Reviewer's report

Title: HPV seropositivity joints with susceptibility loci identified in GWASs at apoptosis associated genes to increase the risk of esophageal squamous cell carcinoma (ESCC)

Version: 3 Date: 12 May 2014

Reviewer: Hong Cai

Reviewer's report:

- Major Compulsory Revisions

1. Authors have added the discussion about social economic status (SES) in the limitation section. However, they have not sufficiently discussed the limitation of hospital-based sampling. Other crucial demographic characteristics in cases and controls, such as the place of origin (citizens vs. rural residents), should also be compared carefully to ensure the comparability between the two groups. It is worrisome that the majority of controls were from city areas (according to “Healthy controls were volunteers from Tongji Hospital Physical Center who had received a comprehensive health examination and were found to be cancer-free”) while cases were from all parts of Hubei province including rural areas. If this is the case, different characteristics such as lifestyles as well as social economic status may confound results and the corresponding impact (selection bias and limited representativeness of the sample) should be discussed.

2. Stratified analyses by smoking/drinking status have not been carried out appropriately. Table S3-S8 should be improved to show the potential gene-HPV interaction by smoking and drinking status. Take Table S3 for example. Among non-smokers, the group of CC and HPV16 negative should be used as reference group as authors did. Also, among smokers, the group of CC and HPV16 negative should be used as the reference group (instead of using the group of CC and HPV16 negative among non-smokers as reference). In addition, the gene-HPV interactions should be assessed by including the gene*HPV 16 interaction term in the logistic regression models.

- Minor Essential Revisions

1. Authors should state how they performed the trend tests. Statistical method such as “Tests for linear trends were performed by treating ordered categorical variables as continuous variables in the regression analysis” should be added.

2. Vertical rules in tables should be avoided.

3. According to Table S9, there was gene-gene interaction with statistical significance. Authors may consider adding the corresponding results in the text.
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: Yes, and I have assessed the statistics in my report.

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