The NF-κB regulator MALT1 determines the encephalitogenic potential of Th17 cells.

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Effector functions of inflammatory IL-17-producing Th (Th17) cells have been linked to autoimmune diseases such as experimental autoimmune encephalomyelitis (EAE), a mouse model of multiple sclerosis (MS). However, what determines Th17 cell encephalitogenicity is still unresolved. Here, we show that after EAE induction, mice deficient for the NF-κB regulator MALT1 (Malt1−/− mice) exhibit strong lymphocytic infiltration in the CNS, but do not develop any clinical signs of EAE. Loss of Malt1 interfered with expression of the Th17 effector cytokines IL-17 and GM-CSF both in vitro and in vivo. In line with their impaired GM-CSF secretion, Malt1−/− Th cells failed to recruit myeloid cells to the CNS to sustain neuroinflammation, whereas autoreactive WT Th cells successfully induced EAE in Malt1−/− hosts. In contrast, Malt1 deficiency did not affect Th1 cells. Despite their significantly decreased secretion of Th17 effector cytokines, Malt1−/− Th17 cells showed normal expression of lineage-specific transcription factors. Malt1−/− Th cells failed to cleave RelB, a suppressor of canonical NF-κB, and exhibited altered cellular localization of this protein. Our results indicate that MALT1 is a central, cell-intrinsic factor that determines the encephalitogenic potential of inflammatory Th17 cells in vivo.

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