Reviewer’s report

Title: Heparin (GAG-hed) inhibits LCR activity of Human Papillomavirus type 18 by decreasing AP1 binding

Version: 1 Date: 29 May 2006

Reviewer: eun hwang

Reviewer’s report:

General
This is a paper with reasonably good experimental data and some interest in general field of cancer biology, and bigger interest in the filed of cervical cancer. Most experiments were carefully designed. One major problem is that the manuscript has a lot of grammatical errors. For example, the first paragraph of the result section (p10) alone bears numerous grammatical errors.

(in the 3rd line, “In order to induce tumors derived from of HeLa cells”;
in the 10th line, “tumors which size was arbitrarily” should be “tumors whose size was arbitrarily”;
in the 11th line, “that were treated with GAG-hed as notice(d) after;”
in the 12th line, “At day 30th”, should be “At day 30”.)

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

And, there is one experiment that requires more careful observation and documentation on the result. Heparin is known to induce cancer cell death through inhibition of transcription factors and causing apoptosis (for example, Berry D, Lynn DM, Sasishekaran R, Langer R., 2004). Therefore, GAG-hed used in this work is expected to induce cell death independently of the inhibition on HPV E6/E7 expression. On page 12, authors described the effect of GAG-hed on HeLa cell viability. Authors documented “the same suppressive effects of GAG-hed--- can be translated into a significative decrease in viability and growth for HeLa cell cultures”. However, authors carried out MTT assay which provides only the relative numbers of live cells. The result presented in Fig.4, does not provide any information on whether the treatment caused only cell growth arrest (usual outcome of E6/E7 inhibition is G1 arrest followed by a state of cellular senescence) or also induced cell death. The cell morphology presented in B does not provide any information on the effect of the treatment, and the text neither described anything on this observation. The authors may also want to observe a longer effect on SW480 cells.

Secondly, in Fig 6., authors provided a model for the effect of GAG-hed on HPV LCR. According to the cartoon in the proposed model and its legend, GAG-hed and AP1 form a stable complex that is incapable of binding to DNA. Is there any evidence for the existence of this complex either from any published report or from the work of the authors’ own? If not, the proposed model should be retracted. If yes, it should be mentioned and discussed.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

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Discretionary Revisions (which the author can choose to ignore)

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

Level of interest: An article of importance in its field

Quality of written English: Not suitable for publication unless extensively edited

Statistical review: No
Declaration of competing interests:

I declare that I have no competing interests.