Reviewer’s report

**Title:** LINE-1 Methylation Status and Its Association with Tetralogy of Fallot in Chinese Infants

**Version:** 1  **Date:** 5 March 2012

**Reviewer:** Apiwat Mutirangura

**Reviewer’s report:**

Sheng W et al reported LINE-1 hypomethylation of heart tissues of patients with Tetralogy of Fallot. The finding is new and performed from a very difficult to get tissues. Although the study will be much more appreciated if authors can provide more information on causes and consequences of these finding, I believe this finding deserved publication. Nevertheless, there are some concerns that should be addressed before publication.

**Major Revision**

- Title: I don’t see a particular reason indicating this finding as “Chinese”. Please consider exclude the term.
- Background regarding the role of LINE-1 methylation was inadequate and not up to date. Author should mention a current report that LINE-1 hypomethylation genome widely down regulated gene containing LINE-1 (published in PLoS One 2011, 6(3):e17934). Please note that the role on gene expression explains phenotypes better than instability.
- To prove that the difference in methylation between test and control was not due to confounding sex and age, authors may do an additional pair t-test by matched age and sex between test (TOF) and control.
- Because differences in number of tests the non significant difference in female group is not conclusive. Equal number of test and control should provide more convincing result. Authors may do two additional pair t-tests (male and female) by matched age between test (TOF) and control.
- Method and data showed no association between promoter methylation and LINE-1 methylation should be provided.

**Minor**

- It will be of great interest to people who are interested in LINE-1 methylation to see the association between CpGs. Example evaluating the correlation between LINE-1 CpGs was reported at Nucleic Acids Res 2008, 36:5704-5712.
- Finally several recent evidences demonstrated independent methylation changes among certain interspersed repetitive sequences. For example methylation of Alu but not LINE-1 is low in aging. So I suggest not defining LINE-1 methylation levels as global methylation levels. Author may do Alu methylation study or edit the word “global” to be more specific (LINE-1).
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'