Reviewer's report

**Title:** DNA methylation analysis reveals distinct methylation signatures in pediatric germ cell tumors

**Version:** 3  **Date:** 24 November 2012

**Reviewer:** Yasuhiko Kaneko

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The authors studied methylation status of cancer-related genes and 5 imprinted genes in 51 pediatric germ cell tumors, and stated that they found distinct methylation signatures. Although their findings are mostly confirmatory, they usefully extend the previous findings on the epigenetic characteristics of pediatric germ cell tumors.

**Major Compulsory Revisions:**

I have the following concerns:

The lengthy discussion should be shortened, and should focus on the subject relevant to their findings.

Examples of irrelevant discussion:

The fifth paragraph of discussion: “In a pathway analysis------for patients with GCTs.” The authors did not study expression of the stem cell marker genes in their GCTs, and the expression studies are mandatory to discuss the relationship between the aberrant expression of stem cell markers and germ cell tumorigenesis.

The sixth and eighth paragraphs: “Our results ------malignant teratoma.” and “Survival rates------that could be used.”

The authors did not provide the data on survivals. Because greater than 95% of children with GCT are cured by the present therapy as they described in the discussion, it is very difficult to identify the prognostic markers. In addition, the fifth reference in this paper stated that methylation of tumor suppressor genes did not affect the outcomes of patients with yolk sac tumor. Thus, the paragraphs may be useless if they do not provide their own data on outcome and the methylation status of the genes.

Table 4: The numbers of YSTs and germinomas in Table 1 differ from the numbers of respective tumors in Table 4. The authors should describe the reason of the discrepancy.

Thirteen YSTs in Table 4 should be classified into male and female tumors, and the respective data should be provided, because the methylation status of the imprinted genes depends on the sex of the host in whom tumors develop.
**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

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