PERIPHERAL NEUROPATHY ORCHESTRATED BY NONNEURAL-SPECIFIC T LYMPHOCYTES.

A. Hess1, H. Insol1, S. Sessler2, S. Schwender2 and R. Dersch2

1Inst. f. Virologie und Immunobiologie and 2ZentraIabor des Medizinischen Klinik der Universität Würzburg, Germany

Introduction: Intracerebral injection of Lewis (LEW) rats with the murine carcinoma J774 (JHMV) typically results in a demyelinating encephalomyelitis accompanied by a mononuclear, paralytic disease. In contrast, no clinical signs can be observed in JHMV infected Brown Norway (BN) rats. In both rat strains CD2+ T-lymphocytes contribute considerably to the inflammatory infiltrate in virus-infected CNS lesions.

Phenotypic and functional properties of these CD2+ T-cells were characterized by flow cytometry and determination of virus-specific cell mediated cytotoxicity at different times past infection. In LEW rats, in average (±SEM) more CD2+ T-lymphocytes were recovered from the CNS compared to the BN rat population. Nevertheless, in both rat strains the majority of these cells is characterized by the loss of the CD4+ antigen, indicating a primed or activated state. In LEW rats maximal infiltrating and tissue destruction as well as clinical symptoms correlate with the climax of clinical symptoms. In BN rats, however, the overall killing capacity of CNS extracted leukocytes is considerably lower compared to LEW rats throughout the infection.

From these data we conclude that CD2+ T-cells could contribute to neurological disease by virus-infected targets in the CNS of LEW rats. This idea is further supported by experiments using irradiated LEW rats that were reconstituted by a purified fraction of naive CD2+ T-lymphocytes before infection. These animals developed enhanced neurological disorders and succumbed earlier to the infection compared to irradiated but not reconstituted animals.

B CELL ACTIVITY IN IMMUNE-MEDIATED NEUROPATHIES: CELLULAR PROCESSING AND IMMUNE-MEDIATED INNERVATION THROUGH CO-MONITORING USING FLOW CYTOMETRY.

C. Heidenreich and R. Behrendt

Department of Neurology, Heinrich-Heine-Universität Düsseldorf, Germany

LIMTED RESTRICTION IN μ/CTR USAGE OF T CELL CLONES SPECIFIC FOR MBP IN PHA-P, EBV, AND LPS ACTIVATION.

S. Heemken, G. K. P. van der Maas and H. M. Metzger

Departments of Neurology and Immunology, University of Utrecht, The Netherlands.

B CELL ACTIVITY IN IMMUNE-MEDIATED NEUROPATHIES: CELLULAR PROCESSING AND IMMUNE-MEDIATED INNERVATION THROUGH CO-MONITORING USING FLOW CYTOMETRY.

C. Heidenreich and R. Behrendt

Department of Neurology, Heinrich-Heine-Universität Düsseldorf, Germany

Introduction: We have previously reported on pokeweed mitogen (PWM) induced synthesis of anti-ganglioside GM1 antibodies (anti-GM1) by peripheral blood mononuclear cells (PBMC) from patients with the acute Guillain-Barré syndrome (GBS) and with multifocal motor neuropathy (MMN) (Heidenreich et al., 1995). The aim of the present study was to confirm these findings and to extend observations to other immune-mediated neurological diseases using a panel of monoclonal antibodies (Mabs) to identify a specific repertoire.

Methods: PBMC were depleted of CD2+ T-cells and CD5+ B-cells by magnetic cell separation. Anti-GM1 synthesis in culture supernatants was quantitated by ELISA. PBMC were also stimulated by a monoclonal antibody to CD2 (CD2-mab) or entoroxin T cell receptor mab with or without interleukin (IL) 2, 4, 5 and 6.

Results: PWM induced anti-GM1 synthesis was inhibited by depletion of T-cells from PBMC, but could be restored in a mixed assay requires CD2 contact of T-cells. Anti-GM1 synthesis after depletion of CD5+ B-cells was not reduced as compared to unseparated cells. In 5 patients anti-GM1 secretion was greatly stimulated in the CD2-mab, whereas entoroxin T cell receptor mabs with or without interleukins (IL) 2, 4, 5 and 6.

Conclusions: These results demonstrate requirement of activated T-cells for in vitro synthesis of anti-GM1 and are in agreement with the hypothesis of non-activated (bystander) T-cell help to ganglioside GM1 specific B cells in MMN and GBS.

B CELL ACTIVITY IN IMMUNE-MEDIATED NEUROPATHIES: CELLULAR PROCESSING AND IMMUNE-MEDIATED INNERVATION THROUGH CO-MONITORING USING FLOW CYTOMETRY.

C. Heidenreich and R. Behrendt

Department of Neurology, Heinrich-Heine-Universität Düsseldorf, Germany

Introduction: We have previously reported on pokeweed mitogen (PWM) induced synthesis of anti-ganglioside GM1 antibodies (anti-GM1) by peripheral blood mononuclear cells (PBMC) from patients with the acute Guillain-Barré syndrome (GBS) and with multifocal motor neuropathy (MMN) (Heidenreich et al., 1995). The aim of the present study was to confirm these findings and to extend observations to other immune-mediated neurological diseases using a panel of monoclonal antibodies (Mabs) to identify a specific repertoire.

