Tailoring hydrogen sulfide as therapeutic target in multiple sclerosis? Upregulation of tolerogenic pathways in dendritic cell and T cells from mice with EAE by the hydrogen sulfide donor GYY4137 and potentially impaired production of endogenous H2S in patients with multiple sclerosis

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May 18, 2020

Abstract

The aim of the study was to examine the in vitro effects of the slow-releasing H2S donor GYY4137 on immune cells involved in the pathogenesis of the central nervous system (CNS) autoimmune disease, multiple sclerosis (MS). GYY4137 specifically potentiated TGF-beta expression and production in dendritic cells and significantly reduced IFN-γ and IL-17 production in the lymph node and spinal cord T cells obtained from mice immunized with CNS antigens. Both the proportion of FoxP3+ regulatory CD4+ T cells in the lymph node cells, and the percentage of IL-17+ CD4+ T cells in the spinal cord cells were reduced upon culturing with GYY4137. Interestingly, peripheral blood mononuclear cells obtained from MS patients had lower expression of the H2S-producing enzyme, 3-mercaptopyruvate-sulfurtransferase (MPST), in comparison to those obtained from healthy donors. A significant inverse correlation between the expression of MPST and several pro-inflammatory factors was also observed. Further studies on the relevance of the observed results for the pathogenesis and therapy of MS are warranted.

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