Author’s response to reviews

Title: A possible role for miRNA silencing in disease phenotype variation in Swedish transthyretin V30M carriers

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Version: 3 Date: 20 August 2010

Author’s response to reviews: see over
Dear Sir

Thank you for the constructive comments from the referees. Please bring forward our appreciation on the work they have laid down on our manuscript.

Please find below a point-to-point answer to the questions raised by the referees. Please note that text we wish to remove is marked like this.

Referee: 1
Reviewer: Wenqiang Yu

The two questions I have proposed for this manuscript are much more important to make your points more clear. Your answers to these question can be accepted but not satisfied.
A1. Thank you for the constructive comments on our manuscript. We also consider these points most important and as we mentioned earlier this experiment will be carried out, but will not be included in this manuscript.

Referee: 3
Reviewer: Joel Buxbaum

Re: my first comment regarding multiple comparisons: It is not clear to me how the authors adjusted for multiple comparisons. They should state the method they used. For instance if the used Bonferroni then a statistically significant difference with 16 comparisons is a P value of <0.003 (0.05/16). Then only rs62093482 would be significant, which is OK regarding the main point of the paper, but rs71383038 and 3794885 would not be significant.
A1. A correction of the manuscript has been made regarding the statistical method and p-values (see corrections in Results, table 1 and method/statistics).

A point I missed in my original review is that the frequency of the significant snp is not stated to differ between early and late onset Swedish FAP cases. If that is correct then it is difficult to accept without further explanation that putative microRNA binding impacts on penetrance. The point made by Soares et al in reference 27 was that the differences were between early and late onset cases in Portuguese patients with early and late onset.
A2. - Although the Swedish population as a group has a low penetrance, differences within the population still exists. The difference within the Swedish population might be explained by other factors such as differences in the regulation of the miRNA itself (see corrections in Discussion).
On page 12 where the authors have inserted a paragraph and quoted ref 24 (their own work) they have not removed the sentence referring to reference 23 which reference 24 indicates was incorrect.

A3. We have clarified the paragraph (see corrections in Discussion)

We believe that our manuscript has improved with the suggested changes and clarifications, and hope that it acceptable for publication in BMC Medical Genetics-journal

Sincerely

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