

3,3',4,4',5-Pentachlorobiphenyl (PCB 126) decreased the ratios of epoxide metabolites of unsaturated fatty acids to their corresponding diols in male rodents

Xianai Wu

Postdoctoral Research Scholar

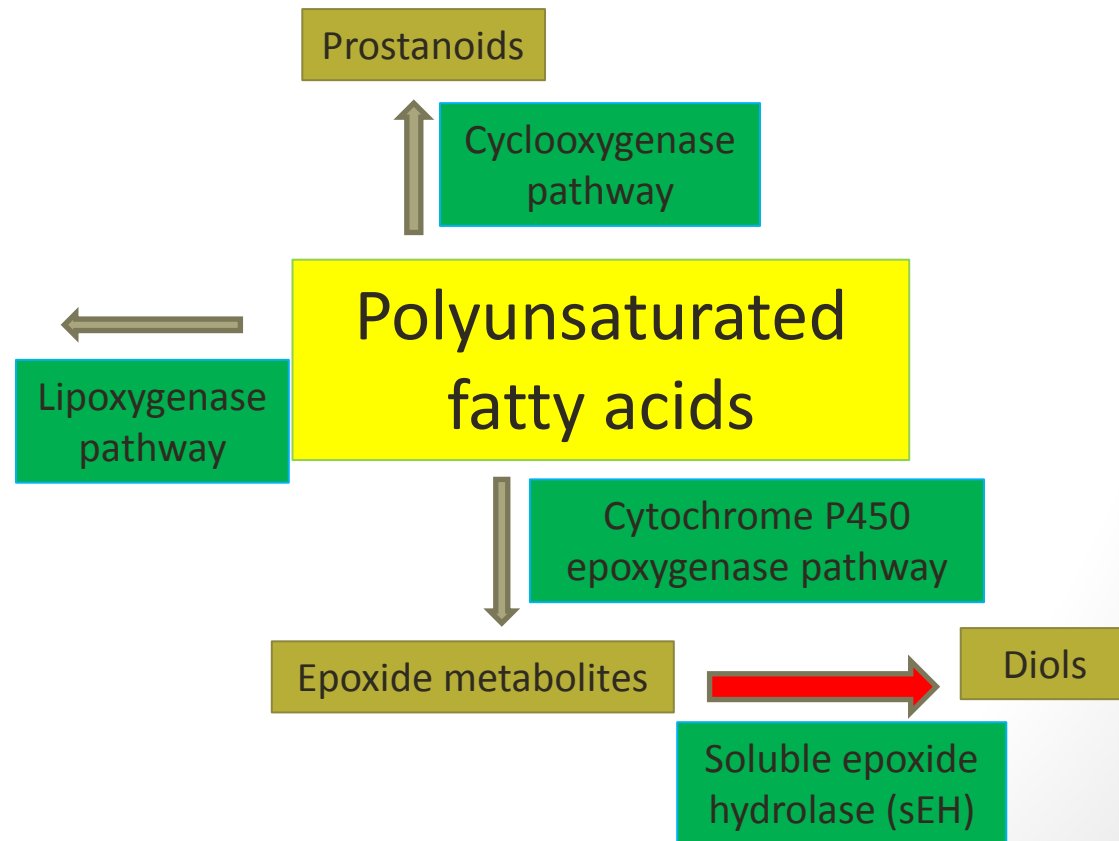
University of Iowa

Department of Occupational and Environmental Health

xianai-wu@uiowa.edu

Background

- 3,3',4,4',5-Pentachlorobiphenyl (PCB 126): Dioxin-like pollutant.
- PCB 126 exposure may affect the global metabolome, including oxygenated metabolites of unsaturated fatty acids (oxylipins).
- Oxylipins: Regulatory lipid mediators implicated in metabolic syndrome.

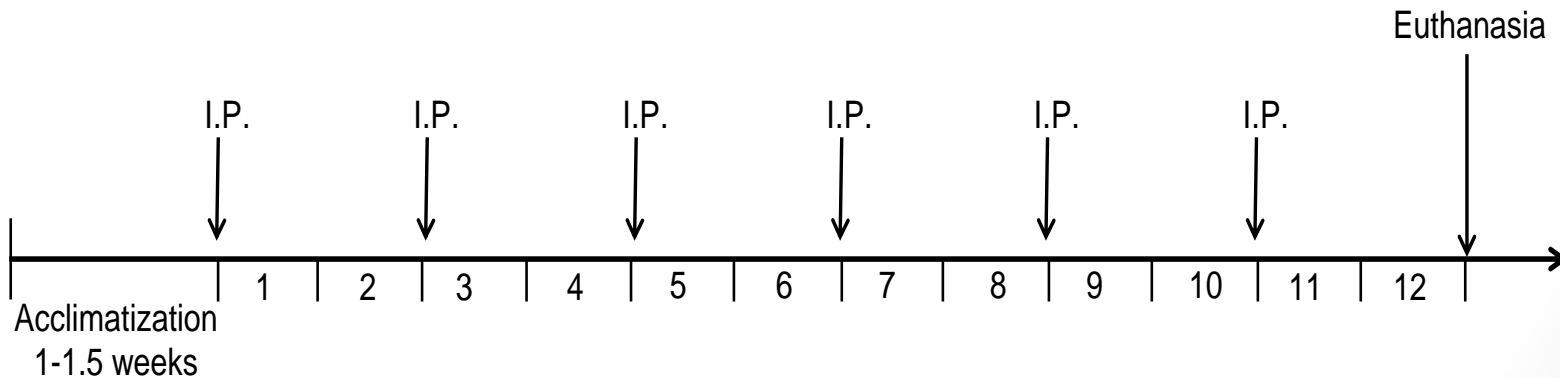


Hypothesis

Chronic exposure to PCB 126 alters the levels of regulatory lipid mediators (oxylipins) in rats.

Experiment design

- Five week old male Sprague-Dawley rats (n=8~10/group, 147 ± 8 g)
- Biweekly I.P. injections of PCB 126 in corn oil for 3 months.
- Cumulative doses: 0, 0.06, 0.3 and 1.2 $\mu\text{mol}/\text{kg}$ b.w.

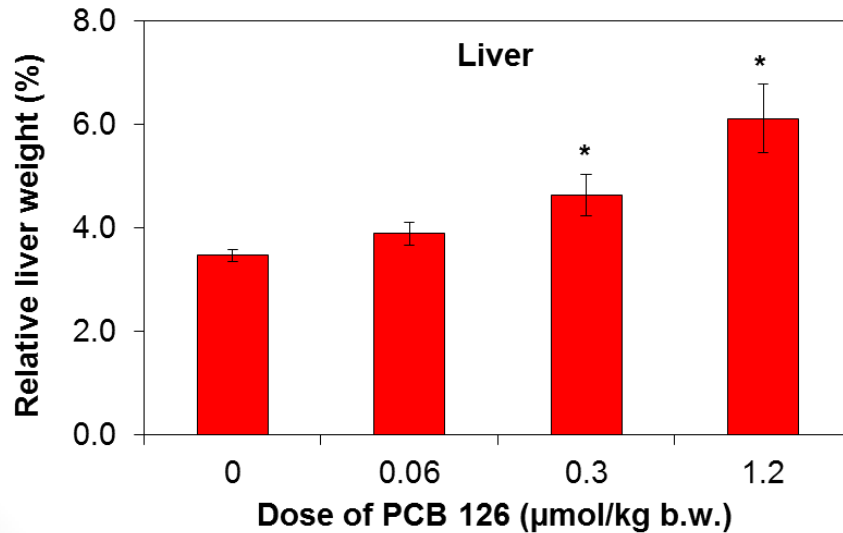
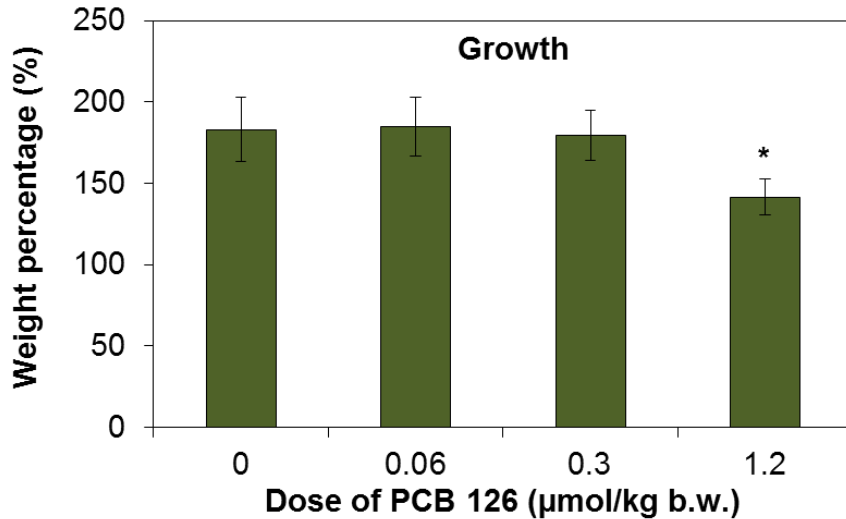


- Tissue (e.g., liver, lung and thymus) were collected

Experimental part

- General toxicity: Body and organ weight
- GC-ECD: PCB 126 levels
- LC/MS/MS: Oxylipin levels
- Determination of epoxide hydrolase activity:
Cytosol, peroxisomes, and microsomes
- Statistical analysis: One way ANOVA and Tukey's Studentized Range (HSD) Test. Comparisons are significant at 0.05 level.

General toxicity



Decreased:

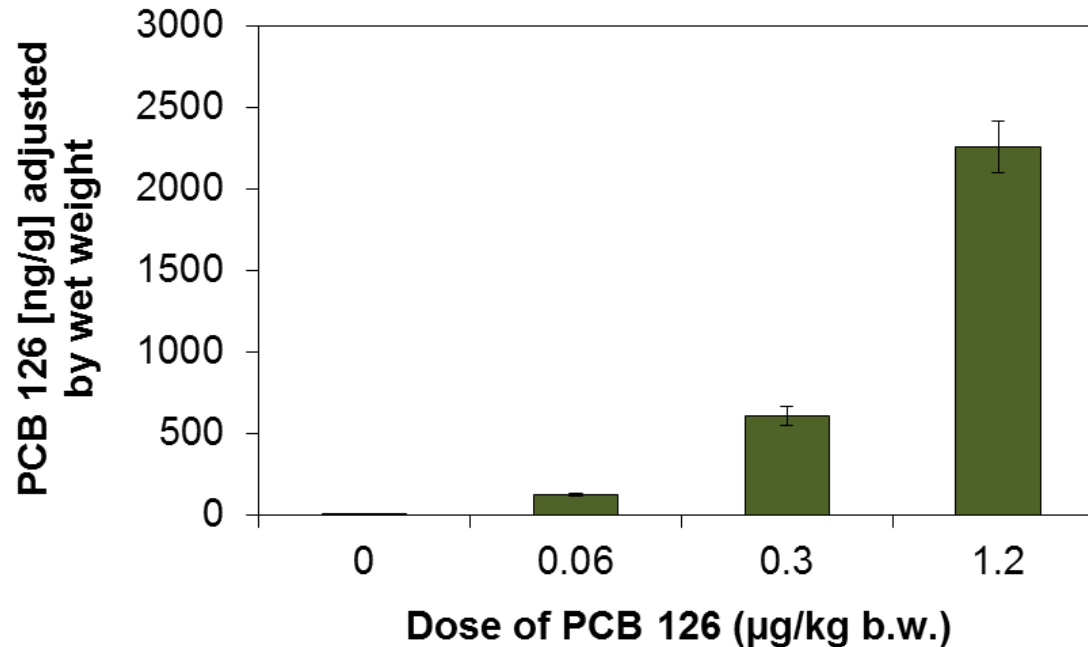
- Growth
- Relative thymus weight

Increased relative organ weights:

