Reviewer’s report

Title: Up-regulation of expression and lack of 5CpG island hypermethylation of p16 INK4a in HPV-positive cervical carcinomas.

Version: 1 Date: 27 December 2006

Reviewer: Nam Hoon Cho

Reviewer’s report:

General

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

The authors failed to identify the extensive methylation within p16 CpG island in 13 primary cervical carcinomas and in 5 cervical cancer cell lines, though cases with partial methylation were seen in a few cases, relatively higher even in normal samples. Then p16 hypermethylation is not a frequent event. There are some potentially serious problems with the manuscript, then needed to be addressed.

1) There are too few numbers of materials to draw a strong conclusion.
2) Table 1 should clarify in more detail according to partial or extensive methylation status and normal versus cancer areas.
3) Methylation-specific PCR primer sites are too restricted beyond the range of the ‘core region’. Authors should protect the chance of false negative results due to the insufficient methods.
4) On immunohistochemical staining, cytopalsmic staining can be just non-specific, not implying true clue to overexpression. Authors should be careful to declare on the ground of more scientific and fundamental evidence.
5) In conclusion, you have to be cautious to mention the last paragraph 'hypermethylation of the gene can not be ..... with persistent HR-HPV infection and up-regulated...' because your research did not contain the convincing data on HR-HPV persistent infection.
6) The references should be extensively searched with more specific regards to p16 hypermethylation in cervical cancers, for instance, "Methylation of p16INK4a is a non-rare event in cervical intraepithelial neoplasia." Diag Mol Pathol 2006; 15:74-82.

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.