CALIFORNIA STATE SCIENCE FAIR
2005 PROJECT SUMMARY

Name(s)

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Project Number

S0412

Project Title

Investigating Multiple Sclerosis: Antibodies to CD44 and a4B1 Differentially Affect Myelin-specific T Cell Responses

Abstract

Objectives/Goals

Multiple sclerosis (MS) is a chronic autoimmune disease that affects approximately 2.6 million people around the world. Previous studies have shown that antibodies to adhesion molecules CD44 and integrin a4B1 prevent central nervous system inflammation and ameliorate the clinical symptoms of experimental autoimmune encephalomyelitis, a murine model of MS. However, the effect of these antibodies on the function of myelin-reactive T cells is still unknown. The present study investigates the molecular responses of myelin-reactive T cells to the two antibodies with the hypothesis that the antibodies will decrease secretion of harmful, pro-inflammatory cytokines and increase the secretion of beneficial, anti-inflammatory cytokines # thus, ameliorating the symptoms of MS.

Methods/Materials

T cells from the spleen and lymph nodes of MBP Ac 1-11 TCR transgenic mice were stimulated with varying concentrations of MBP peptide in the absence or presence of anti-CD44 or anti-a4B1. Thereafter, two assays were performed: Enzyme-linked Immunosorbent Assays (ELISAs) to measure cytokine secretion, and antigen-specific T cell proliferation assay.

Results

First, antibodies did not significantly inhibit T cell proliferation. Second, there was an increase in secretion of the immunosuppressive, anti-inflammatory cytokine Interleukin-10 by both antibodies. Converse from the initial hypothesis, there was an up-regulation of pro-inflammatory cytokines interferon-GAMMA, tumor necrosis factor-ALPHA, and interleukin-12 p40 in cells treated with anti-CD44. A literature search was run and it was found that the specific antibody used for CD44 (IM.7.8.1) was stimulatory. Lastly and most importantly, the pro-inflammatory cytokines were down-regulated by anti-a4B1.

Conclusions/Discussion

The results suggest that, though anti-a4B1 and anti-CD44 both prevent EAE, these antibodies differentially affect pro-inflammatory cytokine production by myelin-reactive T cells. Most importantly, the immunosuppressive role of anti-a4B1 makes it a promising therapy for MS. Anti-a4B1 may prevent CNS inflammation and ameliorate symptoms through the regulation of cytokines. Future research will include in vivo assays to confirm the regulation of inflammatory cytokines by the antibodies. Further studies into associated signal transduction pathways and the effects on myelin-reactive T cells will elucidate the antibodies# role as potential MS-specific therapies.

Summary Statement

The effects of antibodies to CD44 and integrin a4B1 on T cell cytokine secretion and proliferation were investigated; anti-a4B1 was discovered to reduce the release of pathological chemicals as a promising therapy for multiple sclerosis.

Help Received

Used lab equipment at Stanford University in the lab of Dr. Lawrence Steinman, under the supervision of Dr. Shalina Ousman; began project with the Center for Clinical Immunology at Stanford Summer Internship Program