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ESPS PEER REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 13529
Title: IGF-1 mRNA isoforms and IGF-1R mRNA expression in chronic hepatitis C
Reviewer code: 00005177
Science editor: Su-Xin Gou
Date sent for review: 2014-08-27 13:47
Date reviewed: 2014-09-03 19:25

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[ ] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] Existing	[ ] High priority for publication
[Y] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] No records	[Y] Rejection
[ ] Grade D: Fair	[ ] Grade D: Rejected	BPG Search:	[ ] Minor revision
[ ] Grade E: Poor		[ ] Existing	[ ] Major revision
		[ ] No records	

COMMENTS TO AUTHORS

The paper"IGF-1 mRNA isoforms and IGF-1R mRNA expression in chronic hepatitis C" submitted for publication on WJG by Dr. Aldona Kasprzak and coworkers is really interesting since it introduces new factors correlated with the natural history of chronic hepatitis C (CHC). General comment: The Authors concluded that 1)"Differences in quantitative expression of IGF-1 mRNA isoforms in HCV-infected livers, as compared to the control, suggest that HCV may induce alteration of IGF-1 splicing profile" 2)"Increase in grading of HCV-infected livers was linked to decreased IGF-1 mRNA expression, an altered profile of mRNA isoforms and to an increase in IGF-1R mRNA expression" and that 3) "Demonstration of an increased tissue expression of IGF-1R mRNA and the decreased expression level of IGF-1 mRNA isoforms, accentuated in line with increasing liver damage may be of a prognostic significance". Several clinical, virological and genetic prognostic factors have been used to predict the course of the disease and the response to treatment in CHC, predictors of relevant clinical impact in past years, when the percentage of the response to treatment was low or intermediate (between 25-60 %), but of lower practical use in the DAAs era, when no factor may anymore predict the response to treatment since 90-95% of treated cases eradicate HCV infection. Nevertheless, it remains of great importance to extend our knowledge on the pathogenesis and natural history of HCV diseases, also considering that the high cost of the new DAAs will make difficult at present their extensive use in most countries. Under this viewpoint I appreciate the attempt of Dr. Aldona Kasprzak and Coauthors to verify whether the IGF-1 mRNA isoforms and

IGF-1R mRNA expression may have clinical relevance in CHC. However, I should also underline some important limitations of this study. First of all the Authors investigated a limited number of liver biopsies from patients with chronic hepatitis C (34, 32 or 37?) and a only 7 negative tissue controls. I think that, in spite of statistical significance, these numbers are too small to convince the readers that these new prognostic factors may be used in clinical practice. -The Authors evaluated the relationship between their new prognostic factors and the degree of liver necroinflammation and fibrosis comparing G0-G1 versus G2-G4 and S0-S1 versus S2-S4. I think that this choice was strongly influenced by the low number of patients with CHC grade S3 and S4 and more importantly grade G3 and G4 in their study. Examining table 2 we may easily realize that only a few patients in this study had severe CHC or liver cirrhosis. A comparison G0-G2 versus G3-G4 and S0-S2 versus S3-S4 could better clarify the clinical value of IGF-1 mRNA isoforms and IGF-1R mRNA expression. -The Authors should comment on the peculiar composition of their study sample, where only a few patients present severe CHC or liver cirrhosis, and on the effect of this composition on the results. From this viewpoint the Authors should also express their opinion on the possibility to generalized their data. -The usefulness of new prognostic factors of the clinical course of CHC should be compared with that of the other factors (clinical, virological and genetic) so far in use. -The IGF-1 mRNA isoforms and IGF-1R mRNA expression were assessed in liver biopsies with methods of a certain technical complexity, an important limitation in the DAAs era, when a 12 weeks oral treatment may eradicate HCV infection and cure most of treated patients. The Authors should comment on this. -

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[ ] Grade E: Poor		[ ] Existing	[Y] Minor revision
		[ ] No records	[ ] Major revision

COMMENTS TO AUTHORS

In this manuscript, Kasprzak et al., described the expression changes of IGF-1 mRNA isoforms and IGF-1R mRNA in chronic hepatitis C patients. They found that the progression of HCV infection may induce an alteration of IGF-1 splicing profile, as well as that increase in grading of HCV-infected livers was linked to decreased IGF-1 mRNA expression, an altered profile of mRNA isoforms and to an increase in IGF-1R mRNA expression. In general, this manuscript provides important clinical clues for the role of IGF-I family in the pathogenesis of HCV. The entire paper is well-written and well-organized. The statistical analysis is accurate and appropriate. I hereby recommend its possible publication in WJG, unless authors corrected following points: 1. In the INTRODUCTION section, authors should clearly state the research gap and the importance of the current study; 2. The running title should be changed to "Expression of IGF-1 mRNA isoforms in HCV infection"; 3. The first paragraph of MM "Patients": "Infections with other hepatotropic viruses (HBV, HCMV, EBV) or other reasons of liver damage were excluded." Other reasons of liver damage and diseases should be clearly stated; 4. Last paragraph of MM, the company information of statistical software should be indicated; 5. There are several typo and formatting errors throughout the manuscript. Please carefully revise them before re-submission. For example: "histological activity (grading: G0 - no activity, G1 - mild activity, G2 - moderate acitivity, G3 - severe activity)" acitivity should be activity. 6. There are too many citations in the INTRODUCTION section, please cut some of them.