

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 54966

Title: Intratumoral heterogeneity of liver cancer: from single-cell to population-based studies

Reviewer's code: 00055041

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Professor

Reviewer's Country/Territory: Italy

Author's Country/Territory: China

Manuscript submission date: 2020-02-27

Reviewer chosen by: Jia-Ping Yan

Reviewer accepted review: 2020-05-07 11:38

Reviewer performed review: 2020-05-07 17:24

Review time: 5 Hours

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 Grade E: Do not publish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

SPECIFIC COMMENTS TO AUTHORS

The manuscript is interesting and well structured.

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 54966

Title: Intratumoral heterogeneity of liver cancer: from single-cell to population-based studies

Reviewer's code: 02537773

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Academic Research, Associate Professor, Doctor, Lecturer

Reviewer's Country/Territory: Germany

Author's Country/Territory: China

Manuscript submission date: 2020-02-27

Reviewer chosen by: Jia-Ping Yan

Reviewer accepted review: 2020-05-11 07:52

Reviewer performed review: 2020-05-16 17:16

Review time: 5 Days and 9 Hours

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



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SPECIFIC COMMENTS TO AUTHORS

The authors provide very comprehensive review on an interesting topic of intratumoral heterogeneity of liver cancer. The main focus in deed is the hepatocellular carcinoma. Title: since the focus almost solely related to HCC it may be possible to update the title to HCC as otherwise the data to cholangiocellular cancer is missing. The format needs to be updated on the Journals recommendations. Figures are informative and conclusions are well balanced.

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 54966

Title: Intratumoral heterogeneity of liver cancer: from single-cell to population-based studies

Reviewer's code: 00503516

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Associate Professor

Reviewer's Country/Territory: Italy

Author's Country/Territory: China

Manuscript submission date: 2020-02-27

Reviewer chosen by: Jia-Ping Yan

Reviewer accepted review: 2020-05-08 15:23

Reviewer performed review: 2020-05-17 10:40

Review time: 8 Days and 19 Hours

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

SPECIFIC COMMENTS TO AUTHORS

Qi Zhang et al describe the intra-tumoral heterogeneity in hepatocellular carcinoma (HCC). Given the poor effectiveness of available therapeutic approaches to HCC, any novel approach to the disease can be of interest. The work is well written and presented. When the authors write: “In the liver, hepatocytes are organized from the central vein to the portal node, showing a strong regularity of the gene expression profile(5, 6). For example, the expression of Alb, Glul, Cyp2e1, Cyp2f2, and other hepatocyte markers in different locations can be extremely different” I suggest to briefly expand this part indicating the relevance of the oxygen gradient within the hepatic lobule in gene expression. Linked to the above consideration, are the authors aware of any relation between oxygenation and intra-tumoral heterogeneity? It would be nice to briefly discuss this aspect.