Reviewer’s report

Title: Genome-wide rare copy number variation screening in ulcerative colitis identifies potential susceptibility loci

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Reviewer: Sajid Malik

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Comments on the Manuscript: BMC Medical Genetics MGTC-D-15-00134

Genome-wide rare copy number variation screening in ulcerative colitis identifies potential susceptibility loci

Saadati et al. report the analyses of large cohort of ulcerative colitis (UC) and identify rare structural variants with a potential contribution to the risk of UC. This is an interesting study and adds useful data into the existing scenario of GWAS for complex diseases. However, the manuscript would benefit from the following major and minor modifications and may be accepted when the following issues are adequately resolved:

Major changes required:

1. There are several datasets in the study and the sample inclusion scheme is difficult to follow. The authors need to present a flowchart of sample ascertainment, which should clearly show the study populations, previously analysed and newly included samples and inclusion/exclusion criteria. See for instance the flowchart presented in papers: Johnston et al. Am. J. Hum. Genet. 76:609-622, 2005; Hou et al. Nature Genetics 46, 1007-1011, 2014; Park et al. Identification of rare germline copy number variations over-represented in five human cancer types. Mol Cancer. 2015; 14: 25.

2. The authors confined their results to only three rare CNVs. It would be worthwhile to present another work-flow chart / pyramid diagram depicting various tires of analyses pipe line and the filtering scheme, i.e., 151 CNVs □ 24 CNVs □ 3 CNVs.

3. The three identified loci have been mentioned in varying orders in Abstract, Results and Discussion. There should be a consistent sequence for presenting the identified loci.
4. There is no mention of the scheme adopted for the selection of UC patients except: page 8, first paragraph. 'The diagnosis of UC was based on standard clinical, endoscopic, radiological and histological criteria [17].' It would be pertinent to briefly mention the criteria adopted for the characterization of the UC patients, based on scoring method or any other.

Minor changes/modifications required:

1. Page 5. Introduction, line 38. Remove the repetition of '……….of the……….'

2. Page 6. Introduction, line 52. '….in-silico……..' should be written in italics, as mentioned elsewhere in the manuscript (page 13, line 17).

3. There are large number of inconsistencies in the references and many of them do not agree with the BMC Med Genet format.

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.
Yes

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

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