Reviewer's report

Title: PRNP variation in UK sporadic and variant Creutzfeldt Jakob disease highlights genetic risk factors and a novel non-synonymous polymorphism

Version: 1 Date: 18 August 2009

Reviewer: Richard Carp

Reviewer's report:

Major Compulsory Revisions: None.

Minor Essential Revisions:

1. In the Statistical Comparisons section, the last sentence of the first paragraph is confusing. It is not clear what groups are being compared: surely the 129 genotype frequencies of the control groups versus the National CJD Surveillance Unit sCJD cases yielded significant differences. The sentence should be restructured.

2. In Fig. 3, the columns representing male and female cases have not been identified on the figure or the figure legend.

Discretionary Revisions:

1. In the Abstract (Background):

   Whether these polymorphisms are more or less common is irrelevant; what is important is the effect of specific polymorphisms on disease occurrences and/or progression.

2. It would be appropriate to add the following reference in your discussion of Asian data regarding the 129 polymorphism:


3. At the end of the D202D discussion: until one knows the frequency of D202D in the control population, it is pure speculation to suggest a role in vCJD.

4. The speculation about a role of D167G as a cause of a genetic form of CJD is also premature. Again, this polymorphism has not been assessed in the control population.

Level of interest: An article of importance in its field
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.