Reviewer’s report

Title: The (FTO) gene polymorphism is associated with metabolic syndrome risk in Egyptian females: a case-control study

Version: 0 Date: 08 Aug 2017

Reviewer: Shelley Cole

Reviewer’s report:

Addressing Reviewer #1 Comments:

1. Study under-powered and didn't replicate Elouej et al., 2016: The authors have added an additional 56 participants, bringing the total to 197, in an attempt to increase the sample size and power of the study. The authors state that resources limit any additional recruitment. They have added power calculations (though in their response they did not compare the previous power using 141 participants to their improved power using 197). They correctly applied a conservative Bonferroni correction, and the association with ALT levels is no longer significant. They provided more detail in their discussion about how the results of their study replicate, or don't replicate, with others. Their main finding of the association between the FTO variant genotypes and metabolic syndrome does overlap with findings in the Tunisian population (Elouej et al, 2016).

2. FTO variant associations in both dominant and recessive models: The authors have addressed this by adding a discussion of past results as well as theirs.

3. Bonferroni correction: The authors have clarified the post hoc Bonferroni adjustment testing they conducted for pairwise comparisons versus the Bonferroni correction that was applied in the revision to address multiple testing with the quantitative traits.

4. LD at the FTO locus: The authors are unable to type additional FTO variants to address LD in the Egyptian population.

Additional comments:

A. Discussion, page 11, lines 15-18: The results are overstated. This should be rewritten as "Moreover, our study suggests for the first time an association of FTO polymorphism with high ALT levels that seems to be BMI independent, though the association was no longer statistically significant when corrected for multiple comparisons."
B. Discussion, page 11, lines 22-27: Better expressed as "...was also associated with increased ALT levels [58]. This suggests an association of FTO genetic variation with ALT might be mediated through NAFLD, though participants with overt liver disease were excluded from our study. Another possibility is that FTO contributes directly to the regulation of hepatic metabolism [59]."

C. Conclusions, page 12, lines 10-13: The results are again overstated. This should be rewritten as "Moreover, our study suggests a novel BMI and TAG-independent association of FTO genetic variation with elevated ALT levels that needs to be validated in other large sample sizes."

D. When referring to the FTO gene it should be italicized, whereas when referring to FTO protein it shouldn't. This is inconsistently applied throughout.

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?
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I am able to assess the statistics

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