Reviewer's report

Title: Genomic NGFB variation and chronification in multiple sclerosis: case control study and expression analyses

Version: 2 Date: 30 August 2008

Reviewer: Daniela Galimberti

Reviewer's report:

Aims of this work are clear and methods sound. Results obtained add a substantial piece of knowledge about gender-related differences influencing the development of MS.

Regarding the association analysis, the population is large enough to get reliable results. However, whereas one SNP (rs6330) is likely a risk factor, another one (rs11102930) seems to act as a protective factor, raising the question whether NGFB overall effect is to increase or decrease the risk of developing MS in male population. This point should be better addressed.

In addition, when stratifying genetic data according to MS course, Authors should take into account that patients with RR-MS could develop Secondary Progressive (SP)-MS in the future. To overcome this possibility, patients could be stratified in "bout onset“ (RR+SP) and progressive onset (PP). Alternatively, the duration of the disease should be specified for each group, in order to have homogeneous RR and SP populations.

In addition, I suggest some formal changes in order to help readers to get the key-points of the association analysis:

- Table 1 should be split in two smaller Tables, the first regarding rs6330, the second on rs11102930.
- P value, together with OR(CI) of these two SNPs, could be added in the text ("Results” section) to be more easily noticed at a first glance by readers.
- Table 2 describes negative results, therefore could be deleted and included in the supplementary material.

Lastly, clinical criteria used for MS diagnosis should be mentioned when describing patients.

Concerning expression analysis, I would suggest more caution regarding conclusions described. First of all, the group of patients analyzed is quite small (23 males and 10 females) and no controls have been included. In addition, Authors should consider that the following variables could influence results obtained:

- were RR and SP patients having relapses (if any) in an acute or stable phase of the disease at time of sampling?
- were patients under treatment with an immunomodulatory agent?
All these information should be added in the “Methods” section and results discussed on the basis of these data.

**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