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[Lab. of Biochemistry]

**Dietary Prevention of Azoxymethane-Induced Colon Carcinogenesis with Rice-Germ in F344 Rats.**

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The modifying effect of dietary administration of defatted rice-germ (RG) and  $\gamma$ -aminobutyric acid (GABA)-enriched defatted RG on azoxymethane (AOM)-induced colon carcinogenesis was investigated in two experiments with male F344 rats. In the first experiment (the pilot study), the effects of the defatted RG, the GABA-enriched defatted RG and RG on AOM-induced (15mg/kg body wt once a week for 3 weeks) formation of aberrant crypt foci (ACF) were examined. The latter two preparations (2.5% in the diet) significantly inhibited ACF formation. In the second experiment, a long-term study of the effects of RG was done. At the termination of the study, dietary exposure to RG during the initiation phase significantly reduced the incidence of colonic adenocarcinoma. These data suggest that constituents of RG are possible dietary preventatives for human colon cancers.

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[Lab. of Biochemistry]

**Reactive Oxygen Species as a Risk Factor in Verotoxin-1-Exposed Rats.**

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It has been suggested the interaction of *Escherichia coli* O157-derived verotoxins (VTs) with the vascular endothelium plays a central role in the pathogenesis of the thrombotic microangiopathy and ischemic lesions characteristic of hemolytic uremic syndrome (HUS) and *E. coli* O157-associated hemorrhagic colitis. Intravenous administration of both *E. coli* O157-derived VT1 and lipopolysaccharide (LPS) in the rat induced a synergistic increase in thiobarbituric acid (TBA) values in those animal's plasma, as compared with that injected with VT1 or LPS alone. Both RT-PCR and Western blot studies of reactive oxygen species-related enzymes showed that VT1 markedly decreased the expression of catalase mRNA and protein in human aortic endothelial cells, but caused less alteration in the levels of Cu, Zn-superoxide dismutase, and NADPH oxidase mRNA. The accumulated data thus suggest that bacterial VT1 reduces mainly catalase levels in endothelial cells, which is synergistically potentiated by LPS, and that the resulting hydroxyl radical participates in endothelium injury through a marked enhancement of lipid peroxidation, leading to HUS.

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[Lab. of Biochemistry]

**Chemopreventive Effect of Dietary Flavonoid Morin on Chemically Induced Rat Tongue Carcinogenesis.**

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The modifying effects of dietary exposure of the flavonoid morin on 4-nitroquinoline 1-oxide (4-NQO)-induced tongue tumorigenesis, the activities of phase II detoxifying enzymes glutathione S-transferase and quinone reductase in liver and tongue, and cell proliferation activity in tongue were investigated in male F344 rats. Our results indicate that morin acts as a chemopreventive agent against tongue carcinogenesis induced by 4-NQO through modification of detoxifying enzyme activities and/or cell proliferation activities.

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[Lab. of Biochemistry]

**Modifying Effects of a Flavonoid Morin on Azoxymethane-Induced Large Bowel Tumorigenesis in Rats.**

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The modifying effects of dietary exposure to a flavonoid morin during the initiation and post-initiation phases of azoxymethane (AOM)-initiated colorectal carcinogenesis was investigated in male F344 rats. A total of 55 animals were initiated with AOM by weekly s.c. injections of 15 mg/kg body wt for 3 weeks to induce colorectal neoplasms. These results indicate that morin could exert a weak chemopreventive effect on large bowel tumorigenesis induced by AOM when fed during the post-initiation phase.