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Titel des Beitrags:
2-Methoxyestradiol inhibits experimental autoimmune encephalomyelitis through suppression of immune cell activation.

Abstract:
The endogenous metabolite of estradiol, 2-Methoxyestradiol (2ME2), is an antimitotic and antiangiogenic cancer drug candidate that also exhibits disease-modifying activity in animal models of rheumatoid arthritis (RA). We found that 2ME2 dramatically suppresses development of mouse experimental autoimmune encephalomyelitis (EAE), a rodent model of multiple sclerosis (MS). 2ME2 inhibits in vitro lymphocyte activation, cytokine production, and proliferation in a dose-dependent fashion. 2ME2 treatment of lymphocytes specifically reduced the nuclear translocation and transcriptional activity of nuclear factor of activated T-cells (NFAT) c1, whereas NF-κB and activator protein 1 (AP-1) activation were not adversely affected. We therefore propose that 2ME2 attenuates EAE through disruption of the NFAT pathway and subsequent lymphocyte activation. By extension, our findings provide a molecular rationale for the use of 2ME2 as a tolerable oral immunomodulatory agent for the treatment of autoimmune disorders such as MS in humans.

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