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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 63313

Title: Histone methylation in pancreatic cancer and its clinical implications

Reviewer's code: 03475361
Position: Peer Reviewer
Academic degree: MD
Professional title: Doctor
Reviewer's Country/Territory: Japan
Author's Country/Territory: China

Manuscript submission date: 2021-01-27
Reviewer chosen by: AI Technique
Reviewer accepted review: 2021-01-29 04:12
Reviewer performed review: 2021-01-30 08:46
Review time: 1 Day and 4 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish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

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SPECIFIC COMMENTS TO AUTHORS

The manuscript is described the review of epigenetic change (histone methylation) in pancreatic cancer, and its probability of therapeutic target. I think the manuscript is overall well-written, however, genetic mutation such as K-ras, TP53 and SMAD4 are the more critical issues we should overcome than epigenetic abnormalities. The authors should discuss or address the importance of epigenetic change rather genetic mutation.

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 63313

Title: Histone methylation in pancreatic cancer and its clinical implications

Reviewer's code: 03739027
Position: Peer Reviewer
Academic degree: PhD
Professional title: Professor
Reviewer's Country/Territory: Japan
Author's Country/Territory: China

Manuscript submission date: 2021-01-27
Reviewer chosen by: AI Technique
Reviewer accepted review: 2021-01-28 00:29
Reviewer performed review: 2021-02-09 22:45
Review time: 12 Days and 22 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish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	[ ] Yes [Y] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

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SPECIFIC COMMENTS TO AUTHORS

Based on extensive knowledge of histone-modifying enzymes (writers), histone demethylases (elimination), and the PHD finger domains (leaders) that recognize the target histone residues of those enzymes, this review summarized the relationship between histone modification enzymes and the onset, metastasis, and malignancy of pancreatic cancers (PC). In particular, histone H4K20 methylase SMYD3 (KMT3E), histone H3K27 methylase EZH2, and histone H3R8 and H4R3 arginine methylase PRMT5 inhibitors have been introduced as typical epigenetic reagents for PC chemotherapy. Also, it is mentioned that deficiencies in histone methyltransferase or demethylase may inhibit cell proliferation and may not necessarily lead to malignant transformation. The delay in the development of therapeutic agents for histone demethylase inhibitors is also mentioned. In addition, it is mentioned that the arginine demethylase has not yet been clarified. This is a comprehensive review of major histone modification-related enzymes based on many references and is highly informative and can be highly evaluated. However, I would recommend that the authors reconsider the following points before publishing. Major points: - Most of the abstract part is used to explain epigenetics and common malignant cancers. Therefore, the readers may not predict that much information related to PC is provided in this review by this abstract alone. To increase the number of readers of this review, I suggest that the authors minimize the background part for general epigenetics and cancer and provide pancreatic cancer (PC)-specific information about epigenetic regulation and diagnosis, the current situation of the chemotherapy using epigenetic reagents, and about what is expected as advanced PC treatments based on future epigenetic research. - Tables 1-4 have much information and are plentiful. However, rows and groups are difficult to recognize. How about reorienting for more space, reducing the font size, and separating groups with thin lines or grey-and-white columns? Minor points: - P3, line 7: Therefore,

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some researchers have turned to (are focusing on?) epigenetics,…. - P5, line 10: “trypot-phan-aspartic acid 40 domain”…. The "tryptophan-aspartic acid 40 (WD40) domain" may be appropriate for this part. - P7, line 1: PRMT5…leading to the silencing of the cell cycle. Is this description correct? This is the opposite of the PRMT5 feature mentioned in the following statement.: PRMT5 overexpression improves cancer cell survival, proliferation…. - P8, line 20: The following statement is inconsistent with evidence that FBW7 inhibits EZH2 function through its ubiquitin-mediated degradation : EZH2 and FBW7 protein levels are negatively correlated in human PC specimen. The authors may want to say that EZH2 and FBW7 protein levels are oppositely regulated in human PC specimens. - P10, line 14: FBXL10 should be described as KDM2B for the reader's convenience. - P17, line 16: Is it correct that EZH2 is not expressed in normal pancreatic cells? P18, lines 14–15: The expression of EZH2 in PC cells is significantly higher than in normal pancreatic duct cells and fibroblasts. These two are a bit inconsistent. - P20, line 30: Jarid1b should be described as KDM5B for the reader's convenience.