In this manuscript, Dr. Shivakumar and colleagues conducted a two-stage exome-wide sequencing based association study to identify novel endometrial

Cancer related rare variants in a large American population, named MyCode. The study was performed rigorously and the findings are quite interesting.

**Major Compulsory Revisions**

**1, the description/algorithm for case-control enrollment is not clear.**

**2, the distribution of call rate for exome-sequencing should be provided as well some other basic description, such as sequencing depth, etc.**

**3, please provide a work-flow to show the procedure of the study.**

**4, the author only conducted association study to rare variants in current study (MAF<0.05), why not do the analysis to common variants at the same time to show the result for both of them.**

**5, It is very interesting that the authors annotate the significant SNPs with COSMIC database. COSMIC database is collected by somatic mutation while the authors actually obtained germline SNPs. How to understand the overlap? Meanwhile, I am not sure how the author list the tissue-source for the SNPs in Table 4.**

**6. the ways how to merge the SNPs to genes and to pathways will significantly influence the result and affect the repeat to this study, I suggest the authors give me details or provide scripts with github. Meanwhile, all the database or software should be provided with version or date number, such as KEGG (older version or new version?)**

**7, qq-plot should be provided for gene-based and pathway based analysis, as well as survival analysis.**

**8, I suggest the author provide all the scripts for the analysis with github so that readers can easily repeat the result within their own dataset. Meanwhile, the authors should pay attention to increase the reproducibility of the manuscript, for example, Table 3/4 should provide genome reference version for the position, GRCH37 or GRCH38.**

9, It will be nice if the author can provide the difference test for Table 1 between case/control and discovery/validation.