

## ESPS PEER REVIEW REPORT

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

**ESPS manuscript NO:** 12789

**Title:** Control of Stem Cell Fate by Engineering their Micro and Nanoenvironment

**Reviewer code:** 02595715

**Science editor:** Ling-Ling Wen

**Date sent for review:** 2014-07-26 23:10

**Date reviewed:** 2014-08-07 17:35

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

## COMMENTS TO AUTHORS

accept

## ESPS PEER REVIEW REPORT

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

**ESPS manuscript NO:** 12789

**Title:** Control of Stem Cell Fate by Engineering their Micro and Nanoenvironment

**Reviewer code:** 02511983

**Science editor:** Ling-Ling Wen

**Date sent for review:** 2014-07-26 23:10

**Date reviewed:** 2014-08-07 21:44

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 type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

## COMMENTS TO AUTHORS

The manuscript Control of Stem Cell Fate by Engineering their Micro and Nanoenvironment is a useful review with an interesting subject regarding the using of stem cells in regenerative medicine. Although the study is well structured and the subject is actual and interesting, the manuscript needs minor revisions in terms of grammar spelling (see below). In this regard we recommend careful language editing by the authors to ensure that the manuscript meets the Journal's guidelines. We would also advice the authors to explain all the abbreviations (e.g. BMMSCs) for a better understanding of the manuscript. Overall, the quality of the written English is acceptable. However, a few improvements are highly recommended. A thorough review of the punctuation is strongly advised (especially the use of comma). In addition, some sentences could use rephrasing, in order to allow an easier comprehension of the text and to achieve a more academic style. In this regard, we recommend very careful language editing to ensure that the manuscript meets the Journal's standards. Examples: Page 2: "Stem cells are capable of long-term self-renewal and differentiation into specialised cell types, making them an ideal candidate..." - a comma should be added between types and making "The control of stem cell fate has become a major area of interest, in the field of regenerative..." - this is the opposite case: the comma after interest should be removed "...delivered via biomaterials to be able to provide clues to determine stem cell differentiation" - rephrase the sentence, in order to avoid or reduce the repetition of "to" "This review aims to provide an overview of the topographical, chemical and molecular clues that biomaterials can

provide to guide stem cell fate.” – rephrasing is advised so as to avoid the repetition of “provide”  
“An alternative approach is to provide genetic clues including delivering DNA plasmids and small interfering RNAs (siRNA) via scaffolds has also shown to influence stem cell fate.” – rephrase to clarify  
Page 4: “The second type of stem cells, which has attracted extensive research interest are adult stem cells” - replace are with is represented by, since the grammatical concordance requires it (the subject is “type”, the predicate cannot be “are”) “The extracellular matrix in the in vitro stem cell niche is arranged into complex topographic features...” – Italics for “in vitro”  
Page 10: “However, it is thought, that the elasticity of the ECM induces changes in the focal adhesion protein activity and remodeling” - remove comma after thought  
Page 11: “...is provided by the ECM, which regulate a key number of cellular functions...” – replace regulate with regulates, since ECM stands for extracellular matrix  
Page 13: “After functionlisation the gels were able to direct the differentiation...” – add a comma after functionlisation  
Page 14: “With an emergence of plasma surface modification studies over the last five years which can easily modify the chemical properties of the surfaces and coat the surfaces with different functional groups, the use of chemical groups controlling stem cell fate is likely to receive extensive research due to clear evidence that surface chemistry clearly influences stem cell behavior and their differentiation.” – sentence needs rephrasing, since it is too long and the meaning of some parts become somewhat blurred  
Page 18: “Future perspectives” vs. “Future perspectives”? We also recommend the authors to provide the copyright permission for all figures that are included in the manuscript. In conclusion, the manuscript could provide useful information to researchers and clinicians and I recommend the publication after these revisions are made.

