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Downregulation of lncRNA GAS5 confers tamoxifen resistance by activating miR-222 in breast cancer

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Abstract

Long noncoding RNAs (lncRNAs) work as oncogenes or tumor suppressors that play important roles in tumorigenesis and chemotherapeutic drug resistance. This study investigates the role of lncRNA in tamoxifen resistance in breast cancer. A microarray of lncRNAs was screened in the tamoxifen-resistant MCF-7R cells and the parental, non-resistant MCF-7 cells. Downregulation of lncRNA GAS5 was found in MCF-7R cells. Besides, decreased expression of GAS5 was found in breast cancer tissues, which was associated with advanced TNM stage, and shorter overall survival time. We further found that GAS5 overexpression enhanced cell sensitivity to tamoxifen in MCF-7R cells both in vitro and in vivo. Moreover, GAS5 increased sensitivity of breast cancer cells to tamoxifen by serving as a molecular sponge for miR-222, contributing to the suppression of phosphatase and tensin homologs (PTEN) (one endogenous target of miR-222). In addition, we found that inhibition of PTEN was achieved by activating AKT/mTOR signaling pathway with decreased GAS5 expression. Collectively, our study demonstrated that GAS5 enhances the efficacy of tamoxifen in breast cancer and could be a novel prognostic biomarker.