Reviewer's report

Title: Further evidence that mutations in INS can be a rare cause of Maturity-Onset Diabetes of the Young

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Reviewer: Pal R. Njolstad

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Recently, mutations in the insulin gene have been found to cause permanent neonatal diabetes mellitus, maturity-onset diabetes of the young as well as atypical type 1 diabetes. While a mutation in the insulin gene is a relatively frequent etiologic factor in permanent neonatal diabetes mellitus, the latter two groups seem rarely to be associated with insulin gene mutations. Boesgaard and colleagues hypothesized that mutations in the insulin gene can cause maturity-onset diabetes of the young in Danish and Czech probands as well. They also investigated Danish subjects with GAD-negative type 1 diabetes or gestational diabetes. The authors identified a novel mutation in the Danish maturity-onset diabetes of the young material and a previously reported mutation in the Czech cohort. They did not detect any pathogenic mutations in the materials with type 1 diabetes or gestational diabetes. The findings are interesting, in line with other studies and add new knowledge to the field. The paper is well written.

Major questions/comments

1. The authors should define their criteria for “conventional” maturity-onset diabetes of the young. These may vary among various centers.
2. The mean age of onset of diabetes for the Danish maturity-onset diabetes of the young probands was high (24 years). Could several of the probands rather have early-onset type 2 diabetes?
3. What is “family history of diabetes”? Only probands with a diabetic parent or child should be included since the authors were looking for monogenic diabetes.

Minor questions/comments

1. Exchange “A R46Q….” with “An R46Q…..”. The same applies for R6C and L68M.
2. The last sentence of the Background is imprecise. The authors have not investigated type 2 diabetes.
3. Choose either singular or plural for the various species listed in the Results and Discussion.

Level of interest: An article whose findings are important to those with closely related research interests
Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
No