Reviewer's report

Title: CD133+ Adult Human Retinal Cells Remain Undifferentiated in Leukemia Inhibitory Factor (LIF)

Version: 2 Date: 7 July 2008

Reviewer: Gail M Seigel

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Major Compulsory revisions

1. Why was CD133 chosen to purify stem/progenitor cells from the retina (since CD133 is a component of normal photoreceptors)? The observation on page 10 states that 67% of post mortem human retinal cells expressed CD133, but only 31% were purified by magnetic separation. How many cells of this population are progenitor cells and how many are CD133-expressing mature photoreceptors? This seems to confound the findings within this paper.

2. How do the authors reconcile LIF effects on neurosphere formation and cell proliferation in this system, which seems counter-intuitive in relation to its effects on other cell types?

3. How were the designations "lo" and "hi" generated based on flow cytometry?

4. Please show negative controls for Figure 7. Was there an isotype negative control used for immunocytochemistry? If not, it needs to be.

5. Can any of the markers tested by flow cytometry be confirmed by PCR? It is always best to validate using another method.

Minor Essential Revisions

1. Explain how the ability to generate neurospheres from the adult human retina implies that the adult human retina may possess the ability for cellular replacement (page 3). Is neurosphere formation the only criterion for self-renewal?

2. Please use micrograms per ml instead of dilution factors in the Methods section, whenever possible.

3. What do the numbers mean within the histograms of Figure 2? They do not seem to be percentages, as they don't add up to 100%.

Discretionary Revisions

1. Page 11 results could be presented as a Table.

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.