Reviewer’s report

Title: Genomic profiling identifies common HPV-associated chromosomal alterations in squamous cell carcinomas of cervix and head and neck

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Reviewer: William Lockwood

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Wilting et al provide evidence that HPV-positive squamous cell carcinomas have specific alterations that distinguish them from other squamous cell cancers. In addition, they identify organ specific genomic events as well as pan-squamous genomic alterations across cervical and head and neck cancers. While it is clear that identifying regions of genomic alteration associated with HPV infection is necessary to define mechanisms of HPV-mediated carcinogenesis, the current study is entirely descriptive and fails to interpret the results in a biological context.

Major Compulsory Revisions:

The authors use array CGH data to define regions of copy number alteration specific to HPV-positive head and neck and cervical cancers. The approaches used and statistical methods employed are very sound and yield interesting results. However, it is disappointing that the authors do not interpret or discuss their findings to further insights into the mechanism of HPV mediated tumorigenesis.

In its current state, the article solely lists regions of alteration common or specific to each group. The authors should take this information one step further and identify the specific genes and pathways associated with tumorigenesis in each group, particularly HPV positive cancers. For example, in the conclusions, the authors state that 32% of the genes found by Pyeon et al to be differentially expressed between HPV-positive and negative cancers were located within the regions identified in this study. It is unclear why the authors did not investigate these genes and their functions further. Are any of the genes known to interact with E6 and E7? What pathways are these genes involved in? How would this impact the treatment of HPV-positive vs HPV-negative cancers.

Questions of this nature need to be addressed in order to relate the findings to cancer biology

Level of interest: An article of importance in its field

Quality of written English: Acceptable

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