

## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Stem Cells

**ESPS manuscript NO:** 27305

**Title:** Update on acute myeloid leukemia stem cells: New discoveries and therapeutic opportunities

**Reviewer's code:** 01554116

**Reviewer's country:** Spain

**Science editor:** Fang-Fang Ji

**Date sent for review:** 2016-05-23 10:39

**Date reviewed:** 2016-05-23 18:45

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input checked="" type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

## COMMENTS TO AUTHORS

This is an excellent revision on the topic of acute myeloid leukemias and cancer stem cells. The authors gave a comprehensive view in the main aspects of AML, focusing the attention on the translational implications of the knowledge gained through research. The style is clear and highly informative, and the list of references complete enough.

## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Stem Cells

**ESPS manuscript NO:** 27305

**Title:** Update on acute myeloid leukemia stem cells: New discoveries and therapeutic opportunities

**Reviewer's code:** 02446098

**Reviewer's country:** China

**Science editor:** Fang-Fang Ji

**Date sent for review:** 2016-05-23 10:39

**Date reviewed:** 2016-06-02 22:29

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input checked="" type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

## COMMENTS TO AUTHORS

This review is well organized. The topic on acute Myeloid Leukemia Stem cells is well discussed. But, the subtype of AML, such as M1-7, also should be covered.

## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Stem Cells

**ESPS manuscript NO:** 27305

**Title:** Update on acute myeloid leukemia stem cells: New discoveries and therapeutic opportunities

**Reviewer's code:** 00289387

**Reviewer's country:** United States

**Science editor:** Fang-Fang Ji

**Date sent for review:** 2016-05-23 10:39

**Date reviewed:** 2016-06-06 03:41

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input checked="" type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		[Y] No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		[Y] No	

## COMMENTS TO AUTHORS

This is a well written and organized review article that updates the mechanistic insights into cancer stem cells in the pathogenesis and drug resistance of acute myeloid leukemia (AML). The authors primarily presented the signature of leukemia stem cells different from normal stem cells, focusing on the signaling pathways that regulate leukemia stem cell self-renewal and differentiation including surface markers, intracellular mediators, and oncogenes. Accordingly, a variety of therapeutic agents that are currently tested to target these individual molecules in clinical trials were clearly illustrated and summarized in a Figure and a Table. In general, the paper fits well the scope of this journal and will have great potential to help diagnose and treat the disease, given the most recent knowledge about cancer stem cells. A minor concern should be addressed. The discussion of each drug is too long as such the paper appears imbalanced; thereof, a concise revision is highly recommended.

## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Stem Cells

**ESPS manuscript NO:** 27305

**Title:** Update on acute myeloid leukemia stem cells: New discoveries and therapeutic opportunities

**Reviewer's code:** 00504828

**Reviewer's country:** United States

**Science editor:** Fang-Fang Ji

**Date sent for review:** 2016-05-23 10:39

**Date reviewed:** 2016-06-07 04:45

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Minor revision
		BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

## COMMENTS TO AUTHORS

This review manuscript summarizes the current status of leukemia stem cells from biology to prognosis. Extensive literatures are cited and included figures and table are pretty good. The summary of clinical trials (table) must be very useful for physicians. I would like to list several comments below: Major comments 1. Page 6, "Symmetrical vs asymmetrical cell division" and "Quiescence" sections. I think that the descriptions in both sections are too short and somewhat insufficient. The authors can do much better job by doing a bit of homework. "Concise" but "sufficient enough" paragraphs needed. Regarding "Quiescence" and stem cell exhaustion – there are a few very important original research that the authors should cite. 2. Page 7, "Key signaling pathways". Isn't Notch signaling also suggested in LSCs? 3. General comment: I think descriptions in sub-sections under "3. Biology of leukemia stem cells" is superficial. A little bit more in-depth discussion would be appreciated. For example, "symmetrical vs asymmetrical cell division" "quiescence" "key signaling pathways relevant for retaining stemness" may not be sufficient enough. 4. Page 24, line 6 "...human IgG4 monoclonal antibody against CXCR4...". Is this really the correct



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information? I have never heard of IgG4. Minor comments 1. There are several minor grammatical errors. I attach the file (PDF) with correction instead of typing each here. I may miss additional minor errors as . The authors may want to carefully check the text again. 2. Minor polishing of English (just wording) would make the manuscript more attractive. There are also some (a bit) awkward phrasings. 3. Abbreviations. All should be spelled out at their first appearance. For example, "NPM-mutated...(page 8)". 4. Very minor formatting issues (such as font, DOI numbers in the reference section etc.). The authors should carefully check the submission guideline provided by the publisher.