Reviewer's report

Title: Lower CD28+ T cell proportions were associated with CMV-seropositivity in patients with Hashimoto’s thyroiditis

Version: 1 Date: 22 March 2013

Reviewer: Elisabetta Caselli

Reviewer's report:

The authors present data on the detection of altered proportions of peripheral lymphocyte subpopulations in Hashimoto’s patients compared to healthy controls, and correlate these findings to CMV seropositivity. The data are interesting, however the work is essentially observational and has various limitations, therefore I think it needs major revision before publication.

Major Compulsory Revisions.

1. Overall, as the authors write in the Discussion, HT results from local autoimmune mechanisms in the thyroid gland, but this aspect is not addressed by their work. Similarly, the association between CMV infection and immune dysregulation is well known and the paper do not add new data, but rather confirm that virus infection is related to an altered proportion of peripheral lymphocytes, without explaining why it might be associated to HT development.

2. In the absence of an analysis of the presence/expression of CMV at the local level (in the thyroid gland) the correlation of their findings with CMV infection appears not sufficiently supported by data but rather two accidentally concomitant aspects.

3. Since both HT and CMV infection are known to be related to immune dysfunction, it does not surprise that in subjects affected by both conditions the signs of dysregulation are worse than in others.

4. By contrast, the paper would be greatly improved by the analysis of CMV presence and/or expression at the thyroid level, by histochemistry or immunofluorescence, to verify the effective involvement of CMV in the thyroid disease.

5. Similarly, also the analysis (i.e. by ELISPOT) of lymphocyte subpopulations reactivity against CMV should be added, to give strength to the association between CMV infection and alterations of CD4+ and CD8+ lymphocyte populations.

Discretionary Revisions:

1. The number of HT patients (20) should be increased to be more similar to that of HC subjects (70), and HC and HT subjects should be more matched, although differences do not appear statistically significant.

2. In Table 1, CMV seropositivity results report a different number of patients
(HC=49; HT=12): it should be explained why they are different.

3. Due to the high proportion of CMV-positive subjects in the general population, the analysis of CMV-specific IgM response should be added to strengthen the association of HT with CMV.

Minor Essential Revisions:
1. Abstract, page 3, line 9: the term flow cytometry is incorrectly written
2. Background, page 4, line 3: change the verb “were” in “are”

Level of interest: An article of limited interest

Quality of written English: Needs some language corrections before being published

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