USING ZEBRAFISH TO UNDERSTAND MECHANISMS OF BENZO[A]PYRENE

Kristine L. Willett, Cammi Thornton, Xiefan Fang and Jone Corrales

Department of BioMolecular Sciences, School of Pharmacy, University of Mississippi, University, Mississippi, USA

Abstract: Benzo[a]pyrene (BaP) is a well-known but mechanistically complicated carcinogen, reproductive and developmental toxicant. In zebrafish (*Danio rerio*), waterborne or dietary BaP/PAH exposure causes developmental adverse outcomes including growth reduction, neonatal death, cardiac dysfunction, skeletal abnormalities, craniofacial and fin deformities. Likewise, in humans, perinatal PAH exposure causes neural tube, cardiovascular and craniofacial defects, lower gestational size and birth weights, but the persistent consequences of fetal BaP exposure in adults or future generations are less clear. We have found using zebrafish that multigenerational developmental impacts are present in F1 and F2 offspring after parental only BaP exposure. BaP developmental exposure causes significant changes in gene expression when considering the transcriptome. Also global methylation status is decreased in BaP-treated larvae, but the causative role of methylation changes on gene specific effects has been more difficult to establish. Yet using morpholino approaches, like a Cyp19a1b-morpholino, to transiently knockdown protein expression, we established the role of aromatase inhibition as a relevant mechanism in BaP's developmental toxicities. Collectively, this presentation will bring together promoter methylation and transcriptomic changes in developing zebrafish after early life BaP waterborne exposure to predict how these changes may lead to immediate, long-term, and multigenerational toxicities and how these results can contribute to an adverse outcome pathway for BaP-mediated developmental toxicity.