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PERIPHERAL NEUROPATHY ORCHESTRATED BY NON-NEURAL-SPECIFIC T LYMBCOTIIIS.

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Neuronal-specific T cells are held to play a pivotal role in the Guillain-Barré syndrome, and experimental allergic neuritis (EAN). Here, the effects of intravenous accumulation of nonneural-specific T cells on blood-nerve barrier permeability and peripheral nerve function were assessed. Rat ovalbumin (OA)-specific T cells were activated in vitro on day 0 intravenously transferred to female adult Lewis rats. Rats were then given intravenous injections of OA or casein into left and right tibial nerves respectively. On days 3 and 4, selected rats also received intravenous purified immunoglobulin from rabbits with myelin-induced EAN.

Rapid accumulation of O/A T cells and ED1 macrophages and marked increases in blood-nerve barrier permeability in OA but not casein injected nerves followed transfer of 2x10^6 T cells. 5x10^6 T cells induced decreases in proximal/distal CMAP amplitude ratios but also severe reductions in distal CMAP amplitudes and Wallerian degeneration in OA nerves. Denerviation was occasionally observed in nerves proximal to sites of OA injection. 5x10^6 T cells also induced decreases in amplitude ratio but with only minor axonal degeneration and reductions in distal amplitudes. Constriction block and denervation were considerably augmented in animals also receiving anti-myelin antibody.

Intravenous accumulation of nonneural-specific T cells can orchestrate denervation, axonal degeneration, or both.

U1.03

PHENOTYPIC AND FUNCTIONAL PROPERTIES OF CD4+ T-LYMPHOCYTES FROM THE BCSFB IN CNS-RATS WITH CORONAVIRUS-INDUCED ENCEPHALOMYELITIS

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Intracerebral injection of Lewis (LEW) rats with the murine coronavirus HM (JHMV) typically results in a demyelinating encephalomyelitis accompanied by a necrotic, paralytic disease. In contrast, no clinical signs can be observed in JHMV infected Brown Norway (BN) rats. In both rat strains CD4+ T-lymphocytes contribute significantly to the inflammatory infiltrate in virus-induced CNS lesions.

Phenotypic and functional properties of these CD4+ T cells were characterized by flow cytometry and determination of virus-specific cell mediated cytoxicity at different times post infection. In LEW rats, in average 10-times more CD4+ 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 lack of the CD45RC molecule, indicating a primed or activated state. In LEW rats maximal infiltration of these lymphocytes as well as maximal cytoxic activity coincides with the climax of clinical symptoms. In BN rats, however, the overall killing capacity of CNS and peripheral effector cells was lower compared to LEW rats throughout the infection.

From these data we conclude that CD4+ 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 pure CD4+ T cells. This fraction developed enhanced neurological disorders and succumbed earlier to the infection compared to irradiated but not reconstituted animals.

P06.07

LIMITED RESTRICTION IN a3b7b TCR USAGE OF T CELL CLONES SPECIFIC FOR MBP (i.e., BA-90-12-4 and R56-182a) IN HLA-DR1 HOMOGEOUS INDIVIDUALS.

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In order to study the TCR repertoire in response to a given specific peptide/MHC complex, we have taken advantage of a panel of pairs of HLA identical individuals having various levels of relation ranging from monogenic to unrelated individuals. These have been previously defined by PC11 analysis showing the direct correlation between the level of relatedness and the concordance of the corresponding peripheral a3b7b TCR repertoire. By limiting dilution we have generated a panel of T cell clones specific for either MBP a.a. 94-102 or SI05 hap a.a. 3-13. The overall repertoire between, as well as within individuals, were diverse in the Vb region usage and the composition of the CDR3 regions. However, within particular individuals there appeared to be some intra-individual limited restriction. This is illustrated by the occurrence of certain V-b and J-b genes being used by multiple clones from one, or a pair of individuals which are not found or are very limited in the other pairs. On the whole, there was a limited conservation in the response to the different peptides. A high frequency of Vb 2.4, 2, and 7 responded to MBP, whereas these regions were not found in the hap clones. Also, some similarities could be seen in the a3 composition in the CD DR's CDR2 region and Vb specificity, regardless of the individual from which they were isolated. This suggests that there is a selection for these particular CDR3 regions in combination with certain V regions, and that they probably share some structural similarity in the manner of recognition allowing these a3 to contact the peptide/MHC complex in a similar a3m.