Reviewer’s report

Title: Novel ANKRD11 gene mutation in an individual with a mild phenotype of KBG syndrome associated to a GEFS+ phenotypic spectrum: a case report.

Version: 0 Date: 20 Nov 2018

Reviewer: Palma Finelli

Reviewer’s report:

The report by Alves RM et al. entitled "Novel ANKRD11 gene mutation in an individual with a mild phenotype of KBG syndrome associated to a GEFS+ phenotypic spectrum: a case report" deserves consideration.

The clinical case is interesting as it reports the finding of two variants, by WES approach, in a familial case: a novel de novo loss of function variant in ANKRD11 causing a mild phenotype of KGB syndrome and a variant in the SCN9A gene shared by the two sisters both affected by generalized epilepsy with febrile seizures.

"Genotype first" approach help to reach a diagnosis especially for those syndromes characterized by a large phenotype spectrum and sharing clinical signs with other syndromes such as KBG syndrome. Anyway it is increasingly clear that the identification of causal variant in a gene may not be sufficient to fully explain the clinical phenotype, and this study shows how WES has been important to dissect the clinical phenotype identifying other variants that help genotype-phenotype correlation.

There are a few minor amendments:

line 8 pag 5 please specify the aCGH resolution
line 61 pag 5 delete (Goldenberg et al., 2016; Low et al., 2016)
line 15 and 18 pag 6 delete (Parenti et al., 2016) and (Zhang et al., 2004)
line 4 page 11 Figure 1: A-P instead of A-O

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

**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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