- Liver
- Lung
- Spleen

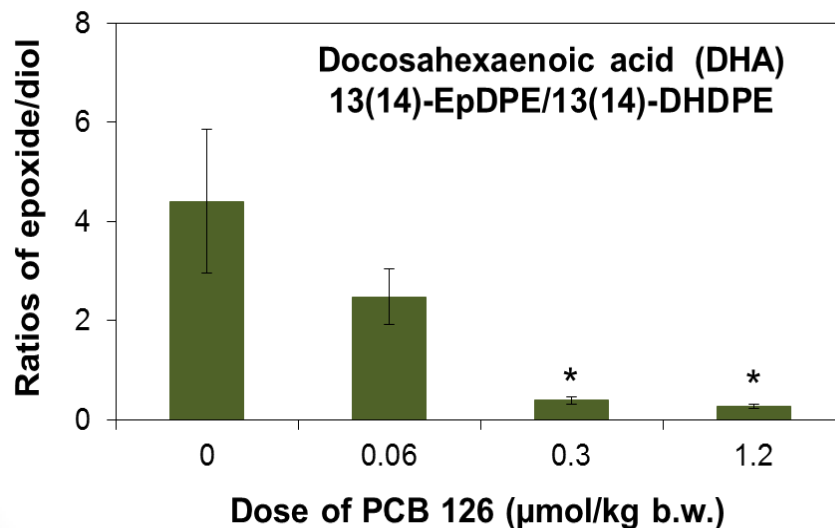
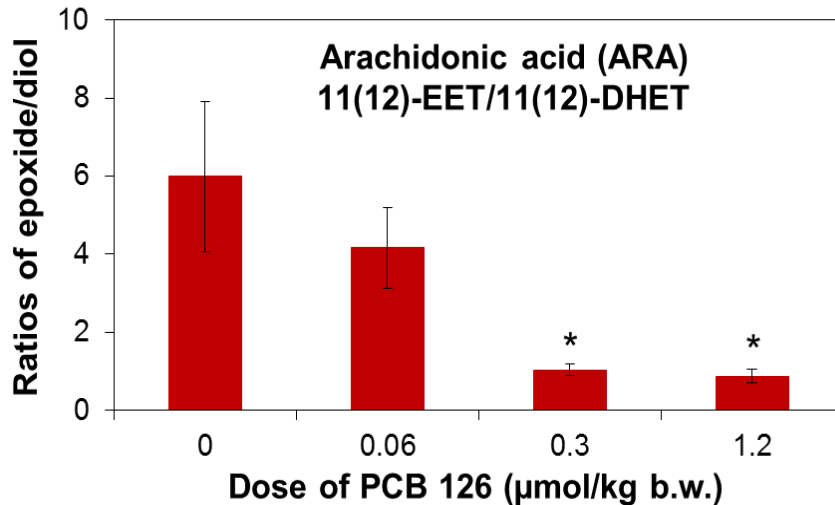
* Significant different from control ($p < 0.05$)

PCB 126 tissue levels



- **Liver:** Dose-dependent increase
- **Plasma:** < Limit of Detection (5.0 ng/mL)

Oxylipins profiling in plasma

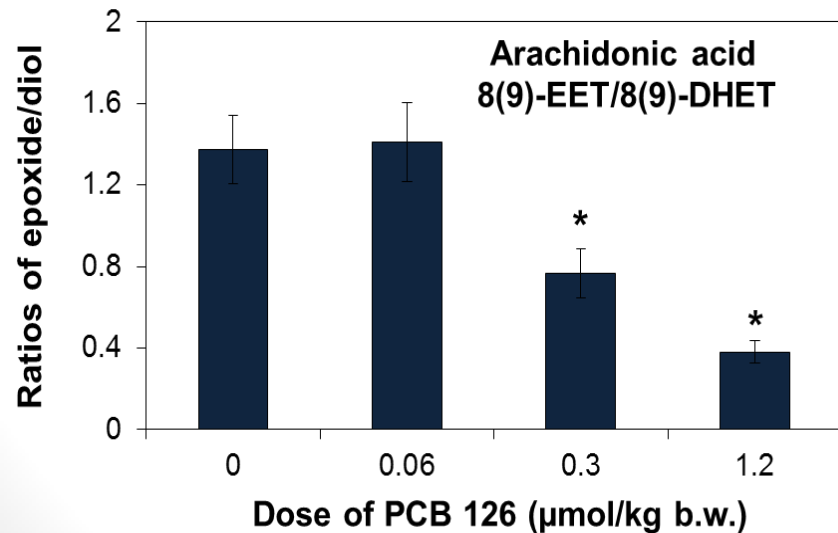
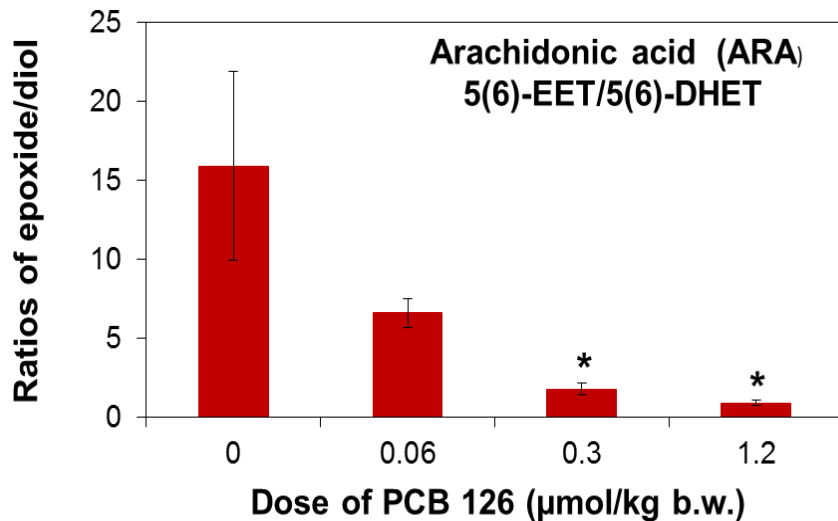


