



## PEER-REVIEW REPORT

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

**Manuscript NO:** 66559

**Title:** Adult neural stem cells and schizophrenia

**Provenance and peer review:** Invited Manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 00505755

**Position:** Editorial Board

**Academic degree:** PhD

**Professional title:** Senior Research Fellow

**Reviewer's Country/Territory:** Japan

**Author's Country/Territory:** China

**Manuscript submission date:** 2021-04-06

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2021-04-07 06:23

**Reviewer performed review:** 2021-04-16 06:35

**Review time:** 9 Days

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<b>Peer-reviewer</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous



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

#### **SPECIFIC COMMENTS TO AUTHORS**

This is a comprehensive mini review in which several genes and signalings are involved.  
The references may be cited appropriately in Table 1.



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**Peer-review model:** Single blind

**Reviewer's code:** 03709824

**Position:** Editorial Board

**Academic degree:** BSc, MSc, PhD

**Professional title:** Full Professor, Professor

**Reviewer's Country/Territory:** India

**Author's Country/Territory:** China

**Manuscript submission date:** 2021-04-06

**Reviewer chosen by:** Ya-Juan Ma

**Reviewer accepted review:** 2021-05-10 08:47

**Reviewer performed review:** 2021-05-11 07:34

**Review time:** 22 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input checked="" type="checkbox"/> Rejection
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#### **SPECIFIC COMMENTS TO AUTHORS**

Although great efforts have been made in writing the above review, it does not add any sparkle that suffices the justification to publish in a high impact journal like WJSCs. It appears merely a discussion of literature, which has been covered in many reviews/options before.



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**Peer-review model:** Single blind

**Reviewer's code:** 05246551

**Position:** Editorial Board

**Academic degree:** BSc, PhD

**Professional title:** Research Assistant Professor

**Reviewer's Country/Territory:** Greece

**Author's Country/Territory:** China

**Manuscript submission date:** 2021-04-06

**Reviewer chosen by:** Ya-Juan Ma

**Reviewer accepted review:** 2021-05-11 12:49

**Reviewer performed review:** 2021-05-19 11:26

**Review time:** 7 Days and 22 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
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<b>Peer-reviewer</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous



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## SPECIFIC COMMENTS TO AUTHORS

Authors Ling Hu and Lei Zhang here present a mini-review type manuscript on the implication of defective proliferation of adult neural stem cells in the pathogenesis of schizophrenia based on data that secondary neurogenesis was found significantly reduced in post-mortem brains of patients diagnosed with schizophrenia. Patients with schizophrenia display an immature dentate gyrus as well as impaired maturation of adult-born neurons. The minireview focuses on the role of schizophrenia risk genes such as DISC1, SNAP-25, NRG1, CACNA1C, and Reelin. Mutations or misexpression of those genes result in defective proliferation, differentiation, migration, and maturation of adult neural progenitors. Authors also focus on the related signaling pathways Wnt and Notch respectively, which play a major role in adult neurogenesis, and their detriment is linked to neurodevelopmental disorders. The manuscript is well written and well organized but is suggested the paragraph about reelin to be moved after the paragraph about the CACNA1C gene in the same part of the manuscript concerning schizophrenia-related risk genes. Moreover, given that the goal of the mini-review is the clarification of the potential contribution of the dysregulated adult neural stem cells in the pathogenesis of schizophrenia one short paragraph could be added to mention other molecules involved in adult neurogenesis and schizophrenia, such as miR-19 which is enriched in adult hippocampal neural progenitor cells, plays a regulatory role in adult hippocampal neurogenesis and it was be found to be involved in the migration of adult-born neurons and schizophrenia. Taking under consideration my suggestions I propose that this manuscript could be published in BPG.



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**Peer-review model:** Single blind

**Reviewer's code:** 02524648

**Position:** Editorial Board

**Academic degree:** PhD

**Professional title:** Postdoctoral Fellow

**Reviewer's Country/Territory:** Spain

**Author's Country/Territory:** China

**Manuscript submission date:** 2021-04-06

**Reviewer chosen by:** Ya-Juan Ma

**Reviewer accepted review:** 2021-05-11 06:48

**Reviewer performed review:** 2021-05-19 14:32

**Review time:** 8 Days and 7 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
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## SPECIFIC COMMENTS TO AUTHORS

Comments to Ms 66559 The manuscript titled "Adult neural stem cells and schizophrenia", by Hu and Zhang is a clearly summarized update on risk genes and signalling pathways that are possibly implicated in the pathogenesis of schizophrenia. The text reads well, with a very small number of typos that will no doubt be easily corrected; nevertheless, one feels that some more detailed information on the results obtained by the cited research would improve the quality of the review. Some minor comments are: Line 11 in Introduction: change "pronged" to "prolonged" 2nd paragraph in Introduction: Instead of "...in which the density of Ki67, the cell proliferation marker, was reduced by 50-60% in the SGZ", use "...in which the number of cells expressing Ki67,..." SCHIZOPHRENIA RISK GENES Disrupted in schizophrenia 1 (DISC1) Instead of: "Girdin, which regulates the differentiation, maturation, migration, and cytoskeleton of ...", use "...migration, and cytoskeletal organization of ..." SNAP-25 Similarly to DISC1 and NRG1, indicate in the title to this section what SNAP-25 stands for: Synaptosomal-Associated Protein, 25kDa (SNAP-25) Some reference is required to accompany the last sentence in the "SNAP-25" section ("Importantly, this immature DG phenomenon has also been observed in the post-mortem brains from schizophrenic patients, suggesting a close link between disrupted maturation of adult-born cells and schizophrenic-like behaviors.") The authors should carefully revise the nomenclature they have used throughout their manuscript to denominate the gene vs the protein and the human vs the murine gene, as this is sometimes confusing (e.g. SNAP-25 mutant, "...regard to the functions of CACNA1C, it has received...", "...reduced gene dosage of CACNA1C...", "Recent studies showed that the plasma levels of secreted Notch ligands (Dll1 and Dlk-1) were



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elevated, whereas the levels of PSEN1, CREBBP and RBPj were decreased in microarray analyses of whole blood from a large sample of SCZ patients”, “It has been reported that Reelin mRNA and protein levels are reduced by almost 50% in cortical and hippocampal regions in post-mortem brains and serum of schizophrenic patients”, “Reelin, and extracellular matrix glycoprotein...”, etc.) Line 12 in the CACNA1C section: Change “adult neogenesis” to “adult neurogenesis” SCHIZOPHRENIA AND RELATED SIGNALING PATHWAYS CONTROLLING ADULT NEUROGENESIS Wnt signaling The following sentence is not clear, it reads as if some part had been duplicated: “The inactivation of GSK-3 $\beta$  finally causes the accumulation and translocation of  $\beta$ -catenin to the nucleus where it binds to and subsequently translocates and binds to the transcription factor Tcf/Lef family and activates target genes”. It would read more clearly if the words “to and subsequently translocates and” were removed. 3rd paragraph: It is not necessary to introduce an abbreviation of cerebrospinal fluid, since this term is only used once. Notch signaling 2nd paragraph, 3rd line: “In neural stem cells...”; correct to “In neural stem cells...” Table 1: Since there is no indication on the table that the results reported are exclusively related to work carried out on animal models, it would be appropriate to add some sentence in the row corresponding to “Neuregulin-1/Effects on adult neurogenesis” that indicated what has been observed in SCZ patients, and not only what is seen following NRG1 treatment.