Dear Editor,

On behalf of my co-authors, we thank you very much for giving us an opportunity to revise our manuscript, we appreciate the editor and the reviewer very much for their positive and constructive comments and suggestions on our manuscript entitled " **Maturity-onset diabetes of the young type 9 or latent autoimmune diabetes in adults: A rare case report and a systematic review"(NO:82297).** Based on these comments and suggestions, we have made careful modifications on the original manuscript (see those in red), which we hope meet with approval. And the manuscript has been polished. We hope that these revisions are satisfactory and that the revised version will be acceptable for publication in the World Journal of Diabetes. Below you will find our point-by-point responses to the reviewers' comments.

We would like to express our great appreciation to you and the reviewer for your comments on our paper. Looking forward to hearing from you.

Thank you and best regards.

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Response to the reviewer 1

Comments: Dear authors firstly, I appreciate your work in this study. It is well-written. But PAX4:c.314G>A variant is classified as VUS (variants of uncertain significance) in databases so its association with disease risk is unclear. According to ACMG criteria it is classified as benign. o PAX4:c.314G>A variant is not novel (it is reported as novel in this report by the authors); it is available in the dbSNP database (rs765561668). o The case that you are presenting has clinical findings related to LADA, but the variant is inherited from the mother. In the manuscript, you notice that the mother does not have any clinical findings related to LADA or MODY types. o If PAX4:c.314G>A variant is related to LADA, you would have detected the same symptoms in her mother too. There are rare cases in which the penetrance and expressivity of inherited genes or variations change in next generations. o The authors did not mention how many genes they performed using High-throughput sequencing, if they used a specified MODY gene panel maybe it would be better to perform whole-exome or whole-genome sequencing to clarify the case. o Functional analysis must be performed to understand the relationship between variant and disease. The PAX4:c.314G>A variant is insufficient to determine your case's clinical situation.

Response: Thanks very much for your constructive comments.

1. You are right, PAX4:c.314G>A has been reported in the dbSNP database, we revised this statement in the article. However, there has been still no article reporting the specific clinical features of patients with this mutation, nor has it been reported that this mutation can be combined with LADA, so from this point, we think it is worth to be reported.
2. We apologize for not specifying what method we used to detect the gene in the article, actually, we used next-generation sequencing (DNBSEQ-T7) to detect 130 genes that related to diabetes, which include 14 pathogenic genes associated with MODY (HNF4A, GCK, HNF1A, PDX1, HNF1B, NEUROD1, KLF11, CEL, PAX4, INS, BLK, ABCC8, KCNJ11, APPL1), and only PAX4:c.314G>A mutation was found.
3. We agree with you on the relationship between PAX4: c.314G>A mutation and diabetes, which was what we want to figure out at first. In the beginning, we wondered whether the patient should be diagnosed as MODY or LADA, taking the results of the patient's examination and the fact that the blood glucose of her mother was normal into account, the final diagnosis was LADA. Many articles have reported that PAX4 gene mutations are associated with diabetes, and PAX4 gene does play a key role in the differentiation of pancreatic islet β cells. Therefore, we suspect that PAX4: c.314G>A mutation may play a facilitating role in the progression of LADA, and further functional experiments worth to be done to validate. We will try to confirm in subsequent experiments. Thank you

very much for your meaningful suggestions, we made some modifications in the article based on your thoughtfull suggestions.

Response to the reviewer 2

Comments: The article was well designed and written. Kudos to the authors.

Response: Thank you very much for your positive comments! We are greatly encouraged by your words and will try to make it better.