COX-2 hypermethylation is a prognostic factor of cervical cancer
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Purpose : Gene silencing caused by aberrant hypermethylation is an important epigenetic event in tumor progression. We hypothesized that the aberrant hypermethylation of a specific tumor suppressor gene may associate with the prognosis of cervical cancer.

Methods : We compared the clinical outcome of 80 women with cervical cancer and their hypermethylation profiles using bisulfate modification and MS-PCR. Informed consents from all subjects were obtained.

Results : Total of 14 genes (p16, APC, RASSF1A, CDH1, FHIT, HLTF1, THBS1, RUNX3, COX-2, DAPK, hMLH1, GSTP1, TIMP3, and p14), which were known to be associated with tumor behavior, was analyzed. Interestingly, by log-rank test, we found that aberrant hypermethylation of COX-2 was significantly associated with poor overall survival of cervical cancer (P=0.001). Immunohistochemistry of COX-2 methylated samples revealed that one subject showed positive COX-2 immunoreactivity despite COX-2 aberrant methylation. Aberrant methylations of other tumor-associated genes were not associated with clinical outcome of cervical cancer.

Conclusion : Our results suggest that aberrant methylation of COX-2 gene may be a poor prognostic factor of cervical cancer. Since COX-2 expression is suggested as a poor prognostic factor in cervical cancer, our results need to be validated in further study.

Aberrant DNA hypermethylation: Distinctive epigenetic marker between adenocarcinoma and squamous cell carcinoma of cervix
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Purpose : Previously, we have reported that DNA hypermethylation of RASSF1A and hMLH1 are epigenetic markers distinguishing adenocarcinoma (AC) and squamous cell carcinoma (SCC) of uterine cervix (Proc of the 30th Annual Meeting of Korean Cancer Association #P-100). In this study, to overcome the caveats of small sample size of the previous study, we investigated the DNA hypermethylation profile with the extended samples.

Methods : Using bisulfate modification and MS-PCR, we determined the DNA hypermethylation profile in 95 cervical cancer patients including 34 AC patients. Informed consents from all subjects were obtained.

Results : We confirmed that aberrant DNA hypermethylation of RASSF1A, which we previously suggested, is significantly increased in ACs of uterine cervix (P<0.001). In addition, we found that hypermethylation of APC, HLTF1, and TIMP tumor suppressor genes is distinctive characteristics of ACs (P<0.001, P<0.001, P<0.001, respectively). In contrast, hypermethylation of CDH1 and THBS1 genes is found to be characteristics of SCCs (P<0.001, P<0.001).

Conclusion : Here, for the first time, we report that not only aberrant methylation of RASSF1A and APC, but also methylation of HLTF1 and TIMP are epigenetic characteristics of ACs of uterine cervix. This suggests that different epigenetic mechanisms may play a role in tumorigenesis of ACs and SCCs.