

## Genetic Alterations of the CDX2 Gene in Gastric Cancer

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Gastric atrophy and intestinal metaplasia are generally considered to be precancerous lesions of the stomach and Cdx2 play an important role in intestinal metaplasia and gastric carcinogenesis. To elucidate the potential etiological role of the Cdx2 gene in the gastric carcinogenesis, we have analyzed the gene mutations and allele loss of the Cdx2 gene in 95 sporadic gastric cancers. We found somatic mutation of the Cdx2 gene in 2 cases. The mutations were missense mutations, P63L in exon 1 and E204K in exon 2 encoding caudal like protein activation region (codon 13~180) and homeobox domain (codon 188~243) of the gene, respectively. In addition, 9 (25.0%) of 36 informative cases at D13S220 and/or D13S260 showed allele loss. In 11 cases with genetic alteration, Cdx2 nuclear staining was observed only in 8 gastric mucosae with intestinal metaplasia. Of these, loss of Cdx2 expression in cancer cells was found in two cases with somatic mutation and three cases with LOH. Interestingly, all of them were of intestinal-type gastric cancers. Thus, these results suggest that genetic alterations of Cdx2 may contribute to the loss of Cdx2 expression and to the development of gastric cancer, especially to intestinal-type.