Reviewer’s report

Title: A Method for Determining Haploid and Triploid Genotypes and their Association with Vascular Phenotypes in Williams Syndrome and 7q11.23 Duplication Syndrome

Version: 0 Date: 30 Jan 2018

Reviewer: Ibtessam Hussein

Reviewer's report:

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The authors presented a method for identifying haploid and triploid genotypes in CNV regions using PennCNV and in-house developed R scripts values and applied the obtained information to test for genotype-phenotype associations. They used samples from individuals with Williams syndrome (deletion 7q11.23) and individuals with Duplication 7q11.23 to test for association between presence of aortic arteriopathy and SNPs of specific genes (genotype), and used SNP-level statistics and GEC software for multiple comparisons. They observed that the G allele in ELN gene increases the severity of SVAS, whereas it is protective against aortic dilatation in Dup 7q.

They concluded that SNP-chip and CNV analysis can be used for genotype-phenotype investigation in other diseases where is less information about genetic mechanisms.

Although the number of patients was small but they used appropriate analysis and statistical methods that could prove the effectiveness of their methods.

The paper is accepted after minor revisions:

1- Page 6- line 38 "interaction between diagnosis (i.e. 7q11.23 copy number) and genotype"
   should write: "interaction between genotype (i.e. 7q11.23 copy number) and phenotype"
   or "interaction between diagnosis and genotype (i.e. 7q11.23 copy number)"

2- According to the data presented in figure (1):
page 8- line 35: "the sentence :"the increase in LRR of duplicated regions (orange lines)"
should write: "duplicated regions(blue lines)"

page 8- line 36: "the decrease in hemideleted regions (blue lines)"
should write " hemideleted regions (orange lines) 

3- In the Abstract both cover page and page (2) in the results paragraph:

"The A allele of SNP rs2528795 in the elastin gene" should write "The G allele of SNP" because the authors concluded in their results that the G Allele increases the risk of aortic stenosis

and is protective for aortic dilatation

4- In the abstract page 1 and 2: "while the G allele of the same SNP was associated with aortic dilation in Dup7"

should write: "while the A allele of he same SNP was associated with aortic dilation in Dup7"

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

No

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

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Acceptable

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