Author's response to reviews

Title: Repeat polymorphisms in ESR2 and AR and colorectal cancer risk and prognosis: results from a German population-based case-control study

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Author's response to reviews: see over
Dear Dr. Frattini,

We appreciate the opportunity to revise our manuscript. We thank the reviewers for their helpful comments and have now revised our manuscript accordingly. Please find below the detailed answers to the comments given by the reviewers.

Yours sincerely, on behalf of all co-authors,

Anja Rudolph, PhD

Enclosures
Reviewer: Susanta Roychoudhury

Major comments

The paper reports case-control study to evaluate the association of two repeat polymorphisms in ESR2 and AR genes, respectively and colorectal cancer from a German population. The authors found only a moderate risk for colorectal cancer with average number of ESR2 CA repeats but without significant heterogeneity with respect to gender. No association also found with AR CAG repeats and colorectal cancer in this population. They also did not observe any association of these two polymorphisms with any prognostic factors and survival. Thus, basically it is a report of negative results. However, this is important in the background that couple of earlier study found association in other populations. The present study design is robust in respect of sample size and statistical analysis. The authors have carefully accounted for all variables in their analysis.

*We thank Dr. Roychoudhury for his detailed review of our manuscript and helpful comments.*

Minor comments:

1. Write full form of SHBG in its first mention.

   *We have corrected this (page 4, lines 79-80): “A CA repeat exists in intron 5 of ESR2, and it was found to be associated with serum androgen, sex hormone-binding globulin (SHBG) and estradiol levels [9, 10].”*

2. Correct the model name of the instrument in which genotyping was performed.

   *We corrected this mistake (page 7, lines 147-150): “The detection was done using the ABI 3130XL Genetic Analyzer (Applied Biosystems, Carlsbad, CA, USA) and the fluorescently labelled DNA fragments were analysed by size using the GeneMapper 4.0 software (Applied Biosystems, Carlsbad, CA, USA).”*

3. What “heterogeneous genotype” is as mentioned in result section (line 238)?

   *The correct expression here would be heterozygous instead of heterogeneous. We changed the respective sentence accordingly (page 10, lines 217-218): “Because the AR gene is X-linked, a heterozygous genotype among men indicates a genotyping error.”*

Reviewer: Silvia Ottaviani

Reviewer’s report:

The data presented in the case-report manuscript is interesting and scientifically sound. The content and organisation of the article are clear and the data discussed appropriately. Though the associations between ESR2 and AR repeat polymorphisms and colorectal cancer risk have been reported previously, this paper provides an incremental advancement on the published data. This is a well-written and presented article that will be of great interest to molecular endocrinologists and related scientists.

*We thank Dr. Ottaviani for her detailed review of our manuscript and helpful comment.*
Minor Essential Revisions:

1. Line 103: abbreviation has been used without the full description. Add: sex hormone-binding globulin (SHBG).

   This has already been corrected according to Dr. Roychoudhury’s comment.