Reviewer’s report

Title: Changes of tau profiles in brains of the hamsters infected with scrapie strains 263K or 139A possibly associated with the alteration of phosphate kinases

Version: 1 Date: 28 April 2009

Reviewer: Pedro Piccardo

Reviewer’s report:

Major Compulsory Revisions.

The work presented in this manuscript is aimed at investigating the possible changes of the microtubule-associated protein tau in scrapie-infected hamsters.

In Methods it is indicated that “Previous studies confirmed that the incubation time of 263K-infected hamsters was 79.1±8.6 days, while that of 139A-infected hamsters was 395±8.5 days. The brains were removed surgically at the 20th, 40th, 50th, 60th and 70th days after inoculation and immediately dissected”

If identical time points (i.e., 20-70 days post inoculation) were taken to collect brain samples from animals inoculated with 263K and 139A scrapie agents it is conceivable that animals infected with 263K agent would include pre-clinical and clinically affected animals. In contrast, animals inoculated with 139A-infected scrapie agent would all be at the preclinical stage of disease. If so, comparison between these 2 groups of animals would not be valid. In addition, progression of disease would only be thoroughly analyzed in animals inoculated with 263K agent. These issues should be clarified.

Were control animals infected with the same inocula used to determine the incubation time for each agent in the set of experiments described in this manuscript or was previous data used to estimate incubation times for each inocula? Data from previous experiments could be used as guide, however a set of controls should be used for each new series of experiments.

How many animals were analyzed per time point? This issue should be clearly presented in materials and method as well as in figure legends.

The PrP banding pattern in figure 1 is not clear (overexposed film? gel overloaded?). The shift in mass of PrP species following PK digestion is not shown. It is suggested to modify Figure 1 in order to clearly show (i) the various PrP bands (non-, mono- and bi-glycosylated PrP isoforms), (ii) to include positive and negative controls, and (iii) to show samples before and after PK digestion.

The resolution of western blots showing tau protein, GSK3# and CDK5 should be improved. For example the various tau protein isoforms are not clearly resolved in the data as shown. High quality western blot data should be used specially when quantitative analysis is being performed.
In conclusion: the proposed set of experiments is of interest not only for the field of transmissible spongiform encephalopathies but also for the broad area of neurodegenerative diseases. However, several issues should be clarified.

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

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests