Reviewer's report

Title: Age-of-onset-dependent Influence of NOD2/CARD15 gene variants on Disease behaviour and treatment in Crohn’s disease

Version: 2 Date: 14 January 2013

Reviewer: Francis Vasseur

Reviewer's report:

The manuscript entitled "Age-of-onset-dependent Influence of NOD2/CARD15 gene variants on Disease behaviour and treatment in Crohn's disease" submitted by Carsten Posovszky et al. aims at evaluating the influence of NOD2 gene variants in disease behavior and treatment of pediatric and adult-onset Crohn’s disease, has been amended by the authors.

The questions suggestions and comments have been taken into account by the authors. Some Minor Essential Revisions remain.

#1 In the sentence "In this retrospective single center study in a tertiary center we report high prevalence of patients with NOD2 variant alleles with 44% in the pediatric- and 42% in adult-onset CD. The frequency of NOD2 variants in our cohort is similar to other European pediatric multicenter cohort studies with a prevalence of 35 upto 45.6% {Lacher, 2010 #19;de Ridder, 2007 #72;Sun, 2003 #82}." The first part of the sentence reports a frequency of patients and the second part of the sentence (beginning with "The frequency of NOD2 variants...") sounds like an allelic frequency although it seems a genotype frequency. This kind of confusion should be corrected.

#2 The previous confusion in mind of the authors as reported in my #1 is evident in the authors response letter. To the previous #41 they answered "Indeed, we compared the NOD2 variant allele frequency but we did not found a statistical difference between the two groups." and refered to allelic frequency although they seem to mean "patients with variant allele?", indeed in the "change in the manuscript" they now use a correct formulation with "the presence of two NOD2 mutant allele was found more frequent in the pediatric-onset CD patients" which refers to patients and thus to genotype frequencies and not allelic frequencies. The authors must be aware of this mistakes and should not confoung between allelic and genotype frequencies.

#3 In the legend of supplemental figure 1, why did the authors do not add the word "allele" to the "patients with NOD2 variant" although they wrote "NOD2 wild-type alleles" just after?

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

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