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: 2 January 2007

Reviewer: ALFONSO DUENAS-GONZALEZ

Reviewer's report:

General
This is a report on the status of p16 (expression and methylation) gene in cervical cancer cell lines and primary tumors. The ms in general terms is well-written

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
The major issue raised in this work is that the results are not concordant with those previously published where methylation frequencies at this gene promoter is substantial. In addition, several studies in cervical cancer patients have also found no expression or down-regulation in the expression of p16 protein. The having different results does not imply that the results are incorrect, however, they need to be discussed in depth in regard to previous ones. Issues such as the number of patients, FIGO stages, race, technics for assess methylation, primer positions, etc must be detailed and compared (preferably in a table) with previous studies. The following is a list of these works (some of them are referenced but not discussed in the manuscript). A satisfactory addressing of this issue is absolutely needed.

Yang HJ, Differential DNA methylation profiles in gynecological cancers and correlation with clinicopathological data.
Jeong DH, Promoter methylation of p16, DAPK, CDH1, and TIMP-3 genes in cervical cancer: correlation with clinicopathologic characteristics.
Int J Gynecol Cancer. 2006 May-Jun;16(3):1234-40.
Yuan JR,[Methylation and aberrant expression of the p16 gene in cervical carcinoma]
Wong YF, Methylation of p16INK4A in primary gynecologic malignancy.
Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Discretionary Revisions (which the author can choose to ignore)

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: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests'