Lymph node-derived donor encephalitogenic CD4+ T cells in C57BL/6 mice adoptive transfer experimental autoimmune encephalomyelitis highly express GM-CSF and T-bet.

Abstract:
Experimental autoimmune encephalomyelitis (EAE) is a relevant animal model for the human demyelinating inflammatory disorder of the central nervous system (CNS), multiple sclerosis (MS). Induction of EAE by adoptive transfer allows studying the role of the donor T lymphocyte in disease pathogenesis. It has been challenging to reliably induce adoptive transfer EAE in C57BL/6 (H-2b) mice. The goal of this study was to develop a reproducible and high yield protocol for adoptive transfer EAE in C57BL/6 mice. A step-wise experimental approach permitted us to develop a protocol that resulted in a consistent relatively high disease incidence of ~70% in recipient mice. Donor mice were immunized with myelin oligodendrocyte glycoprotein (MOG)p35-55 in complete Freund's adjuvant (CFA) followed by pertussis toxin (PT). Only lymph node cells (LNC) isolated at day 12 post immunization, and restimulated in vitro for 72 hours with 10 \textmu g/mL of MOGp35-55 and 0.5 ng/mL of interleukin-12 (IL-12) were able to transfer disease. The ability of LNC to transfer disease was associated with the presence of inflammatory infiltrates in the CNS at day 12. Interferon gamma (IFN?) was produced at comparable levels in cell cultures prepared from mice at both
day 6 and day 12 post immunization. By contrast, there was a trend towards a negative association between IL-17 and disease susceptibility in our EAE model. The amount of GM-CSF secreted was significantly increased in the culture supernatants from cells collected at day 12 post immunization versus those collected at day 6 post-immunization. Activated CD4+ T cells present in the day 12 LNC cultures maintained expression of the transcription factor T-bet, which has been shown to regulate the expression of the IL-23 receptor. Also, there was an increased prevalence of MOGp35-55-specific CD4+ T cells in day 12 LNC after in vitro re-stimulation. In summary, encephalitogenic LNC that adoptively transfer EAE in C57BL/6 mice were not characterized by a single biomarker in our study, but by a composite of inflammatory markers. Our data further suggest that GM-CSF expression by CD4+ T cells regulated by IL-23 contributes to their encephalitogenicity in our EAE model.

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