# Genetic engineering of mesenchymal stromal cells for cancer therapy: turning partners in crime into Trojan horses

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## Reviewers’ Comments to Original Submission

**Reviewer 1: Brigitte Vollmar**  
May 13, 2016

| Custom Review Question(s)                                                                 | Response | Overall Reviewer Manuscript Rating:  |
|-----------------------------------------------------------------------------------------|----------|-------------------------------------|
| Is the subject area appropriate for you?                                                | 5 - High/Yes | 95                                  |
| Does the title clearly reflect the paper’s content?                                     | 5 - High/Yes |                                      |
| Does the abstract clearly reflect the paper’s content?                                  | 5 - High/Yes |                                      |
| Do the keywords clearly reflect the paper’s content?                                    | 5 - High/Yes |                                      |
| Does the introduction present the problem clearly?                                      | 5 - High/Yes |                                      |
| Are the results/conclusions justified?                                                  | 5 - High/Yes |                                      |
| How comprehensive and up-to-date is the subject matter presented?                       | 5 - High/Yes |                                      |
| How adequate is the data presentation?                                                  | 5 - High/Yes |                                      |
| Are units and terminology used correctly?                                               | 5 - High/Yes |                                      |
| Is the number of cases adequate?                                                        | N/A      |                                      |
| Are the experimental methods/clinical studies adequate?                                | N/A      |                                      |
| Is the length appropriate in relation to the content?                                   | 5 - High/Yes |                                      |
| Does the reader get new insights from the article?                                      | 5 - High/Yes |                                      |
| Please rate the practical significance.                                                 | N/A      |                                      |
| Please rate the accuracy of methods.                                                    | N/A      |                                      |
| Please rate the statistical evaluation and quality control.                            | N/A      |                                      |
| Please rate the appropriateness of the figures and tables.                              | N/A      |                                      |
| Please rate the appropriateness of the references.                                      | 5 - High/Yes |                                      |
| Please evaluate the writing style and use of language.                                  | 5 - High/Yes |                                      |
| Please judge the overall scientific quality of the manuscript.                          | 5 - High/Yes |                                      |
| Are you willing to review the revision of this manuscript?                              | Yes      |                                      |

**Comments to Author:**

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The authors provide a well written comprehensive overview on this highly relevant issue. The review article allows the reader to get a perfect insight on the currently available knowledge. I have absolutely no concerns or suggestions for the text body. The only thing I would like to encourage the authors is to put in some illustrative figures and/or schemes. In addition, the manuscript would further benefit from tables being included, e.g. for the common features of MSCs.

Reviewer 2: anonymous
May 27, 2016

Reviewer Recommendation Term: Accept with Minor Revision
Overall Reviewer Manuscript Rating: 70

| Custom Review Question(s)                                      | Response |
|----------------------------------------------------------------|----------|
| Is the subject area appropriate for you?                       | 4        |
| Does the title clearly reflect the paper’s content?            | 4        |
| Does the abstract clearly reflect the paper’s content?         | 4        |
| Do the keywords clearly reflect the paper’s content?           | 4        |
| Does the introduction present the problem clearly?             | 4        |
| Are the results/conclusions justified?                         | 4        |
| How comprehensive and up-to-date is the subject matter presented? | 4        |
| How adequate is the data presentation?                         | 2        |
| Are units and terminology used correctly?                      | 4        |
| Is the number of cases adequate?                               | N/A      |
| Are the experimental methods-clinical studies adequate?       | N/A      |
| Is the length appropriate in relation to the content?          | 3        |
| Does the reader get new insights from the article?             | 4        |
| Please rate the practical significance.                        | 4        |
| Please rate the accuracy of methods.                           | N/A      |
| Please rate the statistical evaluation and quality control.    | N/A      |
| Please rate the appropriateness of the figures and tables.     | 1 - Low/No|
| Please rate the appropriateness of the references.             | 4        |
| Please evaluate the writing style and use of language.         | 4        |
| Please judge the overall scientific quality of the manuscript. | 4        |
| Are you willing to review the revision of this manuscript?     | Yes      |

Comments to Author:
The manuscript "Genetic engineering of mesenchymal stromal cells for cancer therapy - turning partners in crime into Trojan horses" represents a comprehensive review article discussing the field of MSC. The review article gives an excellent overview on the topic and also shed some critical light on the published work in this field. The manuscript is very well written and well structured. I would suggest to incorporate a number of tables and overview diagrams in order to support the subchapters (i.e. the role of MSC in cancer therapy, clinical trials, ...)

