Author's response to reviews

Title: Serum levels of Pancreatic Stone Protein (PSP)/reg1A as an indicator of beta-cell apoptosis suggest an increased apoptosis rate in hepatocyte nuclear factor 1 alpha (HNF1A-MODY) carriers from the third decade of life onward

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Author's response to reviews: see over
Response to the Reviewer Comments.

We thank the reviewer for their constructive comments and suggestions.

Major compulsory revisions;

1. As suggested by the reviewer, family control subjects have now been excluded from the manuscript. This information has been removed from the abstract (page 2, line 16), the subjects section (page 5, paragraph 1, lines 6-8) and the results section (page 7, paragraph 1, lines 7-10). Figure 1 has also been deleted as requested.

2. As suggested by the reviewer, we have now deleted the following statement from the discussion: ‘This may indicate that the rate of beta-cell apoptosis is mild in GCK-MODY patients’ (page 10, paragraph 3, lines 24-25). We have replaced this statement with the following sentence ‘although PSP/reg1a levels were not upregulated in GCK-MODY, we cannot draw any conclusions from the GCK-MODY group due to the limited numbers available’ (page 10, paragraph 3, lines 24-26).

3. We have changed the C-peptide units to ng/ml which is equivalent to mcg/L as suggested. We are confident in our diagnosis of type 1 diabetes mellitus in the three subjects with persistent C-peptide levels outside of the honeymoon period. As specified in the subjects section, they were auto-antibody positive. Clinically, on presentation, all three subjects had osmotic symptoms with ketosis requiring insulin from diagnosis. There was no significant family history recorded in any of the type 1 diabetes mellitus subjects. These three subjects were not newly diagnosed and the duration of their diabetes ranged from 3-33 years. We have now added the following sentence “Clinically, on presentation, all subjects with type 1 diabetes mellitus had osmotic symptoms with ketosis requiring insulin from diagnosis. There was no significant family history recorded in any of the subjects with type 1 diabetes mellitus” to the Methods/Subjects section (page 5, paragraph 1, lines 10-12). As requested by the reviewer, the fasting C-peptide and glucose for the type 1 diabetes mellitus group have been added to Table 1.
4. In the discussion, the line ‘indirect marker of beta cell mass’ has been deleted as requested (page 9, paragraph 2, line 22).

Minor essential revisions;

1. The number of HNF1A-MODY (n=37) cases has been added to the abstract results section (line 19).

2. The amendments to Table 1 have been made as recommended. The numbers for each group have been added. The GCK-MODY diabetes duration has been adjusted to read ‘from birth’. The decimal places are now consistent and appropriate.

3. In the background section, the gene name for the KO mouse is in the lower case (page 3, paragraph 3, lines 18-19). In addition, “maybe” has been replaced by “may be” (page 3, paragraph 3, line 21).