



Benjamin M Segal M.D.

Professor
Director, U-M Multiple Sclerosis Center
Director, Holtom-Garrett Program in Immunology
Department of Neurology
Programs in Immunology and Neuroscience
4009 BSRB
109 Zina Pitcher Place
Ann Arbor, MI 48109-2200
(734) 615-5635
bmsegal@umich.edu
[My website](#)



 [Download](#) this page

Research Interests

Our laboratory studies interactions between the immune and nervous systems in the context of autoimmune demyelinating disease. We pose questions about the influence of the CNS microenvironment on the development of local inflammatory responses and, conversely, about the influence of immune mediators on neuronal and glial survival and regeneration/ repair.

Most of our work focuses on the human disease multiple sclerosis (MS, the second most common cause of neurological disability in young adults) and its animal model, experimental autoimmune encephalomyelitis (EAE). MS is believed to be an autoimmune disease in which the immune system mounts an aberrant attack against proteins in the myelin sheath. In EAE, vaccination of laboratory animals with myelin proteins induces multifocal neuroinflammation and a relapsing paralysis that simulates MS. One part of our laboratory is devoted to human immunological studies (involving the analysis of peripheral blood and cerebrospinal fluid mononuclear cells that are collected from patients with MS or other neurological diseases and healthy controls). Currently we are investigating the relationship between the expression of selected cytokines (such as IL-23 and IL-17) and CNS inflammatory disease activity, as detected by advanced MRI techniques, in individuals with progressive multiple sclerosis. A complementary division of our laboratory is dedicated to animal studies. We are investigating the mechanisms by which leukocyte subsets, chemokine and cytokines act together to induce demyelination and neuronal loss. We are also studying the effects of cytokines and chemokines on CNS progenitor cells and axonal regrowth pathways that could affect attempts to repair damaged CNS tissues.

Some of our ongoing projects are on the following topics: (i) the expression pattern and role of the interleukin (IL)-12 p40 family of monokines in secondary progressive

MS; (ii) the role of IL-12 and IL-23 in T cell homing to the CNS and epitope spreading during the course of EAE; (iii) CNS expression and functional significance of lymphoid chemokines, such as CXCL13 and CCL21, in driving the formation of organized inflammatory infiltrates during relapsing EAE and MS; (iv) the origin and biological activities of dendritic cells that accumulate in demyelinating lesions during EAE; (v) the importance of regulatory T cells for remission during relapsing autoimmune demyelination; (vi) the role of neutrophils and the chemokines that attract them in blood-brain-barrier breakdown during EAE; (vii) effects of chemokines and cytokines on neuroprotection and progenitor cell migration/maturation in the mature CNS; (viii) the role of Nogo and neuropilin signaling on leukocyte activation and function.

Selected References

Segal BM, Shevach EM. IL-12 unmasks latent autoimmune disease in resistant mice. *J Exp Med* 1996;184: 771-775.

Segal BM, Dwyer B, Shevach EM. An IL-12/IL-10 immunoregulatory circuit controls susceptibility to autoimmune disease. *J Exp Med* 1998;187: 537-546.

Chang JT, Shevach EM, Segal BM. Regulation of IL-12 receptor $\alpha 2$ subunit expression by endogenous IL-12: A critical step in the differentiation of pathogenic autoreactive T cells. *J Exp Med* 1999;189:969-978.

Segal BM, Glass D, Shevach EM. IL-10-producing CD4⁺ T cells mediate tumor rejection. *J Immunol (Cutting Edge)* 2002;168: 1-4.

Segal BM. CNS chemokines, cytokines, and dendritic cells in autoimmune demyelination. *J Neurol Sci* 2005;228(2): 210-214.

King I, Segal BM. Cutting edge: IL-12 induces CD4⁺CD25⁻ T cell activation in the presence of regulatory T cells. *J Immunol (Cutting Edge)* 2005;175(2): 641-645.

Deshpande P, Segal BM. IL-12 driven upregulation of P-selectin ligand on myelin-specific T cells is a critical step in an animal model of autoimmune demyelination. *J Neuroimmunol* 2006;173(1-2): 35-44.

Bagaeva LV, Rao P, Powers JM, Segal BM. CXCL13 plays a role in experimental autoimmune encephalomyelitis. *J Immunol* 2006;176(12): 7676-7685.

Kroenke MA, Segal BM. Th17 and Th1 responses directed against the immunizing epitope, as opposed to secondary epitopes, dominate the autoimmune repertoire during relapses of experimental autoimmune encephalomyelitis. *J Neurosci Res* 2007;85(8): 1685-1693.

Deshpande P, King IL, Segal BM. Cutting edge: CNS CD11c⁺ cells from mice with encephalomyelitis polarize Th17 cells and support CD25⁺CD4⁺ T cell-mediated immunosuppression, suggesting dual roles in the disease process. *J Immunol* 2007;178(11): 6695-6699.

Find more publications by [Dr. Benjamin Segal](#)
Last updated 10/19/2007 [Click here to update](#)

00043