Authors’ Response to Reviewers Comments
Jul 05, 2016

We thank the reviewers for their positive comments. We have created and integrated into the manuscript two figures illustrating different aspects of MSC therapy. Figure 1 provides an overview of the strategies for MSC engineering against cancer, while figure 2 details the mechanisms of action of suicide gene based therapies and explains the different strategies of constitutive gene expression vs. tumor-specific expression. We hope these figures help the reader understand the strategies currently most used to target tumors with engineered MSCs.
Reviewers’ Comments to Revision

Reviewer 1: Brigitte Vollmar

Jul 14, 2016

Reviewer Recommendation Term: Accept
Overall Reviewer Manuscript Rating: 95

Custom Review Question(s) | Response
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Is the subject area appropriate for you? | 5 - High/Yes
Does the title clearly reflect the paper’s content? | 5 - High/Yes
Does the abstract clearly reflect the paper’s content? | 5 - High/Yes
Do the keywords clearly reflect the paper’s content? | 5 - High/Yes
Does the introduction present the problem clearly? | 5 - High/Yes
Are the results/conclusions justified? | 5 - High/Yes
How comprehensive and up-to-date is the subject matter presented? | 5 - High/Yes
How adequate is the data presentation? | 5 - High/Yes
Are units and terminology used correctly? | 5 - High/Yes
Is the number of cases adequate? | 5 - High/Yes
Are the experimental methods/clinical studies adequate? | 5 - High/Yes
Is the length appropriate in relation to the content? | 5 - High/Yes
Does the reader get new insights from the article? | 5 - High/Yes
Please rate the practical significance. | 5 - High/Yes
Please rate the accuracy of methods. | N/A
Please rate the statistical evaluation and quality control. | N/A
Please rate the appropriateness of the figures and tables. | 5 - High/Yes
Please rate the appropriateness of the references. | 5 - High/Yes
Please evaluate the writing style and use of language. | 5 - High/Yes
Please judge the overall scientific quality of the manuscript. | 5 - High/Yes
Are you willing to review the revision of this manuscript? | Yes

Comments to Author:
-

Reviewer 2: anonymous

Aug 03, 2016

Reviewer Recommendation Term: Accept
Overall Reviewer Manuscript Rating: 75

Custom Review Question(s) | Response
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Is the subject area appropriate for you? | 4
Does the title clearly reflect the paper’s content? | 4
Does the abstract clearly reflect the paper’s content? | 4
Do the keywords clearly reflect the paper’s content? | 4
Does the introduction present the problem clearly? | 4
Are the results/conclusions justified? | 4
How comprehensive and up-to-date is the subject matter presented? | 4
How adequate is the data presentation? | 2
Are units and terminology used correctly? | 4
| Question                                                                 | Rating |
|-------------------------------------------------------------------------|--------|
| Is the number of cases adequate?                                        | N/A    |
| Are the experimental methods/clinical studies adequate?                 | N/A    |
| Is the length appropriate in relation to the content?                   | 3      |
| Does the reader get new insights from the article?                      | 4      |
| Please rate the practical significance.                                 | 4      |
| Please rate the accuracy of methods.                                    | N/A    |
| Please rate the statistical evaluation and quality control.             | N/A    |
| Please rate the appropriateness of the figures and tables.              | 3      |
| Please rate the appropriateness of the references.                      | 4      |
| Please evaluate the writing style and use of language.                  | 4      |
| Please judge the overall scientific quality of the manuscript.          | 4      |
| Are you willing to review the revision of this manuscript?              | Yes    |

**Comments to Author:**

The manuscript "Genetic engineering of mesenchymal stromal cells for cancer therapy - turning partners in crime into Trojan horses" is now appropriately improved. I have no further comments or suggestions.