Reviewer's report

Title: Familial imbalance in 16p13.11 leads to a dosage compensation rearrangement in an unaffected carrier

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Reviewer: Reinhard Ullmann

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In their manuscript, Delicado and colleagues report an index patient with a familial duplication of 16p13.11 inherited from the mother and present in an uncle and an elder brother. Most interestingly, a concurrent deletion hindered the identification of the duplication in the mother by array CGH. Only when employing alternative methods the additional deletion was identified. Finally, the authors discuss a potential dosage compensation mechanism and emphasized the importance of their findings for genetic counseling of the mother.

Minor essential revisions:
+ the author mention several times that the clinical relevance of the duplication is unclear and that they can not associate it with the brain phenotype of their patient. Actually, there are numerous studies clearly showing statistically significant disease association of 16p13.1, e.g. with schizophrenia and mental retardation. The latter has been comprehensively tested by Mefford and colleagues (Mefford H, Genome Research 2009). Moreover, a 16p13 duplication has already been reported in a patient with brain malformations (Karaminejad et al., 2011)

+ the array used in this study covered "clinically relevant " regions with high density. It’s really a pitty to see neighbouring regions like 16p11 covered by oligos with highest density, while 16p13.11, the region this study is focusing on, is just represented by the oligo backbone. Higher density in the region could provide further information, e.g. reveal further subtle rearrangements that could shed light on the underlying mechanism

+ how was the STR PCR quantified?
+ does a region rich in LCRs really has a repetitive structure
+ the authors tested two different cell types derived from the mother and conclude " that all cell lineages with different genotypes would have been confined to extraembryonic tissue". Are two cell types enough to make this conclusion?

+ the authors say "50% will have a 16p13.11 duplication and the other 50% will have the reciprocal deletion." I recommend to rephrase this sentence to reflect the probabilistic nature of these numbers

Level of interest: An article of importance in its field
Quality of written English: Needs some language corrections before being published

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