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. I recommend to publish the manuscript if the authors could make the following revision.

**Major Compulsory Revisions**

1, A schematic overview or graphical abstract of the study was encouraged to be provided as the Figure 1, including the sample, analysis pipeline and main idea and found of the study.

2, In the abstract, the value of 0.30±0.02 is not clear, what’s that? Beta/M and SD/IQR/95%CI?

3, “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.

4, “Sequencing reads were trimmed to remove the reads containing adapters and low

Quality”, it is not clear how the author to do it.

5, “The chromosome number was deducted by R package HMMcopy”. Deducted should be detected? It is not clear which dataset were applied for this analysis, WGBS or RNA-seq?

6, in “Global abnormality of DNA methylome in human blastocyst”, whether the average methylation level is from same genomic positions?

7, Why use three different notes, AB, BA, or BB, to indicate middle grades?

8, For figure 1A and 1B (Supplementary Figure S1), It would be great if the author could add the boxplot outside the dots so that the quantile of the data distribution could be provided.

9, For figure 1B, more details should be provided, such as CpG shore, CpG shelf, main histone main TF-binding regions from ENCODE Project.

10, For supplementary Figure 1B, why only the Figures of AA and CC were shown?

11, In Supplementary Figure 1D, what does it mean for “DNA” (the first column)?

12, the definition or the database of the above genomic regions was not defined or provided. Please provided the database (include version) or definition.

13, “we regarded the methylome of AA blastocysts as good epigenomic status and used the average methylation level of AA blastocysts (0.30±0.02) as the control. Interestingly, the proportion of blastocysts with a methylation level falling within the range of 0.30±0.02 in different grades is correlated with the live birth rate for that grade”. Not clear what’s 0.02 represent.

14, Supplementary Figure 1C and 1D should have corresponding supplementary tables to show the exact values. Note: all the supplementary tables could be place in one excel in different sheets.

15, Figure S2B is not clear. What does the lines indicate? Different samples? it seems the number of the lines less than the sample size in the present study, right? Or else it is a schematic diagram？ Then why not provided a classic example with the current data in a classic DMR(genes)?

16, “Thus, hypothetically, the DNA methylome of a few TE cells removed from blastocysts could predict the methylome level of AA blastocysts (0.30)”. What’s this 0.30 represents?

17, Why only parts of the sample have “BSCR”? What’s the difference between bisulfite conversion rate calculated by spike-in unmethylated lambda DNA and non-CpG methylation? Or measured by methylation level of chrM?

18, “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”?

19, The following corresponding supplementary Tables should be provided for DMR, Figure 1A, 1B (value and variation), Figure 2A (genomic regions). In additional, the author forget to mention which databased was chose to do the enrichment analysis.