Reviewer’s report

Title: Genetic and clinical characteristics of Chinese children with Glucokinase-Maturity-Onset Diabetes Of The Young (GCK-MODY)

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Reviewer: Mark A. Magnuson

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In this paper the authors describe the clinical features and associated genetic mutation in nine Chinese pediatric GCK-MODY patients. Five of the mutations have been previously reported, although in other ethnic populations, but four were novel. All patients exhibited stable, asymptomatic hyperglycemia characteristic of GCK-MODY.

This study is important in two ways. First, it describes four previously unreported mutations in GCK. Second, and perhaps more important, it demonstrates the existence of GCK-MODY in the Chinese population. As the authors assert, this may improve the diagnosis of GCK-MODY2 in stable, asymptomatic hyperglycemic patients, and avoid unnecessary therapy. Several modifications are recommended prior to publication.

1. The authors state that GCK mutation is a common cause of asymptomatic hyperglycemia in Chinese children; however, with such a small cohort it is not possible to make such a broad statement. The conclusions need to be more tempered.

2. The authors should also be more careful discussing the pathogenicity of the novel GCK mutations since they did not study the kinetics, stability or binding affinity to GCK regulatory protein. Indeed, some statements are overly assertive given the lack of such data. For instance, on p. 12 the phrase "mutation p.Ser151del causes the lack of this bond and leads to a loosened structure of this region" can be predicted, but cannot be treated as a fact without further data. Again, it is recommended that the conclusions be softened. It should also be stated clearly that additional kinetic assays are necessary to establish the actual functional basis for the disease.

3. The statement on p. 4 "Although heterozygous inactivating GCK mutations are diverse, they all lead to the same phenotype of mild fasting hyperglycaemia" is a bit misleading. While it is true that most GCK-MODY mutations impair kinetic activity, some have been shown to exhibit markedly impaired stability with normal kinetics. Thus, the authors may want to reconsider their use of the term "inactivating".
4. Finally, the authors too often extrapolate their very limited clinical findings to broad clinical advice, even though this is a clinically-oriented journal. In this regard, many statements seem inappropriate. For instance, on p. 11 the statement "Diagnostic uncertainty can cause anxiety in both parents and the treating paediatrician" is anecdotal and adds very little. Similarly, it seems out of place to be describing diagnostic protocols when this is not the point of the paper. It is recommended that the discussion be both shortened and rewritten to remove all such extraneous information, and to eliminate the very professorial/lecturing tone that currently exists. By doing so, the article will become more palatable to the reader.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

Not relevant to this manuscript

Quality of written English
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Needs some language corrections before being published

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