Pacific Northwest NATIONAL LABORATORY

Oregon State University

PAHs: New Technologies and Emerging Health Risks

Robyn Leigh Tanguay
Director and Project Lead

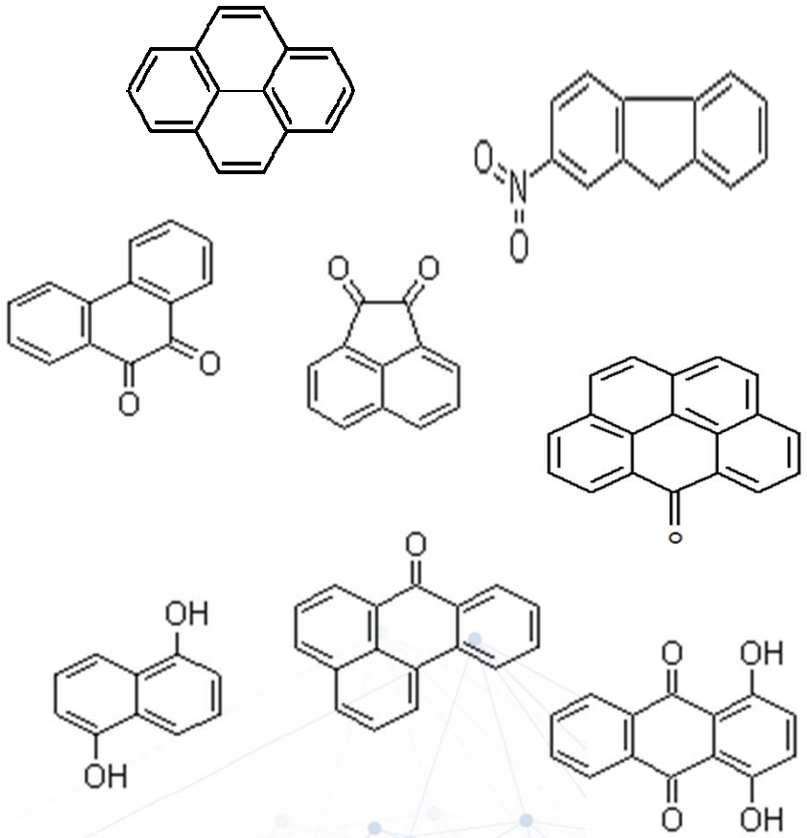
The Problem

- Approximately 53 million people live within 3 miles of a Superfund site.
- PAHs are 3 of the top 10 ATSR Priority List of Hazardous Substances
- More than 100 parent PAH compounds
- Unknown number of PAH derivatives and metabolites
- Parent PAHs arise from industrial processes and from extraction and burning of fossil fuels
- PAHs typically exist in complex environmental mixtures
- Substantially higher concentrations of PAHs in the soil, and water

PAH Health Effects

- Human exposure - primarily via ingestion
- A subset of PAHs are known carcinogens
- The majority of available research in on the US EPA 16 priority PAHs
- Mounting evidence other PAHs are a concern
- Non-cancer affects

Toxicity Mechanisms for Most PAHs Unknown



- Environmentally dynamic
- Parent, substituted compounds
- Toxicity data was scarce for substituted PAHs
- PAHs induce AHR-dependent and AHR-independent developmental toxicity, dependent on structure
- We lack the structural basis to predict toxicity

OSU/PNNL SRP

Overall Mission

Identify polycyclic aromatic hydrocarbons (PAHs) in the environment, to characterize their toxicity, and to specify the levels of those chemicals in the environment below which they pose no threat to human health.

We will supply EPA and other partners with actionable information and with tools that enable them to detect PAHs in the environment, to measure PAH concentrations, and to evaluate remediation.

Overall Center Aims

- Collect PAH mixtures at Superfund sites and assess their toxicity
- Predict and identify new PAH compounds created as a byproduct of remediation at Superfund sites and assess their toxicity.
- Deploy passive sampling technology in a wearable format to assess human PAH exposures.
- Identify gene expression networks targeted by PAH exposure that can serve as early indications of disease.
- Determine how exposure susceptibility across test systems and humans depends upon PAH physicochemical properties, tissue and body composition.

OSU/PNNL Superfund Research Program (SRP):
Polycyclic Aromatic Hydrocarbons: New Technologies and Emerging Health Risks

The mission of the OSU/PNNL SRP is to identify polycyclic aromatic hydrocarbons (PAHs) in the environment, characterize their toxicity, and specify the environmental concentrations below which they pose no threat to human health.

Cores

Administrative Core

Administration

Robyn Tanguay
Director | OSU

Katrina Waters
Deputy Director | PNNL

Research Translation

Stacey Harper
Co-Coordinator | OSU

Diana Rohlman
Co-Coordinator | OSU

Data Management and Analysis

Katrina Waters
Leader | PNNL

Community Engagement

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Co-Leader | OSU

Jamie Donatuto
Co-Leader | Swinomish

Chemical Mixture

Kim Anderson
Leader | OSU

Research Experience and Training Coordination

Andrew Buermeyer
Director | OSU

Craig Marcus
Assistant Director | OSU

Projects

Linking PAH Exposure to Health Outcomes Using Human Primary In Vitro Respiratory Model

Susan Tilton
Leader | OSU

David Williams
Co-Investigator | OSU

Elucidating Metabolic and Physicochemical Mechanisms of PAH Susceptibility in Toxicity Test Systems and Humans

Justin Teeguarden
Leader | PNNL

Jordan Smith
Co-Investigator | PNNL

Predicting the Toxicity of Complex PAH Mixtures

Robyn Tanguay
Leader | OSU

Lisa Truong
Co-Investigator | OSU

Developing and Evaluating Technology to Measure PAH Fate and Exposures

Kim Anderson
Leader | OSU

Identification of Remediation Technologies and Conditions that Minimize Formation of Hazardous PAH Breakdown Products at Superfund Sites

