Promoter CpG methylation of tumor suppressor genes in colorectal cancer and its relationship to clinical features

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Abstract

Aberrant promoter methylation of CpG islands of tumor suppressor genes inhibits expression of the genes and may lead to tumorigenesis. We investigated the aberrant methylation profile of potential tumor suppressor genes of p15, p16, SOCS-1, and Wnt signaling pathway in colorectal cancers and correlated the data with clinical findings. Cancerous and nearby non-cancerous tissues of 185 sporadic colorectal cancer samples were studied. Methylation specific PCR was performed to explore the mechanism of inactivation in p15, p16, SOCS-1, E-cadherin, APC, GSK-3beta, and Axin1 genes. Aberrant promoter methylation in p15, p16, SOCS-1, E-cadherin, APC, GSK-3beta, and Axin1 genes were 5.9, 7.0, 3.8, 5.9, 12.4, 2.2, and 0% for cancerous tissues, respectively, whereas the frequencies were 3.8, 0, 0, 7.0, 2.7, 0.5, and 0% for nearby non-cancerous tissues, respectively. The frequency of aberrant promoter methylation of cancerous tissues was significant higher than non-cancerous tissues in p16, SOCS-1, and APC genes ($p<0.05$) and methylation status of these genes had no clear relationship with clinical parameters. Of the 66 patients who showed at least one aberrant promoter methylation in the tumor-suppressor genes, 5 (7.6%) patients demonstrated multiple methylation phenotype (methylation > or =3) and associated with increased lymph node metastasis ($p=0.036$). Our findings suggest that inactivation of some tumor suppressor genes through aberrant promoter methylation of CpG islands may play a role in the development of colorectal cancer and methylation inactivation of these genes except p16 and SOCS1 may occur at the precancerous stage. Multiple methylation pathways may be involved in the tumorigenesis of colorectal cancer and associated with aggressiveness of clinical disease.