Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

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"

Response: According to your suggestion, we have corrected the word "pronged" to "prolonged" in the revised manuscript.

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,…."

Response: According to your suggestion, we have changed the words "density of" to "number of cells expressing" in the revised manuscript.

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 …"

Response: According to your suggestion, we have changed the word "cytoskeleton" to "cytoskeleton organization" in the revised manuscript.

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)

Response: According to your suggestion, we have changed the word "SNAP-25" to "Synaptosomal-Associated Protein, 25kDa (SNAP-25)" in the revised manuscript.

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.")

Response: According to your suggestion, we have added the reference [8,50] in the last sentence of the SNAP-25 part in the revised manuscript.

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 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.)
Response: According to your suggestion, we have carefully revised the nomenclature of genes/proteins from mouse or human throughout the manuscript.

Line 12 in the CACNA1C section: Change "adult neogenesis" to "adult neurogenesis"
Response: According to your suggestion, we have corrected the word "neogenesis" to "neurogenesis" in the revised manuscript.

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-3β finally causes the accumulation and translocation of β-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.
Response: According to your suggestion, we have deleted the words "to and subsequently translocates and binds" in the revised manuscript.

3rd paragraph: It is not necessary to introduce an abbreviation of cerebrospinal fluid, since this term is only used once.
Response: According to your suggestion, we have deleted the abbreviation "(CSF)" in the revised manuscript.

Notch signaling 2nd paragraph, 3rd line: "In neural stem ells…"; correct to "In neural stem cells…"

Response: According to your suggestion, we have corrected the word "ells" to "cells" in the revised manuscript.

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.

Response: According to your suggestion, we have added the following sentence in the table box of NRG1/Effects on the adult neurogenesis. Nrg1 regulates both excitatory and inhibitory synaptic transmission in the adult brain and abnormal neurotransmission and/or synaptic plasticity have been observed in the schizophrenic brain.

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

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.

Response: According to your suggestion, we have moved the "Reelin" part to the section of SCHIZOPHRENIA RISK GENES, right after the "CACNA1C" part in the revised manuscript.

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.

Response: According to your suggestion, we have added one paragraph concerning the role miR-19 in adult neurogenesis and schizophrenia in the revised manuscript.

Reviewer #3:

Scientific Quality: Grade D (Fair)

Language Quality: Grade B (Minor language polishing)

Conclusion: Rejection

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.

Response: According to your suggestion, we have added some discussion and future direction in the CNCLUSION in the revised manuscript.

Reviewer #4:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

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.

Response: According to your suggestion, we have changed the way in which the references are cited in the table of the revised manuscript.