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Effect of maternal and postweaning folic acid supplementation on mammary tumor risk in the offspring.

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Source

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Abstract

Intrauterine and early life exposure to **folic acid** has significantly increased in North America owing to **folic acid** fortification, widespread supplemental use, and periconceptual supplementation. We investigated the effects of maternal and postweaning **folic acid** supplementation on mammary tumor risk in the offspring. Female rats were placed on a control or **folic acid**-supplemented diet prior to mating and during pregnancy and lactation. At weaning, female pups from each maternal diet group were randomized to the control or supplemented diet and mammary tumors were induced with 7,12 dimethylbenz[a]anthracene at puberty. At necropsy, mammary tumor parameters, genomic DNA methylation, and DNA methyltransferase activity were determined in the offspring. Both maternal and postweaning **folic acid** supplementation significantly increased the risk of mammary adenocarcinomas in the offspring (OR = 2.1, 95% CI 1.2-3.8, P = 0.008 and OR = 1.9, 95% CI 1.1-3.3, P = 0.03, respectively). Maternal **folic acid** supplementation also significantly accelerated the rate of mammary adenocarcinoma appearance (P = 0.002) and increased the multiplicity of mammary adenocarcinomas (P = 0.008) in the offspring. Maternal, but not postweaning, **folic acid** supplementation significantly reduced global DNA methylation (P = 0.03), whereas postweaning, but not maternal, **folic acid** supplementation significantly decreased DNA methyltransferase activity (P = 0.05) in nonneoplastic mammary glands of the offspring. Our findings suggest that a high intrauterine and postweaning dietary exposure to **folic acid** may increase the risk of mammary tumors in the offspring. Further, they suggest that this tumor-promoting effect may be mediated in part by altered DNA methylation and DNMT activity.