



PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Oncology

Manuscript NO: 51417

Title: Roles of cell fusion, hybridization and polyploid cell formation in cancer metastasis

Reviewer's code: 00068720

Position: Peer Reviewer

Academic degree: MSc

Professional title: Attending Doctor, Professor

Reviewer's country: China

Author's country: Sweden

Manuscript submission date: 2019-09-20

Reviewer chosen by: Jia-Ping Yan

Reviewer accepted review: 2019-11-15 05:02

Reviewer performed review: 2019-11-19 06:32

Review time: 4 Days and 1 Hour

| SCIENTIFIC QUALITY | LANGUAGE QUALITY | CONCLUSION | PEER-REVIEWER STATEMENTS |
|--|---|--|---|
| <input type="checkbox"/> Grade A: Excellent | <input type="checkbox"/> Grade A: Priority publishing | <input type="checkbox"/> Accept | Peer-Review: |
| <input checked="" type="checkbox"/> Grade B: Very good | <input checked="" type="checkbox"/> Grade B: Minor language | (High priority) | <input checked="" type="checkbox"/> Anonymous |
| <input type="checkbox"/> Grade C: Good | polishing | <input checked="" type="checkbox"/> Accept | <input type="checkbox"/> Onymous |
| <input type="checkbox"/> Grade D: Fair | <input type="checkbox"/> Grade C: A great deal of | (General priority) | Peer-reviewer's expertise on the |
| <input type="checkbox"/> Grade E: Do not | language polishing | <input type="checkbox"/> Minor revision | topic of the manuscript: |
| publish | <input type="checkbox"/> Grade D: Rejection | <input type="checkbox"/> Major revision | <input checked="" type="checkbox"/> Advanced |
| | | <input type="checkbox"/> Rejection | <input type="checkbox"/> General |
| | | | <input type="checkbox"/> No expertise |
| | | | Conflicts-of-Interest: |
| | | | <input type="checkbox"/> Yes |
| | | | <input checked="" type="checkbox"/> No |



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SPECIFIC COMMENTS TO AUTHORS

This study clarified the recent progress in cell-cell fusion and with a focus on an important role for polyploid cells in cancer metastasis. The paper offers an interesting analysis and their innovation and findings are well emphasized. It is recommended to provide more evidence on the etiology, diagnosis and prognosis in clinical evidence, provide more references, or summary tables.

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

- The same title
- Duplicate publication
- Plagiarism
- No

BPG Search:

- The same title
- Duplicate publication
- Plagiarism
- No



PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Oncology

Manuscript NO: 51417

Title: Roles of cell fusion, hybridization and polyploid cell formation in cancer metastasis

Reviewer's code: 02577402

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Professor

Reviewer's country: China

Author's country: Sweden

Manuscript submission date: 2019-09-20

Reviewer chosen by: Jia-Ping Yan

Reviewer accepted review: 2019-11-14 00:45

Reviewer performed review: 2019-11-19 14:17

Review time: 5 Days and 13 Hours

| SCIENTIFIC QUALITY | LANGUAGE QUALITY | CONCLUSION | PEER-REVIEWER STATEMENTS |
|---|---|--|---|
| <input type="checkbox"/> Grade A: Excellent | <input type="checkbox"/> Grade A: Priority publishing | <input type="checkbox"/> Accept | Peer-Review: |
| <input type="checkbox"/> Grade B: Very good | <input checked="" type="checkbox"/> Grade B: Minor language | (High priority) | <input checked="" type="checkbox"/> Anonymous |
| <input checked="" type="checkbox"/> Grade C: Good | polishing | <input type="checkbox"/> Accept | <input type="checkbox"/> Onymous |
| <input type="checkbox"/> Grade D: Fair | <input type="checkbox"/> Grade C: A great deal of | (General priority) | Peer-reviewer's expertise on the |
| <input type="checkbox"/> Grade E: Do not | language polishing | <input type="checkbox"/> Minor revision | topic of the manuscript: |
| publish | <input type="checkbox"/> Grade D: Rejection | <input checked="" type="checkbox"/> Major revision | <input type="checkbox"/> Advanced |
| | | <input type="checkbox"/> Rejection | <input checked="" type="checkbox"/> General |
| | | | <input type="checkbox"/> No expertise |
| | | | Conflicts-of-Interest: |
| | | | <input type="checkbox"/> Yes |
| | | | <input checked="" type="checkbox"/> No |



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SPECIFIC COMMENTS TO AUTHORS

In this study, the authors reviewed the roles of cell fusion, hybridization and polyploid cell formation in cancer metastasis. It is a good review. However, some issues exist. 1. Citation: When citing others' work, the reference should be immediately follow the sentence regarding the work. Do not delay until one or several sentences away before giving the reference number. For example, in the sentences of "Gauck and co-workers showed that spontaneous fusion of human breast epithelial cells and human breast cancer cells can give rise to hybrid cells that possess CSCs properties. In these studies, the----epithelial cells (49).", the reference number 49 was given at the second sentence following the first one of "Gauck and co-workers---". The reference number 49 should be at the end of "----possess CSCs properties.". A lot of other examples existed. Please check the whole article and correct all these issues. For example, in the same paragraph, "In another example", here a reference number should be given. However, the reference number was given several sentences away. This is not good. 2. Abbreviations: The authors used a lot of abbreviations, some of which are known but others are not known by most readers. For example, what do "MSC, NOD/SCID, WIST, SLUG, SNAIL, BMDC, mSSC, etc." mean? The full phrase should be given at the first time of using an abbreviation. Then, you can always use the abbreviation without mentioning the full phrase. Please check the whole article and correct all similar issues. 3. In the section of "Clinical significance of polyploidization in cancer", "The PGCC's are able to overcome---" should be "The PGCCs are able to overcome---". "from which they are eventually able to come back from and resume growth" should be "from which they are eventually able to come back and resume growth". In summary, it is a good review.

INITIAL REVIEW OF THE MANUSCRIPT



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PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Oncology

Manuscript NO: 51417

Title: Roles of cell fusion, hybridization and polyploid cell formation in cancer metastasis

Reviewer's code: 02683307

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Doctor, Professor, Research Scientist

Reviewer's country: South Korea

Author's country: Sweden

Manuscript submission date: 2019-09-20

Reviewer chosen by: Jia-Ping Yan

Reviewer accepted review: 2019-11-08 07:02

Reviewer performed review: 2019-11-20 08:24

Review time: 12 Days and 1 Hour

| SCIENTIFIC QUALITY | LANGUAGE QUALITY | CONCLUSION | PEER-REVIEWER STATEMENTS |
|--|--|--|---|
| <input type="checkbox"/> Grade A: Excellent | <input checked="" type="checkbox"/> Grade A: Priority publishing | <input checked="" type="checkbox"/> Accept | Peer-Review: |
| <input checked="" type="checkbox"/> Grade B: Very good | <input type="checkbox"/> Grade B: Minor language | (High priority) | <input checked="" type="checkbox"/> Anonymous |
| <input type="checkbox"/> Grade C: Good | polishing | <input type="checkbox"/> Accept | <input type="checkbox"/> Onymous |
| <input type="checkbox"/> Grade D: Fair | <input type="checkbox"/> Grade C: A great deal of | (General priority) | Peer-reviewer's expertise on the |
| <input type="checkbox"/> Grade E: Do not | language polishing | <input type="checkbox"/> Minor revision | topic of the manuscript: |
| publish | <input type="checkbox"/> Grade D: Rejection | <input type="checkbox"/> Major revision | <input type="checkbox"/> Advanced |
| | | <input type="checkbox"/> Rejection | <input checked="" type="checkbox"/> General |
| | | | <input type="checkbox"/> No expertise |
| | | | Conflicts-of-Interest: |
| | | | <input type="checkbox"/> Yes |
| | | | <input checked="" type="checkbox"/> No |



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SPECIFIC COMMENTS TO AUTHORS

This manuscript is a well written review about cell fusion.

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Google Search:

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BPG Search:

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PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Oncology

Manuscript NO: 51417

Title: Roles of cell fusion, hybridization and polyploid cell formation in cancer metastasis

Reviewer's code: 00070894

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Doctor, Professor

Reviewer's country: China

Author's country: Sweden

Manuscript submission date: 2019-09-20

Reviewer chosen by: Jia-Ping Yan

Reviewer accepted review: 2019-11-14 05:48

Reviewer performed review: 2019-11-21 15:47

Review time: 7 Days and 9 Hours

| SCIENTIFIC QUALITY | LANGUAGE QUALITY | CONCLUSION | PEER-REVIEWER STATEMENTS |
|---|---|--|---|
| <input type="checkbox"/> Grade A: Excellent | <input type="checkbox"/> Grade A: Priority publishing | <input type="checkbox"/> Accept | Peer-Review: |
| <input type="checkbox"/> Grade B: Very good | <input checked="" type="checkbox"/> Grade B: Minor language | (High priority) | <input checked="" type="checkbox"/> Anonymous |
| <input checked="" type="checkbox"/> Grade C: Good | polishing | <input type="checkbox"/> Accept | <input type="checkbox"/> Onymous |
| <input type="checkbox"/> Grade D: Fair | <input type="checkbox"/> Grade C: A great deal of | (General priority) | Peer-reviewer's expertise on the |
| <input type="checkbox"/> Grade E: Do not | language polishing | <input type="checkbox"/> Minor revision | topic of the manuscript: |
| publish | <input type="checkbox"/> Grade D: Rejection | <input checked="" type="checkbox"/> Major revision | <input type="checkbox"/> Advanced |
| | | <input type="checkbox"/> Rejection | <input checked="" type="checkbox"/> General |
| | | | <input type="checkbox"/> No expertise |
| | | | Conflicts-of-Interest: |
| | | | <input type="checkbox"/> Yes |
| | | | <input checked="" type="checkbox"/> No |



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SPECIFIC COMMENTS TO AUTHORS

In this review, Shabo et al. summarize the recent progress in cell-cell fusion and polyploid cells in cancer metastasis. There is a large amount of study providing evidence that fusion of cancer cells with other cells participates in tumor stem cell formation, high invasiveness acquisition of tumor, modification of tumor microenvironment, epithelial-mesenchymal transition (EMT). Both of these biological processes are closely related to the invasion and metastasis of tumor. They firstly introduced the concepts and research background of cell fusion and polyploidization. What's more, they elaborated the relationship between cell fusion, polyploidization and cancer. They also indicate that inflammation, hypoxia or starvation may play important role in causing cell fusion and polyploidization in tumours. The last part of the review described the clinical significance of polyploidization and clinical evidence of cell fusion. However, there are some concerns that need to be clarified. 1. This paper intends to summarize the research progress on the role of cell fusion in tumor metastasis. However, the authors wrote at length about cell fusion and polyploidization in the development, growth or progress of tumor. 2. It should be concluded that what's with cell-fusion and polyploidization in step of cancer metastasis, including local invasion and intravasation into vasculature, survival of circulating tumor cells (CTCs), priming of the metastatic niche, extravasation into the secondary site and metastatic colonization of the new tissue. 3. In the last part of the review, the authors emphasised the clinical significance of polyploidization and cell fusion. It is desired to sum up the relative target or direction for tumor diagnosis and treatment.

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BPG Search:

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PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Oncology

Manuscript NO: 51417

Title: Roles of cell fusion, hybridization and polyploid cell formation in cancer metastasis

Reviewer's code: 00053419

Position: Editorial Board

Academic degree: PhD

Professional title: Professor

Reviewer's country: Spain

Author's country: Sweden

Manuscript submission date: 2019-09-20

Reviewer chosen by: Jia-Ping Yan

Reviewer accepted review: 2019-11-18 11:35

Reviewer performed review: 2019-11-22 15:40

Review time: 4 Days and 4 Hours

| SCIENTIFIC QUALITY | LANGUAGE QUALITY | CONCLUSION | PEER-REVIEWER STATEMENTS |
|---|---|---|---------------------------------------|
| <input type="checkbox"/> Grade A: Excellent | <input type="checkbox"/> Grade A: Priority publishing | <input type="checkbox"/> Accept | Peer-Review: |
| <input type="checkbox"/> Grade B: Very good | <input type="checkbox"/> Grade B: Minor language | (High priority) | <input type="checkbox"/> Anonymous |
| <input type="checkbox"/> Grade C: Good | polishing | <input type="checkbox"/> Accept | <input type="checkbox"/> Onymous |
| <input type="checkbox"/> Grade D: Fair | <input type="checkbox"/> Grade C: A great deal of | (General priority) | Peer-reviewer's expertise on the |
| <input type="checkbox"/> Grade E: Do not | language polishing | <input type="checkbox"/> Minor revision | topic of the manuscript: |
| publish | <input type="checkbox"/> Grade D: Rejection | <input type="checkbox"/> Major revision | <input type="checkbox"/> Advanced |
| | | <input type="checkbox"/> Rejection | <input type="checkbox"/> General |
| | | | <input type="checkbox"/> No expertise |
| | | | Conflicts-of-Interest: |
| | | | <input type="checkbox"/> Yes |
| | | | <input type="checkbox"/> No |



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SPECIFIC COMMENTS TO AUTHORS

The manuscript is comprehensively written and the most relevant topics in the field are nicely discussed providing the most relevant literature. The topic is of great interest.

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

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PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Oncology

Manuscript NO: 51417

Title: Roles of cell fusion, hybridization and polyploid cell formation in cancer metastasis

Reviewer's code: 03465354

Position: Editorial Board

Academic degree: PhD

Professional title: Assistant Professor

Reviewer's country: United States

Author's country: Sweden

Manuscript submission date: 2019-09-20

Reviewer chosen by: Jia-Ping Yan

Reviewer accepted review: 2019-11-14 14:37

Reviewer performed review: 2019-11-22 22:19

Review time: 8 Days and 7 Hours

| SCIENTIFIC QUALITY | LANGUAGE QUALITY | CONCLUSION | PEER-REVIEWER STATEMENTS |
|---|---|---|---------------------------------------|
| <input type="checkbox"/> Grade A: Excellent | <input type="checkbox"/> Grade A: Priority publishing | <input type="checkbox"/> Accept | Peer-Review: |
| <input type="checkbox"/> Grade B: Very good | <input type="checkbox"/> Grade B: Minor language | (High priority) | <input type="checkbox"/> Anonymous |
| <input type="checkbox"/> Grade C: Good | polishing | <input type="checkbox"/> Accept | <input type="checkbox"/> Onymous |
| <input type="checkbox"/> Grade D: Fair | <input type="checkbox"/> Grade C: A great deal of | (General priority) | Peer-reviewer's expertise on the |
| <input type="checkbox"/> Grade E: Do not | language polishing | <input type="checkbox"/> Minor revision | topic of the manuscript: |
| publish | <input type="checkbox"/> Grade D: Rejection | <input type="checkbox"/> Major revision | <input type="checkbox"/> Advanced |
| | | <input type="checkbox"/> Rejection | <input type="checkbox"/> General |
| | | | <input type="checkbox"/> No expertise |
| | | | Conflicts-of-Interest: |
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| | | | <input type="checkbox"/> No |



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SPECIFIC COMMENTS TO AUTHORS

The proposed review manuscript by Shabo and co-authors summarizes the current knowledge on the role of cell fusion, hybridization and polyploid cell formation in cancer metastasis. The authors begin their review with introduction of the mechanisms of cellular fusion and polyploidization and the effect of these phenomena on nuclear reprogramming and epigenetic modifications. Further, the authors logically concentrate the reader's attention to the role of cell fusion and epigenetic reprogramming in the formation of pluripotent cancer stem cells and the epithelial to mesenchymal transition (EMT). The authors discuss the role of macrophages and inflammation in cancer cell fusion and move to discussing the clinical significance of polyploidization in cancer. As the authors point out, the knowledge on cell fusion in cancer has the potential for the development of novel cancer therapies. In my opinion as a peer reviewer, this is a well-written, logical and informative manuscript which brings an interesting topic with high significance in the field of cancer growth. Text is written well and the figures are of a good quality. I do not have any comments or suggestion for quality improvement of the manuscript.

INITIAL REVIEW OF THE MANUSCRIPT

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- No



PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Oncology

Manuscript NO: 51417

Title: Roles of cell fusion, hybridization and polyploid cell formation in cancer metastasis

Reviewer’s code: 00077340

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Associate Professor

Reviewer’s country: Japan

Author’s country: Sweden

Manuscript submission date: 2019-09-20

Reviewer chosen by: Jia-Ping Yan

Reviewer accepted review: 2019-11-17 04:37

Reviewer performed review: 2019-11-29 14:34

Review time: 12 Days and 9 Hours

| SCIENTIFIC QUALITY | LANGUAGE QUALITY | CONCLUSION | PEER-REVIEWER STATEMENTS |
|---|---|--|---|
| <input type="checkbox"/> Grade A: Excellent | <input type="checkbox"/> Grade A: Priority publishing | <input type="checkbox"/> Accept | Peer-Review: |
| <input type="checkbox"/> Grade B: Very good | <input checked="" type="checkbox"/> Grade B: Minor language | (High priority) | <input checked="" type="checkbox"/> Anonymous |
| <input checked="" type="checkbox"/> Grade C: Good | polishing | <input checked="" type="checkbox"/> Accept | <input type="checkbox"/> Onymous |
| <input type="checkbox"/> Grade D: Fair | <input type="checkbox"/> Grade C: A great deal of | (General priority) | Peer-reviewer’s expertise on the |
| <input type="checkbox"/> Grade E: Do not | language polishing | <input type="checkbox"/> Minor revision | topic of the manuscript: |
| publish | <input type="checkbox"/> Grade D: Rejection | <input type="checkbox"/> Major revision | <input type="checkbox"/> Advanced |
| | | <input type="checkbox"/> Rejection | <input checked="" type="checkbox"/> General |
| | | | <input type="checkbox"/> No expertise |
| | | | Conflicts-of-Interest: |
| | | | <input type="checkbox"/> Yes |
| | | | <input checked="" type="checkbox"/> No |



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SPECIFIC COMMENTS TO AUTHORS

In this manuscript, the authors review and summarize the role of cell-cell fusion in polyploid cells that influence cancer metastasis. The authors make references to polyploid giant cancer cells and tumor associated macrophages which are related to tolerance to chemo-and radiation therapy. This is an interesting and studying manuscript especially for researchers who are not familiar with this fields. To add more quality to this manuscript, some points below may be considered. In chapter 'Cell fusion, polyploidization and cancer', the word PGCC shows up suddenly. The explanation of how PGCCs are formed and what they are should be inserted with some references and a figure, though some explanations exists in latter half of this manuscript. In chapter talking about TAM, the authors should insert some figures that explains relations between tumor cells and TAMs. Since the authors don't refer to the concrete therapeutic target of TAM, they should add some examples. For example: Noncanonical pathway for regulation of CCL2 expression by an mTORC1-FOXK1 axis promotes recruitment of tumor-associated macrophages *Cell Rep.* 2017 Nov 28;21(9):2471-2486. doi: 10.1016/j.celrep.2017.11.014. In chapter Cell fusion, polyploidization and cancer, a comma is needed between 1911 and a German

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