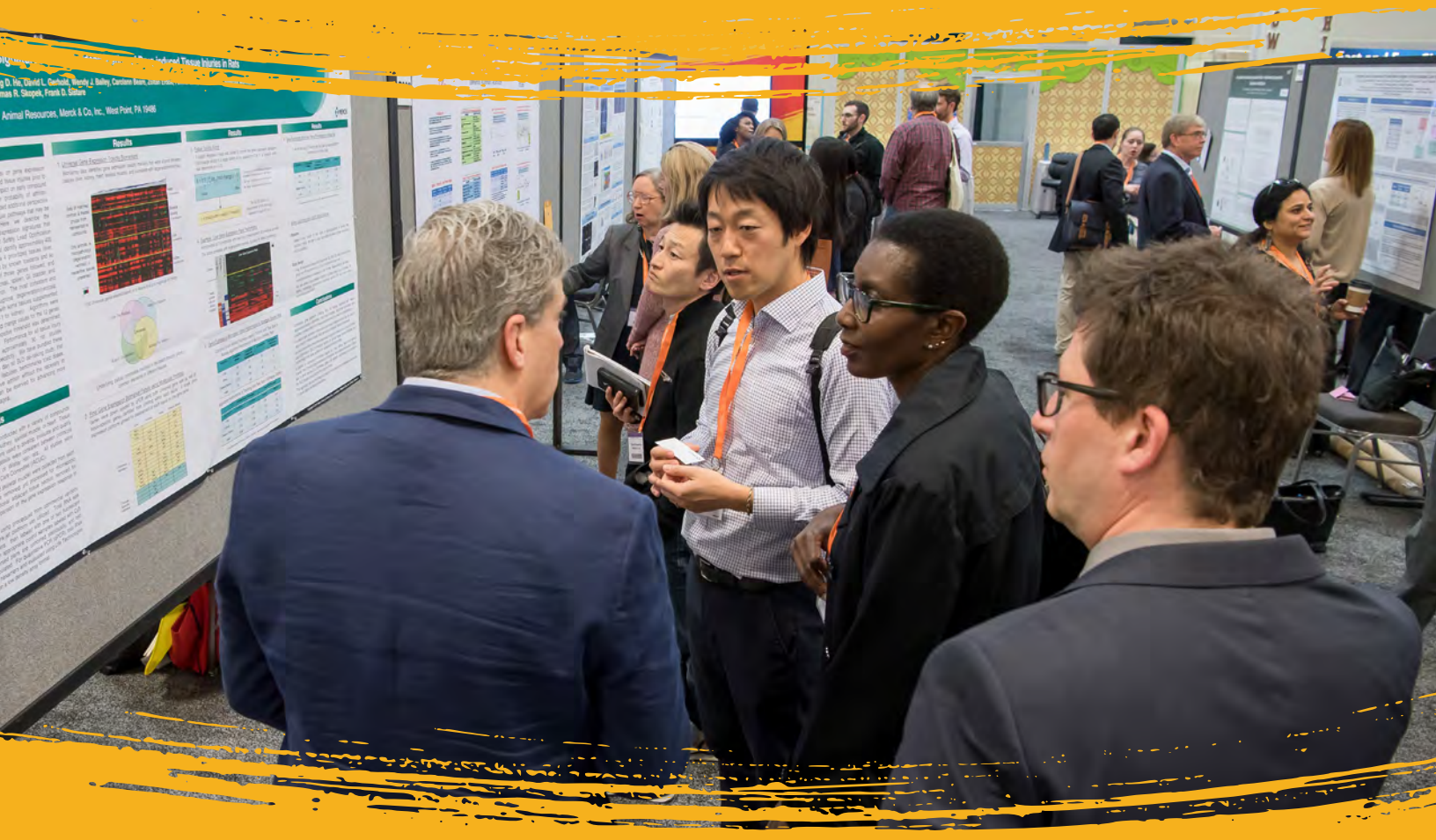

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