Reviewer’s report

Title: The NRG1 exon 11 missense variant is not associated with autism in the Central Valley of Costa Rica

Version: 1 Date: 20 January 2007

Reviewer: James Sutcliffe

Reviewer’s report:

General

The manuscript by McInnes et al describes an analysis of the neuregulin 1 (NRG1) gene in a population isolate located in the Central Valley of Costa Rica (CVCR). Previous studies in this population associating a nonsynonymous variant with schizophrenia and psychosis, prompted analysis of this variant in the available CVCR autism families. The bottom line is that this infrequent coding variant is not apparently associated with autism in these families. The rationale for the experiment is clearly laid out, the data clearly presented, and appropriate conclusions drawn. This is a nice study. While it concluded in a negative result, the findings are no less worth reporting, particularly given the rationale for studying this question in the first place. I have no significant concerns about this report. I have only one question regarding the case with an apparent de novo instance of this variant. If this is true (i.e. assuming paternity is not a problem), can this be a recurring variant? The haplotype studies, which seem to suggest that the Val/Leu change is present on at least two haplotypes, are consistent with this idea. Given that there is uncertainty regarding phase in two families with the different haplotype, a similar uncertainty may exist for this idea. Do the SCZ studies support the variant being a recurrent event? If so, it would be worth mentioning the possibility.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

N/A

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

N/A

Discretionary Revisions (which the author can choose to ignore)

If appropriate, consideration of the possibility of the Val/Leu variant being a recurrent change.

What next?: Accept after discretionary revisions

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

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.