Reviewer's report

Title: Increased phosphorylation of histone H3 at serine 10 is involved in Epstein-Barr virus latent membrane protein-1-induced carcinogenesis of nasopharyngeal carcinoma

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Reviewer: Kai-Ping Chang

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This is an interesting study evaluating the role of histone H3 phosphorylation at serine10 (p-H3Ser10) in Epstein-Barr virus (EBV) latent membrane protein-1 (LMP1)-induced carcinogenesis of nasopharyngeal carcinoma (NPC). Authors demonstrated that EBV-LMP1 can induce phosphorylation of histone H3 at Ser10 via MSK1. Authors therefore concluded that increased phosphorylation of histone H3 at Ser10 is likely a crucial regulatory mechanism involved in LMP1-induced carcinogenesis of NPC. Although the design and novelty of the study may be attractive to our readers, several problems may arise in this study.

Major concerns:

(1). Authors used only one NPC cell line (CNE1, a well-differentiated SCC) to verify the hypothesis. Although the results are very convincing, readers might doubt if similar findings could be reproducible in another NPC cell line, especially in the NPC cell line which was derived from the more common cell type, undifferentiated carcinoma, in NPC. The authors are advised to try another NPC cell line to prove at least that EBV LMP-1 can induce the increased phosphorylation of histone H3 at serine 10.

(2). The expressions of LMP1 were scored as positive and negative when the percentage of stained tumor cells in an entire lesion was #5% and #5%, respectively. This cut-off value is very doubtful. Spearman correlation is also not a proper statistical method to be used under this circumstance. The authors should improve the statistical methods to prove this association in vivo.

(3). P-H3Ser 10 labeling index is also higher in chronic nasopharyngitis compared to that of normal nasopharynx. Authors are advised to provide a reasonable explanation for this phenomenon.

Minor concern:

(1) At page 5, paragraph 2, authors addressed that NPC is a human squamous cell carcinoma. Although this might be true at EM level, this description might still mislead our readers and should be modified and the relative literature should be quoted adequately.
Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

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