Dear Editors and Reviewers:

Thank you for your letter and for the reviewers' comments concerning our manuscript entitled "Molecular diagnosis of Kallmann syndrome with Diabetes by Whole exome sequencing and Bioinformatic Approaches". Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our research. We have studied comments carefully and have made correction which we hope meet with approval. Revised portions are marked in red in the paper. The main corrections in the paper and the responds to the reviewer's comments are as following:

Reviewer 1:

A. Major points 1. Hypogonadotrophic hypogonadism 25 with anosmia (HH25, OMIM 618841) has been attributed to heterozygous mutation in the NDNF gene (Messina A, Pulli K, Santini S, Acierno J, Känsäkoski J, Cassatella D, Xu C, Casoni F, Malone SA, Ternier G, Conte D, Sidis Y, Tommiska J, Vaaralahti K, Dwyer A, Gothilf Y, Merlo GR, Santoni F, Niederländer NJ, Giacobini P, Raivio T, Pitteloud N. Neuron-Derived Neurotrophic Factor Is Mutated in Congenital Hypogonadotropic Hypogonadism. Am J Hum Genet. 2020 Jan 2;106(1):58-70. doi: 10.1016/j.ajhg.2019.12.003. Epub 2019 Dec 26. PMID: 31883645; PMCID: PMC7042563); however, this information is lacking from Table 7.

2. The SOX3 c.699_719del variant has been reported to be "likely pathogenic" (Kim JH, Seo GH, Kim GH, Huh J, Hwang IT, Jang JH, Yoo HW, Choi JH. Targeted Gene Panel Sequencing for Molecular Diagnosis of Kallmann Syndrome and Normosmic Idiopathic Hypogonadotropic Hypogonadism. Exp Clin Endocrinol Diabetes. 2019 Sep;127(8):538-544. doi: 10.1055/a-0681-6608. Epub 2018 Sep 14. PMID: 30216942). However, SOX3 gene is not included in Table 7.

B. Minor points 1. The authors are wellcome to add the relevant OMIM entries for all HH types attributed to genes included in Table 7 [FGFR1 (147950), FGF8 (612702), PROK2 (610628), CHD7 (612370), WDR11 (614858), GNRHR (146110), GNRH1 (614841), KISS1R (614837), KISS1 (614842), TACR3 (614840), TAC3 (614839), ANOS1 (308700), FGF17 (615270), IL17RD (615267), DUSP6 (615269), SPRY4 (615266), FLRT3 (615271), PROKR2 (244200), SEMA3A (614897), HS6ST1 (614880), CCDC141, FEZF1 (616030), and NELF (614838)].

2. TACR3 and GNRHR genes are reported to be linked with nIHH twice in Table 7; duplicated should be ommitted.

Response: For Table 7, we added new genes (NDNF, SOX3) and removed duplicate genes (TACR3 and GNRHR). In addition, we added the Phenotype MIM number of genes based on the OMIM database.

Science editor:

The authors should increase the number of references used in the study and arrange them according to the journal format. Highlight section should be inserted before references. Source of funding should be clearly stated.

Response: I have increased the number of references used in the study and arrange them according to the journal format. Highlight section have been inserted before references. Source of funding have been added.

Company editor-in-chief

1.The authors should sign the Copyright License Agreement; 2. Supplementary comments: This is an Unsolicited basic study manuscript. The Financial support should be clearly stated for the study. The topic has not previously been published in the WJD. 3. The authors should provide a clear statment for funding information in the manuscript file ; 4. PMID and DOI numbers were provided in the reference list for some references only; 5.The “Article Highlights” section is missing. Please add the “Article Highlights” section at the end of the main text

Response： 1.I have signed the Copyright License Agreement; 2. The Financial support have been added. 3. I have provided a clear statement for funding information in the manuscript file ; 4. PMID and DOI numbers were added; 5.The “Article Highlights” section have been added at the end of the main text.

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 did not list the changes but 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

Wang ruixue