Reviewer's report

Title: Enrichment of ultraconserved elements among genomic imbalances causing mental delay and congenital anomalies

Version: 2 Date: 23 August 2010

Reviewer: Guy Froyen

Reviewer's report:

The authors adapted the paper according to most of my comments and questions. However, I still have two major comments for which I would like to have the authors’ response.

Major compulsory revisions:

I am still confused about the number of UCEs included in the CNVs. In table 1, the total number of UCEs in the CNVs is 38, not 29! Since the same set of 9 UCEs are within the CNVs of cases 2 and 7 both should be included, or not? If not, it should be mentioned as ‘29 different UCEs' but then I still don’t see why these 9 ‘same’ UCEs should not be included in the enrichment calculations.

I did not find any reference to the database of UCEs except for the original paper. If anyone would like to check whether any UCE is associated with their CNV, he/she should be able to find these UCEs? Did I overlook this reference? In case of a database please provide the URL; in case of a feature within a genome browser, provide the configuration to be shown.

Minor essential revisions:

It should be mentioned that 114 UCEs are not correctly mapped and why. As it is now, 111 vs 256 is confusing since it does not make 481.

If the paternity of the CNV is important, then why is it not discussed as mentioned in the answer to my question?

In the discussion, I don’t see where the enrichment ratios of 3.7 and 1.7 come from. Please explain or refer to a table, if present there.

I would delete the final sentence in the discussion regarding the inclusion of UCE sequences on oligo arrays because it does not fit with the message of the paper.

Discretionary revisions:

Conclusion: change to ‘… dosage-sensitive genes.’ and ‘… as the gene content or the mode of inheritance.’

Legend to Table 1. ‘… where all the consecutive ..’

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