Reviewer’s report

Title: Protective variant associated with alcohol dependence in a Mexican American cohort

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Reviewer: Ulrich W. Preuss

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Manuscript Number: ?
Title: “Protective variant associated with alcohol dependence in a Mexican American cohort”
Authors: Norden-Krichmar et al
Article Type/Method: ?

The paper reports results from a GWAS in 427 Mexican Americans regarding their risk for alcohol dependence symptoms with focus on the ADH gene cluster on chromosome 4. The subjects were diagnosed using a semi-structured interview (SSAGA). GWAS was performed using an Affymetrix Axiom Exome 1 A chip. Results indicate that an ADH7 variant (rs991316) has a protective influence on the phenotypes. Additional linkage analysis suggested that nearby variants in LD with this SNP are not responsible for the observed associations.

The authors conclude that ADH7 has been previously reported to have a protective role against alcohol dependence in other studies and may also play a protective role in the current sample of Mexican Americans.

The strengths of the paper certainly include the thorough assessment of the subjects and the elaborate genetic analyses as well as the elaborate discussion of results. The paper is well-structured and well-written. Selection of phenotypes and statistical methods are appropriate.

I have only few comments to make:

1. The authors should include a sample-size/power analysis to their study, since the sample is rather small for a GWAS/analysis of the ADH cluster and the authors also use “quantitative” phenotypes (DSM III R and IV symptom counts) and n = 125 of the subjects had an alcohol dependence diagnosis.

2. Previous studies in other ethnicities also identified a number of other ADH gene variants which may influence the risk for alcohol dependence (e.g. ADH1B, C) which did not reach significance in the current study. This may also be due to low sample size and loss of power. Please comment.

3. Please use the term “alcohol dependence” throughout the paper (instead of
“alcoholism”)
4. Please report ethnic background assessments in the results section.
5. Methods: please explain the term “winsorization “
6. Figure 2: please explain the phenotypes (“AlcDep3” and “AlcDep4”) in the legend, as with table 1.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests