Author’s response to reviews

Title: The level of netrin-1 is decreased in newly diagnosed type 2 diabetes mellitus patients

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Author’s response to reviews:

Dear Dr. Alexander Kokkinos,

On behalf of my co-authors, we thank you very much for giving us an opportunity to revise our manuscript. We appreciate editor and reviewers very much for their positive and constructive comments and suggestions on our manuscript entitled “The level of Netrin-1 decreased in newly diagnosed type 2 diabetes mellitus patients”. (ID: BEND-D-15-00134). We are thankful to the referees and the Editor for pointing out some important modifications needed in the report.

Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have studied comments carefully and have made correction which we hope meet with approval. Revised portion are marked in red in the paper. The main corrections in the paper and the responds to the reviewer’s comments are as flowing:

Responds to the reviewer’s comments:
Reviewer 1:

1. Response to comment: several paragraphs clarity and sense of the manuscript is obscured. The meaning of the article is not clearly understood and the discussion section is difficult to read.

Response: Thanks for the referee’s kind suggestion. According to reviewer’s advices, we review the manuscript and make essential parts and revisions are marked.

2. Response to comment: This is not a mechanistic study and it would be more reasonable if they shortened the section referring to the results of other mechanistic studies and explained more the implications of their findings.

Response to comment: Thanks for the referee’s suggestion. We removed some parts including mechanistic especially in inflammation which using track changes. At the same time, we made more implication for the significance of this trial.

1) It is not clear when and how postprandial glucose and insulin levels were measured (2 hours after a test meal, random meal, OGTT?)

Response to comment: During our trial we use 2 hours after a test meal to measure the level of postprandial glucose and insulin (Page 7, Line 133-134).

2) Non-diabetic participants had lower fasting insulin and higher postprandial insulin levels compared with diabetic subjects. How can the authors explain these results?

Response: In patients with type 2 diabetes, higher concentrations of insulin are needed to stimulate peripheral glucose disposal and to suppress hepatic glucose production than are needed in patients without diabetes, implying that initially increased insulin secretion compensates for insulin resistance but overt disease occurs over time as cell compensation fails. In conclusion, a marked deterioration in β-cell function precedes the onset of type 2 diabetes.

3) Did the control group include subjects with prediabetes (IFG or IGT) or were they excluded from the study?
Response: The control group was comprised of 26 aged-matched subjects and all of them with abnormal glucose tolerance at the baseline examination. Meanwhile, we excluded IFG and IGT from the study.

Reviewer 2:

1. Response to comment: what kind of study is?
Response: We defined the study as a research article.

2. Response to comment: exclusion criterias define.
Response to comment: We have tried to define exclusion criteria in the text by highlight (Page 6, Line 105-115).

3. Response to comment: AKI define
Response: We defined AKI as Acute Kidney Injury (Page 5, Line 83)

4. Response to comment: IK-B define
Response: We defined IK-B as inhibiting factor Kappa B.

5. Response to comment: NF-kB define
Response: We defined NF-kB as nuclear factor Kappa B.

6. Response to comment: Better to define abbreviations into the text (HbA1c, TG, TC, HDL, LDL etc.)
Response: We have defined the abbreviations into the text (for e.g. HbA1c) which are marked according to the reviewer’s suggestion.
Reviewer 3:

1. Response to comment: the data about duration of diabetes and diabetes treatment.

Response: Thanks for the referee’s kind suggestion. Our study included 30 patients newly diagnosed with T2DM (T2DM group). All of them had been diagnosed DM within six months, who had no received previous antihyperglycaemic therapy.

2. Response to comment: Many studies explicated in the discussion section should have been written in the background section.

Response: Thanks for the referee’s kind suggestion. We made changes which are marked in the text according to reviewer’s suggestion.

We tried our best to improve the manuscript and made some changes. We appreciate for editors/reviewers’ warm work earnestly, and hope that the correction will meet with approval.

Once again, thank you very much for your comment and suggestions.

Sincerely yours,

Chenxiao Liu

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