## ESPS PEER REVIEW REPORT

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

**ESPS manuscript NO:** 12789

**Title:** Control of Stem Cell Fate by Engineering their Micro and Nanoenvironment

**Reviewer code:** 02594838

**Science editor:** Ling-Ling Wen

**Date sent for review:** 2014-07-26 23:10

**Date reviewed:** 2014-08-11 12:37

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 checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<input type="checkbox"/> High priority for publication
<input checked="" 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 type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No records	<input checked="" type="checkbox"/> Major revision

## COMMENTS TO AUTHORS

This manuscript is generally well written and helpful for the researchers interested in stem cells and regeneration. However, this has critical ethical problem at this form. - The authors included 4 figures derived from other investigators published papers without any specific comments regarding the copyright. The authors have to check this issue. - The authors have to be consistent in abbreviation. For example, adult stem cells were described as ASCs, ADSs, or ADSCs. - The authors described several papers related with surface topography and chemicals in the text. However, the same contents were omitted in the Table 1 and 2. You had better include the facts and references in the tables.

## ESPS PEER REVIEW REPORT

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

**ESPS manuscript NO:** 12789

**Title:** Control of Stem Cell Fate by Engineering their Micro and Nanoenvironment

**Reviewer code:** 02446106

**Science editor:** Ling-Ling Wen

**Date sent for review:** 2014-07-26 23:10

**Date reviewed:** 2014-08-16 04:05

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 type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

## COMMENTS TO AUTHORS

The manuscript ? Control of Stem Cell Fate by Engineering their Micro and Nanoenvironment ?, by Griffin et al. is a review on current strategies aimed to regulate stem cell behaviour by manipulating their niche. In particular, the authors review the three main avenues consisting in using topographical, chemical and genetic clues that biomaterials can provide in a regulatory way to guide stem cell fate. The manuscript is interesting, the cited works are relevant and the references are updated. In addition, the content falls certainly within the scope of the journal. However, I have a couple of major concerns regarding the manuscript: the topic the interaction between stem cells and (bio)materials has already been extensively revised (see References below), especially for what concerns materials as stem cell regulators. The authors should provide justification for the need of an additional review on the topic or better highlight in what consists the originality of their manuscript. While very well chosen and representative, the figures used throughout the manuscript have already been published. Indeed the source is cited, but I think that the authors and/or the Editor should ask permission for reproduction of these data to whom it may concern. There are some typos and some redundant phrases throughout the text, which should be, thus, shortened and double checked. Minor remarks: page 4 line 2 ?therapeutic?, could it be substituted by regenerative? page 4 line 8 ?ability to maintained for?, ??? page 4 line 21 etc. ?In their in vitro environment stem cell fate is determined by a reservoir of biochemical and biophysical clues [6]. The instructions from their stem cell niche will govern their niche environment, controlling ? some words can be eliminated page

5 ?The physical environment has shown to be an alternative means of controlling cell fate[10] ? the phrase can be eliminated page 5 ?Biochemical clues in the form of growth factors and cytokines have also shown to provide important instructions to stem cells in vitro[15]. ? the phrase can be eliminated, redundant with refs 7-9 page 5 ?T(a) topographical, (b) chemical and (c) molecular clues ? I guess the authors ment ?molecular genetic?, otherwise it is not clear which the difference is with chemical page 10 ?The hMSCs adopted the morphology of the differentiated cells. ? the phrase can be eliminated page 11 line 15 ?cue? , could it be substituted by ?clue? for being consistent page 11 line 2, check the plural ?molecules? page 13-14 the work by Coletti D et al. in J Biomed Mater Res A. 2009 Nov;91(2):370-7. doi: 10.1002/jbm.a.32243.seems very relevant for SAM and could be worth citing it page 14 botttom ?transfection efficiency? should be ?applicability? or similar, usually viral infection is quite efficient page 14 bottom ?Adenoviruses have been illustrated to have higher transfection efficieny but their use is less discouraging in vivo responses including early failures has led ? , ??? please rephrase page 15 ?Non-viral gene delivery is the most commonly used in the form of a DNA plasmid, which is usually extracted from bacteria[105]. ? the phrase can be eliminated page 16 ?To provide an overview, siRNAs are 19-22 base pair nucleotides which when delivered into the target cell will cause the specific knockdown of the gene that is complimentary to its sequence. The siRNA causes silencing of the specific gene by unwinding of the double strand in the RNA-induced silencing complex (RISC), followed by recognition and cleavage of the complementary strand of endogenous mRNA[105-108]. Several areas of research have endeavoured to use siRNA to induce specific differentiation of stem cells. ? the paragraph can be eliminated and the notion referred to by the citations, for those who want to have the basics of siRNA. page 17 I guess the symbol TM should be added to ?Oligofectamine and siPORT? page 18 ?Nanotopographies hold great promise due to the