Abstract 376 — Oral Presentation: Session II-1b "Pathways Approach in Toxicology"

Constructing, Quantifying, and Validating an Adverse Outcome Pathway for Vascular Developmental Toxicity

N Kleinstreuer*[1], T Knudsen[2], T Tal[3], T Heinonen[4], J Franzosa[2], N Baker[5], S Padilla[3], E Carney[6], W Casey[7]

[1]ILS/NICEATM, RTP, NC, USA; [2]U.S. EPA/ORD/NCCT RTP, NC, USA; [3]U.S. EPA/ORD/ISTD, RTP, NC, USA; [4]FICAM, University of Tampere, Tampere, Finland; [5]Lockheed-Martin/EPA contractor, RTP, NC, USA; [6]The Dow Chemical Company/Predictive Toxicology Division, Midland, MI, USA; and [7]NIH/NIEHS/DNTP/NICEATM, RTP, NC, USA.

**Presenting author*

Abstract

Embryonic vascular disruption (1) leads to a range of adverse prenatal outcomes. The adverse outcome pathway (AOP) for embryonic vascular disruption was recently entered into the AOP wiki and accepted as part of the OECD workplan. The AOP was built based on molecular initiating events (MIEs) affecting genes from critical pathways (hypoxia/growth factor signaling, chemokine networks, extracellular matrix interactions and vessel remodeling/stabilization) with evidence of abnormal embryonic vascular development in the mammalian phenotype browser of the Mouse Genome Informatics database (http://www.informatics.jax.org/). EPA ToxCast high throughput screening data (2) for assays mapping to targets in the AOP were used to prioritize >1000 chemicals for their potential to disrupt vascular development. A subset of these chemicals are being tested for developmental effects across a wide range of vascular-specific model systems. Preliminary results from functional validation of AOP targets, quantification of MIEs and key cellular events (3), and compound hazard predictions will be discussed. *This abstract does not necessarily reflect EPA policy.* *This project was funded in whole or in part with Federal funds from the EPA, CSS Research Program, Lockheed-Martin contracting, and NIEHS, NIH under Contract No.HHSN27320140003C.*

References

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