Regulation of Metabolism in Triple-Negative Breast Cancer (TNBC)

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Abstract:

Altered metabolism represents a fundamental difference between cancer cells and normal cells. Translational control and metabolic reprogramming are hallmarks of advanced cancers. Many important genes involved in all aspects of cancer development and progression express mRNAs that are selectively translationally regulated, including regulators of cancer cell metabolism. Cancer cells acquire an altered metabolism, switching from oxidative phosphorylation (OXPHOS) to a glycolytic phenotype (Warburg effect), to increase reliance on alternate metabolic pathways for the production of amino acids, lipids, nucleic acids, and energy to support growth, proliferation, and metastasis. Highly metastatic Triple-negative breast cancer (TNBC) is characterized by dysregulated glycolysis. The exact mechanism used in this metabolic reprogramming is largely unknown. Our studies using genome-wide translatomic analysis, qRT-PCR, Western blotting, and metabolomics in TNBC cell line show that silencing DAP5 reduces the translation of mRNAs related to glucose metabolism and glycolytic proteins. We hypothesize that this form of translation is crucial for regulating metabolic mRNAs under stress conditions, when canonical translation is impaired. This mechanism is essential for the metabolic switch that drives TNBC progression and metastasis. Our research aims at identifying a novel mechanism of mRNA translation in the regulation of metastatic cancer cell metabolism in TNBC.

Keywords:

Metabolic reprogramming, Warburg effect,Triple-negative breast cancer (TNBC), translation, Glycolysis.