In this manuscript, Dr. Li and colleagues investigated the relationship between HIF3A genotype, DNA methylation and sex, gestational diabetes, pre-eclampsia, birth weight and gestational age with different statistic method in a large population size from Barwon Infant Study (n=938). It is the largest sample size research I have seen in the same topic research. *T*he study was performed rigorously and the findings are interesting. What’s more genetic and epigenetic variants were considered in the study at the same time. I only have several concerns for the authors to think about again and make further response.

**Major Compulsory Revisions**

1. In the Table 1 and Table 3, beta value in univariate (Table 1) and multivariate analysis(Table 3) for sex is same? Please double check it.
2. The author mentioned cellular heterogeneity and flow cytometry, However, I don’t know how the author adjusted these heterogeneity? No details about this part in the method and result section. The author mentioned sensitive analysis, however, the procedure of the sensitive analysis were not provided.
3. The author apply R2>0.3 as the imputation threshold, I am worrying about the accuracy for the further analysis. Is there any significant change for the most important conclusion in this study if we set R2>0.8 as the threshold? Another R2>0.1 was used again to select tag-SNPs, how about to show the association P-value distribution for all the SNPs?
4. Please show name platform name for the methylation quantification: SEQUENOM MassARRAY EpiTYPER platform. (Page 14, line 21)
5. How to understand the methylation level of 40%-50% in Figure 2? Imprinted genes (one chromosome methylated and another one un-methylated)?
6. It looks the methylation status of HIF3A.1 and HIF3A.2 is almost independent. How to understand this difference?
7. Please provide exact genomic position for HIF3A.1 and HIF3A.2 as chr19:xxx-xxx style so that the reader could map the regions quickly.
8. It is quite interesting result. However, it will be better if the author have some validation cohort or biological interpretation to confirm the most important conclusion.
9. Raw data including IDAT, Beta or M matrix should be deposited in the GEO database.

Minor Revisions:

1. In the study, multiple tests were conducted and I am think multiple test correction should be considered, at least in the discussion section.
2. I am not familiar with the methylation quantify method in this study, I am quite interesting the cost for this assay for each sample. And why the author apply this method rather than the traditional pyrosequencing or targeted BSP sequencing.
3. In table 1, the P-value column is not easy to be understood since it is not very clear which one is reference, for example, row of Gestational diabetes
4. In the background section, the current diagnosis golden standard and common procedure for the diagnosis in author’s hospital should be introduced with more information. Meanwhile,
5. The frequency of drug-related-toxicities in the patient population for capecitabine should be mentioned in line 32 page 5.
6. Too many data not published were listed in the manuscript, please replace them with published literatures.