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Decreased *Helicobacter Pylori*-Associated Gastric Carcinogenesis in Mice Lacking Inducible Nitric Oxide Synthase

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Overproduction of nitric oxide via inducible nitric oxide synthase (iNOS) is suggested to be a significant pathogenic factor in *Helicobacter pylori* (*H. pylori*)-induced gastritis. The purpose of this study was to examine the role of iNOS in *H. pylori*-associated gastric carcinogenesis. Two types of mice were used in this study, iNOS-deficient mice (iNOS-/-) and wild-type littermates. Gastric cancer was generated in mice using a combination treatment comprising N-methyl-N-nitrosourea (MNU) administration and *H. pylori* infection. Fifty weeks after treatment, tumors in gastric tissues from both types of mice were examined using histopathology, immunohistochemistry and immunoblotting for iNOS and 3-nitrotyrosine. The overall incidence of gastric cancer at week 50 was significantly lower in iNOS-/- compared to iNOS wild-type mice ($p<0.05$). When analyzed according to tumor pathology, the incidence of gastric adenocarcinoma was significantly lower in iNOS-/- compared to iNOS wild-type mice ($p<0.05$). Immunostaining for iNOS was clearly observed in the adenocarcinoma cells of iNOS wild-type mice, and was characterized by a strong cytoplasmic expression pattern. 3-nitrotyrosine was expressed mostly in the area of the lamina propria of the gastritis and adenoma lesions in iNOS wild-type mice. Immunoblotting analyses showed iNOS and 3-nitrotyrosine was also expressed in both adenoma and adenocarcinoma tissues from iNOS wild-type mice. iNOS and 3-nitrotyrosine expression was greater in tumor tissues than in non-tumor tissues. These findings suggest that iNOS contributes to *H. pylori*-associated gastric carcinogenesis in mice.

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