Zebrafish offer one of the most promising alternative and cost-effective vertebrate models for predicting prenatal developmental toxicity and fish early life-stage toxicity. Despite significant advancements over the last 10-15 years, targeted assays using zebrafish are needed to better evaluate effects of chemicals on organogenesis and begin classification of chemicals by toxicologically relevant modes-of-action. To this end, using transgenic zebrafish (fl1:egfp) that stably express eGFP within vascular endothelial cells, we developed and optimized two different 384-well-based high-content screening (HCS) assays that enable us to rapidly screen and identify chemicals impacting cardiovascular and early nervous system development at non-teratogenic concentrations. Following static exposure of one embryo per well starting at 5 hours post-fertilization (hpf), automated image acquisition procedures and custom image analysis protocols are used to quantify total body area and spontaneous activity within unhatched live embryos at 25 hpf, and body length, circulation, heart rate, pericardial area, and intersegmental vessel area within hatched live embryos at 72 hpf. Based on a handful of papers we have published over the last several years (see references below), this seminar will summarize how, compared to existing assays using zebrafish, our HCS assays provide comprehensive discovery platforms with 1) increased sample sizes; 2) broad concentration-response format; and 3) the ability to identify chemicals that target cardiovascular and early nervous system function at non-teratogenic concentrations. Over the long-term, we anticipate that these assays will help prioritize chemicals for hypothesis-driven mode-of-action research as well as uncover mechanisms of developmental toxicity for pesticides, understudied high-production volume chemicals, and field-derived environmental mixtures.

References


Dr. David C. Volz received a PhD in 2006 from Duke University’s Nicholas School of the Environment with a Certificate in Toxicology from Duke’s Integrated Toxicology and Environmental Health Program. Following completion of his PhD, Dr. Volz spent three years as a Toxicologist within the Product Safety/R&D division of Syngenta – a Switzerland-based global seeds and agrochemical company – where, among other responsibilities, he led multidisciplinary project teams that supported early- and late-stage product development, regulatory issues, and new business opportunities. In August 2009, Dr. Volz returned to academia as a tenure-track Assistant Professor of Environmental Health Sciences within the Arnold School of Public Health at the University of South Carolina, Columbia. In July 2015, he relocated to the University of California, Riverside as a tenure-track Assistant Professor (Step V) of Environmental Toxicology within the Department of Environmental Sciences. Using zebrafish as a model, Dr. Volz’ long-term research goal is to identify xenobiotic-mediated pathways that contribute to adverse outcomes during early vertebrate development, particularly for understudied high-production volume chemicals. He has authored or co-authored 36 peer-reviewed papers, one book chapter, and presented at numerous national and international meetings on topics ranging from toxicology, high-content screening, molecular biology, chemicals policy, and animal alternatives. Since 2009, Dr. Volz has been actively involved in global, cross-sector efforts to promote development of tiered strategies for regulatory toxicity testing, and has participated in several related expert workshops sponsored by the Society of Environmental Toxicology and Chemistry (SETAC) and ILSI Health and Environmental Sciences Institute (HESI). In addition, Dr. Volz is an Associate Editor for Chemosphere and serves on the Editorial Advisory Board of Environmental Science & Technology Letters, Neurotoxicology and Teratology, and Environmental Toxicology and Chemistry. Dr. Volz’ teaching interests are focused on environmental health, toxicology, and chemical risk assessment, and he has also taught international workshops on risk assessment for industry, government, and academia.