Reviewer’s report

Title: Dissecting the obesity disease landscape: identifying gene-gene interactions that are highly associated with Body Mass Index

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Reviewer: Deepak Perumal

Reviewer’s report:

The authors of the manuscript titled “Dissecting the obesity disease landscape: identifying gene-gene interactions that are highly associated with Body Mass Index” highlight in detail the interactions between SNPs that are associated with BMI using data from a larger cohort. This article presents in detail the large-scale efforts to understand the genetic architecture of obesity through the application of genome-wide association studies and complementary methods, such as pathway analysis. Hence the content of this article is relevant, timely, and of great interest to the audience of this journal.

The article is well written and several points that strengthen this article are,
1. The abstract is concise and sufficient.
2. The article is easy to read and free from grammatical or spelling errors.
3. The methodology and data interpretations are clearly explained. This greatly enhances the validity of the findings.
4. The content of this article is technically accurate and sound.
5. All relevant articles are referred in the manuscript.

However, the authors need to address the below minor points that would further strengthen this article.
1. The authors need to provide an alternate title for the manuscript considering it has been presented in an IEEE meeting previously.
2. The discussion section seems to be too elaborate. The authors could provide a better discussion removing unnecessary explanation.
3. It is well known that highly polygenic traits like BMI appear to be influenced by numerous loci in several different regions in the genome. How do the authors explain this artifact in context of their study?
4. It is not clear whether the authors have estimated SNP based heritability using linear models in order to determine if SNPs within the examined biological pathways explained a disproportionate amount of the heritability for BMI.
5. I am curious to known in addition to gene-gene interactions, whether gene-environment interactions should be taken into account as well to maximize the obesity prediction ability. It seems probable that a combination of non-genetic information will still be needed to optimize the prediction of obesity.
The article is meritorious for publication in Biodata Mining. The authors need to address these minor comments before the article can be considered for publication.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests