Reviewer's report

Title: Association between novel TARDBP mutations and Chinese patients with amyotrophic lateral sclerosis

Version: 1 Date: 15 October 2009

Reviewer: Christopher E Shaw

Reviewer's report:

Association between novel TARDBP mutations and Chinese patients with amyotrophic lateral sclerosis

Hui-Ling Xiong et al.

The authors sequenced exons 2-6 in 71 sporadic and 5 familial ALS cases. They describe a novel mutation in TADBP predicted to cause a single amino acid substitution Ser292Asn (c.875G>A) which is in a highly conserved domain and has a high likelihood of pathogenicity on SIFT bioinformatic modelling. The mutation lies in exon6 and affects the glycine rich C-terminal domain. Three ALS associated TARDBP mutations flank it affecting amino acids at 290 and 294.

The significance of the synonymous SNPs [Gly40Gly (c.120G>A) and Ala366Ala (c.:)] and one intronic SNP [239-18t>c] is unclear as they are not predicted to alter splicing or RNA expression levels of TARDBP. The 1098C>G SNP (Ala366Ala) has previously been detected in one sporadic ALS case and one control.

Specific comments below in black.

When assessing the work, please consider the following points:

1. Is the question posed by the authors well defined?
   Yes

2. Are the methods appropriate and well described?
   Yes, entirely appropriate

3. Are the data sound?
   Yes, I have no concerns about the validity of the mutations.

4. Does the manuscript adhere to the relevant standards for reporting and data deposition?
   Yes it is fairly well written. It needs minor grammatical editing.

5. Are the discussion and conclusions well balanced and adequately supported by the data?
Yes

6. Are limitations of the work clearly stated?
Yes

7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished?
Yes

8. Do the title and abstract accurately convey what has been found?
Yes

9. Is the writing acceptable?
It needs some grammatical correction but it is acceptable as is

Reviewer's report
-----------------
Please number your comments and divide them into
- Major Compulsory Revisions
  NO
- Minor Essential Revisions
  Only revisions suggested are grammatical regarding the use of English
  The author can be trusted to make these. For example, missing labels on figures, the wrong use of a term, spelling mistakes.
- Discretionary Revisions
  These are recommendations for improvement which the author can choose to ignore. For example clarifications, data that would be useful but not essential.
  NONE

Quality of written English
--------------------------
- Needs some language corrections before being published
- Acceptable

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

**Statistical review:** Yes, and I have assessed the statistics in my report.
Declaration of competing interests:

I declare that I have no competing interests