Hardesty, J. E., Al-Eryani, L., Wahlang, B., Falkner, K. C., Shi, H., Jin, J., Vivace, B. J., Ceresa, B. P., Prough, R. A., & Cave, M. C. (2018). Epidermal growth factor receptor signaling disruption by endocrine and metabolic disrupting chemicals. *Toxicological Sciences*, *162*(2), 622-634. https://doi.org/10.1093/toxsci/kfy004

Definitions

- **Epidermal Growth Factor Receptor (EGFR)**: A protein on the cell surface that helps cells grow and divide.
- **Endocrine Disrupting Chemicals (EDCs)**: Chemicals that can interfere with hormone systems.
- **Metabolic Disrupting Chemicals (MDCs)**: Chemicals that can interfere with metabolism, the process by which your body converts what you eat and drink into energy.
- **Phosphorylation**: The addition of a phosphate group to a protein or other organic molecule, which can change how that molecule works.
- **Constitutive Androstane Receptor (CAR)**: A receptor involved in the regulation of genes related to drug metabolism.

Key Findings

- Certain chemicals, including PCBs and pesticides, can inhibit EGFR signaling.
- These chemicals may act by preventing EGFR from functioning properly, which can affect liver and other organ functions.
- The study identified that chemicals like chlordane, trans-nonachlor, PCB-126, PCB-153, and atrazine are potent EGFR inhibitors.
- Human exposure levels to some of these chemicals exceed the concentrations that inhibit EGFR in lab tests.

Introduction

The study aims to understand how certain environmental chemicals disrupt EGFR signaling. These chemicals, which include pesticides and PCBs, are known to interfere with hormone and metabolic systems. Understanding their impact on EGFR can help explain their harmful effects on the liver and other organs.

Main Content

Background

Environmental chemicals, especially EDCs and MDCs, can disrupt various biological processes. This study focuses on their impact on EGFR signaling, which is crucial for cell growth and liver function.

Methods

- **Compound Selection**: Ten chemicals known to activate CAR were selected, including PCBs and pesticides.
- **Cell Culture**: Human liver and skin cells were used for experiments.
- **Assays**: Various assays were conducted to measure EGFR activity, including:
    - **CAR Activity Reporter Assay**
    - **EGF Endocytosis Assay**
    - **EGFR Phosphorylation Assay**
- **Molecular Modeling**: Docking simulations were performed to identify potential binding sites of the chemicals on EGFR.

Results

- The chemicals did not directly activate CAR but inhibited EGFR signaling.
- Chlordane, trans-nonachlor, and atrazine significantly reduced EGFR phosphorylation.
- The chemicals prevented EGF endocytosis, indicating they interfere with EGFR activation.
- Human serum concentrations of some chemicals were found to be higher than the levels needed to inhibit EGFR.

Conclusion

The study shows that many environmental chemicals can inhibit EGFR signaling, potentially leading to adverse health effects. This inhibition can disrupt normal liver function and contribute to diseases like fatty liver disease. Future research should focus on understanding the broader health implications of these findings and developing strategies to mitigate the risks posed by these chemicals.

Word Count: 402