

## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 24212

**Title:** Restored NKG2D expression, altered cytokine production and increased cytotoxicity by NK cells in patients with chronic HCV infection with persistently normal ALT

**Reviewer's code:** 00012216

**Reviewer's country:** Spain

**Science editor:** Ze-Mao Gong

**Date sent for review:** 2016-01-15 09:26

**Date reviewed:** 2016-01-22 02:59

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 checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

## COMMENTS TO AUTHORS

Laszlo Szeray et al carry out a phenotypic and functional analysis of different peripheral lymphocyte subsets to explain the different clinical behaviours between persistent HCV infections with high and persistent normal ALT (PNALT). They found some phenotypical and functional differences in NK and CD8+ cell subsets between PNALT and chronic cases. Interestingly, some of those difference could be due to a TGF- $\beta$ 1 effect. They observed a different NKG2D expression on NK cells from chronic and PNALT patients. Previously it has been described that hepatitis C virus infection downregulates the ligands of the activating receptor NKG2D (Cell Mol Immunol. 2008; 5(6):475-8), but according to current paper this would happen only in chronic but not in PNALT patients. Hepatitis C virus infection downregulates the ligands of the activating receptor NKG2D. Minor comments - In the description of quantitative variables would be more representative of the sample to give the mean plus the standard deviation instead of the SEM, and it would be even better to use non parametric data such as median plus interquartile range. - When authors analyse CD8+ and



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CD4+ cells they should state if they label PBMC with CD3 as well, since NK also express CD8 and macrophages do also express CD4. - Although NK response is impaired in chronic HCV infection, the functional impairment of CD3+/CD8+ cells is observed in HCV-specific cytotoxic T cells. Therefore, to analyse in HCV specific CTLs these phenotypic differences observed in total CD8+/CD3+ cells could add impact to the results. - Authors should show representative examples of the FACS dot-plots obtained, to illustrate the phenotypical differences observed between chronic and PNAL groups.

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**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 24212

**Title:** Restored NKG2D expression, altered cytokine production and increased cytotoxicity by NK cells in patients with chronic HCV infection with persistently normal ALT

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**Science editor:** Ze-Mao Gong

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<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 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 checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		BPG Search:	<input checked="" type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

## COMMENTS TO AUTHORS

NA

## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 24212

**Title:** Restored NKG2D expression, altered cytokine production and increased cytotoxicity by NK cells in patients with chronic HCV infection with persistently normal ALT

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<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 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

This manuscript by Laszlo Szereday et al. presents expression data of various killer inhibitory and activating receptors in natural killer cells from normal healthy subjects as well as from HCV carrier and chronic hepatitis C patients. Although they found no change in the percentage of CD4+, CD8+, regulatory T cells, NK and NK-like cells, a significant reduction in the expression of natural killer group 2 member D (NKG2D) receptor in chronic hepatitis C patients as compared to that in healthy and HCV carriers. The study is straightforward and relevant. Results are convincing, discussion and conclusion are appropriate. Comments: ? All the abbreviations should be expanded for the first time stated in the text. ? ALT is alanine aminotransferase (not aminotransferase as mentioned in the introduction) ? anti-HCV should be indicated as "anti-HCV antibody". ? Page 9:, 2nd para "Than we determined NKG2D, CD160 and KIR2DL3 expression by NK cells by flow cytometry". This sentence should be restructured. ? Page 11, line 3: "Expression of NKG2C was significantly increased on NK cells of patients with chronic HCV

infection compared to healthy controls (Fig. 1g)". This statement is ambiguous and in contrast to the conclusion. It should be stated as; "Expression of NKG2C was higher in NK cells from patients with chronic HCV infection as compared to healthy controls but significantly lower than HCV carriers (Fig. 1g). ? Fig. 1 has several panels but not organized properly, and their description is missing in the legend. Figure legends should walk through the figure. Each of the three rows has same 'healthy control, chronic HCV with elevated ALT and HCV carriers with PNALT' labeling. This could be a single label for all the three rows at the bottom panel only. Similarly other figures should also be organized. ? Figure 5 panel a, b and c are confusing. Each panel should have its subtitle in the figure legend. For example (a) Cytotoxicity of NK cells isolated from healthy, HCV carrier and Chronic HepC patients. (b) Cytotoxicity of TGFbeta-treated NK cells isolated from healthy individuals. (c) Expression of NKG2D, KIR2DL3 and CD160 receptors by TGF beta-treated NK cells In Fig 5, the number of patients is indicated. Does it mean that NK cells from these individuals were mixed and then used in the experiment? If this is so, then it is unacceptable.