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PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Oncology*

Manuscript NO: 77566

Title: Transcriptional factor III A promotes colorectal cancer progression by upregulating cystatin A

Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05562744
Position: Editorial Board
Academic degree: FACS, MD, PhD
Professional title: Professor, Senior Scientist
Reviewer's Country/Territory: Turkey
Author's Country/Territory: China

Manuscript submission date: 2022-05-07

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-06-14 04:14

Reviewer performed review: 2022-06-15 19:48

Review time: 1 Day and 15 Hours

Scientific quality	[Y] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish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	[Y] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No

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

SPECIFIC COMMENTS TO AUTHORS

Title reflects the study Abstract is well written Core tip summarizes the study very well Introduction summarizes the study very well/ Materials and methods section: each porcedure is very well explained. the authors should give more detail about the vector for I believe the vector has two reporter Results: The expression of GTF3A was higher in CRC tissues and lymph node metastatic tissues than in adjacent normal tissues. GTF3A was associated with CRC prognosis. Functionally, knockdown of the Gf3a gene impaired the CRC cell proliferation, invasion and motility in vitro and in vivo. Moreover, RNA-Seq analysis revealed that GTF3A might upregulate the expression cystatin A (CSTA), while the luciferase activity assay showed that GTF3A bound to the promoter of Csta gene and increased the Csta transcription. Furthermore, CSTA regulated the expression of epithelial-mesenchymal transition (EMT) markers. Discussion is well written References are up to date.

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Peer-review model: Single blind

Reviewer's code: 05191118
Position: Peer Reviewer
Academic degree: PhD
Professional title: Assistant Professor
Reviewer's Country/Territory: India
Author's Country/Territory: China

Manuscript submission date: 2022-05-07

Reviewer chosen by: Dong-Mei Wang

Reviewer accepted review: 2022-06-22 03:00

Reviewer performed review: 2022-07-04 20:12

Review time: 12 Days and 17 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
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SPECIFIC COMMENTS TO AUTHORS

The researchers in this study identified the role of GTF3A, an RNA polymerase III transcriptional factor, in promoting progression of colorectal cancer by upregulating Cystatin. The work is well conducted with appropriate controls and I recommend the paper could be published in the "World Journal of Gastrointestinal Oncology" after the authors address the major and minor points. Addressing the comments will improve the quality of the manuscript and the impact of this research work. Major points: 1. Abstract: It is written as "Human tissue microarrays containing 90 pairs of CRC tissues and adjacent non tumor tissues, and human tissue microarrays containing 20 pairs of CRC tissues, corresponding adjacent non tumor tissues and lymph node tissue" … why the authors have not written "Human tissue microarrays containing 110 pairs of CRC tissues and adjacent non tumor tissues and lymph node tissue". This was confusing to me. Then I checked the M&M and it was somewhat clear. But then in the results section it was mentioned only 90 pairs so again I got confused. The authors need to clarify this and make it clear. Also, the authors have not elaborated the detailed source of these two sources. The authors should be more explicit in providing the details for better clarity. 2. The expression of GTF3A in HCT116 cells in Fig. 2A is very low (hardly a band is visible) but again expression is observed in Fig. 2B(b). Why such a discrepancy and why did the authors choose this cell line for knockdown experiments? I understand the selection of SW480 cells but not clear about the selection of HCT116 cells. Why was DLD-1 cells not chosen for this experiment, atleast they had some basal expression (Fig. 2A)? 3. In Fig. 5A and discussion section, Vimentin is mentioned but the blot is not shown. Please add. 4. The manuscript has many typographical errors. Units have sometimes space and

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sometimes not. No uniformity. No space before reference at many places. Spelling mistakes in GTF3A name itself, cell lines names and other words at many places. The authors are seriously requested to look into this aspect thoroughly. 5. At few places, English needs to be improved (especially the titles of results section) for clarity and understanding (few are suggested above). The company that provided English language certificate has not done an excellent job. Minor points: 1. Expand "Csta gene" in abstract 2. Abstract: "were examined for the GTF3A expression" instead of "were examined the GTF3A expression" 3. Abstract: "Functionally, knockdown of the Gf3a gene". The gene name is misspelled. It should have been "Gtf3a". 4. Abstract: "GTF3A might upregulate the expression cystatin A (CSTA)". "of" is missing in the sentence and Cystatin A abbreviation expansion should have been earlier in the abstract and it should be in italics in this sentence. 5. "Progress" cannot be a keyword. Please delete. 6. The coretip last sentence should have been the abstract last sentence. 7. Please write "5S rRNA" instead of "5SrRNA" wherever applicable in the manuscript. 8. Please write this sentence as suggested here. "GTF3A gene is present in all the organisms. Human …" 9. Expand "RNP". 10. Please write this sentence as suggested here. "and the complex functions as a NES to transfer" instead of "and the complex functions as a nuclear export signal to transfer" as NES is already abbreviated earlier in the introduction. 11. Please rewrite this sentence as English is NOT correct and typographical error is present. "So far, several studies suggested that the 5S rRNA bound with L5 and L11 to form the 5S RNP complex, further regulating the MDM2 p53 checkpoint[9-12]." 12. Please rewrite this sentence as English is NOT correct. "Other cysteine protease inhibitors, cystatin SN (CST1) and cystatin S (CST4) are type 2 cystatin proteins; they the enhance the metastasis of various malignant tumors and contribute to the poor survival of patients [20, 21].". The authors can write as "Other cysteine protease inhibitors, cystatin SN (CST1) and cystatin S (CST4), are type 2 cystatin proteins, which enhance the metastasis of various

