Reviewer's report

Title: The CTLA4 variants may interact with the IL23R- and NOD2-conferring risk in development of Crohn's disease

Version: 1 Date: 18 January 2010

Reviewer: Jürgen Glas

Reviewer's report:

Abstract
In the abstract the six CTLA4 polymorphisms tested in the presented study should be listed including rs-numbers. For the polymorphism in IL23R the correct nomenclature should be used, in this case it would be p.Arg381Gln (rs11209026), R/Q and Q/Q are not a clear nomenclature.

Background
The authors did not give an enough comprehensive and representative overview about the most important genetic associations in Crohn's disease. They should cite NOD2 (Nature 411:599-603,2001 and Nature 411:603-6,2001) and IBD5 (Nat Genet 29:223-8,2001) as the most important associations before the era of genome-wide (GWA) studies and the most important associations of the several GWA studies such as IL23R/ATG16L1 (Science 314:1461-3,2006/Nat Genet 39:596-604,2007) PTGER 4 (PLoS Genet 3:e58,2007) and IRGM (Nat Genet 39:830-2,2007) and also the Meta-analysis of these GWA studies (Nat Genet 40:955-62,2008). Citations of loci as for example NELL1, which have not been confirmed in replication studies (ref. 3 and ref. 6 in the reference list), could be deleted.

Results:
In table 2 also the allele frequencies should be included. In table 2 two the rs-numbers of all polymorphisms should also be indicated. The frequencies of the CD associated polymorphisms within NOD2, IL23R and ATG16L1 should be included in table 2, it is not sufficient only to cite previous studies of the authors.

Discussion:
The overview of the GWA studies is not representative, only ref. 4 and ref. 5 are important GWA studies, but not ref. 3 and ref. 6, whereas the most important GWA studies are not cited (see comments to "Background"). As the interaction of CTLA4 and NOD2 variants found in the presented study is relatively weak, it should be discussed that this can be due to the small number of CD patients tested by the authors. Since they cite the study of Machida et al (ref 14) it should also be discussed that different genetic associations can also be the result of ethnic differences, as for example NOD2 mutations are not associated with CD in Asiatic populations.
Methods/Determination of genotypes
The basic characteristics of the control group as indicated in "Subjects" should also be included in table 1.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

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