Reviewer's report

Title: Expression of a Cu,Zn superoxide dismutase typical for familial amyotrophic lateral sclerosis increases the vulnerability of neuroblastoma cells to infectious injury

Version: 3 Date: 30 August 2007

Reviewer: Peter Monk

Reviewer's report:

General
The paper claims to provide evidence for the ‘particular vulnerability of G93A-SOD1 neuronal cells……to inflammation….and suggests early treatment of respiratory infections in ALS patients’ by analysing the responses of a human neuroblastoma cell line transfected with WT or mutant human SOD1. In three sets of experiments, these cells have been treated with hemolysin from S. pneumoniae and with monocyte-derived macrophages stimulated with a TLR-2 agonist. The neuroblastoma cells expressing mutant SOD1 are more likely to undergo apoptosis than cells expressing wt SOD1. In an attempt to provide a mechanism, mutant SOD1-expressing cells are also shown to undergo prolonged increases in intracellular Ca2+ in response to the hemolysin. No attempt is made to provide a mechanism for the increased vulnerability to the activated macrophages.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
The overall impression is of disconnected experiments that have been assembled to make a paper loosely themed upon inflammation. Although the individual experiments appear to be well conducted, there is not a coherent narrative: why are experiments macrophages stimulated by a synthetic TLR2 ligand combined with those using hemolysin directly on neuronal cells? Taken as a preliminary investigation into the potential role of infection in disease progression, the paper is of interest but it does not really support the conclusions that are drawn, regarding the suggestion of more aggressively treating respiratory infections in ALS.

1) A better conclusion might be that further work in this area is certainly justified and that this might lead to changes in treatment.

2) The discussion section is over-long and much of it could be omitted to make the paper easier to read.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
1) Pneumolysin is produced in E. coli. What are the levels of LPS in these preparations?
2) What morphological and functional characteristics were used to assess the macrophages? How long were they cultured? Trypsin can activate macrophages so it would also be useful to know how they were harvested for co-culture.
3) What are the units of the are-under-the-curve figures? Are these meaningful?
4) Vulnerabitivity (p15) is not an English word

Discretionary Revisions (which the author can choose to ignore)

**What next?:** Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

**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'