

PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Oncology

Manuscript NO: 53927

Title: Circular RNA and Its Potentials as Prostate Cancer Biomarkers

Reviewer's code: 02856239

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Associate Professor

Reviewer's Country/Territory: United States

Author's Country/Territory: Canada

Manuscript submission date: 2019-12-31

Reviewer chosen by: Le Zhang

Reviewer accepted review: 2020-02-14 06:12

Reviewer performed review: 2020-02-14 06:55

Review time: 1 Hour

Scientific quality	<input checked="" type="checkbox"/> Grade A: Excellent <input 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 Grade E: Do not publish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 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

This is an interesting review on the potential role of circular RNA in prostate cancer biology. This paper can be improved in following points. There are many environmental and microenvironmental factors that influence molecular mechanisms of carcinogenesis. When discussing circular RNA, the authors can also discuss influence of those factors, eg, smoking, diet, microbiome, etc. There are also influences of germline and somatic genetic variations. Those can be emphasized. In these contexts, as a future direction, research on cancer risk factors, microbiome, immunity, and molecular tissue biomarkers is needed. Hence, the authors should discuss molecular pathological epidemiology (MPE), which can investigate those factors in relation to molecular pathologies in normal or diseased tissue. MPE, its strengths and challenges have been discussed in Gut 2011, Annu Rev Pathol 2019, etc. I believe MPE research can be a promising direction. Please describe strengths and challenges of MPE.

PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Oncology

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Title: Circular RNA and Its Potentials as Prostate Cancer Biomarkers

Reviewer's code: 00068559

Position: Peer Reviewer

Academic degree: MD

Professional title: Professor

Reviewer's Country/Territory: China

Author's Country/Territory: Canada

Manuscript submission date: 2019-12-31

Reviewer chosen by: Le Zhang

Reviewer accepted review: 2020-02-15 03:16

Reviewer performed review: 2020-02-21 10:26

Review time: 6 Days and 7 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 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 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 author gave a review about the circRNA and Its potential as prostate cancer biomarkers. The review is helpful for us to understand the biogenesis, proposed functions, and the mechanistic machinery that drives the genesis of circRNS, as well as the association between circRNA expression with PCa development. Also, the limitation and clinical concerns about circRNA was illustrated.

PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Oncology

Manuscript NO: 53927

Title: Circular RNA and Its Potentials as Prostate Cancer Biomarkers

Reviewer's code: 02445074

Position: Peer Reviewer

Academic degree: PhD

Professional title: Professor

Reviewer's Country/Territory: United States

Author's Country/Territory: Canada

Manuscript submission date: 2019-12-31

Reviewer chosen by: Le Zhang

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Reviewer performed review: 2020-02-22 18:47

Review time: 1 Day

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 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

GENERAL COMMENTS: This review addresses an interesting topic. The report will be

of special interest to oncologists. **SPECIFIC COMMENTS:** 1. Do you think exon-skipping is same as back-splicing? Back-splicing will produce circles with no lariat! 2. RNA binding proteins might facilitate aberrant splicing. However, for HDV the RNA binding protein stabilized the RNA circles AFTER they were formed. Stabilization of RNA circles is needed as the circles increase in size. Viroid circles, typically of 240-400 nt, do not need RNA binding proteins. HDV at 1700 nt does. But, if a mini-HDV of about 350 nt is expressed it has NO NEED of an RNA binding protein (Lazinski et al.) This result is consistent with the viroid size data. Also, in the absence of RNA binding proteins, the spectrum of sizes of circular host cell RNAs rapidly drops off from 400 to 1500 nt. The authors might also cite data that host cell RNases are predominantly exonucleases rather than endonucleases. Hence, RNA circles are favored over corresponding linear RNAs. 3. It needs to be made clearer that while RNA circles can be made and can accumulate, it may be that only a minor fraction of these can be assigned a function. Hansen's study and others are important but special cases. This reviewer suggests adding more doubt regarding success of ascribing functionality to most RNA circles. 4. There are now three published studies that have reported the existence of HDV-like RNA circles. Such studies have been based on computer-based assembly of ten million or more short RNA reads. The legitimacy of this approach, in these studies, for finding circles still needs to be established.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Position: Peer Reviewer

Academic degree: MD, PhD

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Reviewer's Country/Territory: United States

Author's Country/Territory: Canada

Manuscript submission date: 2019-12-31

Reviewer chosen by: Ruo-Yu Ma (Quit in 2020)

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Reviewer performed review: 2020-04-16 09:20

Review time: 1 Hour

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

SPECIFIC COMMENTS TO AUTHORS

The authors successfully addressed the points.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Title: Circular RNA and Its Potentials as Prostate Cancer Biomarkers

Reviewer's code: 00068559

Position: Peer Reviewer

Academic degree: MD

Professional title: Professor

Reviewer's Country/Territory: China

Author's Country/Territory: Canada

Manuscript submission date: 2019-12-31

Reviewer chosen by: Ruo-Yu Ma (Quit in 2020)

Reviewer accepted review: 2020-04-17 12:17

Reviewer performed review: 2020-04-19 02:43

Review time: 1 Day and 14 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 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
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 authors have revised the manuscript according to the peer review comments and

made the corresponding adjustments. The word spelling “discoverie” in the introduction should be checked.