



PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 41840

Title: Single-cell analysis of tumors: Creating new value for molecular biomarker discovery of cancer stem cells and tumor-infiltrating immune cells

Reviewer’s code: 02523682

Reviewer’s country: China

Science editor: Ruo-Yu Ma

Date sent for review: 2018-09-12

Date reviewed: 2018-09-17

Review time: 4 Days

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 polishing	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	(General priority)	Peer-reviewer’s expertise on the topic of the manuscript:
<input type="checkbox"/> Grade E: Do not publish	<input type="checkbox"/> Grade D: Rejection	<input checked="" type="checkbox"/> Minor revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Major revision	<input checked="" type="checkbox"/> General
		<input type="checkbox"/> Rejection	<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This review described the recent methodologies advances for single-cell analysis and discuss the challenges and prospects for molecular characterization and profiling of CSCs as a hallmark of biomarker discovery in oncology. It has important significance to



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7901 Stoneridge Drive, Suite 501,
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understand the methodologies for single-cell analysis. But the depth and logicality about single-cell analysis for CSCs is not enough. In addition, the following issues should be addressed. The title in the part “MOLECULAR BIOMARKERS OF CANCER CELLS AND CSCs” should be consistent to the following content “Proteomics...” Totally, the writing of the manuscript is good, but there are some grammar errors. The authors can make a list to describe different Single-cell based analytic approaches for different CSC markers in different tissue derived tumors.

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

- The same title
- Duplicate publication
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BPG Search:

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- Duplicate publication
- Plagiarism
- No



PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 41840

Title: Single-cell analysis of tumors: Creating new value for molecular biomarker discovery of cancer stem cells and tumor-infiltrating immune cells

Reviewer’s code: 02446370

Reviewer’s country: France

Science editor: Ruo-Yu Ma

Date sent for review: 2018-09-12

Date reviewed: 2018-09-27

Review time: 15 Days

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 type="checkbox"/> Grade B: Very good	<input 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

SPECIFIC COMMENTS TO AUTHORS

The mini-review proposed by Forouharkhou and Radpour discusses about the use of the new “single cell” technology to discover new molecular biomarkers in cancer diagnostic/prognostic/prediction. Overall, the review includes all the interesting and



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new methods to try to find biomarkers for cancer diagnostic, prognostic, and predictive in cancer cells and cancer stem cells. It however lacks, deeper discussion on all aspects: technologies, analyses, and perspectives. The review starts with a general introduction followed by a paragraph on cancer stem cells (CSC) and high-throughput technologies to isolate cancer cells and CSC. This is followed by a paragraph on technologies used to detect biomarkers in cancer cells and CSC. In this paragraph where technologies (proteomics, genomics, epigenomics, transcriptomics) are rapidly described, it would be nice to develop and describe a bit more these technologies that are not always well-known by readers and more particularly to discuss the advantages and drawbacks for each technology and conclude by telling which is more appropriate for each application. In the paragraph transcriptomics, it would be interesting to develop a bit the recent works performed to get molecular signatures of cancer that highlight the great heterogeneity within a tumor but also within single cells. In the single cell based approaches paragraph it would be interesting to develop the part about microfluidic systems as a lot of bibliography exists now. What has been done and what are the trends for the years to come? It would also be interesting to develop a bit more the paragraph on scRNA-Seq and its value for cancer treatment orientation. The authors should also discuss the problem of sequencing errors associated with NGS. What is done at the informatics level (algorithms) to avoid/decrease this problem? Again authors briefly describe single cell methods adapted to biomarker search but then what? A discussion about the best method(s) for diagnostic, prognostic, predictive biomarkers should be included based on the literature.

INITIAL REVIEW OF THE MANUSCRIPT

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PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 41840

Title: Single-cell analysis of tumors: Creating new value for molecular biomarker discovery of cancer stem cells and tumor-infiltrating immune cells

Reviewer's code: 02446277

Reviewer's country: Romania

Science editor: Ruo-Yu Ma

Date sent for review: 2018-09-26

Date reviewed: 2018-10-01

Review time: 5 Days

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

SPECIFIC COMMENTS TO AUTHORS

The manuscript highlight the recent methodologies advances for molecular characterization and profiling of CSC. Very interesting the section related to single-cell based approaches for the detection of molecular biomarkers. However, it would be



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suitable for this part to be more detailed and with more examples, this being the main purpose of the manuscript (according to the title). It would be appropriate to change the manuscript with the reduction of the first part referred to whole cell population analysis, and the extension of the second part focusing on single-cell RNA-Seq, multiplexed error robust fluorescence (MERFISH), quantitative hybridization chain reaction (qHCR), lineage tracing by nuclease-activated editing of ubiquitous sequences (LINNAEUS), single-cell whole exome sequencing (scWES), with a broader description of the method and some examples of use in diagnosis. Overall, the manuscript is well written and definitely helpful.

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PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 41840

Title: Single-cell analysis of tumors: Creating new value for molecular biomarker discovery of cancer stem cells and tumor-infiltrating immune cells

Reviewer's code: 02446191

Reviewer's country: India

Science editor: Ruo-Yu Ma

Date sent for review: 2018-09-26

Date reviewed: 2018-10-12

Review time: 15 Days

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:
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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

The present manuscript focuses on recent advancements towards the discovery of cancer related biomarkers of diagnostic, prognostic and predictive significance. Molecular heterogeneity at cell level and the presence of cancer stem cells advocate single cell



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based analysis/ profiling as a better approach towards improved investigation of more specific biomarkers to identify and target cancer stem cells. Authors should discuss in detail genomics, epigenomics, transcriptomics and proteomics approaches for diagnosis and prognosis in tumor cells as well as CSCs.

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