**Reviewer’s report**

**Title:** Association of Catechol-O-Methyltransferase Single Nucleotide Polymorphisms, Ethnicity, and Sex in a Large Cohort of Fibromyalgia Patients

**Version:** 1  **Date:** 15 Mar 2018

**Reviewer:** Wei Yang

**Reviewer's report:**

Some of my previous points have been adequately explained/addressed.

Below are some that still need attention:

1. When describing the non FM samples, it would be helpful to make it clear that "Subjects were recruited from physician offices and were included in the study only if the physician deemed the genetic test was medically necessary to assess risk of FM."

2. Table 3. Two of the 4 SNPs showed constant change in the FM group across race and gender groups. These are compelling evidences of association. However, for the other two SNPs, rs6269 showed opposite directions in Afnican Americans and Caucasians; In females, rs4818 shows contradictory changes in the combined samples compared to the African American group. In presence of obvious heterogeneity, the test when comparing across race/gender groups should be performed with this in consideration. I would recommend using tests such as "stratified" analysis instead of direct test for frequency difference. Also, it might help to include an extra column to show the estimated effect size, such as odds ratio, so that even when a comparison is not statically significant probably because of small sample sizes, we would see how the effect size compares to the other groups.

3. When describing the results for diplotype associations: "there was an association of diplotypes when analyzed by ethnicity". This is not an association with race groups, not with FM. It shows nothing but ethical differences. I recommend revision to avoid confusion.

4. Some descriptions regarding "controls" should be made clear whether it refers to the non-FM samples or the 1000 genome data. One examples is the first paragraph in the discussions: "Our study demonstrates the minor alleles of rs4680 occurs in higher frequency in FM subjects compare with controls".

**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?
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

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