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ESPS PEER-REVIEW REPORT

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Title: Effect of the maternal-fetal interface immunoregulation on the occurrence of intrahepatic cholestasis of pregnancy

Reviewer's code: 00742368

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	PubMed Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input checked="" type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		[Y] No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

The manuscript was apparently written hastily. Some of the comments from one of the authors are still seen in track changes and they were not adjusted according to the submitted version. Some sentences are truncated and the grammar in several sections is inappropriate which makes it hard to understand an already hard topic. Abbreviations used which are not spelled out. The references do not conform to the style of the Journal. There are a lot of repetitions of the same concept; i.e. the pathogenesis is unclear and needs further studies. Sometimes, the immunologic mechanism that is described in details and brought forward as a possible contributing factor for ICP lacks supporting evidence in the literature. page 3" These factors can lead to vasospasm and hypoxia at the surface of the placenta and decreased vascular permeability"-I believe it is increased vascular permeability. I suggest using this reference : Sepúlveda WH1, González C, Cruz MA, Rudolph MI. Vasoconstrictive effect of bile acids on isolated human placental chorionic veins. Eur J Obstet Gynecol Reprod Biol. 1991 Dec 13;42(3):211-5. Page 3-" These changes can cause metabolic disorders, inadequate intake of trace elements, leading to injuries of the bile duct"-The sentences that proceeded

do not lend support to this statement Page 3; "How the maternal-fetal immune influences ICP has plagued scientists"-missing word after immune Page 4: " Studies have shown that Th2 type factor against Th1 type factor's immune response"; the sentence's meaning is unclear Page 4; ref xiii does not discuss Th3. Perhaps can use reference-Prud'homme GJ1, Piccirillo CA. The inhibitory effects of transforming growth factor-beta-1 (TGF-beta1) in autoimmune diseases. J Autoimmun. 2000 Feb;14(1):23-42. Page 5; BA are produced idiotypically Ab2 fetal half of this graft antigen-incomplete incomprehensible sentence. Perhaps the authors are referring to the mechanism described in this reference. This should be clarified-Reed E1, Beer AE, Hutcherson H, King DW, Suci-Foca N. The alloantibody response of pregnant women and its suppression by soluble HLA antigens and anti-idiotypic antibodies. J Reprod Immunol. 1991 Jul;20(2):115-28. Page 6-typo TBF---TNF Page 6-The expression of TNF- α and IL-1 are decreased in placental tissue in patients with ICP, which promote the secretion of transforming growth factor 1 (TGF-1). Recent studies have found that TNF- α . It is unclear how the expression of TNF in the placenta is decreased while its level in serum is increased in ICP Page 7-, leading to an increase of the Th2-Th1 ratio demonstrating-Shouldn't this be an increase in th1/th2 ratio Page 7; The results from these studies demonstrate that the surface antigen on Th2 cells and NK cells have enhanced cellular immune function, and promote the Th1/Th2 type cytokine balance via Th1, which may be a cause of the liver cell damage noted to be present in ICP-should mention "the lack of such balance may be a cause..... Page 8- thophoblast-typo Page 8; the sentence ". The expression of HLA-II antigen compatibility is high when maternal and fetal HLA-II genes are highly similar." is redundant Page 8; Nowak pointed out that women with activation of killer cell immunoglobulin-like receptor (KIR) gene and the KIR inhibitory receptor gene ratio between 0.33-0.83 were prone to have spontaneous abortion while women with a ratio between 0.86-1.25 tend to have a NK cell protective effect-Unclear. In Nowak's reference: " an excess of inhibitory KIRs (activating-to-inhibitory KIR gene ratios of 0.33 to 0.83) was associated with miscarriage, whereas ratios close to equilibrium (0.86-1.25) seemed to be protective. In addition, the results suggest for the first time that sporadic and recurrent spontaneous abortions as well as miscarriage in the presence or absence of autoantibodies may have different KIR genotypic backgrounds" Page 8; although they explain the effect of KIR activation-inhibition; suggesting tha