Tamoxifen Resistance and its Role in Migration and Invasion of an *In Vitro* Cell Line Model at the Molecular Level.

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Abstract

Metastasis and drug resistance remain a persistent key clinical obstacles to the success of breast cancer treatments. Recent years have seen an intense focus on understanding the factors that influence metastasis and drug resistance. In this study, the changes in MMPs gene expression were tracked together with their regulatory pathways; PI3K, MAPK and NFKβ pathways, which were represented by the most important genes before and during the process of developing tamoxifen-resistance in MCF7 cell line. MMPs gene expression was found to be up-regulated in MCF7 cell line treated with tamoxifen during the development process of tamoxifen resistance using two approaches. Genes up regulation started at 35μM tamoxifen concentration and significant increase in their expression was observed at 50μM and 35μM six times. Furthermore, genes expression was associated with aggressive pattern, clear morphological changes, higher growth rate, increased migration and adhesion potential and tamoxifen insensitivity. On the other hand, PI3K, MAPK and NFKβ pathways, that induce migration through activation of MMPs gene expression and are also linked to tamoxifen resistance, were overexpressed significantly in both approaches. However, the second approach of treatment where cells treated with 35μM several times showed higher gene expression levels than first approach.

Keywords: Breast Cancer, Matrix Metalloproteinases, Migration, Tamoxifen Resistance.