Methods: PBMC were depleted of CD2+ T-cells and CD5+ B-cells by magnetic cell separation. Anti-GM1 synthesis in culture supernatants was quantitated by ELISA. PBMC were also stimulated by a monoclonal antibody to CD2 (CD2-mab) or entoroxin T cell receptor mab with or without interleukin (IL) 2, 4, 5 and 6.

Results: PWM induced anti-GM1 synthesis was inhibited by depletion of T-cells from PBMC, but could be restored in a mixed assay requires CD2 contact of T-cells. Anti-GM1 synthesis after depletion of CD5+ B-cells was not reduced as compared to unseparated cells. In 5 patients anti-GM1 secretion was greatly stimulated in the CD2-mab, whereas entoroxin T cell receptor mabs with or without interleukins (IL) 2, 4, 5 and 6.

Conclusions: These results demonstrate requirement of activated T-cells for in vitro synthesis of anti-GM1 and are in agreement with the hypothesis of non-activated (bystander) T-cell help to ganglioside GM1 specific B cells in MMN and GBS.

B CELL ACTIVITY IN IMMUNE-MEDIATED NEUROPATHIES: CELLULAR PROCESSING AND IMMUNE-MEDIATED INNERVATION THROUGH CO-MONITORING USING FLOW CYTOMETRY.

C. Heidenreich and R. Behrendt

Department of Neurology, Heinrich-Heine-Universität Düsseldorf, Germany

Introduction: We have previously reported on pokeweed mitogen (PWM) induced synthesis of anti-ganglioside GM1 antibodies (anti-GM1) by peripheral blood mononuclear cells (PBMC) from patients with the acute Guillain-Barré syndrome (GBS) and with multifocal motor neuropathy (MMN) (Heidenreich et al., 1995). The aim of the present study was to confirm these findings and to extend observations to other immune-mediated neurological diseases using a panel of monoclonal antibodies (Mabs) to identify a specific repertoire.

Methods: PBMC were depleted of CD2+ T-cells and CD5+ B-cells by magnetic cell separation. Anti-GM1 synthesis in culture supernatants was quantitated by ELISA. PBMC were also stimulated by a monoclonal antibody to CD2 (CD2-mab) or entoroxin T cell receptor mab with or without interleukin (IL) 2, 4, 5 and 6.

Results: PWM induced anti-GM1 synthesis was inhibited by depletion of T-cells from PBMC, but could be restored in a mixed assay requires CD2 contact of T-cells. Anti-GM1 synthesis after depletion of CD5+ B-cells was not reduced as compared to unseparated cells. In 5 patients anti-GM1 secretion was greatly stimulated in the CD2-mab, whereas entoroxin T cell receptor mabs with or without interleukins (IL) 2, 4, 5 and 6.

Conclusions: These results demonstrate requirement of activated T-cells for in vitro synthesis of anti-GM1 and are in agreement with the hypothesis of non-activated (bystander) T-cell help to ganglioside GM1 specific B cells in MMN and GBS.

B CELL ACTIVITY IN IMMUNE-MEDIATED NEUROPATHIES: CELLULAR PROCESSING AND IMMUNE-MEDIATED INNERVATION THROUGH CO-MONITORING USING FLOW CYTOMETRY.

C. Heidenreich and R. Behrendt

Department of Neurology, Heinrich-Heine-Universität Düsseldorf, Germany

Introduction: We have previously reported on pokeweed mitogen (PWM) induced synthesis of anti-ganglioside GM1 antibodies (anti-GM1) by peripheral blood mononuclear cells (PBMC) from patients with the acute Guillain-Barré syndrome (GBS) and with multifocal motor neuropathy (MMN) (Heidenreich et al., 1995). The aim of the present study was to confirm these findings and to extend observations to other immune-mediated neurological diseases using a panel of monoclonal antibodies (Mabs) to identify a specific repertoire.

Methods: PBMC were depleted of CD2+ T-cells and CD5+ B-cells by magnetic cell separation. Anti-GM1 synthesis in culture supernatants was quantitated by ELISA. PBMC were also stimulated by a monoclonal antibody to CD2 (CD2-mab) or entoroxin T cell receptor mab with or without interleukin (IL) 2, 4, 5 and 6.

Results: PWM induced anti-GM1 synthesis was inhibited by depletion of T-cells from PBMC, but could be restored in a mixed assay requires CD2 contact of T-cells. Anti-GM1 synthesis after depletion of CD5+ B-cells was not reduced as compared to unseparated cells. In 5 patients anti-GM1 secretion was greatly stimulated in the CD2-mab, whereas entoroxin T cell receptor mabs with or without interleukins (IL) 2, 4, 5 and 6.

Conclusions: These results demonstrate requirement of activated T-cells for in vitro synthesis of anti-GM1 and are in agreement with the hypothesis of non-activated (bystander) T-cell help to ganglioside GM1 specific B cells in MMN and GBS.