Câncer de mama. O ácido nordihidroguaiarético (NDGA) inibe o IGF-IR e o receptor c-erbB2/HER2/neu e suprime a proliferação.

Nordihydroguaiaretic acid (NDGA), an inhibitor of the HER2 and IGF-1 receptor tyrosine kinases, blocks the growth of HER2-overexpressing human breast cancer cells.


Source

Diabetes and Endocrine Research, University of California, San Francisco/Mt. Zion Medical Center, San Francisco, California, USA.

Abstract

We have reported that nordihydroguaiaretic acid (NDGA) inhibits the tyrosine kinase activities of the IGF-1 receptor (IGF-1R) and the HER2 receptor in breast cancer cells. Herein, we studied the effects of NDGA on the growth of estrogen receptor (ER) positive MCF-7 cells engineered to overexpress HER2 (MCF-7/HER2-18). These cells are an in vitro model of HER2-driven, ER positive, tamoxifen resistant breast cancer. NDGA was equally effective at inhibiting the growth of both parental MCF-7 and MCF-7/HER2-18 cells. Half maximal effects for both cell lines were in the 10-15 microM range. The growth inhibitory effects of NDGA were associated with an S phase arrest in the cell cycle and the induction of apoptosis. NDGA inhibited both IGF-1R and HER2 kinase activities in these breast cancer cells. In contrast, Gefitinib, an epidermal growth factor receptor inhibitor but not an IGF-1R inhibitor, was more effective in MCF-7/HER2-18 cells than in the parental MCF-7 cells and IGF binding protein-3 (IGFBP-3) was more effective against MCF-7 cells compared to MCF-7/HER2-18. MCF-7/HER2-18 cells are known to be resistant to the effects of the estrogen receptor inhibitor, tamoxifen. Interestingly, NDGA not only inhibited the growth of MCF-7/HER2-18 on its own, but it also demonstrated additive growth inhibitory effects when combined with...
tamoxifen. These studies suggest that NDGA may have therapeutic benefits in HER2-positive, tamoxifen resistant, breast cancers in humans.

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