Staci Simonich
Co-Leader | OSU

Lewis Semprini
Co-Leader | OSU

Partners

Oregon State University

Pacific Northwest National Laboratory

EHSC

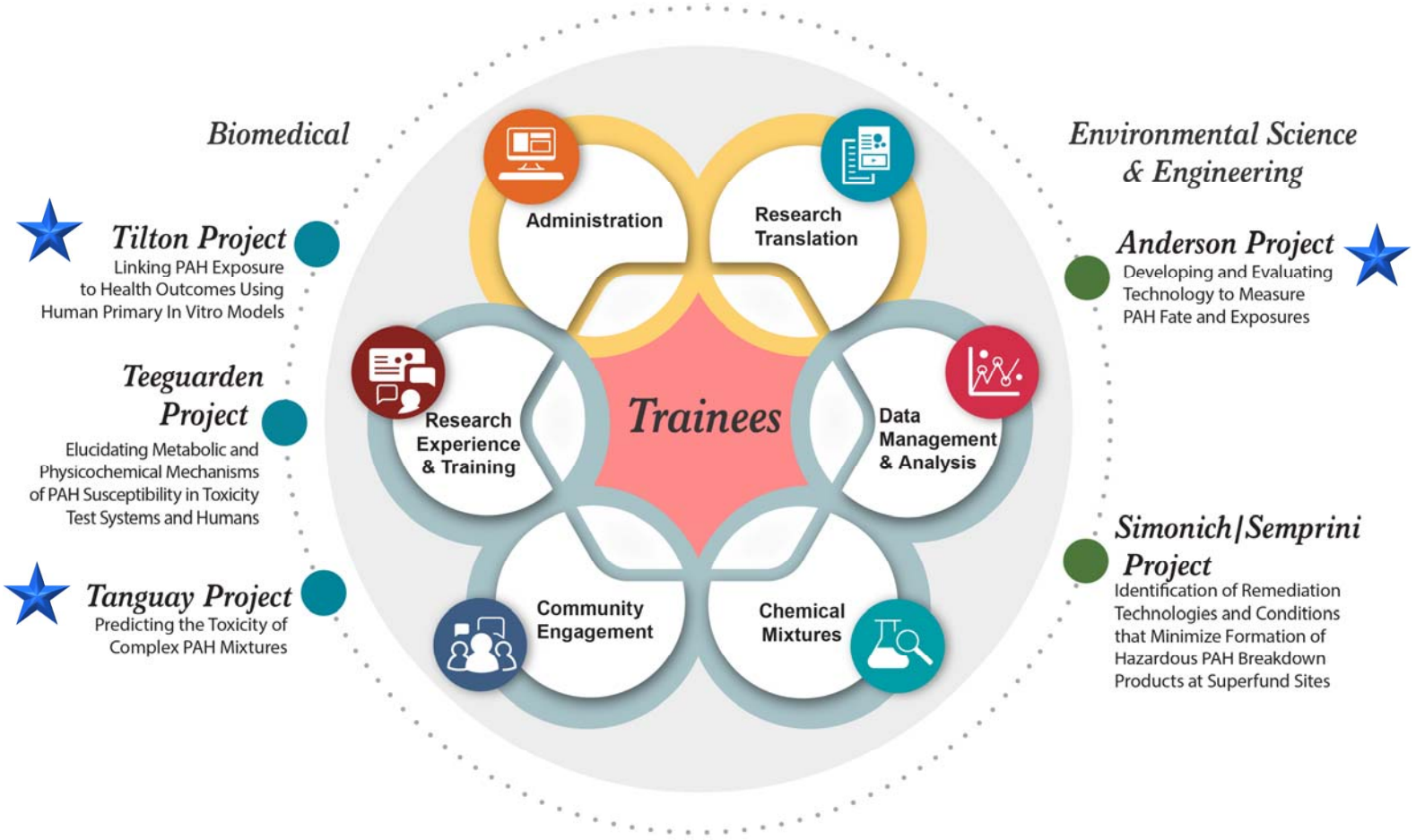
Swinomish Indian Tribal Community

Cayuse – Umatilla – Walla Walla Confederated Tribes of the Umatilla Indian Reservation

NIH National Institutes of Health

Lawrence Livermore National Laboratory

Center Integration



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Predicting the Toxicity of Complex PAH Mixtures

