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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Reviewer reports:

Reviewer #1: The authors studied netrin-1 in 30 patients with newly diagnosed type 2 diabetes and 26 age- and BMI-matched healthy controls. Recent studies have shown that netrin-1 regulates inflammatory cell migration and thus plays an important protective role in inflammation. The authors found that newly diagnosed diabetic patients had lower netrin-1 levels in comparison with healthy subjects and that netrin-1 concentrations were negatively associated with HOMA-IR. This is a well-designed study with interesting results, but its cross-sectional design limits causal inferences.

Major criticism

1. The paper should be edited by a native English-speaker, since there are several paragraphs (especially in the introduction and discussion section) where 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.
2. The authors in the discussion section try to elucidate how lower netrin-1 levels are associated with type 2 diabetes. However, this is not a mechanistic study and no conclusions can be drawn about how netrin-1 is related or not to β-cell dysfunction and insulin resistance. Therefore, 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.

Minor criticism

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

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

3. Did the control group include subjects with prediabetes (IFG or IGT) or were they excluded from the study?

Reviewer #2: We evaluated the manuscript with title: The level of Netrin-1 decreased in newly diagnosed type 2 diabetes mellitus patients. The data are interesting. The major limitation of this study is the small number of patients included in the study.

Nevertheless, the authors found statistical significance in their population.

However, the manuscript needs major revision before it can be proceeded for further evaluation. The authors should take under consideration the following points:

1. The authors should define what kind of study is.

2. The authors should clearly define the exclusion criterias.
3. Line 80. AKI define

4. Line 174. IK-B define

5. Line 175. NF-kB define

6. Better to define abbreviations into the text (HbA1c, TG, TC, HDL, LDL etc.)

7. Maybe the manuscript eventually needs English editing to prescribe more accurately the meanings.

Reviewer #3: The idea of the paper is innovative. As commented, the study population is small, but the data analysis is correct. However, there are some comments to be made:

1. DATA: There is no data about duration of diabetes (only the fact that it is newly diagnosed) and no data about diabetes treatment (and any possible correlations with netrin-1)

2. PAPER STRUCTURE: Many studies explicated in the discussion section should have been written in the background section.

3. LANGUAGE: Many grammar and wording issues that need revision.