Human MHC-II with Shared Epitope Motifs Are Optimal Epstein-Barr Virus Glycoprotein 42 Ligands—Relation to Rheumatoid Arthritis

**Rheumatoid arthritis** (RA) is a chronic systemic autoimmune disorder of unknown etiology, which is characterized by inflammation in the synovium and joint damage. Although the pathogenesis of RA remains to be determined, a combination of environmental (e.g., viral infections) and genetic factors influence disease onset. Especially genetic factors play a vital role in the onset of disease, as the heritability of RA is 50–60%, with the human leukocyte antigen (HLA) alleles accounting for at least 30% of the overall genetic risk. Some HLA-DR alleles encode a conserved sequence of amino acids, referred to as the shared epitope (SE) structure. By analyzing the structure of a HLA-DR molecule in complex with Epstein-Barr virus (EBV), the SE motif is suggested to play a vital role in the interaction of MHC II with the viral glycoprotein (gp) 42, an essential entry factor for EBV. EBV has been repeatedly linked to RA by several lines of evidence and, based on several findings, we suggest that EBV is able to induce the onset of RA in predisposed SE-positive individuals, by promoting entry of B-cells through direct contact between SE and gp42 in the entry complex.

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EBV and Gp42: Links to Rheumatoid Arthritis and Shared Epitope

Abstract

Rheumatoid arthritis (RA) is a chronic inflammatory disease of the joints that can lead to permanent damage and disability. The etiology of RA is complex and includes genetic, environmental, and immunological factors. The shared epitope (SE) is a genetic marker associated with susceptibility to RA in several populations. The EBV-Gp42 complex has been proposed as a potential antigen that could contribute to the pathogenesis of RA. In this review, we explore the evidence linking EBV and Gp42 to RA, focusing on the role of the SE in the regulation of EBV-Gp42 expression and the potential mechanisms by which EBV-Gp42 might contribute to RA. We also discuss the implications of these findings for the development of therapeutic strategies for RA.

Keywords: Epstein-Barr virus, Glycoprotein 42, Rheumatoid arthritis, Shared epitope

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