Reviewer’s report

Title: Autoantibodies Against Retinal Proteins in Paraneoplastic and Autoimmune Retinopathy

Version: 1 Date: 8 April 2004

Reviewer: Pavel Philippov

Reviewer’s report:

The manuscript "Autoantibodies against retinal proteins in paraneoplastic and autoimmune retinopathy" by G.Adamus et al. describes the results of analysis of anti-retinal autoantibodies in sera of 193 retinopathy patients with or without cancer, who have a loss of vision of retinal origin. The experimental results obtained in the work are of interest for understanding of the molecular mechanisms underlying cancer-associated retinopathy and other kinds of retinopathy of the autoimmune origin. The work is also of particular interest for clinicians as the autoantibodies can be used as biomarkers of the disease activity. The work meets the requirements of "BMC Opthalmology" and can be accepted for the publication in the journal as a research article after its minor essential revision.

Now my notes according to Report Template suggested by "BMC Ophtalmology":

Ø Minor Essentional Revisions:
1. To designate anti-retinal autoantibodies, the authors use terms "anti-retinal autoantibodies" (or "autoantibodies") and "anti-retinal antibodies" (or "antibodies"), while in all cases "anti-retinal autoantibodies" (or "autoantibodies") are implied. Thus, it would be better to unify the terms used.
2. In the study, the retinopathy patients were divided into 2 groups: 52 cancer patients with paraneoplastic retinopathy and 141 patients with paraneoplastic autoimmune retinopathy, whose cancer screening by physicians was negative. However, it is known that the CAR symptoms and the underlying autoantibodies can appear long before the diagnosis of cancer. In particular, it follows from the data presented in the manuscript (for example, see Table 3). If so, the question arises whether it is possible that some patients of the 2nd group belong, as a matter of fact, to the 1st group, as their tumors are still "invisable" at the early stage of cancer.
3. It is not clear whether p35 corresponds to transducin or it is a heterogeneous band which contains transducin (see page 10) and other proteins present in Müller cells for example (see page 5). The authors write that "Typically, a serum demonstrated immunostaining of a single retinal protein on a blot" (see page 9) – it would be better to say which bands represent single proteins and which ones contain several antigens.
4. Fig. 1 shows the calculated frequencies of the autoantibodies. However, any examples of the original blots are absent. It is also true for immunocytochemical investigation which is described in detail in the section Methods, but is slightly touched upon in the section Results; thus, the authors write that "…anti-bipolar antibodies could be identified only by immunocytochemistry" (see page 9), but neither the corresponding figure nor the formula "data not shown" is present.
5. In the section Discussion and Conclusion, the authors write "This study confirms that autoantibodies are associated with autoimmune retinopathy". This conclusion is not not quite correct as autoantibodies – in the wide sense – are not always associated with autoimmune retinopathy. Moreover, it is not quite correct even for anti-retinal autoantibodies: recently low-titre anti-recoverin autoantibodies have been detected in cancer patients who have no paraneoplastic retinopathy. In this connection, it is reasonable to mention that such a possibility exists for anti-recoverin autoantibodies similar to anti-Hu autoantibodies.
6. Several questions concerning Fig. 3: (i) what kind of treatment was used in Fig. 3, A?; did the treatment improve the patient's visual fields?; (ii) while the effect of the rituxan treatment on the visual fields is shown in Fig. 3, B, no information on the treatment result is presented in the case of
steroids (see Fig. 3, C); (iii) Fig. 3 demonstrates the dynamics of autoantibody titres in detail, while only one arrow is present in Fig. 3, B to show the improvement of the patient's visual fields. In this connection, the question arises whether it is possible to show the dynamics of the visual fields in more detail.

7. The authors write "We identified a much higher prevalence of anti-retinal antibodies than expected..." (see page 2) and "...possess antibodies against retinal proteins with a higher prevalence than expected." It is not clear what are the reasons of this unexpectedness.

Ø Level of interest: the article meets the requirements of "BMC Ophtalmology".
Ø Quality of the written English: On my opinion, the language is acceptable. (Remember, however, that English is not my native language, hence my evaluation has to be verified by an expert in the field).
Ø Statistical review: Though the manuscript contains statistical calculations, on my opinion, there is no need to verify the calculations by an expert statistician.
Ø Open peer review: no need to include my report on the BMC Ophtalmolgy website, but will be glad, if my review helps to improve and publish the article presented.

What next?: Accept after minor essential revisions

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:

None.