Reviewer’s report

Title: Changes in lymphocyte subsets in patients with Gullain-Barre syndrome treated with immunoglobulin

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Reviewer: I.N. van Schaik

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The authors have investigated T-cell subsets in 38 patients with AIDP and 26 patients with AMAN before and after treatment with IVIg. 30 healthy individuals served as controls.

The main finding is a higher percentage of CD45RO+ T cells in AIDP patients before treatment with a corresponding lower percentage CD45RA+ T cells. After treatment with IVIg the percentage of CD45RA+ T cells was increased as was the CD4+/CD8+ ratio. These changes were not observed in the AMAN group.

The authors conclude that these changes in these subset play an important role in the pathogenesis of AIDP and that the mechanism of action of IVIg acts on these subsets.

Major Compulsory Revisions and additional experiments to be done

Among the membrane antigens that are differentially expressed by reciprocal human T-cell subsets are the CD45RA and CD45RO isoforms, which have been hypothesized to identify "naive" and "memory" T cells. The CD45RA antigen is first expressed by T cells relatively late during their intrathymic maturation and continues to be expressed by most T cells in the immunologically naive neonate. With increasing age and antigenic exposure, CD45RA-/RO+ cells become more prevalent in the circulation and comprise the majority of cells in tissues. Analyses of the functional capabilities of CD4+CD45RA+ and CD4+CD45RO+ cells have shown that proliferative responses to "memory" recall antigens or the ability to provide help for antibody production are functions uniquely performed by CD4+CD45RA-/RO+ cells. The major immunoregulatory functions described for CD4+CD45RA+ cells involve suppression of immune responses, either directly or via the induction of suppressor activity by CD8+ cells. There is considerable experimental support for the hypothesis that CD45RA-/RO+ cells are "memory" cells that derive from virgin CD45RA+/RO- precursors. CD4+CD45RO+ recipient T cells could re-express CD45RA but never revert to a genuine CD4+CD45RA+/RO- naive phenotype.

The findings in the current study are difficult to understand: CD45RO+ cells are expected to outnumber CD45RA+ cells on adults in peripheral blood. Thus the finding that this is not the case in AMAN is more a main finding than the fact that CD45RO+ is higher in AIDP. As RO- cells are derived from RA+ cells and RA+ cells never return to a genuine RA+ state the finding of an increased percentage RA+ cells after IVIg treatment is at least curious. Most problematic is the finding
that the percentage of CD8+ cells was decreased and at the same time the percentage of RA+ cells was increased. This is completely contra-intuitive as the RA cells deliver support to CD8+ cells.

The experiments are too simple and do not elucidate or elaborate on any of these questions.

The effect that IVIg has on these subsets are not really investigated. These experiments should be expanded with in vitro stimulation and suppression work. Furthermore, it would be of interest to treat a few healthy controls with IVIg and see what happens with their subsets. T-cells of GBS patient who are not treated will be available and are of interest. Furthermore, what happens with these subsets after recovery? Only additional experiment can shine some light on this. Because these experiments have interesting and sometimes contra-intuitive result, the experiments should be expanded. That could in the end lead to a very interesting paper.

Minor Essential Revisions

I would like to see scatterplot of the most important experiments. The methods section isn’t clear on the exact methodology used during facs-scanning: e.g. were gates used? How were markes placed and so on.

**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