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PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 42749

Title: Rational use of mesenchymal stem cells in the treatment of autism spectrum disorders

Reviewer's code: 02567328

Reviewer's country: Italy

Science editor: Ying Dou

Date sent for review: 2018-10-10

Date reviewed: 2018-10-17

Review time: 7 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input checked="" type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The review "Rational use of mesenchymal stem cells in the treatment of autism spectrum disorders" is well organized and based on recent literature. Autism and autism spectrum disorders (ASD) are complex pathologies and represent a relevant social

problems. Because the current treatments are only symptomatic, new therapeutic approaches are required. Mesenchymal stem cells could be a good option, as highlighted by the authors but further studies are required. Please the legend of Figure 1 is too long and looks like an abstract. Please modify

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No

BPG Search:

- ☐ The same title
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PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 42749

Title: Rational use of mesenchymal stem cells in the treatment of autism spectrum disorders

Reviewer's code: 03197771

Reviewer's country: Spain

Science editor: Ying Dou

Date sent for review: 2018-11-12

Date reviewed: 2018-11-14

Review time: 1 Day

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input checked="" type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input checked="" type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

Comments to authors: The review article by Liu et al "Rational use of mesenchymal stem cells in the treatment of autism spectrum disorders" summarizes the impact of immune dysfunction on autism spectrum disorder (ASD) laying background for the potential

therapeutic actions of mesenchymal stem cells (MSCs) on these patients at the time that briefly introduces pre-clinical and clinical evidence for the safety of using MSCs for the treatment of ASD. Although the review is well structured and easy to read some room for improvement was detected. For example, original references and details of the NurOwn product and the BTBR original description of the BTBR strain as an ASD animal model (see cite below) would be desirable. Wahlsten D, Metten P, Crabbe JC. Survey of 21 inbred mouse strains in two laboratories reveals that BTBR T/+ tf/tf has severely reduced hippocampal commissure and absent corpus callosum. *Brain Res.* 2003 May 2;971(1):47-54. PubMed PMID: 12691836. Also, the clinical trial evidence for the use of MSC in the treatment of ASD should be more exhaustive and updated. For example, the following reference, among other, should have been included: Chez M, Lepage C, Parise C, Dang-Chu A, Hankins A, Carroll M. Safety and Observations from a Placebo-Controlled, Crossover Study to Assess Use of Autologous Umbilical Cord Blood Stem Cells to Improve Symptoms in Children with Autism. *Stem Cells Transl Med.* 2018 Apr;7(4):333-341. doi: 10.1002/sctm.17-0042. In general, it is recommended to authors an update of the cited references, previous reviews included, to improve the quality of the review. For example, link of immune defects related to ASD is nicely covered by the following review: Estes ML, McAllister AK. Immune mediators in the brain and peripheral tissues in autism spectrum disorder. *Nat Rev Neurosci.* 2015 Aug;16(8):469-86. doi:10.1038/nnrn3978. And in the case of reviews of the use of MSC on the immune system, the selection of reference papers goes up to year 2011 (references 134-136), when more updated reviews are available. Latest cite for the effects of TLRs on immunomodulation by MSCs dates of 2010 (see reference 143). Also, statements should always be documented with references, particularly when dealing with conflictive results. Please add appropriate references to the following statement: "MSCs are capable of crossing the blood brain-barrier and migrating to sites of tissue injury and

inflammation” on pag. 15. Add cites to the following statement: “Several proof-of-concept clinical studies have shown the safety and efficacy of MSCs treatment in autistic patients” on page 19. It is suggested that numberings in Figure 1 are substituted by bullets to avoid readers’ confusion by linking numberings in the different lists presented. The overlap in Venn diagrams does not seem appropriate as no factor is included in the overlapping section. Minor issues: Please review the text for some orthographic mistakes, such as “lable” for: label, “pretreatments” for: pretreated, “Zinc” in a context that should be lower case...etc

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

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- ☐ No

BPG Search:

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PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 42749

Title: Rational use of mesenchymal stem cells in the treatment of autism spectrum disorders

Reviewer's code: 03671529

Reviewer's country: Russia

Science editor: Ying Dou

Date sent for review: 2018-11-12

Date reviewed: 2018-11-26

Review time: 13 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input checked="" type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

It is very interesting review. A small drawback is that the authors cite references for interpretation those works which demonstrated the efficacy of MSCs influence immune processes and inflammation. There are a number of studies that show the rapid

elimination of transplanted MSCs and the absence of any effect from their administration, as well as in vitro.

INITIAL REVIEW OF THE MANUSCRIPT

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BPG Search:

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