Reviewer's report

Title: Association of Estrogen Receptor beta variants and Serum Levels of Estradiol with Risk of Colorectal Cancer: a Case Control Study

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Reviewer: Aung Ko Win

Reviewer's report:

The authors investigated associations of (i) circulating estradiol levels and (ii) ESR2 SNPs rs1256049 and rs4986938 with colorectal cancer risk for Chinese men using a hospital-based case-control study.

Major

Materials
- For cases, what were the selection criteria? Age limits? Selected depending on a family history of colorectal cancer?
- For controls, were they frequency- or individual-matched with cases by age or else?

Methods
- The authors calculated odds ratios for dominant models (CT/TT vs CC).
- Can you present codominant models (CT vs CC and TT vs CC) for each SNP?
- Can you present per allele association (log additive model) for each SNP? i.e. CC=0, CT=1 and TT=2.
- Can you present association between total number of risk allele and colorectal cancer risk (per allele association) for combined two SNPs? i.e. risk allele number will range 0-4.
- Can you present ORs for colon and rectal cancers separately given the authors stated a previous study found that rs1256049 was only associated with rectal cancer?

Results
- Page 8: the authors presented the adjusted OR for serum estradiol. Can you please clarify what this OR represented? Per xx pg/ml or High vs Low level (cut-off?)?
- The authors used the term “adjusted P”. What does it mean? I assumed adjusted OR rather than adjusted P.

Discussion
- Page 10: The authors stated that “....the C allele of rs1256049 conferred an increased risk of rectal cancer....” but they stated in introduction (page 4) “....the T allele of rs1256049 confers increased risk of rectal cancer”. What is the correct one for risk allele of that SNP? The authors should use the same reference allele
in their analyses for comparison.
- The authors should refer a previous finding of association between rs1256049 and colorectal cancer risk in Japanese population.


Minor
- Use “multivariable” instead of “multivariate” analysis.
- Table 2: For rs1256049+rs4986938, the authors stated 0, 1, 2 risk genotype....Please use “allele” instead of “genotype”.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:
No conflict of interest.