Shi, H., Hardesty, J. E., Jan, J., Head, K. Z., Falkner, K. C., Cave, M. C., & Prough, R. A. (2019). Concentration dependence of human and mouse aryl hydrocarbon receptor responsiveness to polychlorinated biphenyl exposures: Implications for aroclor mixtures. *Xenobiotica*, *49*(12), 1414-1422. https://doi.org/10.1080/00498254.2019.1566582

Definitions

- **Polychlorinated Biphenyls (PCBs)**: Chemicals used in industrial products that can cause environmental and health issues.
- **Aryl Hydrocarbon Receptor (AhR)**: A protein that helps cells respond to certain chemicals.
- **Nonalcoholic Fatty Liver Disease (NAFLD)**: A liver disease that occurs when fat builds up in the liver without alcohol use.
- **Luciferase Reporter Assay**: A test that uses light-producing proteins to measure gene activity.
- **EC50**: The concentration of a substance that produces 50% of its maximum effect.

Key Findings

- PCBs activate AhR differently in humans and mice.
- Mice show a stronger response to PCBs compared to humans.
- Specific PCB mixtures affect AhR activation in mice but not in humans.
- These differences are important for understanding PCB effects on liver disease.

Introduction

This study examines how different concentrations of PCBs affect the aryl hydrocarbon receptor (AhR) in humans and mice. AhR is important because it helps the body respond to harmful chemicals like PCBs, which are linked to liver diseases such as nonalcoholic fatty liver disease (NAFLD).

Main Content

Background

PCBs are harmful chemicals that persist in the environment. They can disrupt the endocrine system and metabolism, contributing to diseases like NAFLD. PCBs are classified into dioxin-like (DL) and non-dioxin-like (NDL) types, with DL PCBs being particularly harmful.

Methods

- **Cell Lines and Hepatocytes**: Human HepG2 and mouse Hepa1c1c7 liver cell lines were used.
- **Exposure**: Cells were exposed to various concentrations of TCDD and PCBs 77, 81, 114, 126, and 169.

- **Assays**: Luciferase reporter assays measured AhR activation. Primary human and mouse hepatocytes were used to validate results.

Results

- **TCDD and PCB 126**: Both chemicals activated AhR more strongly in mice than in humans.
    - **EC50 for TCDD**: 0.04 nM in mice vs. 0.45 nM in humans.
    - **EC50 for PCB 126**: 12.3 nM in mice vs. 195 nM in humans.
- **Other PCBs**: PCB 81 activated human AhR more than mouse AhR, while PCBs 77, 114, and 169 were more potent in mice.
- **Aroclor Mixtures**: Aroclor 1260 plus PCB 126 activated mouse AhR but not human AhR.

Conclusion

The study shows that mice respond more strongly to PCBs than humans, indicating species differences in AhR activation. These findings are important for developing accurate animal models to study PCB-related liver diseases and for assessing human health risks.

Word Count: 372