*p16\(^{INK4a}\) Promoter Hypermethylation of Adjacent Non-tumorous Tissue of Gastric Cancer Is Correlated with Glandular Atrophy and Chronic Inflammation*

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**Background** *p16\(^{INK4a}\)* tumor suppressor gene can be inactivated by promoter region hypermethylation in many tumor types including gastric cancers. However, *p16\(^{INK4a}\)* promoter hypermethylation in the surrounding non-tumorous tissues of gastric cancers have not been studied in detail.

**Methods** We examined 46 gastric cancers, corresponding adjacent non-tumorous tissues and 8 gastric tissues of chronic gastritis by performing methylation specific PCR, and analyzed *p16\(^{INK4a}\)* protein expression using immunohistochemistry and Western blot.

**Results** *p16\(^{INK4a}\)* promoter hypermethylation was observed in 43% of gastric cancers and 59% of adjacent non-tumorous tissues, however, none of the samples retrieved from the patients of chronic gastritis displayed *p16\(^{INK4a}\)* promoter hypermethylation. Gastric cancers showed an inverse correlation between vascular invasion and *p16\(^{INK4a}\)* promoter hypermethylation, and adjacent non-tumorous tissues displayed close association between the grade of chronic inflammation, presence of glandular atrophy and *p16\(^{INK4a}\)* promoter hypermethylation. *p16\(^{INK4a}\)* expression was markedly decreased in samples with *p16\(^{INK4a}\)* promoter hypermethylation when compared with samples without *p16\(^{INK4a}\)* promoter hypermethylation.

**Conclusion** These results suggest that *p16\(^{INK4a}\)* promoter hypermethylation is an early and frequent event in gastric carcinogenesis and may serve as a new prognostic biomarker for the risk of gastric cancers.