

Name of Journal: *World Journal of Stem Cells*

Manuscript NO: 02861265

Manuscript Type: REVIEW

Response to editors and reviewers

We thank the editors and the reviewers for their careful work on our review.

As requested, please find below a point by point answer to the reviewers comments.

We also provide the original version of the figure as requested by the editors and we modified the reference style to include PMID and DOI.

In addition, we think that the modifications based on accurate reviewers suggestions had helped to increase the scientific level of our review and we hope that the revised version will fulfill the requirements for publication in *World Journal of Stem Cells*.

Reviewer 1:

"It's a well-structured, well-written review focusing on characterization and potential of urine-derived stem cells. The authors divided this review into three parts. They firstly described the isolation procedure of USCs and summarized phenotype and differentiation capacity of USCs in several published literature. Then, in the second part, they presented and discussed the main applications of USCs. In the last part, they discussed the remaining barriers and challenges in the field of USC-based regenerative medicine. The coverage of this article is very wide and the authors also put forward some of views and opinions on USC. In addition, the tables and figure are well-conducted."

We thank the reviewer for this nice comment.

"However, there have been some published reviews describing the biological characteristics and differentiation potential of USC and possible uses in regenerative medicine [1]. As a novelty paper, it's important to avoid repeated discussions and make new summaries and comments on the content of published articles. So, could you briefly summarize the advantages of this article and how it attracts more readers compared to other reviews? [1] Bento G, Shafigullina AK, Rizvanov AA, Sardão VA, Macedo MP, Oliveira PJ. Urine-Derived Stem Cells: Applications in Regenerative and Predictive Medicine. *Cells*. 2020;9(3):573. Published 2020 Feb 28. doi:10.3390/cells9030573"

We thank the reviewer for this accurate comment.

Firstly, please note that the review mentioned by the reviewer was published February 28th. The redaction of our review was finished at this time and we were mainly performing editing and working on the tables and figures. However, we apologize for not being aware of the publication of this review.

Nevertheless, after a careful reading of this review, we do think that our review differs from the review of Bento et al. on several points:

- Whereas the review of Bento et al. focus on USCs but also largely on epithelial cells, we focus only on UPCs, and directly begin our review with their isolation and description.
- We deeply focus on USC characterization, highlighting the immunophenotyping. Despite that USC characterization is mentioned in the review of Bento et al., we dedicate a large part of our review to this important issue which is often lacking in existing review despite not being an object of consensus in the literature; we gathered all existing data and propose a very complete summary of USC characterization in the Table 1, with an exhaustive list of corresponding references, also highlighting the heterogeneity of the results when appropriate.
- One specificity of our review also relies on the Table 2, which summarize all differentiation protocols found in the literature, gathered by cell type; we also highlighted the existing variability among protocols.
- Moreover, we propose a detailed and didactic figure which summarize the UPC applications, including reprogramming into iPSCs but also their use for cell therapy either directly or indirectly (secretome); this kind of figure cannot be found in existing reviews and will be now at disposal to the readers of *World Journal of Stem Cells*, including neophytes, who want to get a quick and exhaustive summary/view of USC applications.
- Finally, contrary to the review of Bento et al., we also focus on the use of USC for renal repair, especially in the context of Acute Kidney Injury and Chronic Kidney Injury. We tried to emphasize this subject in the R1 version of the manuscript, notably by adding few references that we gathered for this purpose. Modifications have been highlighted in red in the R1 version of this review. This brings also an extra level of specificity to our review taking into account our expertise on kidney repair.

“Minor issues: There is no corresponding reference in the introduction part. For example, “In addition, despite a huge amount of in vivo works... in the hematologic field” and “They have been used for cell-based regeneration strategies... beneficial effects.”, these sentence may need references”

We added references in the introduction, highlighted in red in the R1 version of the review.

“Table 2. It is better to display only one name for the same cell types, that is, to merge cells with the same content into one cell. In that way, readers can clearly see all the cell types of USC differentiation.”

We agree with this comment and we performed this change, highlighted in red in the R1 version of the review.

Reviewer 2:

“The paper: Urine-derived Stem/progenitor Cells: a focus on their characterization and potential is a review article The topic is very important and very interesting”

We thank the reviewer for this nice comment.

“More technical details about isolation and cell expansion are needed in the paper to make it useful for all readers”

We agree with the reviewer comment and added some technical details about USC isolation and cell expansion, highlighted in red in the R1 version of the review.

“The paper need major language review”

When submitting our review, we provided a language editing editorial certification. Indeed, this review has been carefully and comprehensively reviewed by Jeffrey Arsham, cited in the Acknowledgements section of this article. Jeffrey Arsham is an American-born translator. He has a strong expertise in scientific English and has been working for 25 years with the CHU of Poitiers (university hospital of Poitiers), his skill consisting in reading, reviewing and editing manuscripts before their publication in specialized reviews. Moreover, we performed since other careful reviewing/editing of the R1 version of the review in order to add one extra level of verification. We hope that the presented elements will fulfill the reviewer requirement regarding language quality.

“ Clinical results can be reviewed and put in a table”

We are not sure to perfectly understand the reviewer comment. Regarding USCs, there are no clinical trials going on for now, i.e. no clinical results to include and review. We stay at the reviewer disposal if we understood this comment in a wrong way.



RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: World Journal of Stem Cells

Manuscript NO: 57237

Title: Urine-derived Stem/progenitor Cells: a focus on their characterization and potential

Reviewer’s code: 02444715

Position: Peer Reviewer

Academic degree: FRSC, MD, PhD

Professional title: Professor

Reviewer’s Country/Territory: Egypt

Author’s Country/Territory: France

Manuscript submission date: 2020-05-29

Reviewer chosen by: Ya-Juan Ma

Reviewer accepted review: 2020-07-28 19:03

Reviewer performed review: 2020-07-28 19:05

Review time: 1 Hour

Scientific quality	<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
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input checked="" 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 type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Peer-reviewer statements	Peer-Review: <input type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS



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Now I think the paper is more informative with details about the technique and application. The language still need a mojour revision

We thank the reviewer for his/her comment and are glad to read that our revised version of the manuscript fulfill the reviewer's requirements.

Regarding the language, we performed one extra careful reading of the manuscript. More importantly, as requested by WJSC policy, our manuscript was re-read carefully and reviewed by Jeffrey Arhsam, a US-born translator working for years with scientific editing. We provided one language certification to the editors as requested.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: World Journal of Stem Cells

Manuscript NO: 57237

Title: Urine-derived Stem/progenitor Cells: a focus on their characterization and potential

Reviewer's code: 03550401

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Professor

Reviewer's Country/Territory: China

Author's Country/Territory: France

Manuscript submission date: 2020-05-29

Reviewer chosen by: Ya-Juan Ma

Reviewer accepted review: 2020-07-28 10:17

Reviewer performed review: 2020-07-31 01:27

Review time: 2 Days and 15 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 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
Conclusion	<input checked="" type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
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



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The authors addressed all comments. No additional comments.

We thank the reviewer for his/her comment and are glad to read that our revised version of the manuscript fulfill the reviewer's requirements.