Author's response to reviews

Title: Common variation in EMSY and risk of breast and ovarian cancer: a case-control study using HapMap tagging SNPs

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Common variation in *EMSY* and risk of breast and ovarian cancer: a case-control study using HapMap tagging SNPs. Benusiglio et al., submission to BMC Cancer.

**Reviewer’s report version 2**

Jennifer HU

Here is how we have addressed Dr Hu’s comments.

**Major compulsory revisions**

1. *If authors do not wish to run some exploratory analysis, please include their justification in the paper.*

We have added the following paragraph to the discussion, page 12:

“Some authors have advocated the use of histopathologic or demographic data that subclassify individuals in order to identify homogenous subsets for analysis [35]. In the absence of any main effect or strong biological rationale, we have not carried out subgroup analyses as much larger sample sizes would be required to obtain reliable results. The number of possible post-hoc, subgroup analyses is large and there is a strong possibility that one or more tests will be statistically significant simply by chance [36].”

2. *Regarding the existence of coding polymorphisms in the gene, Dr Hu said: it will be important for authors to include the response to her previous comments in their paper.*

- We have added the following to the results section (page 10):
“At the time of study, there were four putative, non-validated coding SNPs mentioned in the dbSNP database (www.ncbi.nlm.nih.gov/SNP/): rs1954782, rs11822571, rs3753051 and rs1047196. We did not detect any of them.”

- We have also given an estimated sensitivity for the screening method used (DHPLC [94%]), in the discussion (page 11, middle paragraph).

- After the revised manuscript was submitted, genotyping data for a synonymous coding SNP in exon 19 was made available on the dbSNP database. We were able to assess that our set of SNPs tagged it very well and have added the information to the manuscript. The following paragraph was added to the discussion (page 12), after the results description for the leave-one-out procedure: “After this study was completed and the first version of the manuscript submitted, genotyping data in a white American population for rs3753051, a synonymous coding SNP in exon 19, were released in dbSNP. We were able to assess how this polymorphism was tagged by our set of SNPs as genotypes from the same individuals were also available for 5’up t>g, IVS9 a>g, IVS16 a>g and 3’down c>t; SNP rs3753051 was perfectly tagged (r² = 1) by 5’up t>g.”