Reviewer’s report

Title: Disentangling the Genetics of Sarcopenia: prioritization of NUDT3 and KLF5 as genes for lean mass & HLA-DQB1-AS1 for hand grip strength with the associated enhancing SNPs & a Scoring system

Version: 1 Date: 26 Nov 2019

Reviewer: Zhihui Zhang

Reviewer's report:

The manuscript aimed to combine the results from GWAS and eQTL and use Mendelian randomization to identify risk variants located in TAD regions that contribute to hand grip and lean muscle mass. However, the paper is not organized well, and the evidence is too weak to support the author's conclusion. Here, I highlighted some required changes to improve the manuscript:

1) Page 1 line 21 "It might also allow us to identify drugs...". This sentence is really confused. I am not sure if the author wants to say that the knowledge of genetics underline muscle mass will help us to identify new drugs or to identify potential side effects of muscles caused by using existing drugs. Please edit this sentence and, also, I don't think this sentence is necessary.

2) The introduction part is poorly organized. For example, at the first paragraph, the author first mentioned GWAS studies related to lean muscle mass at the beginning but described the overall development of GWAS in the middle of the paragraph. At the end, the author wrote that the downstream research of GWAS is valuable and the costs of the treatment of the disease is high. However, I don't know what the relationship between these two statements is. Another example is the third paragraph of the introduction, the author mentioned knocked out of genes based on the results from GWAS and eQTL. However, this statement totally interrupts this paragraph and is not necessary. The whole introduction part is very incoherent and require to re-write.

3) Method part is too simple, and more details are required. For example, how did the author combine different results from multi-GWAS studies? What is the population included in these GWAS studies? How did the author perform TAD analysis? What types of software and statistical methods included in each analysis? And so on.

4) So many issues in results part as well. For example, the author didn't mention what cutoff used to select the significant genes for the following analysis? In addition, the beginning of the second paragraph in the results part, that descripts details of TAD, should be in the introduction part.

5) The author should not organize the figures in different orders as the orders mentioned in the paper. The format of the references needs to change as well.
Overall, the author didn't organize the paragraph very well to support the conclusion.

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

No

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

No

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

No

**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.

I am able to assess the statistics

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

Needs some language corrections before being published

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