Robyn L. Tanguay

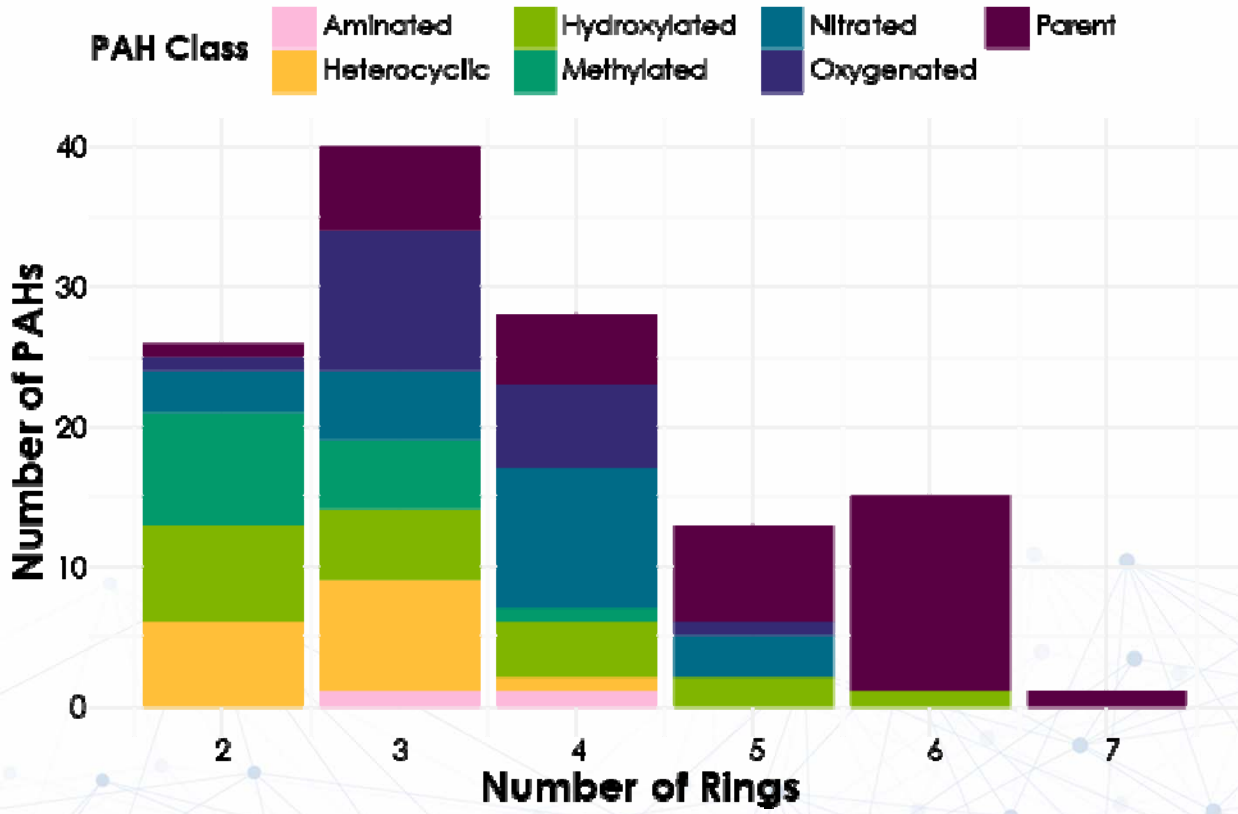
Project Aims

- Determine how the developmental impacts of PAH exposure depend on the composition of PAH mixtures and the chemical structures of environmentally transformed PAHs
- Measure the uptake and metabolism of biologically active PAHs
- Develop diagnostic gene expression pathways for classes of PAHs, determine how those pathways vary as a function of dose
- Determine adult and transgenerational consequences following transient developmental exposures to individual PAHs, real-world mixtures, and model mixtures.

OSU/PNNL SRP

Comparative PAH Toxicity Assessment

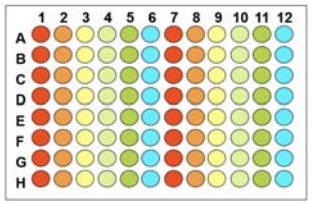
Assembled Library of PAHs for Comparative Analysis



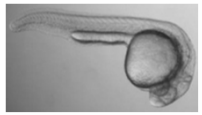
Kim Anderson -
SRP Chemical Mixtures Core

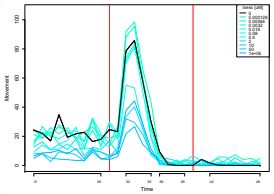
High-Throughput PAH Assessments

6 hpf — 24 hpf — 120 hpf

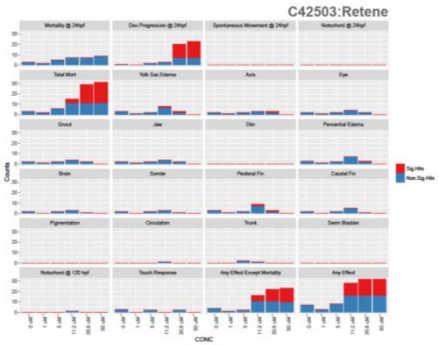


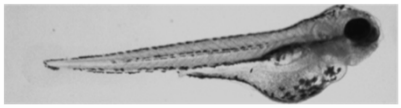
Exposure
- Dechorionated
- 6 hpf to 120 hpf
- 5 concentrations
- N=32/Concentration

