

PEER-REVIEW REPORT

Name of journal: *World Journal of Stem Cells*

Manuscript NO: 76157

Title: Changes of cell membrane fluidity for mesenchymal stem cell spheroids on biomaterial surfaces

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 02505493

Position: Editorial Board

Academic degree: DPhil

Professional title: Professor

Reviewer's Country/Territory: Greece

Author's Country/Territory: Taiwan

Manuscript submission date: 2022-03-05

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-03-12 07:20

Reviewer performed review: 2022-03-21 08:19

Review time: 9 Days

Scientific quality	<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 Grade E: Do not publish
Language quality	<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
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No

Peer-reviewer statements	Peer-Review: [<input checked="" type="checkbox"/>] Anonymous [<input type="checkbox"/>] Onymous Conflicts-of-Interest: [<input checked="" type="checkbox"/>] Yes [<input type="checkbox"/>] No
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SPECIFIC COMMENTS TO AUTHORS

The present study aims to investigate the linkage between cell membrane fluidity and cell morphological change of MSC spheroids on the surface of biomaterials. The authors have used different materials as substrates, they have cultured the cells on the surface of each substrate to create spheroids and investigated the linkage between cell membrane fluidity and cell morphological change. Moreover, they have co-cultured MSC with other types of cells to generate cell co-spheroids. Through these approaches, they have investigated cell-cell interactions and cell membrane exchange in the various spheroids obtained. Their results indicated the appearance of some vesicle-like bubbles on the outer layer of MSC spheroids. Be deeper examination of bubbles formation they have found that these bubbles were originated from the dynamic movement of cell membrane during the formation of spheroids. They have finally concluded that this phenomenon may explain the various complicated physiological alterations of cells during spheroid formation. The work is interesting. The text is well-written. However, there are some points requiring correction and/or clarification, as follows. 1. The text needs minor language revision. 2. Since the abbreviation CS is largely used in the case of chondroitin sulfate, a common constituent of ECM, it is suggested to use a different abbreviation for chitosan, or, better, no abbreviation. 3. Give information on the supplier of the various cells and describe the MSCs (page 10, line 7). 4. It is suggested to the authors to examine or to provide some evidence whether the vesicle-like bubbles represent a new form of exosomes or of giant plasma membrane vesicles. 5. Describe in detail the conditions for cross-linking of HA-coated CS membranes (page 10, 1st line).

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Reviewer's code: 05247020

Position: Peer Reviewer

Academic degree: PhD

Professional title: Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: Taiwan

Manuscript submission date: 2022-03-05

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-03-22 09:20

Reviewer performed review: 2022-03-24 07:02

Review time: 1 Day and 21 Hours

Scientific quality	<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
Language quality	<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
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

Peer-reviewer statements	Peer-Review: [<input checked="" type="checkbox"/>] Anonymous [<input type="checkbox"/>] Onymous
	Conflicts-of-Interest: [<input type="checkbox"/>] Yes [<input checked="" type="checkbox"/>] No

SPECIFIC COMMENTS TO AUTHORS

The authors submitted a manuscript investigating the effect of different biomaterials substrates on the cell membrane fluidity and cell morphological changes of MSCs spheroids. Cell membrane is made up of a complex structure of lipids and proteins that diffuse laterally giving rise to what we call membrane fluidity. Membrane fluidity is a key property for maintaining cell functionality, and depends on lipid composition and cell environment. The manuscript's perspective is somewhat innovative for the research on cell membrane fluidity. Overall, this manuscript is better designed, executed, written, and the logic is relatively clear. Nonetheless, there are a number of issues that need to be noted.

1. In the Results section, the authors should add more quantitative descriptions as appropriate.
2. The author should give a reasonable explanation for the cause of the vesicle-like bubbles in the Discussion section.
3. It is debatable whether the experimental results in the manuscript can be used as a direct indicator of cell membrane fluidity.
4. In the Materials and Methods section, the writing format of the source of the reagents and instruments used should be consistent. The source of some reagents and the model of some instruments should be specified. For example, what is the source of MSCs?
5. There are some errors in grammar and format in the whole manuscript: inconsistencies; spelling mistakes; single and plural expressions; the use of prepositions and definite/indefinite articles. For examples: p(in italics), p; 's, 's; "the HA power" should be changed into "the HA powder"; The definite article "the" and the indefinite article "a" are missing from some sentences.