BIOGRAPHICAL SKETCH

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NAME OF SPONSOR (CO-SPONSOR)	POSITION TITLE
Stephen D. Miller, Ph.D.	Cong. John E. Porter Professor of Microbiology-Immunology; Director, Immunobiology Center
eRA COMMONS USER NAME STEPHENMILLER	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Penn State University, Univ. Park, PA	B.S.	1969	MICROBIOLOGY
Penn State University, Univ. Park, PA	M.S.	1973	IMMUNOLOGY
Penn State University, Univ. Park, PA	PH.D.	1975	IMMUNOLOGY
Univ. of Colorado Medical School	POSTDOC	1975-78	CELL. IMMUNOLOGY

A. Positions and Honors:

POSITIONS:

NIH Postdoctoral Research Fellow (with Henry N. Claman, M.D.), Univ. of Colorado Health Sci. Ctr., Denver, CO, 7/75-6/78

Instructor, Department of Medicine, Division of Clinical Immunology, Univ. of Colorado Health Sciences Ctr., Denver, CO, 7/78-6/80

Assistant Professor, Departments of Medicine and of Microbiology-Immunology, Univ. of Colorado Health Sciences Ctr., Denver, CO, 7/80-6/81

Department of Microbiology-Immunology, Northwestern Univ. Medical School, Chicago, IL, – Professor and Director of The Interdepartmental Immunobiology Center (9/92-Present); Congressman John E. Porter Professor (10/00-Present): Associate Professor (9/86-8/92); Assistant Professor (7/81-8/86)

HONORS:

USPHS Air Pollution Control Graduate Fellowship, 6/69-6/70 & 6/72-6/73

NIH Individual Post Doctoral Fellowship (AI-05593) 10/77-7/78

NIH Young Investigator Award (AI-14913) 8/78-7/81

Member - Honor Society of Phi Kappa Phi (1975); Am. Society for Microbiology (1975); Am. Association of Immunologists (1977); Chicago Association of Immunology (1981); International Society of Neuroimmunology (1987); Am. Assoc. Advancement of Science (1986), Society for Neuroscience (2006)

Editorial Board - *J. Immunology* (1982-85, Section Editor: 1995-2000); *Regional Immunology* (1/92-12/98), *J. Neuroimmunology* (1/94-12/99); *Virology* (2001-Present); *Cellular Immunology* (Deputy Editor, 1999-Present); *Viral Immunology* (2000-Present); *J. Autoimmunity* (2001-Present)

Ad Hoc Reviewer - NINDS Site Visitor, Immunological Sciences and Neurology C Study Sections, National Science Foundation, Veterans Administration, *Science*, *J. Immunology*, *Immunopharmacology*, *Regional Immunology*, *J. Neuroimmunol., J. Virology, J. Clin. Invest., Immunity, J. Exp. Medicine, Nature Med.*

HHMI/NSF Predoctoral Fellowship Immunology and Cell Biology Review Committee (1999-2003, Chair 2002-03)

NIH Neurology C/Neurologic Sciences 3 (NLS 3) Study Section, Regular Member (9/93-6/97)

National Multiple Sclerosis Society Study Section Panel B, Regular Member (1/98-12/03)

NIH – 'Immune Tolerance Network' Steering Committee: 11/01-Pres.

Juvenile Diabetes Research Foundation (JDRF) Immunology Study Section: 01/04-Pres.

National Multiple Sclerosis Society 'Fast Forward' Scientific and Business Advisory Committee: 01/08-Pres.

American Association of Immunologists – Publications Committee: 2000-04 (Chair, 2002-04); Council (*Ad hoc* member; 2002-04)

Pennsylvania State University, Eberly College of Science Outstanding Alumni Science Award: September, 2003

Fellow of the American Association for the Advancement of Science, Elected 10/04

Fellow of the American Academy of Microbiology, Elected 05/07

B. Relevant Peer-Reviewed Publications (selected from 276 total published and in press papers):

McRae, B. L., C. L. Vanderlugt, M. C. Dal Canto, and S. D. Miller. 1995. Functional evidence for epitope spreading in the relapsing pathology of EAE in the SJL/J mouse. *J. Exp. Med. 182:75-85.*

