Reviewer's report

Title: Functional polymorphism of the NFKB1 gene promoter is related to the risk of dilated cardiomyopathy

Version: 1 Date: 16 October 2008

Reviewer: Jürgen Glas

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Background
For the NFKB1 -94 insertion/deletion polymorphism its SNP-ID rs28362491 should be added. It is correct that this polymorphism has originally been associated with ulcerative colitis (ref 15). It is also correct that the results of several replication studies were inconsistent, but in part the authors cite these replication studies incorrectly. The single study which could confirm the original association (ref 21) should be already cited in this section. The study cited in ref 16 dealt with celiac disease and is not relevant in this context and can be deleted. In addition to the negative replication study in ref. 17 two further negative studies (Gut 54:1205-6,2005; Inflamm Bowel Dis 12:606-11, 2006) should also be cited. Furthermore significant associations of the NFKB1 -94 insertion/deletion polymorphism with other disease entities (inflammatory disorders, tumors etc.) should be listed.

Methods/Determination of genotypes
The criteria for diagnosis of DCM should described briefly.
Have the results of genotyping been confirmed by sequence analysis at least in a few samples?

Results:
The authors should address the power of their study providing a power calculation.
The comparisons of genotype frequencies, allele frequencies and phenotype (=carrier) frequencies should be described in more detail within the text. It should be pointed out more clearly that the comparison of ATTG1/ATTG2 + ATTG2/ATTG2 vs. ATTG1/ATTG1 refers to the ATTG2 phenotype. Additionally the comparison of the ATTG1 phenotype should also be given in the text and in table 1. In table 1 the three parts genotype frequencies, allele frequencies and phenotype (=carrier) frequencies should be separated more clearly and the comparison ATTG1/ATTG1 vs. ATTG2/ATTG2 should be removed from the table.

Discussion:
The authors should discuss the main limitations of their study, particularly the relatively small size of their study population and the lack of replication of the
significant associations in a second independent cohort of patients with DCM. Finally, it should also be mentioned that investigating a single or a few gene polymorphisms is rather an ineffective tool for unraveling the genetic background of a disorder with complex genetic background such as DCM and that currently the best strategy would be a genome-wide association study. Such genome-wide association studies could identify susceptibility genes for several disorders as Crohn's disease, diabetes, rheumatoid arthritis, multiple sclerosis etc., this is reviewed for example in Nat Rev Immunol 8:631-43, 2008.

References:

Within the reference list the numbers in brackets after the volume numbers should be deleted.

**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.