### **Reviewer Report**

Title: Accelerated deciphering of the genetic architecture of agricultural economic traits in pigs using the low coverage whole-genome sequencing strategy

**Version: Original Submission** Date: 1/18/2021

**Reviewer name: Martien Groenen** 

### **Reviewer Comments to Author:**

The authors have performed an extensive QTL analysis based on a large number of SNPs in a large Duroc population. The results presented show the power and cost-effectiveness of a low coverage sequencing strategy and increase our insight in the molecular mechanisms behind quantitative traits. Unfortunately, the paper is not written very well and at many places tends towards story telling. The authors point towards a large number of potential candidate genes, many of which have already been identified in previous studies to affect the traits studied in the current study. There is nothing wrong with that, but very often this results in an extensive discussion without any direct evidence that helps to further identify the causal variant responsible for the observed QTL. The discussion therefore could be much shortened which greatly would benefit the readability of the paper. The same is true for the results section, which for over 50% is already discussion rather than presenting the results. E.g. see the discussion about the ABCD4 gene in the results. Furthermore, the involvement of the ABCD4 gene on teat number has been extensively been discussed in several previously published studies. The authors often fail to provide proper references, and where they do the references mentioned do

The authors often fail to provide proper references, and where they do the references mentioned do not always provide evidence for the claims that are made. Some examples:

Lines 175-177: Refers to a previous study but no reference is shown.

Line 210: Refers to a former study reporting PROX2 could be the causal gene. But again, the reference of this study is not provided.

Line 57 states recently developed methods, yet the references are for papers up to 10 years old. I wouldn't call that "recent".

Line 71: Reference 21 is rather old to be used in this context.

Line 329: References 40 and 41 are not good references for the statement made in lines 326-329. For the evaluation of the SNP calling procedure based on BaseVar-STITCH (lines 108-137) it is unclear exactly what data sets are used and how reliably individual genotypes are for animals that have only be sequenced at a very low coverage. This paragraph needs to be clarified.

Lines 397-398: The comment "delivers fewer loci for fewer phenotypes" is rather odd. Fewer than what? And why would that be fewer? Is this statement based on other studies, on the estimated heritabilities? The authors studies 21 different phenotypes. However, many of these are highly correlated and this should be stated more clearly.

Minor comments:

Line 19: "populations"

Line 18-21: This is not a good English sentence

Line 22: Replace "discovered" by "describe"

Lines 22-25: This reads like the authors have performed LCS on all animals and then in addition have also done whole genome sequencing of all individuals.

Line 26: replace "in" by "for"

Line 36: insert "can be" between "and widely".

Line 45: "relies"

Line 45: Strange sentence "which perceive linkage"

Line 74: "describes"

Line 74-75: The infinitesimal model is not specific for "human quantitative traits". Change sentence.

Line 79: Replace second "process" by "produce"

### Methods

Are the methods appropriate to the aims of the study, are they well described, and are necessary controls included? Choose an item.

### **Conclusions**

Are the conclusions adequately supported by the data shown? Choose an item.

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Are you able to assess all statistics in the manuscript, including the appropriateness of statistical tests used? Choose an item.

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