Reviewer's report

Title: Ovarian cancer risk and common variation in the sex hormone-binding globulin gene: a population-based case-control study

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Reviewer: Qiuyin Cai

Reviewer's report:

General

This manuscript evaluated the association between the genetic polymorphisms of SHBG and ATP1B2 genes and epithelial ovarian cancer risk. The D356N polymorphism of SHBG gene has been suggested to be associated with other hormonally-related cancers such as breast cancer; little is known about the association of SHBG polymorphisms with ovarian cancer. Results from this study may contribute to our understanding of this association. The major concern of this study is that this study has a small sample size. The statistical power is low, especially for the functional polymorphism D356N.

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

1. Previous studies suggest that D356N polymorphism was associated with circulating levels of SHBG in post-menopausal women. Although the power is limited due to the small sample size, analyses stratified by menopausal status should be conducted.

2. On the LD analysis between rs6559 and rs1799941 polymorphisms, the authors used both D’ and r2 methods. The results, however, contradict each other (D’=1 but r2 = 0.03). D’ analysis is not appropriate when frequency of a particular allele is very low.

3. In addition to haplotype analysis, it will be interesting to see if there is any joint effect of rs1799941 and rs6259 polymorphisms on the ovarian cancer risk.

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

1. For the haplotype analysis (Table 3), the author did not use the highest frequent haplotype group (35% in control) as a reference group. Why?

2. It will be helpful to present some background information for ATP1B2 gene. What is the function of this gene? Is there any functional interaction between SHBG and ATP1B2 genes?

3. The title of Figure 1 states that the LD map is for the TP53 gene and its franking region. Is this a typo or did the authors use the wrong LD map?

Discretionary Revisions (which the author can choose to ignore)

What next?: Accept after minor essential revisions
Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No

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