Investıgatıon of the Effect of Celastrol on Trıple Negatıve Breast Cancer Cells

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Abstract:

Breast cancer is a malignant tumor, starts in the breast cells and metastases to other organs. It has the highest mortality rate in women. Since receptors, estrogen receptors, progesterone receptors, and human epidermal growth factor receptor 2, are not found in triple-negative breast cancer (TNBC), it represents the most aggressive type of breast cancer with high drug resistance, poor prognosis. It cannot be targeted therapeutically. Therefore, identifying novel molecular targets and developing alternative therapeutic strategies are urgently needed. FOXM1 is a protooncogenic transcription factor, plays a crucial role in promoting cancer cell proliferation, and tumorigenesis of TNBC. We previously demonstrated that in vivo targeting of FOXM1 suppresses TNBC tumor growth in mice. To identify potential inhibitors, utilizing *in silico* docking and molecular dynamics studies we screened the FDA-approved compounds and found that Celastrol interacts with FOXM1. In the study, MDA-MB-231, BT-549, and BT-20 cell lines were used. MTS analysis was performed to investigate the effect of Celastrol molecule on cell viability, clonogenic analysis was performed to investigate its effect on clone formation. Since cell death was observed, Annexin-V analysis to investigate the type of cell death, and western blot analysis were performed to investigate the effect on the expression of FOXM1 and its down targets. As a result of the experiments, it was determined that Celastrol reduces cell viability and colony formation, induced apoptosis. Expression of FOXM1 was inhibited in TNBC. Our results shows celastrol may important inhibitor for the suppression of the expression of FOXM1.

Keywords:

Breast cancer, Triple-negative breast cancer, Celastrol, FOXM1.