Habil, M. R., Salazar-González, R. A., Doll, M. A., & Hein, D. W. (2023). Effect of N-acetyltransferase 2 genetic polymorphism on 4,4'-methylenebis(2-chloroaniline)-induced genotoxicity and oxidative stress. *Archives of Toxicology*, *97*(6), 1773-1781. https://doi.org/10.1007/s00204-023-03508-1

Definitions

- **N-acetyltransferase 2 (NAT2)**: An enzyme that helps process certain chemicals in the body.
- **Genetic Polymorphism**: Variations in a gene among individuals that can result in different traits.
- **4,4'-Methylenebis(2-chloroaniline) (MOCA)**: A chemical used in making plastics that can be harmful.
- **Genotoxicity**: The ability of a substance to damage genetic information in cells.
- **Oxidative Stress**: Damage caused by free radicals, which are unstable molecules that can harm cells.

Key Findings

- The genotoxicity and oxidative stress caused by MOCA vary depending on the NAT2 genetic variant.
- Individuals with the NAT2*7B variant are at higher risk for MOCA-induced DNA damage and oxidative stress.
- The study confirms that NAT2 genetic polymorphisms influence how MOCA is metabolized and its harmful effects.

Introduction

This study examines how different genetic versions of the NAT2 enzyme affect the body's response to MOCA, a harmful chemical used in the plastic industry. Researchers aimed to understand if certain genetic variations make individuals more susceptible to MOCA's damaging effects.

Main Content

Background

MOCA is used in making plastics and can be found in the environment near industrial sites. It is known to cause cancer in animals and is suspected to be harmful to humans. This study focuses on how different versions of the NAT2 enzyme, which varies among people, affect the processing of MOCA and its harmful effects.

Methods

- **Cell Studies**: Chinese hamster ovary (CHO) cells and human liver cells with different NAT2 variants were used to study the effects of MOCA.

- **Genetic Analysis**: The cells were tested for their ability to process MOCA and the resulting DNA damage and oxidative stress.
- **Comparison of NAT2 Variants**: The study compared cells with three NAT2 variants: NAT2*4 (rapid acetylator), NAT2*5B* (slow acetylator common in Europeans), and NAT2*7B (slow acetylator common in Asians).

Results

- **MOCA Processing**: Cells with the NAT2*4 variant processed MOCA more efficiently than those with NAT2*5B or NAT2*7B.
- **DNA Damage**: Cells with NAT2*7B showed the highest levels of DNA damage and oxidative stress when exposed to MOCA.
- **Genetic Differences**: The NAT2 genetic differences significantly impacted how cells responded to MOCA, with the NAT2*7B variant showing the highest risk.

Conclusion

The study concludes that the genetic variation in the NAT2 enzyme significantly affects the body's response to MOCA exposure. People with the NAT2*7B variant are at higher risk for DNA damage and oxidative stress from MOCA. These findings highlight the importance of considering genetic differences in assessing the risk of exposure to harmful chemicals and suggest that individuals with certain genetic backgrounds may need more protection from environmental toxins like MOCA.

Word Count: 419