Reviewer's report

Title: Effects of lifestyle and single nucleotide polymorphisms on breast cancer risk: A case-control study in Japanese women

Version: 2 Date: 12 September 2013

Reviewer: Francesco Gianfagna

Reviewer's report:

This is a replication study of breast cancer candidate SNPs in the Japanese population. It is an interesting study, since data from Japanese population are few. However, the authors should clarify the following points, regarding methods used for subgroup analyses.

Major Compulsory Revisions

1. A lot of analyses were performed, a further adjustment for multiple choice should be used. While the tested associations between genotypes and disease are few, and anyway concordant among the genotypes and the models used for each SNPs, the subgroup analyses are full many. False discovery rate adjustment should be used (preferred to more conservative methods), at least for subgroup analyses.

2. The authors should clarify the criteria for cut-offs used in subgroups definitions. While quartiles were used for some variables, no criteria were specified for other ones, finally some variables were used as continuous. This issue strengthens the need of a multiple choice correction.

3. In discussing the significant results of subgroup analyses, the Authors did not take into account the corresponding results in the opposite subgroup or in the whole sample result. In most cases, these results are similar to (or anyway not significantly different from) the whole sample results. Therefore, the results are those expected in case of null gene-environment interaction. Heterogeneity tests as #² have to be applied to assess differences between subgroups.

Discretionary Revisions

1. It is not clear why the Authors stratified for phenotypes and tested the genotypes in association with disease, while they not decided for the opposite choice. It could be more easy to read and compare the results with the literature.

2. Further comments should be added about the role of genes.

Minor essential revisions - Minor Issues not for publication

1. Please note that the first ref 8 cited in the text is not the correct one, which lacks in references list.
2. In methods (Subjects section), you could specify if participants were consecutively admitted.

3. Some sentences needing a check:
- at the end of introduction, "genETic factors such as..." should be used instead of "genOMic factors..."
- in methods, “(BMI) was calculated as body weight/the square of height” instead of “the square of height/body weight”
- in discussion, “although these SNPs are lococated in the same chromosome REGION”, region could be added
- in discussion, “upstream of the translational start site”, not “transcription” (wrong in ref 15 also, yes, please check)

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:
I declare that I have no competing interests