Reviewer’s report

Title: Prevalence of Genetic Polymorphisms in the Promoter Region of the Alpha-1 Antitrypsin (SERPINA1) Gene in Chronic Liver Disease: a Case Control Study

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Reviewer: Michele Zorzetto

Reviewer’s report:

In this paper Karin F. Fok and co-workers typed 297 patients with liver diseases from various aetiologies and 297 healthy controls for three different SNPs of alpha1 antitrypsin (c.1973T>C, S and Z), in order to understand the role of alpha 1 alleles in liver disease. They found no associations between the alpha 1 SNPs and liver disease.

Major
1) The principal limit of this work is represented by the fact that the patients group is composed by diseases very different one to the other. This could cause an over or underestimation of the actual contribute of the SNPs. Moreover the patients group is not in Hardy-Weinberg equilibrium for the c.-1973T>C SNP. If a population is not in Hardy-Weinberg equilibrium two different events could be happened:
   · The population is stratified for a particular feature
   · Some mistakes in genotyping occurred
Therefore is possible that Fok et al. stratified the patients for some features.
2) The only positive associations is between the heterozygous for S allele and the subgroup of DILI patients. This group is very small (11 patients) then the data is not so significant
3) Haplotype. The table 2 is not clear. It seems not an haplotype reconstruction distribution but a multiple genotypes. Probably is better to reconstruct the haplotype with a software dedicate (e.g hplus http://cougar.fhcrc.org/hplus/).
4) It would be interesting also calculate the linkage between the different SNPs (D’ or r2)

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.
Declaration of competing interests:

I declare that I have no competing interests