Wise, J. T. F., Yin, X., Ma, X., Zhang, X., & Hein, D. W. (2023). Stable Isotope Tracing Reveals an Altered Fate of Glucose in N-Acetyltransferase 1 Knockout Breast Cancer Cells. *Genes*, *14*(843). https://doi.org/10.3390/genes14040843

Definitions

- **N-Acetyltransferase 1 (NAT1)**: An enzyme that helps modify drugs and other foreign chemicals in the body.
- **Knockout (KO)**: A type of genetic manipulation where a specific gene is completely turned off or deleted.
- **TCA/Krebs Cycle**: A series of chemical reactions used by all aerobic organisms to generate energy.
- **Metabolomics**: The study of small molecules (metabolites) within cells, biofluids, tissues, or organisms.
- **Stable Isotope Tracing**: A method used to track the movement and chemical changes of substances in biological systems by using isotopes.

Key Findings

- NAT1 knockout in breast cancer cells changes how glucose is processed in these cells.
- The lack of NAT1 reduces the presence of important metabolites in the TCA/Krebs cycle.
- NAT1 knockout cells produce more lactate, indicating a shift towards a different energy-producing process.
- Changes in amino acid levels and other metabolic pathways were observed, suggesting broad impacts on cellular metabolism.

Introduction

This study investigates how the absence of the enzyme N-acetyltransferase 1 (NAT1) affects the metabolism of glucose in breast cancer cells. NAT1 is often found in higher levels in breast cancer, and understanding its role could help develop new treatments.

Main Content

Background

N-acetyltransferase 1 (NAT1) is an enzyme that modifies and processes drugs and other chemicals in the body. It is found in many tissues and is upregulated in certain types of breast cancer, which means its levels are higher than normal. This upregulation suggests that NAT1 may play a role in the energy

metabolism of breast cancer cells. Understanding how NAT1 affects these processes can provide insights into new therapeutic targets for breast cancer treatment.

Methods

- **Cell Lines**: Breast cancer cells (MDA-MB-231) and two NAT1 knockout versions of these cells were used.
- **Isotope Tracing**: Cells were fed with glucose labeled with a special carbon isotope ([U-13C]-glucose) to track how it was processed.
- **Analysis**: The metabolites produced were analyzed using advanced techniques (2DLC-MS).

Results

- **TCA/Krebs Cycle**: Knockout cells had lower levels of several key metabolites (like citrate and malate) in the TCA/Krebs cycle.
- **Lactate Production**: Increased lactate levels in knockout cells indicate a shift towards anaerobic metabolism (less oxygen use).
- **Amino Acid Metabolism**: Changes in the levels of certain amino acids, such as aspartic acid and glutamic acid, were observed.
- **Nucleotide Metabolism**: Decreased levels of some nucleotides suggest changes in DNA and RNA building blocks.

Conclusion

The study found that NAT1 knockout in breast cancer cells leads to significant changes in how these cells use glucose and produce energy. These findings suggest that NAT1 plays a critical role in cellular metabolism and could be a target for new breast cancer treatments. The altered metabolic pathways in NAT1 knockout cells provide insights into potential therapeutic strategies to hinder cancer cell growth by targeting their energy production mechanisms.

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