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CD40-CD40 ligand interactions in experimental allergic encephalomyelitis and multiple sclerosis

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Abstract

We investigated the role of CD40-CD40 ligand (CD40L) interactions in multiple sclerosis (MS) and experimental allergic encephalomyelitis (EAE). Activated helper T cells expressing CD40L (gp39) surface protein were found in MS patient brain sections, but not in brain tissue sections of normal controls or patients with other neurological disease. CD40L-positive cells were co-localized with CD40-bearing cells in active lesions (perivascular infiltrates). Most of these CD40-bearing cells proved to be of the monocytic lineage (macrophages or microglial cells), and relatively few were B cells. To functionally evaluate CD40-CD40L interactions, EAE was elicited in mice by means of proteolipid-peptide immunization. Treatment with anti-CD40L monoclonal antibody completely prevented the development of disease. Furthermore, administration of anti-CD40L monoclonal antibody, even after disease onset, shortly before maximum disability score was reached led to dramatic disease reduction. The presence of helper T cells expressing CD40L in brain tissue of MS patients and EAE animals, together with the functional evidence provided by successful experimental prevention and therapy in an animal model, indicates that blockade of CD40-CD40L-mediated cellular interactions may be a method for interference in active MS.

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