Reviewer's report

Title: LINE-1 methylation is inherited in familial testicular cancer kindreds

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Reviewer: Jian-Xin Gao

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Although a large volume of data has implicated that retrotransposon LINE-1 might play an important role for tumor development, little is known for the role of LINE-1 in tumor development. Mirabello et al report here that LINE-1 methylation is inherited in familiar testicular cancer kindreds. They demonstrate that the inheritance is gender-specific. Importantly, they also show that LINE-1 methylation of affected father is strongly correlated with affected son, suggesting that epigenetic susceptibility of testicular germ cell tumors (TGCT) is heritable. This finding might be as well applicable to other types of cancer. Therefore, the paper provides valuable information of LINE-1 methylation status effecting on the susceptibility to TGCT and is publishable, despite the fact that the data presented is preliminary. However, the authors should address the following issues before publication:

1. Throughout this paper, the authors used terms “global methylation” interchangeably with “global (LINE-1) methylation”. Because global methylation is usually referred to the methylation status of genome or all DNA, LINE-1 methylation or “global (LINE-1) methylation” should be used in the text to avoid confusing for readers.

2. The authors cited in the discussion that genomic DNA methylation is lower in the patients with seminoma than in non-seminoma controls. However, LINE-1 methylation is not significantly different between these two groups. This suggests that LINE-1 methylation status may be associated with the susceptibility but not the establishment of seminoma. Thus, it would be necessary to show genomic DNA methylation between these two groups in this paper, which will give rise to a positive control (reproducibility) as well as a technical control for LINE-1 methylation (it would be questionable should the levels of genomic DNA methylation be the same between seminoma and non-seminoma controls). Otherwise, the authors should at least explain the contradiction beyond expectation.

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.

**Declaration of competing interests:**

I declare that I have no competing interests.