Author's response to reviews

Title: Genome-wide copy number variation (CNV) in patients with autoimmune Addison's disease

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Author's response to reviews: see over
19. July 2011

Dear Sir,

Re: MS 1428746228535142

Thank you very much for the positive response and constructive criticism of our paper "Genome-wide copy number variation (CNV)" in patients with autoimmune Addison’s disease. The manuscript has now been revised accordingly (detailed below). We hope you will find the revised version suitable for publication. All authors have read and approved the revised version.

Sincerely yours,

Ingeborg Brønstad
Comments to reviewer’s report:

1. The referees point is well taken. We have now focused the text on GWAS and Taqman replications and limited the presentation of the candidate gene analysis in the text. The bulk of this information has been moved to Additional files. Regarding the request for some additional work to characterise the protein products, we agree that this is relevant. However, we feel that to commence on the characterisation on two proteins of mostly unknown function is a new project in itself and beyond the scope of the current paper.

2. The size of the CNVs associated were all ≥ 100 Kbp, which was set as a cut off limit for the GWAS. This has been added in the revised manuscript (see Methods page 8 and heading of Table 1, page 19). Neither frequent nor novel CNVs covering micro RNAs were detected in our GWAS. The exact size and localisation of the CNVs varied slightly between patients, but in every case encompassed the listed genes. This information is now included in the legend to Table 1.

3. Corrections for multi-testing have not been made for the P values in Table 1. However, the genes with significant association to Addison’s disease were taken forward to replication studies to obtain more reliable results. In the revised version we found it more correct to use the Fisher’s Exact test for testing of statistical differences, since not all data sets were compatible with the Chi Square test. Fisher’s exact test is in general more conservative, but the significant differences found with Chi Square test were still valid upon using Fisher’s exact test in our data set.