Tamoxifen Resistance in MCF-7: Tracking the Changes in PI3K/AKT/PTEN Signaling Pathway and Their Role in Glucose and Glutamine Metabolism During Resistance Development

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Abstract

Breast cancer is one of the leading causes of cancer death worldwide. What worsens its clinical outcomes is drug resistance that is still a big challenge to resolve to make a better prognosis. In this study, we aimed to determine the changes in PI3K/AKT/PTEN pathway gene expression levels during the process of developing tamoxifen-resistance in correlation to the changes in metabolic rate of glucose in tamoxifen-resistant and tamoxifen-sensitive MCF-7 cell lines were monitored and correlated with the changes in PI3K/AKT/PTEN molecular pathway. An upregulation of AKT/PI3K pathway genes was noticed at 30μM tamoxifen concentration in treated cells; a significant increase in all gene expression was seen at 35μM six times and 50μM concentrations. PTEN and GSK3 ß genes were found to be downregulated in TAM-R MCF-7 cells. Loss of GSK-3ß activity in MCF-7 breast cancer cells promotes drug resistance and increased glucose metabolism. In conclusion, it was found that TAM-R cells may be able to synthesize their needs of glutamine and increased glucose metabolism in correlation to the molecular changes of GSK-3ß and GLUL gene expression.

Keywords: Glucose, GLUL, PI3K/AKT/PTEN Pathway, Tamoxifen Resistance.