METABOLIC CHANGES IN BREAST CANCER CELLS RESISTANT TO TAMOXIFEN

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Breast carcinoma is the leading type of cancer among women and its incidence is increasing. Despite the targeting of estrogen receptor (ER)-positive cases by hormone therapy, primary and secondary resistance often lead to cancer progression and death. It is therefore important to identify predictive molecular biomarkers and to understand molecular mechanisms behind the primary and secondary resistance. Our aim was to search for diagnostic or therapeutic markers within metabolic phenotype. In this project, we used a novel cell model of secondary resistance to tamoxifen (Tam5R) in breast carcinoma cell lines MCF7 and T47D. We use metabolomics and lipidomics to characterize metabolic phenotype and we focused on metabolic pathways commonly upregulated or downregulated in both cell lines. Metabolomics and lipidomics profiling revealed several mitochondrial and extramitochondrial metabolic pathways, upregulated in Tam5R cell lines, particularly glycerophospholipid and ceramide synthesis. Synthesis of phosphatidylinositol and cardiolipin was significantly upregulated in Tam5R cells compared to control cells. Silencing of several enzymes affected cell growth of Tam5R cells but not control cells, which implies that certain metabolic targets might contribute to the development or maintenance of hormone treatment resistance. Subsequently, we aim to perform a functional analysis of those metabolic pathways in order to understand their role in growth advantage and their contribution to cancer development. Our findings have important implications for understanding functional changes underlying hormone therapy in breast carcinoma and provide a valuable foundation for further investigations of anabolic metabolism in cancer.

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