Author's response to reviews

Title: Association study of genetic variants of pro-inflammatory chemokine and cytokine genes in systemic lupus erythematosus

Authors:

Elena E Sanchez (elena@ipb.csic.es)
Jose Mario JM Sabio (masabio@terra.es)
Jose Luis JL Callejas (JLCALLEJA@telefonica.net)
Enrique E De Ramon (ederamont@telefonica.net)
Rosa R Garcia-Portales (rosagaport@hotmail.com)
Francisco J FJ Garcia-Hernandez (fjgarciahernandez@hotmail.com)
Juan JJA Jimenez-Alonso (juanjimenez@juntadeandalucia.es)
Maria Francisca MF Gonzalez-Escribano (mariaf.gonzalez.sspa@juntadeandalucia.es)
Javier J Martin (martin@ipb.csic.es)
Bobby P BP Koeleman (b.p.c.koeleman@med.uu.nl)

Version: 7 Date: 10 May 2006

Author's response to reviews: see over
Dear Editor,

We are pleased to send you a revised version of our manuscript entitled “Association study of genetic variants of pro-inflammatory chemokine and cytokine genes in systemic lupus erythematosus”. The manuscript has modified taking into account the reviewer’s suggestions. In the following paragraphs we comment the changes that we have included in the reviewed version of the manuscript.

Answer to reviewer Jing-Long Huang

We appreciate the comment of the reviewer and indeed we agree that data on replication or nonreplication of genetic gene variations previously reported to be associated are of importance and will contribute to the elucidation of the genetic background of complex genetic disease.

1. “..genotyping of these genes was not performed (or failed) in 10 to 20% of the study subjects, and the results may be biased.”

We agree with the reviewer that ideally all subject can successfully be genotyped. In our study we indeed had a relative high percentage of subjects that failed genotyping. These subjects were the same between the different polymorphisms tested. Most likely the failed genotypings were due to the relative low concentration of DNA in these particular subjects.

However, we do not believe that our results were biased because of the failed genotyping. Bias could occur if one of the genotype categories had a higher drop-out rate than the other. This appeared not to be the case, failed genotyping occurred randomly throughout the data. Furthermore, the tested polymorphisms were all in Hardy Weinberg Equilibrium, which is expected to be distorted if the above bias occurs. Also, lack of true association could only occur if the associated genotype fails specifically in the cases only. This seems a very unlikely scenario. We therefore do not believe that our lack of association is a type II error as stated in the article, last page discussion:

“The fact that we do not observe an association and fail to confirm some previous studies may be caused by a Type II error (false-negative). This is however unlikely because our sample has more than 80% power to detect the relative risk similar to the
other studies at the 5% significance level. Furthermore, the genotype frequencies did not differ from Hardy-Weinberg expectations, and allele and genotype frequencies in our Spanish population are similar to those reported previously in other Caucasian populations.”

2. “Sufficient details were not provided regarding the roles of these polymorphisms in clinical manifestations of SLE.”

The results have been modified providing additional information regarding the roles of these polymorphisms in clinical manifestations of SLE. In addition, a new table after stratified SLE patients according the presence of renal involvement has been included for each polymorphisms genotyping of these genes (table 4).