Methylation levels of LINE-1 repeats and CpG island loci are inversely related in normal colonic mucosa

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Hypermethylation of CpG island loci within gene promoter regions is a frequent event in colorectal cancer that is often associated with transcriptional silencing and has been referred to as CIMP+. DNA hypomethylation can occur in concert with CIMP+, although these two phenomena appear not to be related in colorectal cancer. The authors investigated here whether the methylation level of LINE-1 repeats, a surrogate marker for genomic methylation, was associated with the level of CpG island methylation in colorectal cancers and in matching normal colonic mucosa from 178 patients. The MethyLight assay was used to quantitate the methylation of CpG islands within the MLH1, P16 (INK4A), TIMP3, DAPK, APC, ER and MYOD genes. A real-time, methylation-specific polymerase chain reaction assay was also used to quantitate the methylation of LINE-1 repeats. In colorectal cancer, no associations were seen between methylation levels in LINE-1 repeats and CpG island loci, including a new CpG island panel that was recently proposed for CIMP+. In normal colonic mucosa, however, the methylation level of LINE-1 repeats was inversely correlated with CpG-island methylation of the MLH1, P16, TIMP3, APC, ER and MYOD genes. The methylation level of LINE-1 repeats in normal colonic mucosa also showed significant associations with common polymorphisms in the methylene tetrahydrofolate reductase and methylene tetrahydrofolate dehydrogenase genes involved in methyl group metabolism. Further investigation of genomic and CpG island methylation in normal colonic mucosa and the possible influences of environmental and genetic factors may provide new insights into the development of CIMP+ colorectal cancer.

[Reference]

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