The Transcription Factor NFAT1 Regulates Dendritic Cell Activation and Systemic Autoimmunity

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Transcription factor nuclear factor of activated T cells (NFAT) plays a pivotal role in maintaining lymphocyte homeostasis. Modulation of NFAT activity has been considered as an important target to suppress diverse hyper-immune disorders. Myasthenia gravis (MG) is a systemic autoimmune disease caused by autoantibodies specific for nicotinic acetylcholine receptor (AChR) at the neuromuscular junction (NMJ). CD4+ T cells have crucial roles in the development of MG. Although the importance of NFAT in CD4+ T cells activation and differentiation has been intensively studied, the role of NFAT in progression and pathogenesis of MG is still poorly investigated. In this study, we addressed the role of NFAT1 in the development of experimental autoimmune myasthenia gravis (EAMG). NFAT1 knockout (NFAT1 KO) mice showed higher susceptibility to EAMG development, which was mediated by upregulated effector function of AChR-reactive lymphocytes. NFAT1 KO mice showed increased AChR-reactive lymphocyte proliferation, Th1 and Th17 cells related inflammatory cytokines production and anti-AChR reactive IgG levels. Dendritic cells (DCs) derived from NFAT1-deficient mice showed pre-activated phenotypes that expressed higher levels of costimulatory molecules such as CD40, CD80, CD86 and MHC class II. Furthermore, DCs from NFAT1 KO mice effectively induced increased CD4+ T cells proliferation as compared with wild-type DCs. Our data collectively suggest the deficiency in NFAT1 led to dysregulated DC functions as well as enhanced production of pro-inflammatory cytokines by T cells, which aggravates the progression of EAMG.