Author's response to reviews

Title: Common Polymorphisms of Calpain-10 and the Risk of Type 2 Diabetes in a Tunisian Arab Population: a case-control study

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Author's response to reviews: see over
February 20, 2010

Scott Edmunds, Ph.D.
Senior Scientific Editor
BMC-series Journals
BioMed Central
Floor 6, 236 Gray's Inn Road
London, WC1X 8HL

Dear Dr. Edmunds,

Please find enclosed a revised version of the manuscript entitled:

**Common Polymorphisms of Calpain-10 and the Risk of Type 2 Diabetes in a Tunisian Arab Population: a case-control study**

Intissar EZZIDI, Safia MESSAOUDI, Molka CHAIEB, Maha KACEM, Ghada M AL-KHATEEB, Touhami MAHJOUB, Wassim Y ALMAWI and Nabil MTIRAOUl, which we submit for consideration for publication in BMC Medical Genetics, after having addressed additional comments of reviewer #1. Attached also is our point-by-point response to reviewer’s comments. The changes made in the text were marked in blue.

None of the authors has any potential financial conflict of interest related to this manuscript

All authors have carefully examined and approved of the changes made to the manuscript, and understand and accept that in the event of its publication, all copyright shall be transferred to BMC Medical Genetics. We look forward to hear from you favorably in due course.

Sincerely,

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RESPONSE TO REVIEWER #1 COMMENTS

Reviewer: 1. The authors only selected three SNPs based on previous reports; and as such, limitations of such a narrow focus should be discussed in the discussion section. Specifically, the authors restricted their study population to only Tunisians of Arab descent, the authors should address whether three SNPs are sufficient to capture the genetic variability in the population of Arab descent.

Authors: A point well-taken and appreciated.

Changes: The Discussion section was modified as per the reviewer's comment.

Reviewer: 2. More details on matching method would be helpful. Was it an individual matching or a frequency matching? If individual matching, how close a set of controls with respect to matching factors was chosen for each case?

Authors: Will do.

Changes: More information on selection of control subjects was added to the revised text.

Reviewer: (i) The authors stated that they used two-way ANOVA in table 2 to compare genotype distributions between groups. Two-way (or two factor) ANOVA (analysis-of-variance) is generally used to compare a continuous variable by two factors?

Authors: The actual test used for comparing allele and genotype frequencies was Pearson chi square test. The reference to two-way ANOVA was a mistake where placed (categorical comparisons).

Changes: The reference to two-way ANOVA was removed from Table 2.

Reviewer: It is recommended that, in matched case-control studies, we should control for matching factors regardless of “statistical significance” for the difference between cases and controls to reduce bias introduced by matching (Rothman KJ, Greenland S, Lash TL, Modern Epidemiology, 3rd. ed). Thus, the authors’ response, “We did not include them (i.e. age and gender) in the model, since they were not significantly different…..”, is not justified.

Authors: While we still maintain that the only covariates to include in regression analysis are those that show statistical significance between study and reference groups, we did take the reviewer's comment into consideration and recalculated the aOR (95% CI). As expected, no difference in the overall conclusion was seen.
Changes: The aOR (95% CI) was recalculated after forcing age and gender into the model. Appropriate modifications were made in the text (Results section).

Reviewer: The authors should consider clearly stating the reference groups they used to calculate odds ratios (Table 5 and 6). For example, you may write as “odds ratios were calculated for carriers versus all non-carriers”. In this case, all non-carriers would be a reference group?

Authors: Will do.

Changes: Appropriate modifications as per the reviewer's comment were made where indicated.

Reviewer: Authors wrote that homozygosity for the UCSNP-19 was associated with increased body weight among patients. Does this suggest that CAPN10 plays an important role in determining adiposity? Is there any previous reports regarding the relation between CAPN10 and measures of adiposity such as BMI or waist-hip-ratio? How does this relate to the risk of diabetes? Authors might well consider describing the findings in detail and discussing about this issue in discussion section.

Authors: A point well-taken.

Changes: The Discussion was modified, taking into consideration the reviewer's comment.

Reviewer: Please provide the results of the Hardy-Weinberg Equilibrium test.

Authors: Will do.

Changes: Hardy-Weinberg Equilibrium (HWE) data were added to the revised text.

Reviewer: Please provide the number of patients and controls for each cell in Table 5.

Authors: Will do.

Changes: Appropriate modification to Table 5 was made as per the reviewer's comment.

Reviewer: Typographical error in Introduction section: (i) “,and as at-risk diplotypes….. were reported for many populations” was written twice in the same sentence.

Authors: We thank the reviewer for pointing out this obvious typographic error.

Changes: The typographic error was corrected as pointed out by the reviewer.