Abstract:
The pathology of ankylosing spondylitis, reactive arthritis, and other spondyloarthopathies (SpA) is closely associated with the human leukocyte class I Ag HLA-B27. A characteristic finding in SpA is inflammation of cartilage structures of the joint, in particular at the site of ligament/tendon and bone junction (enthesitis). In this study, we investigated the role of CD8+ T cells in response to the cartilage proteoglycan aggrecan as a potential candidate autoantigen in BALB/c-B27 transgenic mice. We identified four new HLA-B27-restricted nonamer peptides, one of them (no. 67) with a particularly strong T cell immunogenicity. Peptide no. 67 immunization was capable of stimulating HLA-B27-restricted, CD8+ T cells in BALB/c-B27 transgenic animals, but not in wild-type BALB/c mice. The peptide was specifically recognized on P815-B27 transfectants by HLA-B27-restricted CTLs, which were also detectable by HLA tetramer staining ex vivo as well as in situ. Most importantly, analysis of the joints from peptide no. 67-immunized mice induced typical histological signs of SpA. Our data indicate that HLA-B27-restricted epitopes derived from human aggrecan are involved in the induction of inflammation (tenosynovitis), underlining the importance of HLA-B27 in the pathogenesis of SpA.