

## PEER-REVIEW REPORT

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

**Manuscript NO:** 62758

**Title:** Molecular alterations in pancreatic tumors

**Reviewer's code:** 03262127

**Position:** Peer Reviewer

**Academic degree:** MD, PhD

**Professional title:** Surgeon

**Reviewer's Country/Territory:** Russia

**Author's Country/Territory:** Italy

**Manuscript submission date:** 2021-01-17

**Reviewer chosen by:** Jia-Ping Yan

**Reviewer accepted review:** 2021-01-18 00:14

**Reviewer performed review:** 2021-01-20 06:36

**Review time:** 2 Days and 6 Hours

<b>Scientific quality</b>	<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 Grade E: Do not publish
<b>Language quality</b>	<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
<b>Conclusion</b>	<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
<b>Re-review</b>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<b>Peer-reviewer statements</b>	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 authors have done a great work to systematize modern knowledge about genetic alterations in pancreatic tumors. In general, the article is written at a very high level. The reviewer has only one principal ("fundamental") comment and two technical ones. 1) The article refers mainly to the genre of basic science. However, in my opinion, it would be correct to bring the work a little closer to clinical practice by adding to each paragraph devoted to a particular mutation, a small summary of the preferred chemotherapy option for such a mutation, if these data are available in the literature. 2) The field of research, namely molecular oncology, involves a huge number of abbreviations, mainly related to the names of genes. However, the work contains a number of other abbreviations that are not explained when they first appear in the text (IPMN, PDAC, MCN, LOH), or are not explained at all (GTP, WNT, TRK, ACC, NGS). Two times (Abstract and Introduction, page 5) IPMN was misspelled as IMPN. 3) The titles of the journals in the Reference section should be presented in abbreviated form as in PubMed (see Guidelines for Manuscript Preparation and Submission).

## PEER-REVIEW REPORT

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

**Manuscript NO:** 62758

**Title:** Molecular alterations in pancreatic tumors

**Reviewer's code:** 03091510

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Doctor

**Reviewer's Country/Territory:** Norway

**Author's Country/Territory:** Italy

**Manuscript submission date:** 2021-01-17

**Reviewer chosen by:** Jia-Ping Yan

**Reviewer accepted review:** 2021-01-18 11:32

**Reviewer performed review:** 2021-01-22 18:31

**Review time:** 4 Days and 6 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<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
<b>Conclusion</b>	<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
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

## **SPECIFIC COMMENTS TO AUTHORS**

Visani et al have written a nice review on molecular alterations in pancreatic tumors. The 3 tables give an overview of the most important genetic alterations identified in the most common types of pancreatic tumors. My comments are minor. -Correct IMPN to IPMN on page 3 and 5. -Use the term Serous Cystic Neoplasm (SCN) and not SCA. -In the abstract: “e.g., pancreatic ductal adenocarcinomas, IMPN, Cystic Neoplasms, solid pseudopapillary tumors”. IPMN and SPN are cystic neoplasms. I suggest to remove cystic neoplasms from this sentence. -Ref 55 and 56. I suggest to replace these two references with Goggins et al, Gut 2020, “Management of patients with increased risk for familial pancreatic cancer: updated recommendations from the International Cancer of the Pancreas Screening (CAPS) Consortium”. In these recommendations; for BRCA2 germline mutated individuals an agreement of 93 % for surveillance was reached if at least one affected FDR, or at least two affected relatives of any degree, whereas for BRCA1 germline mutated individuals an agreement of 69.6 % for surveillance was reached if at least one affected FDR. Moreover, surveillance with EUS and/or MRI is recommended to be performed in a research setting by multidisciplinary teams in centres with appropriate expertise. Please modify the sentence regarding annual screening of individuals with BRCA1/2 mutations. -The authors state: “The presence of a KRAS mutation in EUS-FNA material may support a re-evaluation of the original cytopathology report (especially if doubtful), an indication for a second FNA or surgery, and allows to a significant reduction of false-negative diagnoses”. Is a cytology specimen as good as a biopsy to identify the different molecular alterations in pancreatic tumors. (EUS-FNAC (cytology) versus EUS-FNAB (biopsy)). Please add some comments to this point in the last part of the paper. -Are any of the molecular alterations presented currently used in routine diagnostics? Is it possible to add a table on molecular alterations routinely used in the clinic?

## PEER-REVIEW REPORT

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

**Manuscript NO:** 62758

**Title:** Molecular alterations in pancreatic tumors

**Reviewer's code:** 03004570

**Position:** Editorial Board

**Academic degree:** MD

**Professional title:** Professor

**Reviewer's Country/Territory:** Turkey

**Author's Country/Territory:** Italy

**Manuscript submission date:** 2021-01-17

**Reviewer chosen by:** Jia-Ping Yan

**Reviewer accepted review:** 2021-01-18 17:35

**Reviewer performed review:** 2021-01-28 08:39

**Review time:** 9 Days and 15 Hours

<b>Scientific quality</b>	<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
<b>Language quality</b>	<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
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<b>Peer-reviewer statements</b>	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**

This manuscript is a nice, comprehensive and informative review about the molecular alterations in pancreatic tumors. Authors have benefited from 116 references. Some small typewriting errors such as IMPN in the abstract and LOF in Table 3 should be corrected as IPMN and LOH, respectively. On the other hand, authors mention MSI in Acinar cell carcinoma section, but not in PDAC in general. Although it was very low (0.8 %) in PDAC (\*), NCCN recommends MSI and/or MMR testing in metastatic disease (\*\*). I recommend adding this latest information to the manuscript to increase its quality. (\*): Hu ZI, et al. Clin Cancer Res. 2018 Mar 15;24(6):1326-1336. (\*\*): Pancreatic adenocarcinoma. NCCN Guidelines Version 1. 2021

## PEER-REVIEW REPORT

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

**Manuscript NO:** 62758

**Title:** Molecular alterations in pancreatic tumors

**Reviewer's code:** 03733262

**Position:** Editorial Board

**Academic degree:** MBChB, MRCP

**Professional title:** Adjunct Professor

**Reviewer's Country/Territory:** Singapore

**Author's Country/Territory:** Italy

**Manuscript submission date:** 2021-01-17

**Reviewer chosen by:** Jia-Ping Yan

**Reviewer accepted review:** 2021-01-27 08:08

**Reviewer performed review:** 2021-01-28 15:08

**Review time:** 1 Day and 7 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<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
<b>Conclusion</b>	<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
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	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**

Good effort with general overview of the topic Authors to highlight the role of fine needle biopsy (FNB) in EUS for tissue acquisition to improve the tissue yield for molecular analysis Can authors discuss the role of culture of PDAC tumoroids and its clinical utility? Authors need to demonstrate/ elaborate how this bench data translate into real world clinical practice.



## RE-REVIEW REPORT OF REVISED MANUSCRIPT

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

**Manuscript NO:** 62758

**Title:** Molecular alterations in pancreatic tumors

**Reviewer's code:** 03091510

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Doctor

**Reviewer's Country/Territory:** Norway

**Author's Country/Territory:** Italy

**Manuscript submission date:** 2021-01-17

**Reviewer chosen by:** Chen-Chen Gao

**Reviewer accepted review:** 2021-02-28 15:52

**Reviewer performed review:** 2021-03-03 17:15

**Review time:** 3 Days and 1 Hour

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

## SPECIFIC COMMENTS TO AUTHORS

The authors have satisfactory addressed all my suggestions and comments in the revised

manuscript. This is a nice and clinically relevant review on molecular alterations in pancreatic tumors. In my opinion the manuscript is suitable for publication in WJG.