Reviewer's report

Title: Familial Frontotemporal Dementia with Neuronal Intranuclear Inclusions is not a Polyglutamine Expansion Disease

Version: 1 Date: 18 July 2006

Reviewer: Andrew Lieberman

Reviewer's report:

General

Familial FTLD-U with neuronal intranuclear inclusions constitutes a subset of FTLD. Based on the common pathology between these cases and the polyglutamine expansion disorders, Mackenzie et al sought to determine whether a CAG or CAA repeat expansion occurs in these patients. Using DNA derived from five FTLD-U cases with neuronal intranuclear inclusions from four different families, the authors determined repeat lengths in 63 genes encoding stretches of at least five glutamines. This group of genes was identified by a genome wide computational analysis (described elsewhere), and includes nine genes known to cause human disease. Their results were compared with repeat ranges identified in 94 control samples. No significant repeat expansions were detected, leading the authors to conclude that there is no evidence for a polyglutamine expansion in FTLD-U with neuronal intranuclear inclusions.

The report is well written, and the authors have used an appropriate method to test their hypothesis. Their data are presented and discussed succinctly. I have just a few minor suggestions.

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

None.

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

The title to Table 1 should be modified to read “CAG or CAA repeat expansions”.

In the Conclusions, the authors note that they screened “most of the genes” with at least five CAA or CAG repeats encoding glutamine in the human genome. Since their computational analysis is not yet published, it is unclear whether they mean that they screened all of the predicted genes of interest (although there may be others), or that additional genes were identified but not screened. If it is the latter, how many genes were not evaluated and why?

Discretionary Revisions (which the author can choose to ignore)

The authors may wish to expand on their final sentence of the Discussion, and note that ubiquitinated intranuclear inclusions are known to occur in triplet repeat disorders encoding amino acids other than glutamine (eg alanine) and in disorders caused by expansions in untranslated regions.

What next?: Accept after minor essential revisions

Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:
I declare that I have no competing interests.