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**HLA-DPB1 and TAP1 Polymorphisms in Sarcoidosis**

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(CHEST 1997; 111:738)

Sarcoidosis is a chronic, antigen-driven disorder of unknown etiology. It has been established that there is oligoclonality of the T-cell receptor (TCR) expression at disease sites and that antigen triggering through the TCR is major histocompatibility complex (MHC)-restricted. In berylliosis, an association with HLA-DPB1 alleles with a Glu residue at position 69 exists. Because the genetic predisposition to complex diseases is likely to be multifactorial and because previous HLA/sarcoidosis associations are not consistent, it is likely that other class II region genes may be involved. The TAP1 gene, encoded between HLA- DP and -DQ loci of the MHC class II region and containing polymorphisms at sites corresponding to positions 333 and 637 of the protein, produces a transporter molecule involved in endogenous antigen processing. In animal models, TAP1 has been shown to affect foreign antigen uptake and subsequent immune function, and therefore it seems a suitable candidate gene for involvement in the immunologic processes seen in sarcoidosis. We have investigated HLA-DPB1 and TAP1 alleles in two populations of sarcoid patients from the United Kingdom (UK) and Poland.

To investigate the involvement of Glu 69+ HLA-DPB1 alleles in sarcoidosis in the UK population, we have typed HLA-DPB1 alleles by polymerase chain reaction/sequence-specific oligonucleotide (PCR/SSO). Although no individual HLA-DPB1 allele was significantly associated with sarcoidosis, there was an association with Glu 69+ alleles (p=0.01). To investigate whether this association was ethnic-independent, we have characterized HLA-DPB1 Glu 69+ alleles among 47 Slavonic-Polish sarcoidosis patients. It was found that Glu 69+ DPB1 allele frequencies were decreased in the Polish patients studied compared with the UK patients (p=0.0002). To investigate TAP1 polymorphism involvement in sarcoidosis, we have characterized TAP1 alleles in 38 white English individuals with sarcoidosis, 47 Polish patients with sarcoidosis, and 140 English unrelated control subjects, using amplification refractory mutation system-polymerase chain reaction (ARMS-PCR).

Our results showed that allelic variant frequencies of TAP1 alleles were similar among sarcoidosis and control groups in the UK white population. At specific sites, there was a small increase in Val residues at position 333 among English sarcoidosis patients compared with control subjects (47 of 140 [33.6%] vs 17 of 38 [44.7%]), but no difference at position 637 in both UK groups. On comparison of these results with the Polish sarcoidosis population, we found that TAP1C and TAP1D were increased in the Polish group (15 of 94 [16%] vs 3 of 76 [3.9%]; p=0.02) and that the presence of Val at position 333 was less frequent in the Polish group (14 of 47 [29.8%] vs 17 of 38 [45.3%]) compared with the UK patients. No significant difference between the UK and Polish groups was seen at position 637. Further examination of MHC region genes is crucial for elucidation of the genetic predisposition to sarcoidosis. Such studies must involve multiple distinct ethnic groups to identify and confirm ethnic-independent factors involved in this disease.