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ESPS Peer-review Report
Name of Journal: World Journal of Stem Cells
ESPS Manuscript NO: 4279
Title: Neural stem cells isolated from amyloid precursor protein-mutated mice: a tool for in vitro studies and drug discovery
Reviewer code: 00504913
Science editor: Song, Xiu-Xia
Date sent for review: 2013-06-25 14:18
Date reviewed: 2013-07-23 23:33

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[Y] Grade A: Priority Publishing	Google Search:	[ ] Accept
[Y] Grade B (Very good)	[ ] Grade B: minor language polishing	[ ] Existed	[ ] 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:	[Y] Minor revision
[ ] Grade E (Poor)		[ ] Existed	[ ] Major revision
		[ ] No records	

COMMENTS TO AUTHORS
The manuscript entitled " Neural stem cells isolated from amyloid precursor protein-mutated mice: a tool for in vitro studies and drug discovery" by Dr. Baldassarro and coworker is a scientific paper that illustrates an in vitro model based of neural stem cells derived from transgenic animals useful for the study of pathological mechanisms of Alzheimer disease (AD) and for testing new molecules for a therapy. The author proposed Neural Stem Cells (NSCs), isolated from the subventricular zone (SVZ) of Tg2576 mice, as a new study tool that represent an appropriate AD in vitro model resembling some cellular alterations observed in vivo. Overall, this is a well-written and well-conceived manuscript. The work is original, well organized and coherent with the title proposal. The methods appear adequate and the paragraphs are complete and exhaustive. The organisation of results and graphs is well structured. The discussion focuses on the validation of the proposed model through the citation of relevant papers. As is, the only major criticism is that the authors did not sufficiently argument why they selected the SVZ as neurogenesis brain region for obtaining neurospheres. Indeed emerging evidence indicates that altered neurogenesis in the adult hippocampus represents an early critical event in the course of AD. This point should be addressed more thoroughly in the introduction. Another (minor) point is that sometimes in the manuscript it is not so clear what kind of NSCs have been used for experiments (primary, secondary, undifferentiated, differentiated etc.) a diagram illustrating this point could help to better understand the used methods.

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SPS Peer-review Report
Name of Journal: World Journal of Stem Cells
ESPS Manuscript NO: 4279
Title: Neural stem cells isolated from amyloid precursor protein-mutated mice: a tool for in vitro studies and drug discovery
Reviewer code: mail
Science editor: Song, Xiu-Xia
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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[Y] Grade B (Very good)	[Y] Grade B: minor language polishing	[ ] Existed	[ ] 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:	[Y] Minor revision
[ ] Grade E (Poor)		[ ] Existed	[ ] Major revision
		[ ] No records	

Materials and methods: a detailed description is provided

Results: are interesting but the clinical relevancy has not been established

Discussion is well organized, but is not thorough.

References: OK.

Tables and figures: need revision.

The manuscript grade: unsure.

language evaluation Grade B: minor language polishing

Detailed comments: This manuscript characterized a potentially useful in vitro model for Alzheimer's disease. The authors isolated neural stem cells from the subventricular zone of Wild type and Tg2576 mice, and then studied the phenotypes of primary and secondary neurospheres. They found that primary, not the secondary, neurospheres derived from Tg2576 show a decrease in population doubling, and differentiated NSCs from Tg2576 show decreased MAP2+ and increased GFAP+ cells. In addition, a clear decrease in neurites number and length was also observed in differentiated Tg2576 neurons. Furthermore, microarray study found that 11 genes were up-regulated in Tg2576 NSCs.

The data reported in this manuscript are interesting, but the clinical implication is unclear. This is a problem, but actually is not my main concern. My real concern is the clinical relevancy of this model, because Alzheimer's disease is normally **NOT** considered as disease of neural stem cells.

Minor concerns are:

1) Fig 1A needs a negative control to prove the specificity of 6E10.
2) Can authors explain why only primary, not the secondary, neurospheres derived from Tg2576 show a decrease in population doubling? Technical reasons?
3) Are you sure that the fig 2B&D are the pictures of MAP2 staining? They are more like the Tuj staining in fig 2A&C.