Leggett, C. S., Doll, M. A., States, J. C., & Hein, D. W. (2021). Acetylation of putative arylamine and alkylaniline carcinogens in immortalized human fibroblasts transfected with rapid and slow acetylator N-acetyltransferase 2 haplotypes. *Archives of Toxicology*, *95*(1), 311-319. https://doi.org/10.1007/s00204-020-02901-4

Definitions

- **N-acetyltransferase 2 (NAT2)**: An enzyme that helps process and detoxify certain chemicals, including carcinogens.
- **Haplotype**: A group of genes within an organism that was inherited together from a single parent.
- **Aryl amines and alkylanilines**: Chemical compounds that can be found in tobacco smoke and industrial products, known to cause cancer.
- **Genotoxicity**: The ability of a substance to damage genetic information in cells, which can lead to cancer.
- **Fibroblasts**: Cells in connective tissue that produce collagen and other fibers.

Key Findings

- NAT2 genetic variations (haplotypes) affect how well the enzyme processes certain carcinogens.
- Rapid acetylator haplotypes (NAT2*4) show higher activity in processing carcinogens compared to slow acetylator haplotypes (NAT2*5B and NAT2*7B).
- This difference in enzyme activity influences the level of DNA damage and the potential risk of cancer.

Introduction

The study investigates how genetic differences in the NAT2 enzyme affect its ability to process carcinogenic chemicals found in tobacco smoke and industrial products. The focus is on comparing the enzyme activity of different NAT2 haplotypes and understanding how these differences might impact cancer risk.

Main Content

Background

Exposure to carcinogens like arylamines and alkylanilines is linked to an increased risk of bladder cancer. These chemicals are metabolized by the NAT2 enzyme, which has different genetic variations (haplotypes) that can influence its activity. Understanding how these genetic differences affect carcinogen metabolism can help assess cancer risk.

Methods

- **Cell Culture**:
    - Immortalized human fibroblast cells were used.
    - Cells were genetically modified to express different NAT2 haplotypes (NAT2*4, NAT2*5B, NAT2*7B) and the enzyme CYP1A2.
- **Measurement of Enzyme Activity**:
    - N-acetyltransferase activity was measured using high-performance liquid chromatography (HPLC) to analyze how well the enzyme processed various carcinogens.
- **DNA Damage Assessment**:
    - Tests were conducted to measure DNA damage in the cells after exposure to carcinogens.

Results

- **Enzyme Activity**:
    - Cells with the NAT2*4 haplotype showed higher activity in processing carcinogens compared to those with NAT2*5B and NAT2*7B haplotypes.
- **DNA Damage**:
    - Higher enzyme activity in NAT2*4 cells correlated with increased DNA damage when exposed to carcinogens.

Conclusion

The study shows that genetic variations in the NAT2 enzyme significantly impact its ability to process carcinogens and influence the level of DNA damage in cells. Individuals with the NAT2*4 haplotype may have a higher risk of cancer due to more efficient processing of carcinogens, leading to greater DNA damage. Understanding these genetic differences is important for assessing individual cancer risk and developing strategies for prevention and treatment.

Word Count: 403