In vivo Toxicity Testing

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Office of Research and Development

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Goals

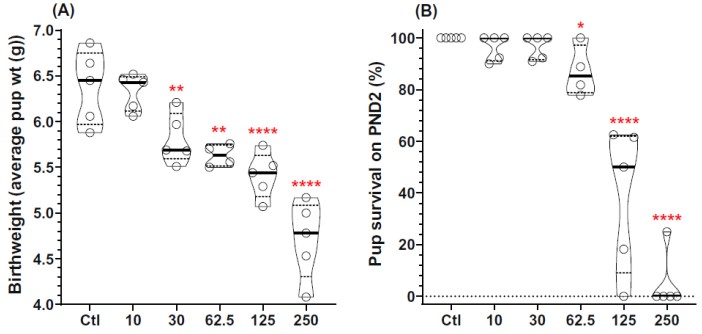
- In vivo developmental, liver, thyroid, or immune endpoints are the basis for essentially all risk assessment points-of-departure
- Unstudied PFAS have been detected in human serum and/or drinking water
- Monitoring studies consistently demonstrate co-exposure to multiple PFAS
- ORD research filling data gaps to:
  - Generate toxicity data for unstudied PFAS with human exposure
  - Characterize Adverse Outcome Pathways associated with exposure during pregnancy
  - Investigate cumulative effects of co-exposure to multiple PFAS
  - Evaluate PFAS estrogenicity in vivo
  - Evaluate how changes in thyroid hormones relate to functional deficits
- Results will advance PFAS toxicology, strengthen scientific basis of state/federal PFAS risk assessments, and provide data to inform PFAS regulatory actions

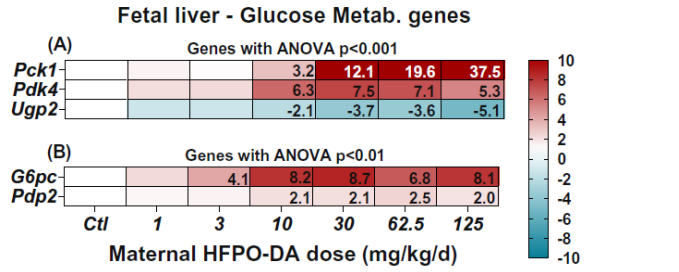
Approach

- ORD in vivo research largely focused on oral exposure to PFAS during pregnancy
- Hypothesis-driven study designs with measurement of critical key events and adverse outcomes in maternal and F1 animals
  - Organ weights, viability, clinical chemistry
  - Thyroid hormone concentrations
  - Test compound concentrations
  - Tissue-specific gene expression
  - Histopathology
  - Studies largely conducted in dose response across a range of legacy and emerging PFAS
- Novel data-rich approaches included such as RNA-Seq, targeted metabolomics, and multiple confocal microscopy

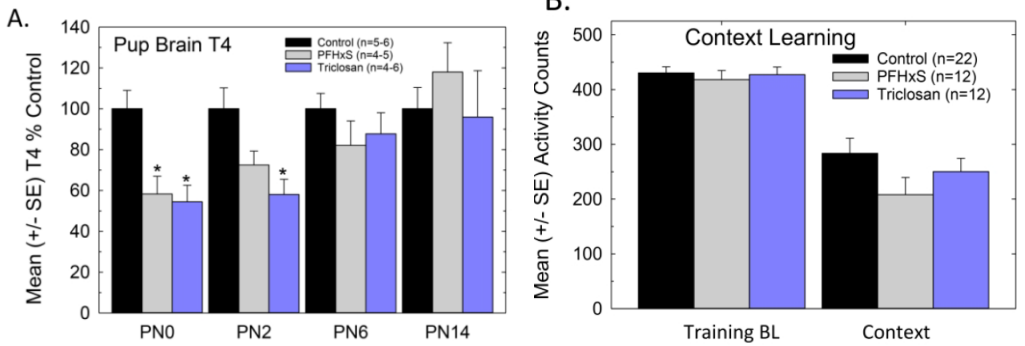
Current Status

- **Publications to-date:**
  - Conley et al. 2019. Adverse maternal, fetal, and postnatal effects of hexafluoropropylene oxide dimer acid (GenX) from oral gestational exposure in Sprague-Dawley rats. doi: 10.1289/EHP4372
  - Conley et al. 2021. Hexafluoropropylene oxide dimer acid (HFPO-DA or GenX) alters maternal and fetal glucose and lipid metabolism and produces neonatal mortality, low birthweight, and hepatomegaly in the Sprague-Dawley rat. doi: 10.1016/j.envint.2020.106204.
  - Gilbert et al., 2021. Thyroid Disruptors: Extrathyroidal Sites of Chemical Action and Neurodevelopmental Outcome-An Examination Using Triclosan and Perfluorohexane Sulfonate. doi: 10.1093/toxsci/kfab080.
- **Completed and on-going studies with anticipated publications**
  - RNA-Seq of the developing rat brain and liver following maternal PFHxS exposure
  - Developmental toxicity of Nafion byproduct 2, PFMOAA, and two PFAS mixture studies
  - Uterotrophic studies of several ER active PFAS





Conley et al., 2021 doi: 10.1016/j.envint.2020.106204



Gilbert et al., 2021 doi: 10.1093/toxsci/kfab080

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