Methylation-silencing RCC1 expression is associated with tumorigenesis and depth of invasion in gastric cancer.

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ABSTRACT

Introduction: Regulator of chromosome condensation 1 (RCC1) is a critical cell cycle regulator. We firstly identified RCC1 gene hypermethylation in gastric tumor tissues using the differential methylation hybridization (DMH) microarray, but the role of RCC1 in the pathogenesis of gastric carcinoma is largely unknown.

Methods: Three gastric cancer cell lines (AGS, MKN45, and TSGH9201) were used to analyze RCC1 gene methylation, mRNA and protein expressions. Furthermore, 85 pairs of matched human gastric carcinoma samples in a tissue microarray were used to analyze RCC1 expression by immunohistochemistry staining.

Results: A differential methylation pattern was found in TSGH9201 (100%), MKN45 (87%), and AGS (62%) cell lines at the 9th CpG site of RCC1 exon 1. RCC1 mRNA and protein expressions in AGS cells were significantly higher than in TSGH9201 and MKN45 cell lines (P < 0.05). Tissue array data showed that RCC1 expression was detected in 21% (18/85) of gastric carcinoma tissues and in 80% (76/95) of adjacent non-tumor tissues. The expression of RCC1 in gastric carcinoma tissues was significantly lower than in adjacent non-tumor tissues (P < 0.001). Furthermore, an association between RCC1 expression and clinicopathological features showed that RCC1 expression was closely correlated with tumor differentiation and depth of invasion (P < 0.05).

Conclusions: Our data indicate that RCC1 expression is frequently lost in poorly differentiated gastric cell lines and gastric carcinoma tissues. Loss of RCC1 expression is correlated with tumor differentiation and depth of invasion. These findings suggest that RCC1 may play a tumor suppressor role in gastric carcinoma.

Keywords: DMH microarray, gastric carcinoma, RCC1, DNA methylation, tumor tissue array, immunohistochemistry...

REFERENCES

[7] Correa P. Human ga...