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Title: TCR V-beta usage in patients with sarcoidosis

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Body: Sarcoidosis is a granulomatous disease of unknown aetiology, mainly affecting the lungs. Elevated numbers of activated T cells are found in bronchoalveolar lavage (BAL) fluid. HLA-DRB1*0301+ (DR3+) patients, who typically have Löfgren's syndrome, are characterized by good prognosis and an accumulation of lung CD4+ T cells using the T cell receptor (TCR) gene segment Valpha2.3 (AV2S3). However, the corresponding β-chains that are part of the TCR have been poorly characterized, and there is only limited knowledge about the TCR usage in non-acute patients. We used antibody staining and flow cytometry to characterize TCR Vbeta usage in CD4+ and CD8+ T cell subsets in blood and BAL fluid samples from different sarcoidosis patient groups as well as from healthy controls. Overall, the TCR Vbeta usage of Valpha2.3 + CD4+ T cells was quite diverse, indicating a predominant role in antigen recognition only for the alpha chain in these T-cell expansions. However, a preference for selective use of Vbeta 22 was noted in one patient. A higher degree of selective Vbeta expression in both BAL and blood of non-acute patients may be due to epitope spreading over time, with more antigenic epitopes available to trigger distinct T cells. The higher non-random TCR Vbeta usage in the lung compared to blood could be related to antigenic triggering at the site of active disease, although more BAL samples of healthy individuals should be analyzed to estimate the normal differences between lung and blood in this respect.