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PEER-REVIEW REPORT

Name of journal: *World Journal of Diabetes*

Manuscript NO: 71017

Title: Molecular diagnosis of Kallmann syndrome with diabetes by whole exome sequencing and bioinformatic approaches

Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05430684
Position: Peer Reviewer
Academic degree: MD, MSc, PhD
Professional title: Chief Doctor
Reviewer's Country/Territory: Greece
Author's Country/Territory: China

Manuscript submission date: 2021-08-24

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-08-25 07:32

Reviewer performed review: 2021-08-28 17:29

Review time: 3 Days and 9 Hours

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No

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Peer-reviewer statements	Peer-Review: [ ] Anonymous [Y] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

I studied carefully the manuscript entitled "Molecular diagnosis of Kallmann syndrome with Diabetes by Whole exome sequencing and Bioinformatic Approaches" by Shuangshuang Sun and Ruixue Wang. The manuscript contains novel pieces of information and thus it is believed taht it will be of substantial interest to the specialized readership of the Journal. However, before considering publication, permit me to raise some queries to the authors: 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

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(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. 3. The manuscript has to be scanned for typos and syntax errors. I remain at your disposal for any revised version of the manuscript.