

# 1. The earliest stages of immune-mediated inflammatory disease

## A1 THE INTERACTION BETWEEN HLA SE ALLELES AND SMOKING AND ITS CONTRIBUTION TO AUTOIMMUNITY AGAINST SEVERAL CITRULLINATED ANTIGENS

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**Objective** Recent data suggest that a gene-environment interaction exists between smoking and the HLA SE alleles in shaping the autoimmune reaction towards specific citrullinated antigens. Here, we determined the effects of HLA SE alleles and TE (tobacco exposure) on the immune response against various citrullinated antigens. These associations were analysed in the anticitrullinated peptide antibody (ACPA) - positive stratum to control for the possibility that found associations are explained by the known interaction between HLA SE alleles and TE on the ACPA status.

**Methods** The reactivity of 661 RA patients against several citrullinated antigens from vimentin, fibrinogen, enolase and myelin basic protein was determined by ELISA. The effects of the HLA SE alleles and TE were assessed by logistic regression analysis. Biologic interaction was analysed by investigating if the effects of the risk factors combined exhibited departure from additivity.

**Results** A significant interaction between TE and HLA SE alleles appeared present for the presence of ACPA as reported previously. When these interaction effects were studied for several ACPA 'fine-specificities' significant interactions were noted for several citrullinated peptides. However these interactions were not present after stratification for ACPA status, indicating that the interaction between TE and HLA SE alleles does not influence autoimmunity towards specific citrullinated antigens, but rather to ACPA development.

**Conclusion** Our data indicate that the gene-environment interaction between HLA SE alleles and smoking does not shape the reactivity of the ACPA response.