

PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 48075

Title: The Role of bioactive lipids in cancer stem cells

Reviewer's code: 02446101

Reviewer's country: China

Science editor: Ying Dou

Reviewer accepted review: 2019-04-12 10:15

Reviewer performed review: 2019-04-12 10:37

Review time: 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 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 checked="" type="checkbox"/> Grade D: Fair	<input checked="" 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 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

SPECIFIC COMMENTS TO AUTHORS

This review highlights recent findings on the role played by lipid metabolism in CSCs, focussing on the specific mechanism by which bioactive lipids regulate the fate of CSCs and their involvement in signal transduction pathways. The manuscript does provide some ideas to the readers. However, there're still several issues which should be



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addressed. 1. The manuscript is not well organized. It's too difficult for the readers to understand it. 2. Maybe the section of "Reactive oxygen species" should be deleted. 3. Some old references should be deleted. So, major revision should be recommended.

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 Stem Cells

Manuscript NO: 48075

Title: The Role of bioactive lipids in cancer stem cells

Reviewer's code: 01851506

Reviewer's country: Japan

Science editor: Ying Dou

Reviewer accepted review: 2019-04-12 07:01

Reviewer performed review: 2019-04-19 09:16

Review time: 7 Days and 2 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 checked="" 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

SPECIFIC COMMENTS TO AUTHORS

The authors summarized the status quo of the lipid functions in cancer stem cells (CSCs), in particular, focusing on the specific mechanisms underlying how the lipid controls CSC fates within the cells, or how it serves as a signal transducer to favor the cancer cell survival. While it is known that CSCs possess an enhanced lipid metabolism, the

rational behind it has remains unexplored. It is, therefore, intriguing that the authors discussed the *raison-d'etre* of such a phenomena in CSCs in this review. In general the text is well written and comprehensive, however, the reviewer has some concerns as follows. 1. It would have been better to discuss a little bit more whether a low blood cholesterol level correlates with lower cancer incidents (HMG-CoA section). Since there is another report that says contrary, why and how such an opposite conclusion has been drawn? Readers are eager to know it from this review. 2. While the authors described that "ABC transporter hyperactivity is possibly due to their exportation of signalling molecules, including lipids"(lipid biomolecules in CSCs section), it is not clear whether the authors have presented evidence that ABC transporter indeed has an ability to transport (export) steroid hormones, cholesterol, and metabolites. 3. The font size in the Figure 1 and 2 is too small. Readers would have a difficulty to see the figures. Furthermore, name of the each cell organelle should be described (mitochondria etc). 4. There is no explanation of G6P, F6P etc. in the Figure 1. 5. There is no explanation of "red" font such as DGAT, PPAP etc. in the Figure 2.

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

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- ☐ Yes ☐ No

BPG Search:

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[] Plagiarism

[Y] No

PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 48075

Title: The Role of bioactive lipids in cancer stem cells

Reviewer's code: 02446280

Reviewer's country: Russia

Science editor: Ying Dou

Reviewer accepted review: 2019-04-16 12:39

Reviewer performed review: 2019-04-24 06:08

Review time: 7 Days and 17 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input 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
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			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The manuscript entitled "Role of bioactive lipids in cancer stem cells" by Begicevic et al addresses very intriguing issue of tumor heterogeneity, resistance to antiproliferative therapy, and cancer cells lipid metabolism turnover. The manuscript is well written, title and abstract reflect the main idea of the manuscript. The manuscript is well illustrated



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and cites recent scientific papers of the field. However I would like to attract Authors attention for some specific points. Introductory chapter starts with very strong statement of tumor hierarchy based on the cited references. Although this speculation is very attractive it is just a model as it pointed out in the cited literature. It is just a model streaming out of stem cells popularity. In reality, there are just a few strong experimental evidences of this. In the next few sentences Authors confused stem cells primary functional characteristics and just some signatures of it. Actually stem cell is the cell that has an ability for self renewal and differentiation. It is really not important to work on the single cell level and use single cell dissociation as well as immunodeficient mice, but it is important to isolate homogenous cell population and by sequential transplantation to demonstrate that this homogenous cell population differentiates in a variety of cell types including initial homogenous cell population. These homogenous cells could carry some non-functional markers (physiological, like transporter activity, metabolic activity or just some surface protein expression) that could be used to characterise these cells as homogenous. However, their stemness should be proved functionally on selfrenewal and differentiation. Next chapter also contains some controversial statements. "While CSCs share the same genetic profile to their progeny, they have differing epigenetic profiles, which results in a change to a number of signalling pathways 31-32." It is absolutely unclear what is the progeny of tumor initiating cells? Where when how the progeny was found, genetically analysed? See cited papers Suva et al "Cellular transformation is a stepwise process involving accumulation of genetic!!! and epigenetic hits. Once initiated, additional and potentially divergent alterations may occur, establishing a tumor with genetic heterogeneity!!!!" Genetic profiles maybe completely different even within somewhat homogenous CSC population but epigenetic hits make them similar as stem cells. And indeed, environmental stimuli pressure influences tumor evolution. I hope my comments will improve the paper and



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will make cancer stem cells concept more clear for the Readers.

INITIAL REVIEW OF THE MANUSCRIPT

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