Dear Editors and Reviewers:

Thank you for your letter and for the reviewers' comments concerning our manuscript entitled "A novel gene mutation in type 7 maturity-onset diabetes of the young: a case report" (ID:80275). Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have studied comments carefully and have made correction which we hope meet with approval. Revised portion are marked in red in the paper. The main corrections in the paper and the responds to the reviewer's comments are as flowing:

Responds to the reviewer's comments:

Reviewer #1:

Response to comment: (The authors are kindly requested to add the novelty and the useful elements of their case report in the paper. What new does this paper add to the current knowledge?)

Response: MODY7 is caused by mutations in the transcription factor Kruppel-like Factor 11 (KLF11) gene. This variant impairs insulin secretion from pancreatic beta cells, possibly by repressing insulin promoter regulation activity. Our report shed light on the molecular mechanisms underlying the pathogenesis of MODY7. First, the novelty of our report is that the clinical and functional characteristics of the novel KLF11 mutation c. G31A have not yet been reported to date. The KLF11 (c. G31A) mutation in this patient expand the genotype and clinical spectrum of MODY7. Second, considering the clinical characteristics of the family, the gene mutation of KLF11 which has obvious heredity can cause MODY7. In this paper, the patient's mother, second aunt, and maternal grandmother had the same gene mutation, thus confirming the characteristics of dominant inheritance of the gene mutation. The patient's mother and maternal grandmother had a history of diabetes,

and the young aunt had a history of impaired glucose tolerance, thus indicating that the clinical characteristics caused by the same mutation were different. It add a date to the MODY7 database and provide a basis for the study of MODY7. In addition, there is currently no clear treatment plan about MODY7. Most scholars administer oral sulfonylureas for MODY7. In our report oral hypoglycemic drugs which were discontinued in the later stage and dietary interventions are beneficial for MODY7. It provides support for MODY7 treatment. Finally, all of the above are described in the manuscript.

Special thanks to you for your good comments.

Reviewer #2:

1. Response to comment: ("MODY7 is caused by mutations in the transcription factor Kruppel-like Factor 11 (KLF11) gene" Please add the reference for the statement.)

Response: Frist, considering the Reviewer's suggestion, we add the reference for the statement. " Another report identified a novel KLF11 Pro193Thr variant in a three generation family with MODY7[4]. These findings shed light on the molecular mechanisms underlying the pathogenesis of MODY7. Therefore, MODY7 is caused by mutations in the transcription factor Kruppel-like Factor 11 (KLF11) gene. A new KLF11 variant was associated with early childhood-onset type 1B diabetes in 2019[5]. As such, KLF11 is a valid candidate gene to determine the genetic predisposition to early onset and type 2 diabetes, as defects in this gene may lead to early onset diabetes[6]. However, KLF11, due to its role as a MODY gene, is a potential therapeutic target for maturity-onset diabetes. Moreover, Wu S et al. document a novel heterozygous KLF11 variant (p. Pro349Ser) as a potential monogenic mutation associated with MODY7 in a family. This variant impairs insulin secretion from pancreatic beta cells, possibly by repressing

insulin promoter regulation activity[13].” Second, we report that MODY7 is caused by mutations in the transcription factor Kruppel-like Factor 11 (KLF11) gene in the discussion of the manuscript. The reason is as follows:

A study found that the KLF11 gene in islet β cells is a PDX-1 transcriptional regulator dependent on P300, which promotes and maintains insulin synthesis and plays an important role in the normal development of the pancreas and the maintenance of islet β cell function, which is the core mechanism of MODY7 occurrence[11]. In 2012, Lomberk et al. found that mutations in the KLF11 gene cause MODY7 and neonatal diabetes; in this study, the A347S gene variant was found in MODY7 patients, which disrupts KLF11-mediated increases in basal insulin levels and promoter activity and attenuates glucose-stimulated insulin secretion. This mechanism contributes to our understanding of the complex gene regulation in MODY[12].Therefore, KLF11, as a transcription factor that is widely expressed in a variety of tissues in vivo, regulates blood glucose homeostasis by a very complex mechanism. It not only directly regulates insulin gene expression, but it also interacts with different target genes to jointly regulate the level of glucose metabolism in the body, thus ultimately leading to the occurrence of MODY7.

2. Response to comment:( The authors did not show the sequences of the other 13 MODY genes. Are there any other mutations in those genes in the family?)

Response: We are very sorry for our negligence of showing the sequences of the other 13 MODY genes. There are not other mutations in those genes in the family. So we don’t show the sequences of the other 13 MODY genes. As Reviewer suggested that We add the supplement that the sequences of the other 13 MODY genes are normal in the manuscript.

3. Response to comment:( It would be helpful if the authors modify the sequencing picture (Figure 1b), making it more straightforward to find out the mutant DNA base.)

Response: It is really true as Reviewer suggested that it would be helpful to find out the mutant DNA base. Therefore, I modify the sequencing picture (Figure 1b). A heterozygous c. G31A transition mutation causing the substitution of aspartic acid by asparagine at codon 11 is shown by a red arrow.

Special thanks to you for your good comments.

We tried our best to improve the manuscript and made some changes in the manuscript. These changes will not influence the content and framework of the paper. And here we list the changes and marked in red in revised paper.

We appreciate for Editors/Reviewers' warm work earnestly, and hope that the correction will meet with approval.

Once again, thank you very much for your comments and suggestions.

Yours sincerely,

12,Dec,2022.