Cell Type Specific Expression of Tumor Necrosis Factor-α in the CNS and Pituitary of Transgenic Mice


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275 Proinflammatory Cytokines, Neurotrophic Factors, and Reactive Astroglialosis during CNS Trauma
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Following injury to the adult CNS, astrocytes become reactive and produce neurotrophic factors in what appears to be a failed attempt to promote recovery. Identification of the molecular mediators of this process known as astroglialis is necessary in order to establish suitable conditions for axonal regeneration and remyelination. In a corticectomy model of injury in adult mice, proinflammatory cytokines IL-1 and TNF-α mRNA levels become elevated within 1 hour as measured by RT-PCR. By in situ hybridization, IL-1 is localized in a specific population of cells around the injury site and within the corpus callosum. This elevation of proinflammatory cytokines precedes the rise in GFAP mRNA, the earliest discernible manifestation of astroglialis, and the upregulation of neurotrophic factor transcripts such as CNF. Current experiments test the hypothesis that proinflammatory cytokines activate astrocytes to become reactive and influence their production of neurotrophic factors.

276 Expression of the Anaphylatoxin C5a Receptor by Glial Cells and T Lymphocytes in Experimental Allergic Encephalomyelitis
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In this study, we investigated the expression of the C5aR in spinal cords of Lewis rats with experimental allergic encephalomyelitis (EAE). Using in situ hybridization (ISH) we analyzed the kinetics of C5aR expression at different time points of EAE (preclinical stage, clinical peak, remission phase). While C5aR mRNA was constitutively expressed at variable low levels in neurons, some blood vessels and a subpopulation of astrocytes in healthy control rats, it was markedly detected in inflammatory cells invading the CNS at the all stages of EAE. Using a combination of ISH and immunohistochemistry we identified multiple cell types expressing the C5aR in the CNS of EAE rats. Based on cell morphology the C5aR mRNA was localized in activated microglial cells and round ED1-positive cells corresponding to monocytes/macrophages. In addition, hypertrophic astrocytes strongly expressed both C5aR mRNA and GFAP particularly during disease remission. Surprisingly, C5aR mRNA was also detected in infiltrating T lymphocytes recognized by an anti-TCR antibody. The potential involvement of C5aR and its receptor in cell trafficking and activation of CNS immunocompetent cells is discussed.

277 Inhibition of IFN-gamma Induced Class II Transactivator and Class II MHC Expression in Microglia
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Microglia are the brain's resident macrophage and when activated have functions including cytokine production and antigen presentation. The class II genes in the major histocompatibility complex (MHC) locus encode proteins that present antigen to CD4+ T-cells, leading to their activation and the development of an antigen specific immune response. In microglia, class II MHC expression is upregulated by interferon-γ (IFN-γ). Class II MHC gene expression is controlled by the class II transactivator (CIITA) transcription factor. IFN-γ induced expression of the CIITA gene is controlled by one of its four promoters (Promoter IV). In this study, we investigated the effects of TGF-β1, IL-4, and IL-10 on IFN-γ induced class II MHC and CIITA expression. By FACS analysis, we show that IFN-γ induced class II MHC protein expression is down-regulated by TGF-β1, IL-4 and IL-10. Using a RT-PCR assay, we show that TGF-β1, IL-4 and IL-10 inhibit CIITA mRNA and IFN-γ induced class II MHC mRNA expression. Studies are ongoing to understand the molecular mechanisms underlying the inhibitory effects of these cytokines.