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ANSWER TO THE REVIEWERS

Manuscript ID: 77652

Title: Alcohol-related diseases and liver metastasis: the role of cell-free network communication

The manuscript has been improved according to the REVIEWERS' suggestions as follows. We have added the answers to their related questions (bold) to facilitate understanding of the replies. All changes are marked in red in the manuscript and italics in this text. The authors appreciate the effort to evaluate to improve our work.

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 77652

Title: Alcohol-related diseases and liver metastasis: the role of cell-free network communication

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 06286468

Position: Peer Reviewer

Academic degree:

Professional title:

Reviewer's Country/Territory: Reviewer_Country

Author's Country/Territory: Spain

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Manuscript submission date: 2022-05-12

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-05-13 12:22

Reviewer performed review: 2022-05-20 15:49

Review time: 7 Days and 3 Hours

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

1、 Studies in recent years have found that not only miRNAs in extracellular vesicles play a role in intercellular communication, but also other substances play a similar role, and it is recommended to supplement, such as those reported in "Exosomes Regulate the Epithelial-Mesenchymal Transition in Cancer " and " Role of exosomal non-coding RNAs from tumor cells and tumor-associated macrophages in the tumor microenvironment " and it is also recommended to cite more research findings in recent years.

As the reviewer kindly comments, three new references have been incorporated in the following paragraph: *"Recent studies have shown that the exosomal content (proteins, miRNA, non-coding RNA) can help diagnose and treat cancer [20–22]".*

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22 Zhang K, Erkan EP, Jamalzadeh S, Dai J, Andersson N, Kaipio K, Lamminen T, Mansuri N, Huhtinen K, Carpén O, Hietanen S, Oikkonen J, Hynninen J, Virtanen A, Häkkinen A, Hautaniemi S, Vähärautio A. Longitudinal single-cell RNA-seq analysis reveals stress-promoted chemoresistance in metastatic ovarian cancer. *Sci Adv* 2022; **8**: eabm1831. [PMID: 35196078 DOI: 10.1126/sciadv.abm1831]

2、 The first appearance of "extracellular vesicles" was abbreviated as EVs and a uniformly abbreviation can be used in the following content.

As the reviewer kindly comments, the use of the abbreviation EVs has been included throughout the text.

3、 More new insight for future research should be shown in the article.

As the reviewer kindly comments, a new paragraph has been added: "Recent studies have shown that the exosomal content (proteins, miRNA, non-coding RNA) can help diagnose and treat cancer [20–22]. Therefore, understanding communication networks and extracellular vesicles as biomarkers can contribute significantly to developing strategies to address the serious public health problems associated with alcohol consumption and cancer".

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Reviewer's code: 06298691
Position: Peer Reviewer
Academic degree:

Professional title:

Reviewer's Country/Territory: Reviewer_Country

Author's Country/Territory: Spain

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Reviewer chosen by: AI Technique

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Review time: 10 Days and 8 Hours

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No

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Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

In this study, the authors describes the involvement of EV signaling during cancer progression in the alcohol environment is unknown. Therefore, understanding communication networks and the role of extracellular vesicles as biomarkers can contribute significantly to developing strategies to address the serious public health problems associated with alcohol consumption and cancer.

1. The language throughout the manuscript needs a thorough editing—some examples are listed here but this is not exhaustive: Alcohol induced gut dysbiosis is thought to play a role in alcohol dependence and regulating effects, including neurological and endocrine signaling and alterations of the immune system. Alcohol induced should be corrected to alcohol-induced.

As a reviewer kindly suggested, a native speaker has checked and modified all English spelling errors detected. All changes are marked in red in the manuscript.

2. The author's comments are well-reasoned and well-argued and suitable for publication.

We thank you for considering our work interesting. We appreciate the comments you make to improve the quality of our work and the time of dedication provided.

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Reviewer's code: 06214653
Position: Peer Reviewer
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Professional title:

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Author's Country/Territory: Spain

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Review time: 8 Days and 10 Hours

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
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Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The authors talked about the role of EVs in alcohol-related illnesses and cancer metastasis.This is an important paper. While I have minor concerns. Did EVs mediate liver-intestine communication through intestinal barrier dysfunction or gut dysbiosis?

According to the authors of this study, multiple mechanisms are attributed to alcohol-induced cancer risk, including toxic products and reactive oxygen species generated by ethanol metabolism. Additionally, cellular factors produced in response to injuries, such as protein, lipids, and microRNAs, can be packaged and released in extracellular vesicles

All changes are marked in red in the manuscript. We hope that these changes fulfill the requirements to make the manuscript suitable for publication in Archivum Immunologiae et Therapiae Experimentalis.

Sincerely yours.