Reviewer's report

Title: What is the potential of Oligodendrocyte Progenitor Cells to successfully treat human spinal cord injury?

Version: 1 Date: 10 July 2011

Reviewer: Karin Nilsson

Reviewer's report:

1. Does the debate present a novel argument, or a novel insight into existing work?
Yes, the authors critically discuss the potential pros and cons of using OPC as therapeutics in SCI. Their main argument is that the role for demyelination in SCI is not clear, and therefore remyelination processes by transplanted OPC may not be the most fruitful way to cure SCI. Even if remyelination would be successful there are many remaining problems, and these could be discussed.

2. Does the debate address an important problem of interest to a broad biomedical audience?
Yes, but the manuscript needs improvement to give a more comprehensive view of the problem and its potential solutions.

3. Is the piece well argued and referenced?
In general yes, but the paper needs to be updated. The Geron trial started almost a year ago and updates have been given at conferences. These should be mentioned, although no conclusions can be made until the trial is finished.

Furthermore, there are very few references to papers published the last few years. The field is moving quickly and a multitude of publications have appeared in 2010-2011. Only two references are from 2010 and none from 2011. The reference list needs to be updated.

4. Has the author used logical arguments and sound reasoning?
Yes, but as stated above, there are missing parts. Background data should be given on stem cells and progenitor cells to provide the reader with knowledge on the cells to be grafted. The part about safety and purity needs to be developed. A major concern in grafting ES-cell derived progenitor cells is the risk of teratoma formation. Several labs have addressed this by xenofree culture of human ES-cells. This should be referred to as a possibility to avoid the risk of serious set-backs should SCI patients present with signs of tumors derived from the grafted progenitors.

5. Is the piece written well enough for publication?
Yes
- Discretionary Revisions (which are recommendations for improvement but which the author can choose to ignore)

1. Potential benefits other than remyelination could be more precisely discussed, i.e. trophic support for survival of other cells and previous experience in this matter. In several experimental CNS trauma papers a large number of grafted progenitor cells never differentiate to the desired progeny, but still provide improved motor or cognitive functions. The paper would benefit from discussing this.

2. Also, even if remyelination would be successful there are many remaining problems, and these could be discussed.

- Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

3. When references are given to web sites the date of making the reference should be noted as the web sites are constantly modified. This is lacking for some references.

- Major Compulsory Revisions (which the author must respond to before a decision on publication can be reached)

4. The paper needs to be updated both for the main issue of debate, The Geron trial and for experimental SCI treatment. The GRNOPC1 started in October 2010, and updates have recently been given at conferences. These should be mentioned, although no firm conclusions could of course be made until the trial is finished and the data collection complete.

5. Furthermore, there are very few references to papers on experimental SCI treatment and progenitor cells published the last few years. The field is moving quickly and a multitude of publications have appeared in 2010-2011. Only two references are from 2010 and none from 2011. The reference list needs to be updated.

6. Background data should be given on stem cells and progenitor cells to provide the reader with knowledge on the cells to be grafted. The part about safety and purity needs to be developed. A major concern in grafting ES-cell derived progenitor cells is the risk of teratoma formation. Several labs have addressed this by xenofree culture of human ES-cells. This should be referred to as a possibility to avoid the risk of serious set-backs should SCI patients present with signs of tumors derived from the grafted progenitors.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a
statistician.

Declaration of competing interests:

I declare that I have no competing interests