特別講演 1

Two New Approaches to Study the Role of HLA-B 27 in Arthritis

Department of medicine, UCLA

David Yu

That HLA-B 27 is crucial in the cause of the spondyloarthropathies is certain, but the mediating process remains an enigma. The focus has been on the ability of HLA-B 27 to present bacterial derived peptides to TCR. However, our recent finding that such CD 8+ T cell response did not parallel disease activity relegates the role of the peptides. Reports that expression of HLA-B 27 on a cell alters its susceptibility to invasion or intracellular replication by bacteria also demand more novel hypotheses. We are examining two possibilities. The first possibility is that the HLA-B 27 serves as a ligand for a specific protein of the arthritis-causing bacteria. Bacterial proteins were extracted by detergent. Complexing with HLA-B 27 was recognized by a higher stability achieved by the HLA-B 27. The positive protein was partially purified by HPLC. Sequence analysis was carried out by mass spectrometry. The encoding bacterial gene was cloned and expressed in a prokaryotic expression vector. The results of these experiments lead to the identification of a bacterial protein which can bind to HLA class I alleles including HLA-B 27. As an alternate approach, we postulate that HLA-B 27 is capable of modifying certain signal transduction pathways of the cells. To provide the activating signals, we exposed HeLa cells to invasive *Salmonella typhimurium*. HeLa cells transfected with HLA-B 27 were used for comparison. Expression of the early genes of activation was used as the assay parameter. We noticed that the presence of HLA-B 27 modified the generation of the AP-1 families as measured by RT-PCR. At the functional level it modified activities of these transcription factors as measured by gel shift assay. Multiple mRNA differentiated HLA-B 27 negative from HLA-B 27 positive cells as assayed by a differential display method. Among the proteins induced by the invasion process, the IL 6 was secreted at a higher level in the HLA-B 27 positive cells. The results of the experiments outlined in the above two projects indicate that the activity of HLA-B 27 is not confined to T cell immune response. The study of HLA-B 27 arthritis encompasses multiple fields in clinical immunology.