Reviewer’s report

Title: A systematic review of genetic mutations in pulmonary arterial hypertension

Version: 1 Date: 06 Jun 2017

Reviewer: Diana Valverde

Reviewer's report:

An interesting work that shown a way to select the genes related to PAH that could be implemented in a panel for genetic screening.

There is a typo in the abstract for the name of the gene AVRL1, I think it should read ACVRL1.

The authors stated that the main cause of familial PAH is a mutation in the citoplasmatic tail of BMPR2, in reference 6 there is not information about this fact. It seems that only mutations in the cytoplasmic tail are responsible for familial PAH, the described mutations in BMPR2 gene are distributed along all the coding sequence.

Please, revised the nomenclature of the genes, genes have to be written in italics to distinguish them from proteins.

Results section

They described 21 genes with evidences of mutations. They described 9 poorly studied, 6 that appeared only in two abstracts and three genes that appeared in three abstracts. That's make nineteen genes, what about the others?

In the next paragraph the say angiotensin II for AGTR1; please describe the gene with the entire name.

The authors did not found mutations in EDNRA, NOS2, SERPINE1, SIRT3 and TPRC6, what about TBX4, THBS1 and TOPBP1 that are included in the table?

A reference is needed for the next paragraph.

Discussion section

Second paragraph, lane 58, "which were mapped" replace better for " which were included". In this paragraph authors mentioned reference 16 but until now it never have been referred to the text. Change the numeration.
Reference 17 is missing in the text.

The authors referred mutations in the 5′UTR region for many genes, they have to be aware that for BMPR2 gene also mutations in this region have been described with a positive confirmation of its implication in expression. Viales et al, Plos One 2015.

The sentence beginning with "Due to… "needs a reference. Lane 51. Next sentence too.

Check reference 8

Check in the text 15 and 16 references.

Typo in Figure 2, "nut" instead of "but".

Additional files, File 1: Position, it is referred to what?

Check the spelling for ACVRL1 gene.

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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