* Significant different from control ($p < 0.05$)

Levels of 24 oxylipins changed:

- Eleven epoxide/diol ratios decreased (epoxide \downarrow and diol \uparrow)
- Leukotriene B4 \uparrow , 6-keto-PGF1 α \uparrow

Oxylipins profiling in liver



*Significant different from control ($p < 0.05$)

Levels of 27 oxylipins changed:

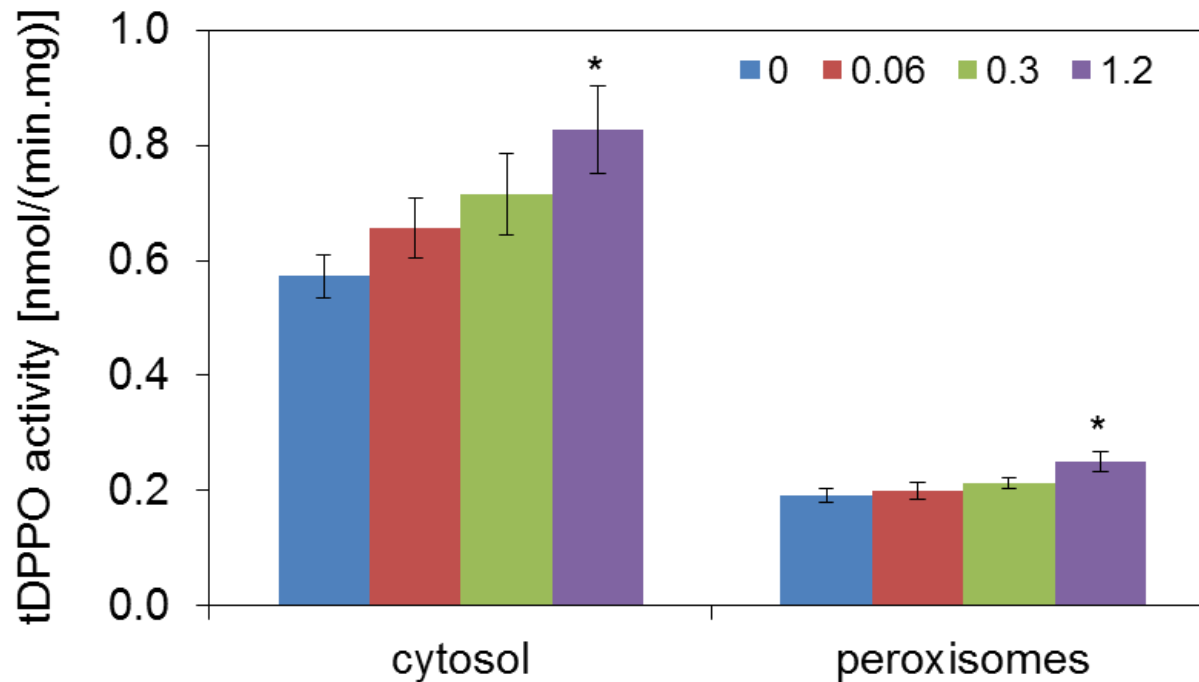
➤ Eleven diols \uparrow , 1 epoxide \downarrow (most epoxides unchanged)

➤ Five epoxide/diol ratios decreased

➤ Increase: 8-Hydroxyeicosatetraenoic acid (HETE), 5-oxo-EET, lipoxin A4, leukotriene B3

➤ Decrease: 15-deoxy-PGJ2

Activities of soluble epoxide hydrolase slightly increased



- tDPPO (trans-diphenylpropene oxide), substrate for sEH
- Incubation tDPPO (50 μ M), 15 min at 30 °C
- *Significant different from control (p<0.05)

Future directions

Test whether sEH inhibition can attenuate PCB 126–induced hepatic steatosis by reduced systemic inflammatory status in rat.

Acknowledgements

- **Iowa Superfund Research Program: Semi-volatile PCBs: Sources, Exposures, Toxicities**
 - Mentor: Dr. Hans-Joachim Lehmler
 - Program Director: Dr. Larry Robertson
 - Colleagues for animal work

- **UC Davis Superfund Research and Training Program**
 - Drs. Jun Yang, Christophe Morisseau, Todd Harris
 - Program Director: Dr. Bruce Hammock
 - Colleagues at UC Davis

- **NIEHS/Superfund grants ES013661, ES04699**
- **K C Donnelly externship 2011**