

Abstract

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Reduction of estrogen-induced transformation of mouse mammary epithelial cells by N-acetylcysteine.

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BACKGROUND: A growing number of studies indicate that breast cancer initiation is related to abnormal estrogen oxidation to form an excess of estrogen-3,4-quinones, which react with DNA to form depurinating adducts and induce mutations. This mechanism is often called estrogen genotoxicity. 4-Catechol estrogens, precursors of the estrogen-3,4-quinones, were previously shown to account for most of the transforming and tumorigenic activity.

METHODS: We examined whether estrogen-induced transformation can be reduced by inhibiting the oxidation of a 4-catechol estrogen to its quinone.

RESULTS: We demonstrate that E6 cells (a normal mouse epithelial cell line) can be transformed by a single treatment with a catechol estrogen or its quinone. The transforming activities of 4-hydroxyestradiol and estradiol-3,4-quinone were comparable. N-Acetylcysteine, a common antioxidant, inhibited the oxidation of 4-hydroxyestradiol to the quinone and consequent formation of DNA adducts. It also drastically reduced estrogen-induced transformation of E6 cells. These results strongly implicate estrogen genotoxicity in mammary cell transformation.

CONCLUSION: Since N-acetylcysteine is well tolerated in clinical studies, it may be a promising candidate for breast cancer prevention.

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