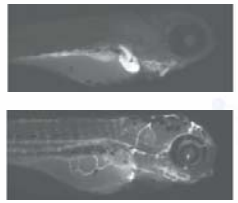




24 hour evaluations
- Behavior
- Morphology

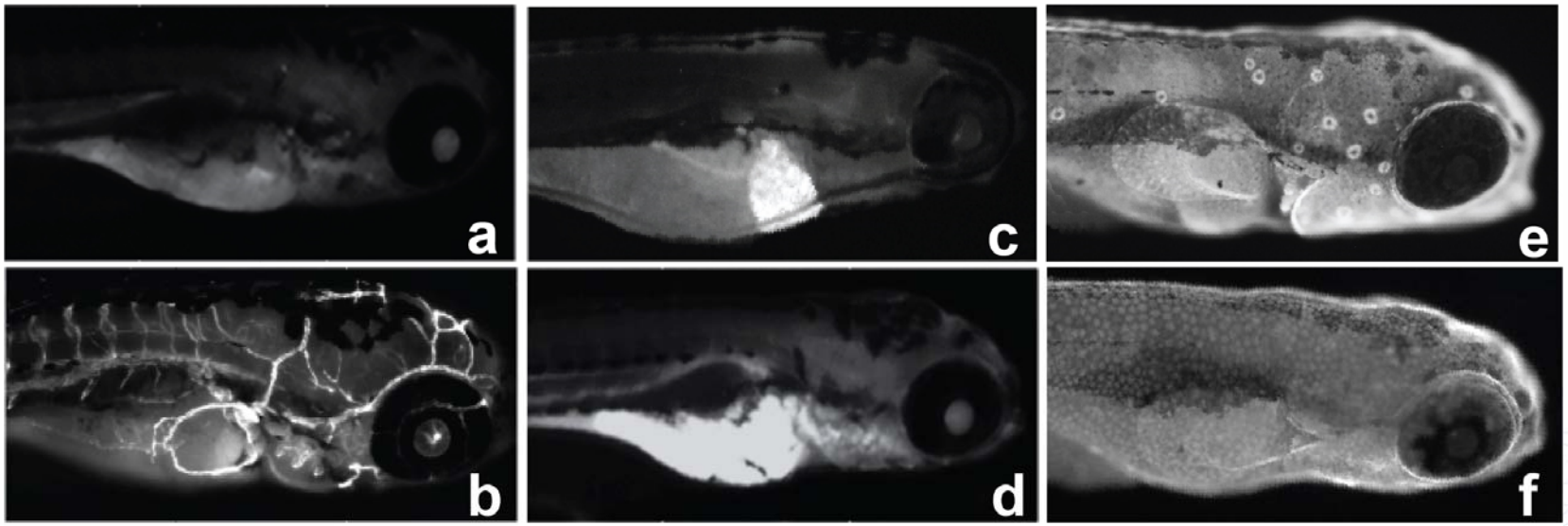






