HLA Class II Molecules and Asthma Induced by Toluene Diisocyanate

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Key Words

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Exposure to toluene diisocyanate (TDI) is associated with a variety of chronic disorders of the lung, including asthma [1]. TDI-induced asthma has been the most common cause of occupational asthma in industrialized countries for many years. Since TDI is a low-molecular-weight compound, it is likely that the immune response is directed to neoantigens formed by the reaction of TDI with body proteins [2]. Individual differences in HLA class II molecules may alter the ability of the molecules to bind peptides and to change the nature of T cell recognition. In a previous collaborative study [3], we observed that HLA class II molecules are involved in conferring susceptibility or resistance to asthma induced by TDI. HLA products or genes seem to represent a risk or a protective factor in asthma associated with specific sensitization to allergens. In the present study we extended our previous observations, and studied the distribution of alleles of the different HLA class II genes in 30 subjects with TDI-induced asthma, in 126 healthy controls and in 12 TDI-exposed asymptomatic subjects, using PCR sequence-specific oligotyping (SSO technique). We found a positive association with the DQB1*0503 allele and a negative association with the DQB1*0501 allele. We also analyzed the differences between hypervariable amino acid residues in the two DQB1 alleles involved in the disease and we found a single amino acid difference at position 57, with aspartic acid in DQB1*0503 and valine in DQB1*0501.

TDI is a chemical characterized by the presence of an -N=C=O group. It could act through different mechanisms. First, it could modify the structure of MHC class II molecules, or self peptides, at the surface of B cells or other antigen-presenting cells in a way that the modified epitopes would be recognized as foreign by the T cells. Second, it could alter the structure or the specificity of the T cell receptor. Third, it could react with other membrane proteins, such as adhesion molecules, and thus behave as a superadhesion molecule. It has also been suggested that DQ molecules could act as dominant suppressor genes able to regulate the suppressor-inducer network. Therefore, TDI might also involve dysfunction in the suppressor-inducer

network. The results of the present study suggest that the amino acid residue variation at position 57 of the DQB1 chain identifies a marker of susceptibility in TDI-induced asthma. The interaction between genetic susceptibility with an adverse environment in occupational asthma deserves further investigation.

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