Reviewer’s report

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

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Reviewer: Roman Junik

Reviewer’s report:

The manuscript of Martina Prelog et al. is a piece of well done work and it is worth to be published in BMC Endocrine Disorders. However, some parts should or might be improved.

Minor Essential Revisions

Methods:

Study population:
“HC (healthy controls) according to WHO definition without any therapy, autoimmune disorders, endocrinologic diseases, cancer or other immunological impairments were recruited at the outpatient clinics …”

If they were healthy, what was the reason for following them in the outpatient clinics? If they were ill, what were the diseases?

Lymphocyte phenotypes:
Please correct the spelling Fluoreszeinisothiocyanat = fluoresceinisothiocyanat

The Authors state „CD28 is a co-stimulatory molecule, … for naïve T cells”. This is a description of molecules/cells and depictions/phenomenon’s but not a description of method(s). This paragraph should be transferred to the “Background” or “Discussion” section of the manuscript.

Quantification of TREC (TRECs?) numbers:
“TRECs are stable circular DNA fragments … from the thymus”. As above.

Results

Patients:
“Despite the wide age-range in HT and HC, no significant differences were present between the groups regarding age (table 1)”.

Age (in years): HC 13,7 ± 4,0; HT 20,2 ± 16,2.

The lack of significant differences in age between the groups is likely due to the wide range of age in HT group (± 16,2) as compared with HC (± 4,0). Obviously, a population of HT consisted of subsequent patients, whom the authors were following in the outpatient setting. However, it seems like comparing
predominantly adolescents and children at pre-pubertal age (mean age 13.7) from HC group with predominantly adult patients from HT group (with the oldest being probably >35 years old), may introduce potential bias. It even raises a question as if it makes sense to compare an immune system of a child/adolescent and a person in the middle of his/her life?

As a matter of fact, the authors raise this issue in the „Discussion” section "A more significant loss of CD28 in our group may be also influenced by the relative higher age of HT patients compared to that study [23], as CD28 expression is dramatically affected by age [3, 24] and changes of CD28-expressing T cells may be more pronounced in older HT patients”.

How did the authors address that? It will be worthwhile to provide a logistic regression model adjusting for age.

Table 1: TSH of HT was 9.1 ± 13.6 mU/L. This means that in HT group there were euthyroid persons as well as patients with clinically overt hypothyroidism. The question is as above: are immunologic parameters in hypo- and euthyroid patients comparable?

Perhaps, the lack of „correlations between lymphocyte subpopulations and hormone levels (and what about TSH?) or thyroid hormone substitution …” results from the heterogeneous HT population?

Additionally: T3 is belived to be a thyroid hormone and T4 is a prohormone of the thyroid gland. The standard approach to thyroid hormone substitution consists of a therapy with levothyroxine, while triiodothyronine is rarely used because of her shorter half life introducing wide variations in the hormone levels. Were all HT patients really treated with liothyronine?

**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