Reviewer’s report

Title: Targeted/exome sequencing identified mutations in ten Chinese patients diagnosed with Noonan syndrome and related disorders

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Reviewer: Reuben Pengelly

Reviewer's report:

The authors present a case series showing their experience in utilising exome sequencing in Noonan syndrome, identifying pathogenic mutations consistent with prior literature. The paper is overall well written, however there are a number of errors, particularly in the methods which require revision prior to this being acceptable for acceptance.

1. Introduction - remove results from this section

2. Subjects - Just to confirm that only 10 individuals were sequenced, with 100% diagnostic rate, or are only diagnosed patients presented?

3. Methods 2.2, Whole exome sequencing - this section has numerous errors of fact and statements that do not make sense. This section requires revision by someone familiar with the process of whole exome sequencing. To highlight particular issue (not necessarily exhaustive): 1) The whole exome enrichment kit is not detailed, only the library preparation kit, which capture kit was utilised? 2) Variants are identified by the use of a genotyping calling tool such as GATK or Samtools, not reference databases 3) You claim to annotate variants following filtering, how is the filtering information added? 4) Clarify and justify why 'variants whose frequencies (in what?) were <0.1% were filtered out.

4. Methods 2.2 - Tools used and reference databases need to be cited

5. Results 3.2 - Again, requires revision as per methods 2.2. Total reads, is this per person average, total accross 10 samples? Also, for average coverage, what is your denominator for these coverages, capture kit baits, genes?

6. Novel variants - PTPN11 K70R has been previously reported (rs397516801) and BRAF F468C has been reported in leukemia (http://onlinelibrary.wiley.com/doi/10.1111/bjh.12735/full). These should be discussed more fully as this substantially adds to the evidence base for these variants and acknowledges prior work.

If these issues are addressed fully, then this manuscript would be suitable for acceptance.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

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

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.

Not relevant to this manuscript

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

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