Author's response to reviews

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

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We thank the reviewers for their helpful comments. Below, we provide a detailed response to the reviewers’ questions

Reviewer 1

The revision seems to be well down. However, I had a little concern on the new sentence below.

Page 8, the first paragraph: we found that methylation at SOX2 was correlated with expression (r=0.44, p=0.008)

We usually find that the promoter (or CpG island) methylation of a gene is inversely correlated with expression. Please provide the explanation for the contradictory finding between methylation and expression.

• We thank the reviewer for pointing out this error. In the analysis, we inadvertently used the average #Ct value rather than the 2 –#Ct. The #Ct value has an inverse relationship with expression; therefore, the expression does follow the expected pattern. We have corrected this mistake and the correct correlation coefficient is -0.40.

Page 7, the third paragraph: GERs should be spelled out when it is used at the first time in the paper.

• We have made the suggested change
Reviewer 2

1. The authors indicate they have examined expression of Sox2 by qPCR (as opposed to qRT-PCR); no data is shown

• We thank the reviewer for pointing out this typo. We have corrected the text to reflect that we used qRT-PCR. We also have added the expression data for SOX2 in Supplementary Table X. In addition, we have added expression data for the de novo methyltransferase DNMT3B, which also supports our findings of higher methylation in YST.

2. They also use gene expression data to corroborate their methylation analyses which implicates Wnt signaling - the figure add has no annotation; statistical corroboration - so its difficult to place this heat map in the context of the paper.

• We apologize for this deficiency. We have now included the qRT-PCR data as supplemental tables 2-8, including the raw Ct values and fold-change/fold-regulation with P-values.

Quality of written English: Not suitable for publication unless extensively edited

• We have edited the document for clarity.