Dear editor

We would like to thank the editor and the reviewers for their conscientious reviews, and insightful comments and suggestions to improve the manuscript. In the response below, we have addressed all the concerns raised by the editor and the reviewers in the revised manuscript. We hope the editor and the reviewers will find that our revised manuscript has improved and is suitable for publication. All changes have been marked in blue.

We hope our paper could achieve the academic standards of your magazine and be published finally.Thank you very much.

Yours Sincerely,

Zeyu Wu, Bing Chang

Response to Reviewers Comments

Manuscript NO: 58573

Title: Pituitary stalk interruption syndrome and liver changes: from clinical features to mechanisms

Authors: Zeyu Wu, Yiling Li,Bing Chang

Reviewers' comments:

Reviewer #1: The manuscript is good and interesting. The title reflects the main subject. The abstract summarizes and reflects the work. The key words reflect the focus of the manuscript, but they does Their summary was well written that pointed the most relevant aspects of the Pituitary stalk interruption syndrome. The Illustrations and tables are good quality and appropriately illustrative of the paper contents. At least two need to be corrected. The reference number 1: Wang CZ, Guo LL, Han BY, Su X, Guo QH, Mu YM. Pituitary Stalk Interruption Syndrome: From Clinical Findings to Pathogenesis. J Neuroendocrinol. 2017;29(1):10.1111/jne.12451. doi:10.1111/jne.12451 and the reference number 68: Enoch Cobbina & Fatemeh Akhlaghi. Non-alcoholic fatty liver disease (NAFLD) – pathogenesis, classification, and effect on drug metabolizing enzymes and transporters. Drug Metabolism Reviews. 2017;49:2, 197-211, DOI: 10.1080/03602532.2017.1293683. The manuscript is well, concisely and coherently organized and presented but I would suggest them to apply relevant items of PRISMA to your narrative review.

Response: Thank you for pointing out the problem. We have adjusted the format of the references. We searched from the PUBMED database and list related literatures about the gene

or chromosome mutations of PSIS,sa shown in table 1 .

Table 1 Gene/chromosome mutations related to PSIS

References	Gene/ Chromosome
Liu Z and Chen X [39] 2020	*ROBO1*
Wang CZ *et al* [40] 2020	*NBPF9*
Bashamboo A *et al* [29] 2016	*CDON*
Guo QH *et al* [35] 2017	*NCOR2*，*NKD2*，*ZIC2*，*MAML3*
Bashamboo A *et al* [32] 2017	*ROBO1*
Zwaveling-Soonawala N *et al* [33] 2018	*DCHS1*，*ROBO2*，*CCDC88C*， *KIF14*，*KAT6A*，*GLI2*，*PROK2*，*NR0B1*，*DCHR7* ，*CCD2DA*
Yang Y *et al* [26] 2013	*HESX1*， *LHX4* ，*SOX3*
Tatsi C *et al* [30] 2013	*TGIF*，*SHH*
Wang *et al* [41] 2019	*MUC4*，*NBPF10*
El Chehadeh-Djebbar S *et al* [38] 2011	17q21.31 microdeletion

Reynaud R *et al [27]* 2012	*PROKR2，HESX1*
Fang X *et al* [42] 2020	*PTCH1, PTCH2, GLI2, TCTN1, ATR, GLI1, CDON, CREBBP, KIF7, LHX4, HHAT, STK36, MAPK3, SMO, PRKAR2A, PRKAR2B, EGR4，SPG11，AHI1, CHD7, CAD, CEP152, CEP290, DHCR24, DMXL2, FREM1, GPSM2, ISPD, NIN, ROBO2, SIX4, SLIT2, WDR11, ASPM, CENPJ, CEP41, DIS3L2, DISC1, DSC2, GH1, GNAS, LRP2, MARCKS, MYH10, NPHP1, NSD1, OTUD4, PCSK1, POMGNT1,PSEN1, RNF111, STIL, TACR3, TBC1D32, VIPR2, WNT5A, ZEB2, ZNF423*
Reynaud R *et al* [43] 2006	LHX4
Dateki S *et al* [44] 2019	*ROBO1*
McCormack SE *et al* [34] 2017	*PROKR2，WDR11*
Demiral M *et al* [45] 2020	*GLI2*
Reynaud R *et al* [4] 2011	*HESX1，LHX4*
Diaczok D *et al* [23] 2008	*OTX2*
Han BY *et al* [28] 2016	*PROKR2*

Coutinho E *et al* [46] 2019	*HESX1*
Vetro A *et al* [37] 2014	Chromosome 2p25 and 2q37
Woods KS *et al* [24] 2005	*SOX3*
Castinetti F *et al* [25] 2008	*LHX4*
Karaca E *et al* [31] 2015	*GPR161*
Carvalho LR *et al* [22] 2003	*HESX1*
Fernandez-Rodriguez E *et al* [11] 2011	*PROP1*
Yang A *et al* [36] 2019	De novo 18p deletion

Reviewer #2: While the review provides useful information on a variety of topics, it is essentially formed by three different parts: a mini-review of PSIS, a case-report of a patient with liver disease due to PSIS and an overview of the effect of pituitary hormones on the liver. The authors could separate these parts and provide different interesting manuscripts such as a review of the PSIS, a review of the effects of pituitary hormones on the liver or a case-report of the patient combined with a review of the literature regarding PSIS effects on the liver. However, the article as it stands contains too much information and confuses the readers, especially the readers of a journal that has gastroenterology as its main topic.

Response：Thank you for your review and evaluation. This is a good suggestion.We planned to write this review due to the case of PSIS related cirrhosis we met. We are writing another reviews about the effects of different pituitary hormones on liver.

Reviewer #3: This is a good review article. I would suggest to apply relevant items of PRISMA to your narrative review. I know that PRISMA is for systematic reviews, but it still has items that can be relevant to narrative reviews as well. This will heavily improve the quality of your review. So Please apply its applicable guidelines, and also send a PRISMA checklist with your revision. Minor language polishing is needed.

Response: Thank you for your review and evaluation. This is a good suggestion. There are few articles about PSIS and NAFLD.

In order to improve the quality of this review,we searched from the PUBMED database and list related literatures about the gene or chromosome mutations of PSIS acroding to some search strategy,as shown in table 1 .

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