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malignant tumors and contribute to the poor survival of patients [20, 21].” 13. Please rewrite this sentence as English is NOT correct. “In the present study, we showed that GTF3A was highly expressed in CRC, and that GTF3A bound to the promoter of Csta to facilitate Csta transcription, which regulates EMT markers and promotes CRC progression.”. The authors can write as “In the present study, we showed that GTF3A was highly expressed in CRC, and it bound to the promoter of Csta to facilitate Csta transcription, which then regulated EMT marker expression and promoted CRC progression.” 14. “The knockdown efficiency was determined using RT-qPCR” instead of “The knockdown efficiency was filtered using RT-qPCR”. 15. “The lentivirus titers were quantified” instead of “The lentivirus titers were qualified”. 16. “Following the manufacturer’s instructions, the crude lysate was centrifuged and the supernatant was collected to measure the protein concentration using the BCA Protein Assay Kit (CWBIO, Beijing, China).” instead of “Following the manufacturer’s instructions, the cell lysates were obtained by centrifugation and the protein concentration was measured using the BCA Protein Assay Kit (CWBIO, Beijing, China).”. 17. “moving the detached cells”. Incorrect English. Please rephrase. 18. “enriched longRNA (> 200 nt) was interrupted”. Incorrect English. Please rephrase. 19. “To determine the expression of GTF3A in CRC tissues,” instead of “To clarify the expression of GTF3A in CRC tissues,” 20. Rephrase the title “Knockdown Gtf3a gene inhibiting CRC cell proliferation” and “Knockdown Gtf3a inhibiting CRC cell motility and invasion” and “GTF3A protein regulating CSTA by binding to the CSTA promoter” and “GTF3A mediating the CRC cell EMT by through regulating the expression of CSTA” and “GTF3A promoting CRC cell growth in vivo”. Incorrect English in all these titles in results section. Please rephrase. 21. Please correct the spelling of HCT116 cells in “Gtf3a knockdown SW480 and HC116 cells”. 22. Please correct GTF3A instead of GTF3 in this sentence “Next, a dual luciferase assay was carried out to determine whether the interaction of GTF3 with the Csta promoter

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increase". 23. Please correct "Gtf3a" in this sentence "Both RNA-Seq and RT-qPCR showed that Csta expression was dramatically decreased in Gf3a knockdown cells". 24. Conclusion: "increased in the expression of CSTA, enhanced the EMT process" instead of "increased in the expression of CSTA enhanced the EMT process", Please add "," after CSTA in this sentence. 25. Please write "Western blotting" instead of "Western-blotting" throughout the manuscript. 26. "The fluorescence staining of the GTF3A and Csta promoters were colocalized to a large extent as indicated" instead of "The fluorescence locations of the GTF3A and Csta promoters were approximately coincident, and indicated". Note: The authors should give page numbers and line numbers in the manuscript.

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RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Gastrointestinal Oncology*

Manuscript NO: 77566

Title: Transcriptional factor III A promotes colorectal cancer progression by upregulating cystatin A

Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05191118
Position: Peer Reviewer
Academic degree: PhD
Professional title: Assistant Professor
Reviewer's Country/Territory: India
Author's Country/Territory: China

Manuscript submission date: 2022-05-07

Reviewer chosen by: Jing-Jie Wang

Reviewer accepted review: 2022-07-26 12:34

Reviewer performed review: 2022-08-10 01:26

Review time: 14 Days and 12 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
Peer-reviewer	Peer-Review: [Y] Anonymous [ ] Onymous

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statements	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The authors have addressed the comments raised by the reviewers and I believe the manuscript can now be accepted for publication