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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 22801

Title: Human cytomegalovirus encoded US28 may act as a tumor promoter in colorectal cancer

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Science editor: Ya-Juan Ma

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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 checked="" 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 checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

In this study the Authors explored the role of the HCMV-encoded US28 in the pathogenesis of colorectal cancer. To this purpose, they performed both ex vivo and in vitro studies. In the ex vivo study, they analyzed by immunohistochemistry the expression of the US28 protein in colorectal cancer samples and in adjacent noncancerous samples and correlated this the US28 levels to the clinicopathological features (histological grade, metastasis, Dukes' stage and survival). In the in vitro study they analyzed the effect of US28 gene overexpression in LOVO colorectal cancer cells on viability, resistance to chemotherapy, cell cycle and invasion of cells exhibited higher viability, greater chemotherapy resistance, accelerated cell cycle progression and increased invasion. They purchased evidence that US28 expression was increased in colorectal cancer tissues, compared with the adjacent noncancerous tissues, and that US28 overexpressing LOVO cells exhibited greater chemotherapy resistance, accelerated cell cycle progression and increased invasion as compared with control cells (non-transfected or transfected with the empty vector). They conclude that US28 expression predicts a poor prognosis and may act as a promoter in the pathogenesis of colorectal

cancer. In this study, while the in vitro experiments are well performed and the results obtained sustain the Author conclusions, in the ex-vivo analyses, even if carried out on an adequate and statistically significant number of patients, there are some critical points that must be clarified and answered, otherwise the manuscript is not acceptable for publication. Major points: 1) RESULTS (pg.11, lanes 22-29): paragraph "US28 expression in colorectal carcinoma and adjacent noncancerous colorectal tissue": Are the Authors sure that the US28 expression is negative in cancer tissues from patients negative for HCMV infection? In other words: can the authors exclude that the positivity observed is not due to some cross-reaction of the US28-specific antibody used with some other protein over-expressed in cancer tissue (for example, human chemokine receptors)? A control performed on samples from HCMV negative patients should be added to confirm the specificity of the antibody used. 2) RESULTS (pg.12, lanes 8-9): paragraph "Relationship between US28 expression and age, sex, tumor site, histological grade, metastasis, Dukes' stage and prognosis": The Authors wrote: "High US28 expression was associated with metastasis, advanced stage and poor patient prognosis"... In Table 1 it is shown that in the advanced stages (C-D) the % of highly positive tissues is about 27.3% (15 out of 55 total at C-D stage) vs about 52% of highly positive cancer in the early stages (25 out of 48 total at A-B stage)... this means that at advanced stage the % of highly positive tissues decrease and not increase... 3) DISCUSSION (pg14, lanes 8-9): "For the colorectal tumor patients with follow-up data, our results indicated that high US28 expression was correlated with histological grade, metastasis and Dukes' stage...." Based on the data reported in Table 1, it seems that high US28 expression is inversely correlated with the histological grade and Dukes' stage, while it is directly correlated with metastasis. The Author should better clarify and discuss this point. Minor points: 4) In some points of the manuscript the English is not fluent or with grammar errors, and should be revised with the help of a native English auditor. An example (pg.13 lanes 9-14): "As shown in Figure 7, compared to the nontransfected control group and the negative control, transfection with pCMV6-entry-US28 resulted in a 82.9% (P=0.001) and 93.9% (P=0.000) increase respectively, in the invasion of cells into the transwell plate chamber." English is not fluent: it should be better: "As shown in Figure 7, transfection with pCMV6-entry-US28 resulted in a 82.9% (P=0.001) and 93.9% (P=0.000) increase of cells invasion ability, compared to