

# letters

## RE: Association of human leukocyte antigen-DRB1 with anti-cyclic citrullinated peptide autoantibodies in Saudi patients with rheumatoid arthritis

**To the Editor:** We read with interest the study reported by Alrogy et al.<sup>1</sup> Firstly, we would like to thank the authors for their interesting findings. In this cross-sectional study, the authors nicely demonstrated a strong association between the presence of the HLA-DRB1 shared epitope and the development of anti-cyclic citrullinated peptide (anti-CCP) antibodies in a small group (76 patients) of Saudi patients with rheumatoid arthritis (RA).

The association of the 04\* allele and the protective effect of the 03\* and 07\* alleles reported in this study seems to be in agreement with the findings of a recent meta-analysis that reported on the association between HLA haplotypes and RA in 475 patients from different Arab populations (Moroccan, Tunisian, Algerian, Egyptian and Syrian).<sup>2</sup> This study, therefore, extends our knowledge of this association to a further Arabic population. It must be stressed, though, that the meta-analysis also reported an association with allele \*10 and a protective effect by alleles \*11 and \*13. Whether the effect of these latter three alleles absolutely does not involve Saudi patients, perhaps, remains to be confirmed in further larger studies.

It would be interesting to know if the authors recorded the number of smokers in both groups and whether this had any effect on the results of anti-CCP antibody positivity. Anti-CCP antibodies are autoantibodies that recognise citrulline, which is the product of the action of the enzyme peptidylarginine deiminase (PAD) on the amino acid argi-

nine. The expression of this enzyme in the lung may be increased by smoking and may thus contribute to more citrullination and consequently to anti-CCP antibody positivity.<sup>3</sup>

It would also be of interest to know if the male-to-female ratio which seems very discrepant between the two groups (9:1 for the study group and 1:1 for the control group) had any effect on the findings of the study. RA, like many autoimmune diseases, is influenced by hormonal factors.

Finally, we would like to make one more point which relates to the parity of the females in the control group. If it was recorded, did it match that of the study group? Again, hormonal factors may be at play here and this should be borne in mind when interpreting the findings of this study. Nevertheless, this may be difficult to correlate as most patients in the study groups were females, but the control group had equal distribution of genders.

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## Reply

We would like to thank the authors of the letter commenting on our recent paper on the association between anti-CCP and the shared epitope status in Saudi patients with RA.<sup>1</sup> Unfortunately, we do not have data on the smoking history of our patients. We agree that smoking is a risk for the development of anti-CCP.<sup>2</sup> Nevertheless, studies on the epidemiology of smoking in Saudi Arabia suggest that smoking is more prevalent among Saudi males.<sup>3</sup> Even though we had more females in our cohort, it might be difficult to decide whether this has direct influence on our findings. A bigger sample size with more males will be needed to answer this question. As for parity of the controls, again this information was not available and will need to be addressed in the future.

We thank you again for your interest in our paper and we do hope that all unanswered questions will be tackled in future studies.

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