Reviewer's report

Title: Autism genetic database (AGD): a comprehensive database including autism susceptibility gene-CNVs integrated with known noncoding RNAs and fragile sites

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Reviewer: Jacob A Vorstman

Reviewer's report:

Major compulsory revisions

1. The authors present a new database and propose that, in addition to existing databases, visualizes ncRNAs and fragile sites. While they discuss (to some extent) the putative importance of ncRNAs they fail to explain the (putative) relevance of fragile sites other than referring to a respectable, but rather speculative paper by Kooy et al. I think the paper would benefit from a well-motivated explanation by the authors as to why the addition of ncRNAs and fragile sites are important for autism research.

2. Unlike what the authors claim, The Autism Chromosome Rearrangement Database does in fact offer the possibility to visualize ncRNAs (MicroRNAs) in relation to autism-associated chromosomal abnormalities. Thus, this is not a new feature.

Minor Essential Revisions

3. (Background). The authors describe that that ASDs are heterogeneous but “share a core deficit in social-cognitive processing”. This claim is not supported by literature findings. The social-cognitive deficits found in ASD patients are not consistent among all patients.

4. (Background). The author’s statement that “several candidate genes have been linked...but the etiology of most cases remains unknown” lacks precision. There are several ASD-associated genes, -although none with conclusive evidence (!) -, which when present may account for a small effect. To date, at the population level the proportion of variation (in ASD liability) that can be explained by the identified ASD risk genes remains very small. Thus, even when present in an autistic individual, these genetic variations explain at best a (small) part of the etiology.

5. (Conclusions). It is not very clear how the stratification method (using ncRNAs in the vicinity of reported ASD loci) can enable researchers “to apply screening criteria and select a more homogeneous group of subjects”?
Discretionary Revisions

(Background). The authors describe that CNVs may affect gene function and then continue to state that the biological relevance of CNVs remains to be revealed. This reasoning is not logical.

(Background). Perhaps the nature and function of microRNAs and snoRNAs can be explained.

Typos:
(abstract): the sentence “When it applicable links to…” appears to be grammatically wrong.

Database
The database is set up in a way that performing queries is possible intuitively and without a priori knowledge.

Level of interest: An article of importance in its field

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