MAPK3 deficiency drives autoimmunity via DC arming.

DC are professional APC that instruct T cells during the inflammatory course of EAE. We have previously shown that MAPK3 (Erk1) is important for the induction of T-cell anergy. Our goal was to determine the influence of MAPK3 on the capacity of DC to arm T-cell responses in autoimmunity. We report that DC from Mapk3(-/-) mice have a significantly higher membrane expression of CD86 and MHC-II and--when loaded with the myelin oligodendrocyte glycoprotein--show a superior capacity to prime naïve T cells towards an inflammatory phenotype than Mapk3(+/+) DC. Nonetheless and as previously described, Mapk3(-/-) mice were only slightly but not significantly more susceptible to myelin oligodendrocyte glycoprotein-induced EAE than WT littermate mice. However, Mapk3(+/+) mice engrafted with Mapk3(-/-) BM (KO-->WT) developed a severe form of EAE, in direct contrast to WT-->KO mice, which were even less sick than control WT-->WT mice. An infiltration of DC and accumulation of Th17 cells was also observed in the CNS of KO-->WT mice. Therefore, triggering of MAPK3 in the periphery might be a therapeutic option for the treatment of neuroinflammation since absence of this kinase in the immune system leads to severe EAE.