

ESPS PEER REVIEW REPORT

Name of journal: World Journal of Stem Cells

ESPS manuscript NO: 13418

Title: In vivo imaging of endogenous neural stem cells in the adult brain

Reviewer code: 02397930

Science editor: Xue-Mei Gong

Date sent for review: 2014-08-22 15:05

Date reviewed: 2014-09-17 02:04

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input checked="" type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input 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	<input type="checkbox"/> Existing	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

COMMENTS TO AUTHORS

The review from Rueger & Schroeter is a very nice, well written, overview of the imaging techniques use to monitor neural stem cells in vivo. I just have two minor issues. It would be useful to add a comment on what is known about the potential toxicity of [18F]FLT. It would be helpful to detail more the legend of Figure 1 to help the reader interpreting each panel. In particular, what are the white circles pointing at?

ESPS PEER REVIEW REPORT

Name of journal: World Journal of Stem Cells

ESPS manuscript NO: 13418

Title: In vivo imaging of endogenous neural stem cells in the adult brain

Reviewer code: 02446041

Science editor: Xue-Mei Gong

Date sent for review: 2014-08-22 15:05

Date reviewed: 2014-08-30 08:47

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input 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	<input type="checkbox"/> Existing	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

COMMENTS TO AUTHORS

Comment: The authors outline and examine the current imaging modalities (optical, PET, MRI) suitable to screen eNSC in trial models. Extraordinary stress is put on the capability of ideal imaging system for a conceivable clinical interpretation on the specificity (signal versus noise ratio) and resolution acquired, a balance that conflicts each other but essential for any meaningful imaging. They insightfully assess the non-invasive imaging will help to encourage an interpretation into the clinical setting, a way that is supported by their own data. Overall, it's insightful, informative, well written with clarity. Specific comment: 1) "Endogenous neural stem cells (eNSCs) in the adult mammalian brain can be mobilized by e.g. pharmacological methods to facilitate regeneration and enhance functional recovery in neurological disease." How can they propose to track down these endogenous eNSCs over a lifetime of the body? What's minimum number of eNSCs monitored using the method? How did they use the non-invasive imaging of tumor cell proliferation with PET to locate if tumor cells cease the proliferation? 2) They should clearly provide the guideline to strike a balance of the specificity (signal versus noise ratio) and resolution acquired, such as Stem Cell Rev. 2010 Jun;6(2):317-33. doi: 10.1007/s12015-010-9130-9. (A biological global positioning system: considerations for tracking stem cell behaviors in the whole body.) 3) Page 4: "More biomarkers were consecutively identified including Sox2, sonic hedgehog (Shh) pathway components, PDGF, EGFR, GFAP, Hes3, Hes5, Musashi, and CD133" - It's a conundrum that these molecules are present in other cell types - how do the authors distinguished these different cells (somatic versus stem cells)?

4) Page 7: Stroke mediated focal cerebral ischemia induces pro-inflammatory cytokine production causing neuroinflammation, detrimental to normal tissues. However, neuroinflammation also induces prepare and fortify eNSCs after stroke. What's threshold or time course for such balance of pro-inflammatory cytokine production to achieve benefits but avoid detrimental? For example, Page 8 –“ since immune cells proliferate in the ischemic brain just as eNSCs do, and [18F]FLT-PET does not differentiate between stem cell- and immune cell-derived proliferation.” How can you track eNSCs instead of immune cells? Or both? Or just one type of cells? How can they differentiate them?