Author’s response to reviews

Title: Spectrum of mutations in monogenic diabetes genes identified from high-throughput DNA sequencing of 6,888 individuals

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Author’s response to reviews:

Reviewer 1 comments:

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Comment: The authors have addressed most of the reviewer's concerns in their rebuttal letter. In the overall conclusion, as well as in the abstract of the paper, the authors should emphasize that the findings from their study confirm that MODY is still largely under-diagnosed in the general population (particularly presenting with early-onset diabetes, when it is clinically defined as type 2 diabetes). In such cases, genetic testing is indeed strongly recommended for a definitive, etiological diagnosis.

Response: We have edited the ‘Conclusion’ section to emphasize this point (page 24, “CONCLUSION):

Our results confirm previous reports that MODY is under-diagnosed, particularly in individuals presenting with early onset diabetes and clinically labeled as type 2 diabetes, and in such cases, genetic testing can provide an etiological diagnosis. With the continuing reduction in costs of
DNA sequencing, genetic screening of all known monogenic diabetes genes in individuals with early onset diabetes should be routinely considered since it can identify individuals with undiagnosed MODY as well as atypical forms of monogenic diabetes.

Similarly, we have edited the ‘Abstract’ to emphasize this point (page 3):

“Our results confirm that MODY is under-diagnosed, particularly in individuals presenting with early onset diabetes and clinically labeled as type 2 diabetes, and sequencing of all monogenic diabetes genes should be routinely considered in such individuals. Genetic information can provide a specific diagnosis, inform disease prognosis and may help to better stratify treatment plans.”

Editorial comments:

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Comment: Please include a list of abbreviations

Response: We have added a list of abbreviations (end of page 26 and start of page 27). We have also made some minor edits to the text of the paper to be consistent with these abbreviations.

Comment: You have mentioned that this study was approved by an ethical committee; please include the reference number for this approval.

Response: We have added the reference numbers for the approval to page 26:

The study was approved by the Institutional Review Board (IRB) of Ulm University, Ulm, Germany; (registration numbers 42/2004 and 189/2007) and the Chamber of Physicians, State Baden-Wuerttemberg, Germany (registration number 133-2002) and is in accordance with the ethical principles of the Helsinki Declaration.

Additional edits:

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1. We have added a description of the Additional Files on page 27 & 28.

2. We have removed URLs from the text and added them to the references or cited the relevant papers (changes are highlighted in the Word document).