Reviewer's report

Title: Novel GATA4 promoter mutation associated with congenital heart disease in South Indian patients

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Reviewer: Saverio Sabina

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TITLE
The title of the paper appears misleading, because the authors are not assessing the association of a novel mutation with CHD in South India population, rather they are trying to assess the association of a pool of mutations with CHD in an ethnic group living in southern India.

ARTICLE
The aim of the authors is the association of some GATA4 mutations to Congenital Heart Disease (CHD) in an ethnic group, those people which speaking the Dravidian language (Dravidians) and living in southern India. However, the selection of the study population is not clear. The assumption that the authors make to justify the setting of their discussion, namely the high rate of consanguineous marriages in the Dravidians, do not directly imply the high frequency of three mutations in these people (the cited supplementary figure 2 unfortunately does not provide this information either). In addition, the articles cited to endorse a low frequency of mutations in patients with CHD of other populations, were not carefully studied. For example, the authors report that Peng and colleagues [11] found a frequency of 1.48% (2/135) of mutations in VSD Chinese patients, whereas Peng and colleagues report 1 mutation in 82 Chinese VSD (1.22%) and 1 mutation in 12 Chinese TOF (8.33%). Similarly, all the CHD Germans reported in [12] are 205, while the Germans VSD are only 6, so that the percentage of mutations is 16.7% (1/6) and not 0.49% (1/205), as reported by the authors of the article under review. According to these published data, the reference samples for analysis on individual CHD are not significant.

In general, I think the authors have submitted a paper that still needed to be well thought out and harmonized. Although they found 6 mutations not in Hardy-Weinberg equilibrium, they reported these mutations in many tables and figures. The mutations were also considered in the 3'UTR in silico analysis. Moreover, they reported that for SV patients they haven't found any mutations (this finding is not strange if we consider that the reference population was only of 3 subjects). Nevertheless, SV patients were reported in tables and figures. Information and data provided by the authors (including the supplementary material) are redundant and often misleading.

Level of interest: An article of limited interest
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