

## ESPS PEER REVIEW REPORT

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

**ESPS manuscript NO:** 12623

**Title:** Neural differentiation from embryonic stem cells in vitro: an overview of the signaling pathways

**Reviewer code:** 02446243

**Science editor:** Xue-Mei Gong

**Date sent for review:** 2014-07-18 10:46

**Date reviewed:** 2014-08-04 17:23

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ Y ] Grade A: Excellent	[ Y ] Grade A: Priority publishing	Google Search:	[ ] Accept
[ ] Grade B: Very good	[ ] Grade B: Minor language polishing	[ ] Existing	[ ] High priority for publication
[ ] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] No records	[ ] Rejection
[ ] Grade D: Fair	[ ] Grade D: Rejected	BPG Search:	[ ] Minor revision
[ ] Grade E: Poor		[ ] Existing	[ Y ] Major revision
		[ ] No records	

## COMMENTS TO AUTHORS

In the present review the authors describe different signaling pathways involved in neural differentiation of ESCs in vitro. The review is very interesting and well written, however some aspects need to be pointed out: -Among the different pathways analyzed the authors do not mention the role of calcineurin and  $Ca^{2+}$  in neural differentiation (Cho A, Tang Y, Davila J, Deng S, Chen L, Miller E, Wernig M, Graef IA. Calcineurin signaling regulates neural induction through antagonizing the BMP pathway. *Neuron*. 2014 Apr 2;82(1):109-24. doi: 10.1016/j.neuron.2014.02.015; Leclerc C, Néant I, Moreau M. Early neural development in vertebrates is also a matter of calcium. *Biochimie*. 2011 Dec;93(12):2102-11. doi: 10.1016/j.biochi.2011.06.032. Epub 2011 Jul 3. Review) and the role of purinergic receptors on stem cells pluripotency and neural differentiation (Glaser T, de Oliveira SL, Cheffer A, Beco R, Martins P, Fornazari M, Lameu C, Junior HM, Coutinho-Silva R, Ulrich H. Modulation of mouse embryonic stem cell proliferation and neural differentiation by the P2X7 receptor. *PLoS One*. 2014 May 5;9(5):e96281. doi:10.1371/journal.pone.0096281. eCollection 2014). - To complete the review authors should also add a paragraph concerning the effect of physical stimuli, such as electromagnetic fields, and radiofrequency waves, on neuronal differentiation in ESCs, (Piacentini R, Ripoli C, Mezzogori D, Azzena GB, Grassi C. Extremely low-frequency electromagnetic fields promote in vitro neurogenesis via upregulation of  $Ca(v)1$ -channel activity. *J Cell Physiol*. 2008 Apr;215(1):129-39; Maioli M, Rinaldi S, Santaniello S, Castagna A, Pigliaru G,



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Gualini S, Fontani V, Ventura C. Radiofrequency energy loop primes cardiac, neuronal, and skeletal muscle differentiation in mouse embryonic stem cells: a new tool for improving tissue regeneration. *Cell Transplant*. 2012;21(6):1225-33. doi:10.3727/096368911X600966. Epub 2011 Sep 22). - Moreover authors should better elucidate how these pathways are integrated to induce early neuroectodermal precursors . - Minor comments: -page 4 “5 mM RA treatment”, perhaps the authors intended 5 uM RA -page 7, line 21 “abovementioned” should be corrected -page 13 line 15 “that that” should be corrected

## ESPS PEER REVIEW REPORT

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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	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"/> Existing	<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"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS TO AUTHORS

This is a well written, comprehensive review about the neuronal differentiation of ES cells. I have the only concern about the lack of clarification of the respective experiments and pathways regarding mouse and human ES cells. I suggest that, especially when human ES cells are discussed, this should be clearly stated in the various sections of the manuscript.