Reviewer's report

Title: No evidence for association between tau gene haplotypic variants and susceptibility to Creutzfeldt-Jakob disease

Version: 2 Date: 23 September 2007

Reviewer: sabina capellari

Reviewer's report:

The manuscript by Sanchez-Juan et al. reports the findings of an association study between tau gene haplotypic variants and susceptibility to CJD. The authors studied 6 MAPT haplotype tagging SNPs and did not find any statistically significant difference between sCID cases and controls in the frequencies of either single locus variants or haplotypes. The question posed by the authors is sound, and the methods applied are appropriate and sufficiently described.

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

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

I understand that the lack of differences between groups justify the pooling of the data but since the gold standard of genetic association studies requires ethnically matched controls it appears appropriate to include a comment about this aspect in the discussion. Indeed, the role of ethnicity on the association of MAPT H1 haplotypes and disease has been also recently pointed out (Winkler et al, Eur J Hum Genet 2007).

Controls and vCJD groups are not age-matched. Furthermore, the disease groups comprise a high proportion of “probable” CJD cases. Also these limitations of the study should be mentioned in the discussion.

A part of the discussion is just a repetition of the result section and should be reduced (while the remaining part should be expanded as stated above).

Table 2 is mentioned before table 1

pag 15 “sequences” is misspelled

Consistency in the indication of frequencies must be checked in Table 5 and 6

The titles of tables 4 and 6 do not read well

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Discretionary Revisions (which the author can choose to ignore)
It could be interesting for the reader to also have the data showing the MAPT haplotype association with sCJD considered as individual groups (as in Table 3).

**What next?:** Accept after minor essential 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 have no competing interest