DEFESA DE TESE

TESE DE DOUTORADO DE ***JOYCE HISAE YAMAMOTO*** *DEFENDIDA NO DEPARTAMENENTO DE OFTALMOLOGIA DA UNIVERSIDADE DE TÓQUIO, JAPÃO, EM 18 DE AGOSTO DE 1992, SOB O TÍTULO "CELLULAR IMUNE RESPONSES TO RETINAL SPECIFIC ANTIGENS IN PATIENTS WITH ENDOGENOUS UVEITIS".*

ABSTRACT: Autoimmunity to retinal specific antigens has been suggested to play a major role in the pathogenesis of some uveitis. This assumption is based on 1) the similarities of clinical and histopathological features of experimental autoimmune uveoretinitis (EAU) to many human uveitic conditions, and 2) the presence of autoimmune responses to the retinal antigens in uveitis patients.

The two main uveitopathogenic retinal specific antigens that induce EAU are S-antigen and interphotoreceptor retinoid-binding protein (IRBP). Through the recent advances in molecular biology, the main uveitopathogenic fragments in the sequence of S-antigen and IRBP are known to be peptides M and N, and the peptides R-4 and R-14, respectively. In the present study the lymphocyte proliferative responses to S-antigen, IRBP and their respective uveitogenic peptides were analyzed in patients with endogenous uveitis (i.e., Behçet's disease, Vogt-Koyanagi-Harada's disease (VKH) and sarcoidosis), in patients with retinitis pigmentosa, in patients with Behçet's disease without uveitis and in normal controls. Among the uveitic entities studied, Behçet's patients presented the highest responses to S-antigen and to IRBP, while VKH patients had the lowest responses. The responses to S-antigen in Behçet's patients with uveitis were correlated to active uveitis, short disease duration and young age. Retinitis pigmentosa patients also showed high responses to S-antigen. The responses to the retinal antigens were correlated to the severity of retinal damage. Several Behçet's patients with uveitis and retinitis pigmentosa patients, both with severe retinal involvement, responded to both retinal antigens, S-antigen and IRBP. Peptide M was a relevant lymphocyte proliferative site of S-antigen in Behçet's patients with uveitis. Behçet's patients without uveitis did not respond to S-antigen, but a certain percentage responded to IRBP, to the S-antigen-derived peptides, and to IRBP-derived peptides. The T cell responses to peptide M were inhibited by antibodies against CD4 and HLA-DR molecules. Monoclonal antibody anti-CD8 molecule inhibited the responses of some patients. The presence of cellular autoimmunity to retinal antigens and their uveitogenic peptides in patients with various clinical entities suggests that cellular autoimmunity is secondary to retinal damage. Nevertheless, it is correlated to uveitis activity and may contribute to the recurrent course and chronicity of retinal disorders.

However, in Behçet's disease, autoimmunity to S-antigen-derived peptide M and/or IRBP may also play a pivotal role in the induction of the ocular disease.