

## PEER-REVIEW REPORT

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

**Manuscript NO:** 57895

**Title:** Prediction of clinically actionable genetic alterations from colorectal cancer histopathology images using deep learning

**Reviewer's code:** 05265621

**Position:** Peer Reviewer

**Academic degree:** PhD

**Professional title:** Professor

**Reviewer's Country/Territory:** United States

**Author's Country/Territory:** South Korea

**Manuscript submission date:** 2020-06-28

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2020-06-28 14:59

**Reviewer performed review:** 2020-06-28 16:15

**Review time:** 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 Grade E: Do not publish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 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**

This is a well written, interesting study to evaluate the feasibility of identifying actionable mutations in colorectal cancer by H&E slides image reviewed by computer with deep learning process. The authors used TCGA database as the main training cohort then the cases from St. Mary hospital as the validation cohort. The study showed predictions of mutation might be feasible by H&E slides using the deep learning-based identifiers. There are some comments would like the authors to address: 1. The benefits of this methods and its clinical meanings are not well discussed in the present article. The authors mentioned this methods may help to get more accurate molecular tests since this may avoid/balance the tumor heterogeneity. However, highly doubt a whole slide image review will be able to address this issue. Then if we are using representative slides from different location of the tumor, it will add the time and costs for this process. 2. More importantly, the authors used the mutation identifier for each mutation including APC, KRAS, PIK3CA, SMAD4, and TP53. However, in the real world, these mutations are so commonly seen in colorectal cancer and a lot of patients have a combination of these mutation instead of only one mutation, how to use the current identifier to predict mutation in these patients will be a challenge. 3. It will be interesting to do a head-to-head comparison between the mutation panel test (molecular test) and this method. It might be reasonable to consider add a table to summarize the pros and cons for each test and may also emphasize the complementary parts of the tests.

## PEER-REVIEW REPORT

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

**Manuscript NO:** 57895

**Title:** Prediction of clinically actionable genetic alterations from colorectal cancer histopathology images using deep learning

**Reviewer's code:** 02533652

**Position:** Editorial Board

**Academic degree:** PhD

**Professional title:** Academic Research, Assistant Professor, Chairman

**Reviewer's Country/Territory:** Saudi Arabia

**Author's Country/Territory:** South Korea

**Manuscript submission date:** 2020-06-28

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2020-06-28 08:27

**Reviewer performed review:** 2020-07-07 08:07

**Review time:** 8 Days and 23 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 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
<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



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#### **SPECIFIC COMMENTS TO AUTHORS**

Dear Authors, I must congratulate you for this novel study in the cancer diagnosis filed which would definitely improve the personalized medicine. I is a commendable attempt in the field of histopathology. However the manuscript which is submitted for the possible publication has many flaws which need to be addressed for it to be suitable for audience. 1. Introduction and Discussion of the manuscript is too long. Need to reduce it. In the last paragraph of the Introduction section authors are describing the methods which is not needed. 2. Methodology section should be crisp and focus only on how the study and experiments were designed and done. 3. Results section consists of too much redundancy, and repetition of methodology which is also present in discussion 4. Authors need to specify the various limitation of the study, especially when dealing with two different sample - frozen and Formalin fixed. 5. There is a need of language sanitation of the manuscript by a native speaker. Regards

## RE-REVIEW REPORT OF REVISED MANUSCRIPT

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

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**Title:** Prediction of clinically actionable genetic alterations from colorectal cancer histopathology images using deep learning

**Reviewer's code:** 05265621

**Position:** Peer Reviewer

**Academic degree:** PhD

**Professional title:** Professor

**Reviewer's Country/Territory:** United States

**Author's Country/Territory:** South Korea

**Manuscript submission date:** 2020-06-28

**Reviewer chosen by:** Pan Huang

**Reviewer accepted review:** 2020-08-21 11:23

**Reviewer performed review:** 2020-08-21 11:40

**Review time:** 1 Hour

<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 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 checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

## SPECIFIC COMMENTS TO AUTHORS



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Thanks a lot for the authors replies. It is a job well done, congratulations!