Hein, D. W., Salazar-González, R. A., Doll, M. A., & Zang, Y. (2023). The effect of the rs1799931 G857A (G286E) polymorphism on N-acetyltransferase 2-mediated carcinogen metabolism and genotoxicity differs with heterocyclic amine exposure. *Archives of Toxicology*, *97*(2697-2705). https://doi.org/10.1007/s00204-023-03577-2

Definitions

- **Polymorphism**: A variation in a gene that can result in different traits among individuals.
- **N-acetyltransferase 2 (NAT2)**: An enzyme that helps break down certain chemicals in the body.
- **Heterocyclic Amines (HCAs)**: Chemicals formed when meat is cooked at high temperatures, which can be harmful.
- **O-acetylation**: A chemical process that adds an acetyl group to a molecule.
- **Genotoxicity**: The ability of a substance to damage genetic information in cells.

Key Findings

- The G857A (G286E) polymorphism in the NAT2 gene affects the enzyme's ability to process HCAs differently, depending on the type of HCA.
- This polymorphism changes the rate at which NAT2 processes certain HCAs, impacting their potential to cause DNA damage.
- The study highlights the importance of genetic differences in how people respond to exposure to harmful chemicals in cooked meat.

Introduction

This study investigates how a specific genetic variation (G857A, also known as G286E) in the NAT2 gene affects the metabolism and genotoxicity of heterocyclic amines (HCAs), which are harmful chemicals formed during the cooking of meat. The goal is to understand how this genetic difference impacts the body's ability to process these chemicals and its implications for cancer risk.

Main Content

Background

N-acetyltransferase 2 (NAT2) is an enzyme involved in breaking down harmful chemicals, including HCAs. The NAT2 gene has different versions (polymorphisms) that can change how well this enzyme works. HCAs are found in cooked meat and can cause cancer. The study looks at how the G857A polymorphism in NAT2 affects the metabolism of three HCAs: IQ, MeIQx, and PhIP.

Methods

- **Genetic Analysis**: Researchers used yeast cells to express different versions of the NAT2 enzyme, including the normal version (NAT2*4) and the variant with the G857A polymorphism.
- **Metabolism Testing**: They measured the ability of these enzymes to process the HCAs by looking at the O-acetylation activity.
- **Genotoxicity Assessment**: They tested how these different enzymes affected DNA damage in cultured cells.

Results

- **Enzyme Activity**: The G857A polymorphism reduced the enzyme's ability to process N-hydroxy-IQ and N-hydroxy-MeIQx but did not affect N-hydroxy-PhIP processing as much.
- **DNA Damage**: Cells with the G857A variant showed different levels of DNA damage when exposed to the HCAs, depending on the type of HCA.
- **Oxidative Stress**: The polymorphism also affected the levels of reactive oxygen species (ROS), which can cause additional damage to cells.

Conclusion

The study found that the G857A polymorphism in the NAT2 gene affects how the body processes certain harmful chemicals found in cooked meat. This genetic variation can change the risk of DNA damage and potentially cancer, highlighting the need to consider genetic differences in assessing health risks from dietary exposures. More research is needed to understand fully how these genetic differences impact health and to develop strategies for personalized health recommendations.

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