Reviewer’s report

Title: Genes encoding critical transcriptional activators for murine neural tube development and human spina bifida: a case-control study

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Reviewer: Henk Blom

Reviewer’s report:

This is an interesting study with an original approach and is well executed.

The statistics look appropriate but are to some extend too complex for me to evaluate and the editors may consider to consult a biostatistician.

I have only some minor remarks (Discretionary Revisions). I leave it up to the authors to include them or not.

1. The DNA samples are collected during the time folic acid food fortification is introduced to the USA. May this have affected the results of this study? I know that some mice models respond to folic acid therapy, although they may not be among the ones selected in this study.

2. Two haplotype blocks show significant association with spina bifida risk. In EP300 this may be explained by the high risk alleles. In TFAP2A such high risk alleles seem not present. The authors may consider sequencing this block to check if additional genetic variants are present that may explain the increased risk.

3. Although spina bifida is a multifactorial disease it can not be excluded that the studied genes may contain relative rare mutations that may cause some of the spina bifida. In the near future high throughput sequencing may reveal such genetic variants in the current patient group.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests.