Dr. Li and colleagues provided a large genome-wide epigenetic profiling research to the cells in the different stage of embryonic development. The study was performed rigorously and the findings sound quite interesting. Although the authors solved majority of my previous comments, there are still few more question should be response further.

**Major Compulsory Revisions**

1, In the updated schematic overview, please remove ‘maybe’, we need provided definite conclusion to the community, vague statement is not suitable especially for the schematic overview which will be deeply remembered by the readers.

2, Is there any possibility to move current Figure 4 to Figure 1? Or else, I prefer to give another schematic overview in the beginning of the manuscript in which the strategy, study design, sample size and analysis could be shown. In some certain, maybe you don’t need to show the conclusion in the schematic overview.

3, In the updated abstract, 0.30±0.02 is still shown without any annotation, please remove 0.02 or noted as 0.30±0.02 (standard deviation). Meanwhile, I find huge number of such problem existed in the full manuscript, please change them carefully, without annotation, nobody knows what it is.

4, “For PCA analysis, the methylomes with the genomic coverage higher than 15% were included”. It is not clear what does the authors want to indicate. I think, here, the author wants to indicate the samples. please replace methylomes with ‘samples’. What’s more, in the page 7, How does the value: 95% CI 0.29-0.31 was calculated? I don’t understand why the author place a 95% CI here, what’s the statistic inference for this 95% CI?

5, in “Global abnormality of DNA methylome in human blastocyst”, whether the average methylation level is from same genomic positions? The methylation level in different genomic position is quite different, if the genomic regions were not same, then such kind of comparison doesn’t make any sense. This section should be re-analyzed to keep the CpG site 100% same among different samples.

6, In Supplementary Figure 1D, what does it mean for “DNA” (the first column)? Okay, then I think the author should be give explicit information for all the analysis, such as “DNA repeat elements in RepeatMasker” UCSC? Ensembl?

7, Figure S2B, why only select subset of the samples, rather than all the samples? maybe another boxplot with dotted points can be provided to show the methylation status for all the samples in the DMR regions.

8, “Notably, the P value of the homogeneity of variance between high-grade and low-grade TEs is 0.03, and the P value between high-grade and middle-grade is 0.05”. Which matric/measurement does the author use to represent “homogeneity”? Then why there is nothing description for Bartlett's test in the method section? I recommend the author to revise the manuscript by another biostatistician, the current statistical statements were not religious enough, vague concept such as divergent and homogeneity should be replaced with explicit matric such as variation or standard deviation. Please provide line number so that corresponding comments could map to page and line number.