Reviewer's report

Title: MHC2TA mRNA levels and human herpesvirus 6 in multiple sclerosis patients treated with interferon beta along two-year follow-up

Version: 1 Date: 23 July 2012

Reviewer: Konstantin Balashov

Reviewer's report:

The authors studied MHC2TA expression in patients with MS. This represents an interesting topic as MHC2TA polymorphism affects susceptibility to MS (Nat Genet. 2005; 37: 486-94).

However, the results shall be provided in a more transparent manner.

MAJOR DEFICIENCIES

Materials and Methods:
Please provide detailed information on control (healthy) subjects studied. Normalization ratios (NR) in Figure 1 were calculated using gene expression data in both patients and control subjects. No information on healthy subjects (age, gender, other medical problems, medications taken) was provided in Material and Methods.

Results:
Please clarify which particular statistical test was used for each p value listed.

Figure 1B:
Please clarify if MHC2TA expression in patients with allele C was normalized against healthy subjects with allele C or the total population of healthy subjects. The control for MS patients with allele C shall be non-MS subjects with allele C. If information on allele C in control subjects is not available, relative gene expression instead of normalized ratio for MHC2TA shall be provided.

Figure 1C:
Please clarify if MHC2TA expression in patients with active HHV-6 infection was normalized against control subjects with active HHV-6 infection or against the population of all control subjects. The control for patients with MS and active HHV-6 infection shall be non-MS subjects with active HHV-6 infection. If information on HHV-6 infection in control subjects is not available, relative gene expression instead of normalized ratio for MHC2TA shall be provided.

Please provide information on MHC2TA expression in patients with active HHV-6 infection at each time point. For example, it would be important to know MHC2TA expression at the 12 month visit for those 19 patients who had active HHV-6 infection at the 12 month visit.
Table 1:
Please add information on the prevalence of HHV-6 DNA expression in the serum of control (“healthy”) subjects.

Table 2:
a) Two additional groups (“MHC2TA mRNA level increased + HHV-6 in serum” and “MHC2TA mRNA level decreased without HHV-6 in serum”) shall be added.
b) The prevalence if IFN-beta neutralizing antibodies after two years of IFN-beta treatment for all four groups shall be provided. The abstract states, “no differences were found between patients with and without Nabs”. However, no data was provided in Results.
c) As Betaseron and Rebif have higher clinical efficacy than Avonex (based on frequency of clinical relapses in patients with MS), the proportion of patients treated with each of the three drugs shall be provided for all four groups.

MINOR SUGGESTIONS

Abstract:
Please correct the error in the "results" section of the abstract. It shall read as follows: "...MHC2TA mRNA levels were significantly LOWER among MS patients with HHV-6 active infection..."

Table 2:
It would be very interesting to know EDSS and Relapse rate in 23 patients who converted from HHV-6 DNA positive status at the basal visit to HHV-6 DNA negative status at the 6-month visit (described on page 9, lines 20-21). It may be reasonable to include this "HHV-6 converters" group in Table 2.

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 declare that I have no competing interests