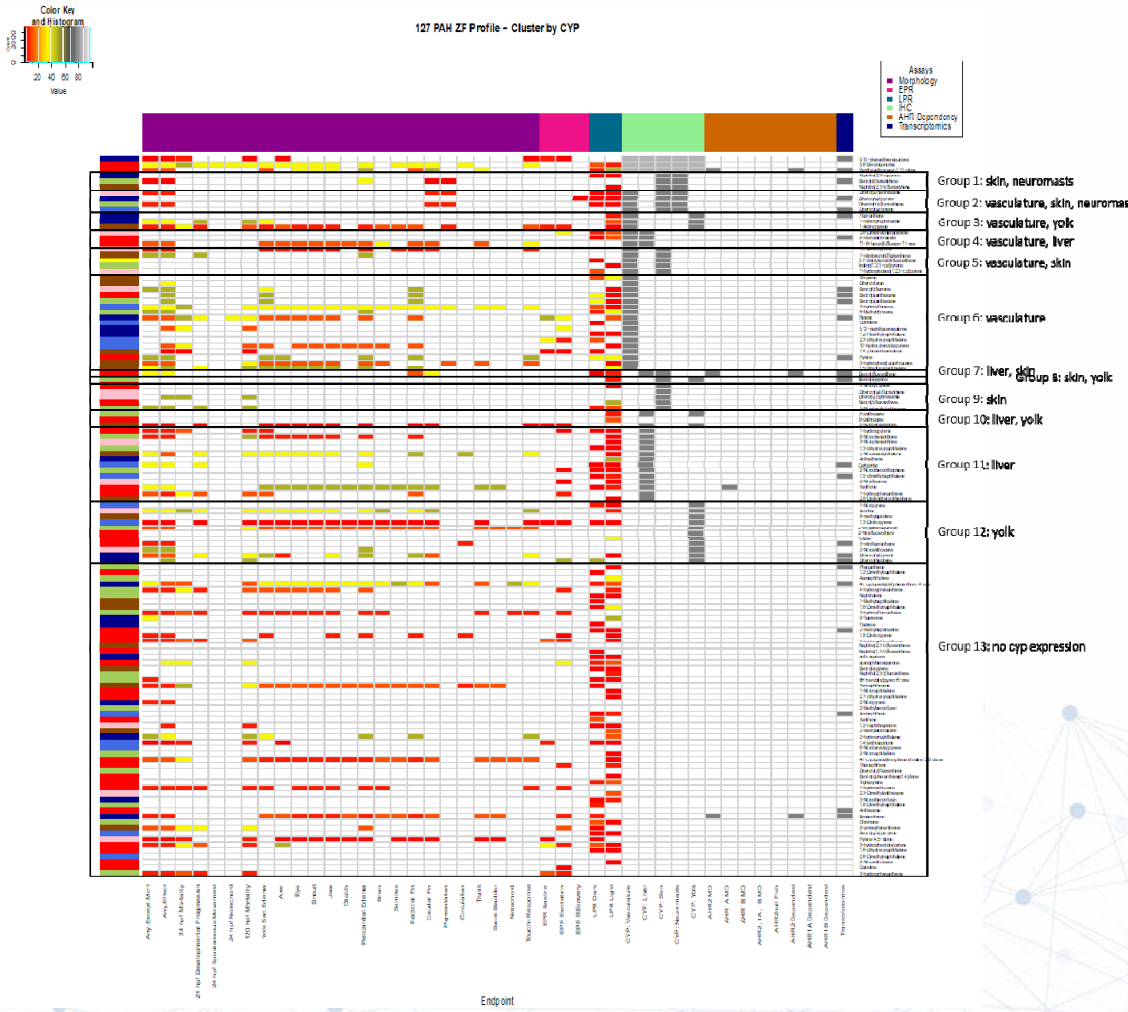
5 day evaluations
- Morphology
- Behavior
- CYP1A Localization

CYP1A Expression Pattern as an Exposure Biomarker of AHR Activation



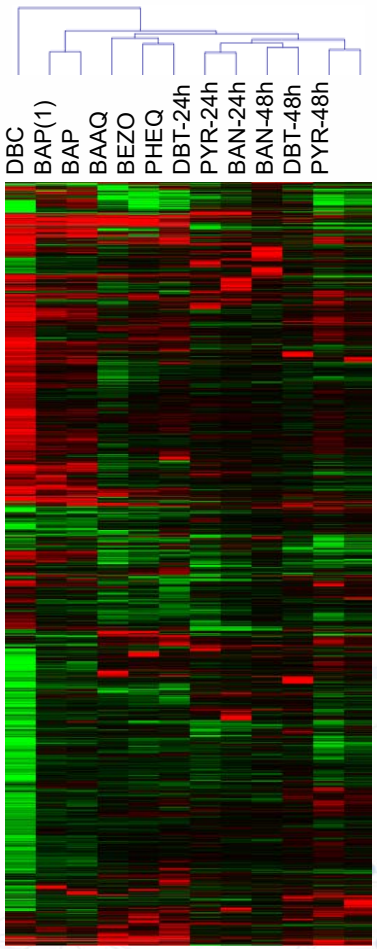
120 hpf

127 PAH Clustered by CYP1A Expression

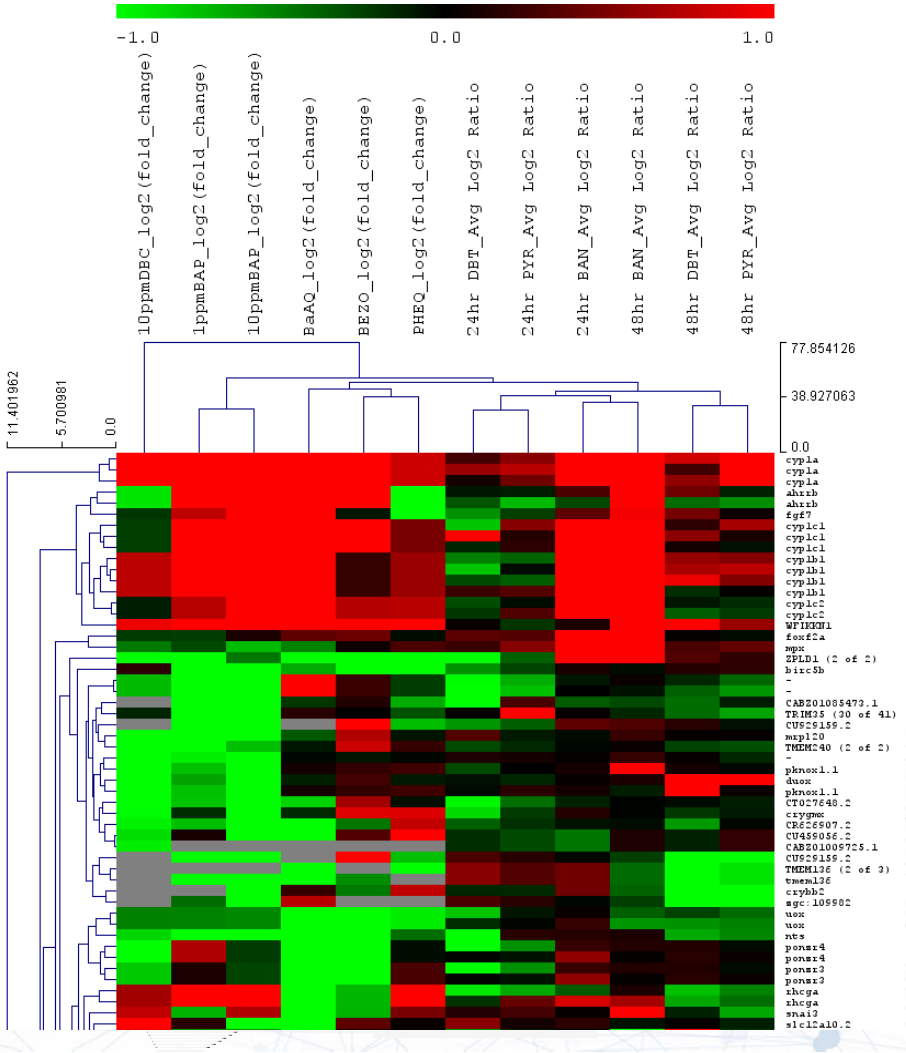


RNA-SEQ Analysis (Embryonic Expression)

OSU/PNNL SRP



Designed to identify **Causal** Changes in gene expression



Measuring Development Origins Of Health Diseases DOHaD

- Swimming activity
- Anxiety
- Aggression
- Social Interactions
- Learning

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Thank you

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