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CANCER

FOLATE PREVENTS GASTRIC CANCER

Folate protects against *Helicobacter*-associated gastric cancer in mice by increasing global DNA methylation and preventing inflammation, according to researchers from the USA and Canada. "Folate is one of the most widely available and effective methyl donors. We wanted to investigate its efficacy and ability to reverse gastric cancer progression," explains lead author Tamas Gonda.

Folate is a methyl donor with a major role in methylation reactions. Folate supplementation can reverse global DNA hypomethylation, prevent DNA damage and improve DNA repair; however, a conflicting picture has arisen from epidemiological and intervention studies into the protective effects of folate in various cancers.

Gonda and colleagues used a hypergastrinemic mouse model (INS-GAS) that progressively develops gastric dysplasia and carcinoma, which is accelerated by infection with *Helicobacter felis*. These mice had low folate levels and reduced global DNA methylation in their stomachs compared with uninfected, wild-type mice. Serum homocysteine levels, which are an inverse indicator of methyl donor status, were increased in the *H. felis*-infected INS-GAS mice, indicating reduced levels of methyl donors.

The researchers found that increasing grades of neoplasia were associated with progressive loss of DNA methylation. By measuring homocysteine levels, they were also able to show that methylation loss correlated with a decrease in levels of methyl donors.

Folate supplementation reversed methyl donor deficiency, prevented loss of DNA methylation and reduced gastric dysplasia, but did not inhibit *H. felis* colonization. The researchers also observed a decrease in proinflammatory lymphocyte numbers after folate supplementation, indicating that the T-cell-driven carcinogenesis that is associated with *Helicobacter* infection could be interrupted.

The researchers will now focus on the relationship between inflammation and methyl donor supplementation. "The interaction between methylation changes and inflammation has important implications for chemoprevention of inflammation-driven cancers," concludes Gonda.

Andy McLarnon

Original article Gonda, T. A. *et al*. Folic acid increases global DNA methylation and reduces inflammation to prevent helicobacter-associated gastric cancer in mice. *Gastroenterology* doi:10.1053/j.gastro.2011.12.058