Reviewer’s report

Title: Rare variant of HSPG2 is not involved in the development of adolescent idiopathic scoliosis: evidence from a large-scale replication study

Version: 0 Date: 17 Nov 2018

Reviewer: Keith Douglas Baldwin

Reviewer's report:

Thank you for this opportunity to review this paper regarding genetic predisposition in adolescent idiopathic scoliosis. It is a question that comes up quite often in discussions with patients as such it is a salient item to discuss and consider in research.

I will freely admit that my knowledge in the area of genetics and techniques involving gleaning knowledge in this regard is quite limited. As such I highly recommend to the editorial staff to get a reviewer who is knowledgeable in this subject matter to review the technical aspects of this paper to assess their merits. I will comment only on the clinical applicability of their work.

Firstly this is a negative paper in the sense that the authors find that in the Chinese population this particular allele of interest was not associated with the phenotypical expression of AIS.

I would ask were the standard criteria used to rule out AIS by the senior spine surgeon (less than 7 degrees of axial rotation on Adams forward bend)? They mention they used Adams forward bend just not the criteria they used.

I see a cursory description of HSPG2 in scoliosis as far as single versus double curves. Is there any specific Lenke pattern associated, the numbers are so big, I would think there would be enough data to assess this.

I think this study is important and I think there is something here. The discussion is good. Can the authors frame the discussion for the common surgeon in terms of what they should take away
from the article? I think the discussion is almost there but I was confused by a lot of the genetic detail in reading it.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Unable to assess

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.

Unable to assess

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If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review

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

Acceptable

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