題名:Theanaphthoquinone inhibits fatty acid synthase expression in EGF-stimulated human breast cancer cells via the regulation of EGFR/ErbB-2 signaling

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上傳時間:2009-08-25T02:39:09Z

摘要:Fatty acid synthase (FAS) is a major lipogenic enzyme catalyzing the synthesis of long-chain saturated fatty acids. Most breast cancers require lipogenesis for growth. Here, we demonstrated the effects of theanaphthoquinone (TNQ), a member of the thearubigins generated by the oxidation of theaflavin (TF-1), on the expression of FAS in human breast cancer cells. TNQ was found to suppress the EGF-induced expression of FAS mRNA and FAS protein in MDA-MB-231 cells. Expression of FAS has previously been shown to be regulated by the SREBP family of transcription factors. In this study, we demonstrated that the EGF-induced nuclear translocation of SREBP-1 was blocked by TNQ. Moreover, TNQ also modulated EGF-induced ERK1/2 and Akt phosphorylation. Treatment of MDA-MB-231 cells with PI 3-kinase inhibitors, LY294002 and Wortmannin, inhibited the EGF-induced expression of FAS and nuclear translocation of SREBP-1. Treatment with TNQ inhibited EGFinduced EGFR/ErbB-2 phosphorylation and dimerization. Furthermore, treatment with kinase inhibitors of EGFR and ErbB-2 suggested that EGFR/ErbB-2 activation was involved in EGF-induced FAS expression. In constitutive FAS expression, TNQ inhibited FAS expression and Akt autophosphorylation in BT-474 cells. The PI 3-kinase inhibitors and tyrosine kinase inhibitors of EGFR and

ErbB-2 also reduced constitutive FAS expression. In addition, pharmacological blockade of FAS by TNQ decreased cell viability and induced cell death in BT-474 cells. In summary, our findings suggest that TNQ modulates FAS expression by the regulation of EGFR/ErbB-2 pathways and induces cell death in breast cancer cells.