High animal fat intake enhances prostate cancer progression and reduces glutathione peroxidase 3 expression in early stages of TRAMP mice.

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Abstract

BACKGROUND: Prostate cancer is the most frequently diagnosed cancer in Western men, and more men have been diagnosed at younger ages in recent years. A high-fat Western-style diet is a known risk factor for prostate cancer and increases oxidative stress.

METHODS: We evaluated the association between dietary animal fat and expression of antioxidant enzymes, particularly glutathione peroxidase 3 (GPx3), in the early stages of transgenic adenocarcinoma of the mouse prostate (TRAMP) mice. Six-week-old male nontransgenic and TRAMP mice were placed on high animal fat (45% Kcal fat) or control (10% Kcal fat) diets and sacrificed after 5 or 10 weeks.

RESULTS: The histopathological score increased with age and high-fat diet consumption. The histopathological scores in dorsal and lateral lobes increased in the 10-week high-fat diet group (6.2 ± 0.2 and 6.2 ± 0.4, respectively) versus the 10-week control diet group (5.3 ± 0.3 and 5.2 ± 0.2, respectively). GPx3 decreased both at the mRNA and protein levels in mouse prostate. GPx3 mRNA expression decreased (~36.27% and ~23.91%, respectively) in the anterior and dorsolateral prostate of TRAMP mice fed a high-fat diet compared to TRAMP mice fed a control diet. Cholesterol treatment increased PC-3 human prostate cancer cell proliferation, decreased GPx3 mRNA and protein levels, and increased H2 O2 levels in culture medium. Moreover, increasing GPx3 mRNA expression by troglitazone in PC-3 cells decreased cell proliferation and lowered H2 O2 levels.

CONCLUSIONS: Dietary fat enhances prostate cancer progression, possibly by suppressing GPx3 expression and increasing proliferation of prostate intraepithelial neoplasia (PIN) epithelial cells.


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KEYWORDS: GPx3; TRAMP; cholesterol; high-fat diet; prostate cancer

PMID: 25053105 [PubMed - in process]