



PEER-REVIEW REPORT

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Title: The Role of Relevant Immune-Modulators and Cytokines in Hepatocellular Carcinoma and Premalignant Hepatic Lesions

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" 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 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		<input type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

COMMENTS TO AUTHORS

In this manuscript Zekri et al. indicate that NKG2D, CD40, IL-2 and IL-10 plays a role in the development and progression of HCC. First, the authors showed that mDCs and CD40+ pDCs were decreased in HCC patients compared with healthy. Moreover, some relevant Immune- Modulators including NKG2D, CD40, IL-2 and IL-10, are dysregulated in HCC patients. Although it is an interesting study investigating the role of immune-modulators and Cytokines in HCC, further modifications are mandatory before publication. major concerns: 1. What is the relationship between these factors? Does they alone or in combination for the development of HCC? 2. Does the dysregulation of these factors correlated with the clinical characteristics of patients or related to the prognosis of patients? Please classified.



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Answering reviewers

1. The immune defense mechanism(s) plays an important role in the inhibition or progression of cancer (Ostrand-Rosenberg et al. 2016), and it is formed of many immune cells (CDs, CTL, TH, Treg, NKs etc), cytokines and immune-modulators that interplay together and co-operate to produce the final response, and this was confirmed by the significant correlation found between them as shown in table (4). We reported that NKG2D, CD40 expressed on DCs, IL-2 and IL-10 might be implicated in HCC pathogenesis, however we cannot concern with each one alone, e.g Tregs and MDSCs secrete immune-suppressive cytokines, such as IL-6, IL-10, and TGF- β (9). IL-10 inhibits CD40 expression on DCs (26), and consequently inhibits expression of IFN- α and IL12.
2. Many thanks for this valuable suggestion, and we will do it in a further study. However in the current study we aimed at investigating the pathogenesis of HCC and determining the immunological markers that could play a role in its development. This was assessed in relation to other premalignant hepatic diseases like HCV chronic hepatitis and liver cirrhosis compared to normal control.