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A18 A GENE–ENVIRONMENT INTERACTION BETWEEN HLA SE ALLELES AND SMOKING AFFECTS THE REACTIVITY OF ACPA TO VARIOUS CITRULLINATED ANTIGENS

D van der Woude, W G Alemayehu, N A Daha, W Verduyn, R R P de Vries, J J Houwing-Duistermaat, T W J Huizinga, R E M Toes *Leiden University Medical Center, The Netherlands*

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Objective It has recently been postulated that a specific interaction exists between genotype, smoking and autoimmunity to citrullinated α-enolase peptide (CEP-1), and that therefore, the major genetic and environmental susceptibility factors for RA are mainly associated with the development of anti-CEP1-positive disease. It is unclear however, if this interaction is truly specific for citrullinated α-enolase.

Methods The reactivity of 745 RA patients to cyclic citrullinated peptide and to two citrullinated peptides derived from vimentin (cVim) and fibrinogen (cFib) was determined by ELISA. The separate effects of the human leucocyte antigen shared epitope (HLA SE) alleles and smoking 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 The ACPA reactivity profile was affected by a significant biological interaction between the HLA SE alleles and smoking. Both the separate effects of HLA SE alleles and

smoking, as well as their combined effects were strongest for the anti-cVim-positive subset. This resulted in an OR of 58 (95% CI 19.6 to 174.9) in the anti-cVim-positive subset for smokers who were homozygous for the HLA SE alleles, compared to an OR of 5.4 (95% CI 2.1 to 14.2) in the anti-cVim-negative subset.

Conclusion The gene-environment interaction between the HLA SE alleles and smoking is not specific for citrullinated α-enolase, but rather extends to other citrullinated antigens as well. This implies that gene-environment interactions may predispose to a broader citrullinated epitope recognition profile, possibly by influencing the magnitude of the anti-citrullinated protein response.

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