PEER-REVIEW REPORT

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No

| Peer-reviewer statements | Peer-Review: [   ] Anonymous   [Y] Onymous |
| | Conflicts-of-Interest: [   ] Yes   [Y] No |

SPECIFIC COMMENTS TO AUTHORS

This is an in-depth review of the current state and prospects of HTS in in-vitro neurogenesis. It will be certainly used as a reference to those that want to engage the field. I have corrected some minor wording and language issues as suggested in the file.

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statements	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

I would like to thank the authors for their well written topic. The manuscript is written with concentrating on the technical point of view, and in my opinion would benefit more and increase the broad-spectrum of readers if a clinical and medical background and introductory paragraphs before the applications part could be added, as this is a part of integrated medicine.   English editing certificate is not present, only the manuscript file is uploaded under the name of the required certificate. English language needs revision for grammatical and syntax corrections.   #Title: the word " Prospection" is not used in the right meaning, could the authors use prospects instead? This applies to the whole document.   #Introduction: 1- The authors wrote: "Therefore, categories of testing candidates are also developing from molecular aiming at diverse">> could they elaborate molecular what? did they mean molecular markers? 2- I recommend adding this reference: Azari, H., & Reynolds, B. A. (2016). In Vitro Models for Neurogenesis. Cold Spring Harbor perspectives in biology, 8(6), a021279. https://doi.org/10.1101/cshperspect.a021279 3- Only one reference is from 2021, out of 211 references this seems a very low number, in addition there was a lot of progress last year too in the publication in this area. examples to last year publications: A.   Shin,   H., Jeong, S., Lee, J. H., Sun, W., Choi, N., & Cho, I. J. (2021). 3D high-density microelectrode array with optical stimulation and drug delivery for investigating neural circuit dynamics.   Nature   communications,   12(1),   492. https://doi.org/10.1038/s41467-020-20763-3 B.   Lam D, Fischer NO, Enright HA. Probing function in 3D neuronal cultures: A survey of 3D multielectrode array advances. Curr Opin Pharmacol. 2021 Oct;60:255-260. doi: 10.1016/j.coph.2021.08.003. Epub 2021

Sep 1. PMID: 34481335. #Figures: Figures are well-drawn and self explanatory. However, they sometimes lack explanation of the abbreviations. Also, why did the authors chose certain and specific markers in figure 1 while the comment on the figure is relatively a general comment?, please modify, if you want to use a general model do not specify the genetic markers or add the work (for example). # The subtitle " Prospection Developing organoids/spheroids-based HTS system: " . I found the authors using a medical term that is known mainly in psychology, could they redefine the term in light of neurogenesis research or use another term? # The authors did not explain the concept of "the conversion efficacy" in the text, only in the supplementary table, and this is an important outcome of the research topic in question, and should be explained clearly in the text, a long with the research limitations resulting from it, and how to overcome those limitations. # Overall: I think the authors should explain that 3D brain structures act as "Microphysiological systems (MPS)" to recapitulate the brain physiology, and discuss more the clinical impact of this approach in the text, along with the possible understanding of the pathophysiology of some neurological effects of drugs or diseases. The clinical background is minimally explained in the text, with concentrating on the technical parts of the topic. I think clinicians could benefit more of this review if its impact and benefits on clinical research were clearly delineated. Even in the part " Applications of HTS on neurogenesis" the authors preferred to explain the technical difficulties that could be encountered rather than explaining the clinical impact on the medical research field or why applications is needed in the first place instead of the real world cases studies. Could the authors kindly modify their text? I suggest that after each application the authors add a subtitle "limitations" and explain the limitations in this area instead of in the application part for the presentation to be more clear.

PEER-REVIEW REPORT

Name of journal: *World Journal of Stem Cells*

Manuscript NO: 73978

Title: Application and Prospects of High-throughput Screening for In Vitro Neurogenesis

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05156586

Position: Editorial Board

Academic degree: PhD

Professional title: Assistant Professor

Reviewer's Country/Territory: South Korea

Author's Country/Territory: China

Manuscript submission date: 2021-12-10

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-01-14 06:09

Reviewer performed review: 2022-02-03 03:18

Review time: 19 Days and 21 Hours

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SPECIFIC COMMENTS TO AUTHORS

The authors demonstrated about high-throughput screening (HTS) to enable to establish new and fast developing technology for the facilitation of in vitro neurogenesis using stem cells and organoids. It is very important technology to study the regulation of disease-mediated circumstance and the development of new drug. This manuscript is written in a well-organized format and covers everything from the description of the HTS system to the in vitro culture system (organoid) and microfluidic device related to neurogenesis. If some minor issues are resolved, it would be good to be published in WJSC. 1. In chapter of "Current in vitro neurogenesis methods", the authors described stem cell differentiation to generate neuronal cells from embryo to adult. However, Figure 1 does not match the description. From the point of view for organoid production, it would be good choice to focus on the neurogenesis of PSCs and write the text. And, the authors should add references to compose Figure 1 to the figure legend. 2. The authors focused on the neural organoid functioning neurogenesis with 3D culture system, and these contents was displayed in Ref. 77 to 87. Organoids induced to a specific part of the brain have different characteristics (induction method, time, conditions, etc.), however the authors listed only the types of brain organoid in parallel without specific mention.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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SPECIFIC COMMENTS TO AUTHORS

I would like to thank the authors for their detailed replies. In answer to the authors' question for the word prospection: In psychology, prospection is the generation and evaluation of mental representations of possible futures. So I recommend this word is omitted from the text (which is already done).