Author’s response to reviews

Title: The influence of the rs1137101 genotypes of leptin receptor gene on the demographic and metabolic profile of normal Saudi females and those suffering from polycystic ovarian syndrome

Authors:

Maha Daghestani (mdaghestani@ksu.edu.sa)
Mazen Daghestani (mhdaghestani@uqu.edu.sa)
Mamoon Daghistani (mdaghist@hotmail.com)
Geir Bjørklund (bjorklund@conem.org)
Salvatore Chirumbolo (salvatore.chirumbolo@univr.it)
Arjumand Warsy (aswarsy@gmail.com;aswarsy@ksu.edu.sa)

Version: 3 Date: 28 Feb 2018

Author’s response to reviews:

Re: The influence of the rs1137101 genotypes of leptin receptor gene on the demographic and metabolic profile of normal Saudi females and those suffering from polycystic ovarian syndrome. BMWH-D-17-00231R2

Dear Sir

Thank you for your comments and the reviewers comments on our above mentioned paper. We have made all the suggested alterations and the paper in its modified form is enclosed. The changes made are listed below:

Answer to Editor Comments:

In addition to the reviewers' comments below, please address the following editorial requests in your revision:

1) Please indicate exact pages for each item on your STROBE checklist.

Answer: Done
2) Consent to publish: this refers to consent for the publication of identifying images or other personal or clinical details of participants that compromise anonymity. Since no such data is reported in your manuscript, please just write "Not applicable".

Answer: Done.

3) Availability of data and materials: please provide name and contact details of the person that readers can contact to obtain the data.

Answer: Done.

4) Please remove the funding information from the Acknowledgments section.

Answer: Done

5) Under the heading "Funding", please state the role of the funding body in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript.

Answer: Done

Answer to Reviewer reports:

Uma Addepally (Reviewer 1): Comments

1. In the anthropometric measurements and metabolic profile of POCS patients and controls (table 1), the crucial factors like Leptin, Ghrelin and HOMA-S the p values are much higher than 0.05. Does it give any significance between PCO and controls?

Answer: No, the high p value indicates there there is no significant difference in the levels of these parameters in PCOS and control group.

Q2. Does any allelic position specificity of Grouping of three genotypes-AA,AG and GG of rs1137101 exists.

Answer: No such specificity exits for the three genotypes.
Q3. Although several variants are involved with rs1137101 any specific reason to consider Gln233Arg.

Answer: The variants of rs1137101, are interesting to study as they have been associated with a number of diseases. As presented on Page 4, they are linked to insulin resistance, metabolic syndrome, dyslipidaemias, diabetes mellitus, obesity, cancer and others. Since PCOS is associated with insulin resistance, metabolic syndrome, dyslipidaemias, obesity, this SNP presented as an important genetic variant to be studied in PCOS patients.

Q 4. Some places it is mentioned as Glu233 (Gln233).

Answer: Thank you for pointing out this mistake. It is corrected. It is a Gln and not Glu.

Q5. if there is no difference between PCO and control for rs1137101 (non synonymous polymorphism), what is the role of Gln 223 in leptin binding or in transmembrane signaling (line no 6 in results).

Answer: An important point. Thank you. We have added an answer to this in the discussion (at end of the second last paragraph of the discussion) and conclusion as follows:

In Discussion: The results of this study highlight an important point, i.e. the polymorphic change resulting from the substitution of an A by G, changing the codon, CAG to CGG, and replacing Gln, a neutral amino acid by Arg, a basic amino acid, brings about an effect thereby affecting the value of different anthropometric and biochemical parameters, both in normal control and PCOS patients. The exact mechanism by which these changes are brought about need functional and in-silico studies, whereby the mechanism of leptin-LER-R interaction can be evaluated.

In Conclusion: Further studies are warranted to determine the mechanism of interaction between leptin and its receptor, which results when Gln, a neutral amino acid, is replaced by Arg, a basic amino acid.

Reviewer 2: Singh Rajender (Reviewer 2): I found the study to be well conducted and a straight association study. This methods are appropriate and results are well presented. In the introduction, rather than mentioning about the controversy among association studies, I would suggest the authors to mention that no study (if so) has been conducted on Saudi Arabian women. That would make a case for this investigation.
Answer: Thank you Sir for your valuable comment. The statement that this is the first study of rs1137101 in Saudi PCOS, in added.