Author’s response to reviews

Title: Functional study of DAND5 variant in patients with Congenital Heart Disease and laterality defects

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Author’s response to reviews:

Lisbon, July 6th 2017

Professor Giovanni Neri

Editor, BMC Medical Genetics, Clinical-Molecular Genetics and Cytogenetics

Dear Professor Giovanni Neri,

enclosed, please find the version of our manuscript by Cristo et al. on “Functional study of DAND5 variant in patients with Congenital Heart Disease and laterality defects” (MGTC-D-17-00126R1) to be submitted for your consideration for publication in BMC Medical Genetics as a Research Article.

Here, as you may appreciate, in this revised version of the manuscript we were able to address all the reviewer’s comments and suggestions. We included the suggestions form the reviewers and the manuscript has been clearly improved and for that we do thank them.
All the contributors have read and approved the submission of this manuscript. We declare no conflict of interest. The results in the manuscript have not been published, or submitted for publication elsewhere.

Looking forward to hearing from you. Sincerely yours,

Prof. José A. Belo, PhD

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Reply to the Reviewers:

Reviewer 1 (Alex Postma)

a) the manuscript has changed in structure. My general feeling is that the results section is too short now. I would include some data from the discussion, particularly on exac in the results section.

R: Due to the new structure of the manuscript, Reviewer 1 suggested that some data from the discussion should be included in the results section. We rearranged the text accordingly (changes are in red).

b) I think you performed statistics on your luciferase assay as you write about significant differences. Yet there are no stars or description of your statistics, please include these so we may be able to judge what is and what isn’t statistically significant.

R: The description of the statistics was included and the asterisks indicating the significant differences were added in Figure 2

Reviewer 2 (Georges Nemer)

Addressed no further questions.

Reviewer 3 (Denise Kay) raised the following concerns:

1. pg. 13, lines 328-329. That no other variants were detected in the DAND5 gene could also be a function of the small size of the gene, and the authors should also acknowledge this in this paragraph.
R: The size of the gene was acknowledged as suggested (changes are in red).

2. Please add a statement to the conclusion that screening a larger sample is required to determine whether the DAND5 variant is a true CHD risk factor or a benign variant.

R: The statement was added to the conclusion (changes are in red).