Author's response to reviews

Title: The PTPN22 C1858T gene variant is associated with changes in residual beta-cell function in new-onset type 1 diabetes

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Version: 3 Date: 23 February 2011

Author's response to reviews: see over
Dear Editor-in-Chief and Associate Editor
Thank you very much for the possibility to submit a second revised version of our manuscript. We have with great effort revised our paper and addressed the reviewer’s comments and are hereby giving a point-by-point response to the concerns. The changes in the manuscript are highlighted in yellow.
Sincerely yours,
Lotte Brøndum Nielsen

Reviewer’s report
Title: The PTPN22 C1858T gene variant is associated with changes in residual beta-cell function in new-onset type 1 diabetes
Version: 2 Date: 3 February 2011
Reviewer: Raffaella Buzzetti
Reviewer’s report:
The Authors answered most of the questions raised, however, some points remain to be clarified.
Minor essential revisions
1) Patients were recruited in 18 centres representing 15 countries in Europe and Japan. The patients had different origins. The HLA risk alleles are different in different populations but, the HLA classification (high, moderate and low) was the same for all patients. This incongruence should be explained.
Answer: We acknowledge the reviewer’s point and have taking the issue into consideration. The four Japanese patients included in this study carry low and moderate HLA risk alleles according to Caucasian classification (three low, 1 moderate), with the more precise \( \text{DRB1} \) genotypes: 01/09, 04/08, 04/09, 09/09. These patients are specified in the HLA risk description in Table 1, highlighted separately next to the numbers for the Caucasian patients. The \( \text{DRB1} 04/09 \) genotype is classified as high risk in Japan. All analyses were repeated without the Japanese patients and it did not influence the results, this is underscored in the Statistical section (P5 L10-12).

2) The prevalence of ZnT8 at onset, should be added.
Answer: Unfortunately, we do not keep serum samples from these patients at the exact time of onset. The time point nearest to onset at which we have serum samples (and ZnT8Ab measurements) is 1 months after diagnosis. The ZnT8Ab prevalence at 1 month after onset is described in the results section (P6 L10-12).

Level of interest: An article of importance in its field
Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:
'I declare that I have no competing interests' below.
Reviewer's report
Title: The PTPN22 C1858T gene variant is associated with changes in residual beta-cell function in new-onset type 1 diabetes
Version: 2 Date: 23 January 2011
Reviewer: Takuya Awata
Reviewer's report:
Minor Essential Revisions:
1. I understand the "mixed-meal". Please explain it for readers in the manuscript briefly.

Answer: The mixed-meal test has briefly been described in the method section (P4 L10-13).

2. In the 2nd paragraph of Results, the quotation of "Figure 1A" should be "Figure 1B", and "Figure 1A" should be quoted above.

Answer: The reference to “Figure 1A” has been changed to “Figure 1B” (P5 L22) and “Figure 1A” is referred to in the part of the Results dealing with the PTPN22 gene and stimulated C-peptide levels (P5 L19).

Level of interest: An article of importance in its field
Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:
I declare that I have no competing interests.