Miller, S. D., C. L. Vanderlugt, D. J. Lenschow, J. G. Pope, N. J. Karandikar, M. C. Dal Canto, and J. A. Bluestone. 1995. Blockade of CD28/B7-1 interaction prevents epitope spreading and clinical relapses of murine EAE. *Immunity. 3:739-745.*

Miller, S. D., C. L. Vanderlugt, W. Smith Begolka, W. Pao, R. L. Yauch, K. L. Neville, Y. Katz-Levy, A. Carrizosa, and B. S. Kim. 1997. Persistent CNS infection with Theiler's virus leads to myelin-specific autoimmunity via epitope spreading. *Nature Med. 3:1133-1136.*

Katz-Levy, Y., K. L. Neville, J. Padilla, S. M. Rahbe, W. S. Begolka, A. M. Girvin, J.K. Olson, C. L. Vanderlugt, and S. D. Miller. 2000. Temporal development of autoreactive Th1 responses and endogenous presentation of self myelin epitopes by CNS-resident APCs in Theiler's virus-infected mice. *J. Immunol. 165:5304-5314*.

Vanderlugt, C. L., T. N. Eagar, K. L. Neville, K. M. Nikcevich, J. A. Bluestone, and S. D. Miller. 2001. Pathologic role and temporal appearance of newly emerging autoepitopes in relapsing experimental autoimmune encephalomyelitis. *J. Immunol. 164:670-678*.

Olson, J. K., A. M. Girvin, and S. D. Miller. 2001. Direct activation of innate and antigen presenting functions of microglia following infection with Theiler's virus. *J. Virol. 75:9780-9789*.

Vanderlugt, C. L. and S. D. Miller. 2002. Role of epitope spreading in immune-mediated diseases: Implications for immunotherapy. *Nat. Rev. Immunol. 2:85-95.*

Tompkins, S. M. and S. D. Miller. 2002. An array of possibilities for MS. *Nat. Med. 8:451-453.*

Neville, K. L., J. Padilla, L. A. Matis, and S. D. Miller. 2002. Myelin-specific tolerance attenuates the progression of a virus-induced demyelinating disease: Implications for the treatment of MS. *J. Neuroimmunol. 123:18-29.*

Croxford, J. L., J. K. Olson, and S. D. Miller. 2002. Epitope spreading and molecular mimicry as triggers of autoimmunity in the Theiler's virus-induced demyelinating disease model of multiple sclerosis. *Autoimmunity Rev. 1:251-260*.

Girvin, A. M., K. B. Gordon, C. J. Welsh, and S. D. Miller. 2002. Differential abilities of CNS-resident endothelial cells and astrocytes to serve as inducible antigen presenting cells. *Blood. 99:3692-3701.*

Kohm, A. P., P. A. Carpentier, H. A. Anger, and S. D. Miller. 2002. ***Cutting Edge:*** $CD4^+CD25^+$ T regulatory cells suppress antigen-specific autoreactive immune responses and CNS inflammation during active experimental autoimmune encephalomyelitis. *J. Immunol. 169:4712-4716.*

Mack, C. L., C. L. Vanderlugt-Castaneda, K. L. Neville, and S. D. Miller. 2003. Microglia are activated to become competent antigen presenting cells and potent effector cells in the inflammatory environment of the Theiler's virus model of multiple sclerosis. *J. Neuroimmunol. 144:68-79.*

Howard, L. M., K. L. Neville, L. M. Haynes, M.C. Dal Canto, and S. D. Miller. 2003. CD154 blockade results in transient reduction in TMEV-induced demyelinating disease. *J. Virol. 77:2247-2250.*

Olson, J. K. and S. D. Miller. 2004. Microglia initiate CNS innate and adaptive immune responses through multiple Toll-like receptors. *J. Immunol. 173:3916-3924.*

Carpentier, P. A., W. S. Begolka, J. K. Olson, A. Elhofy, W. J. Karpus, and S. D. Miller. 2005. Differential activation of astrocytes by innate and adaptive immune stimuli. *Glia 49:360-374.*

McMahon, E. J., S. L. Bailey, C. L. Vanderlugt-Castenada, H. Waldner, and S. D. Miller. 2005. Epitope spreading initiates in the CNS in two mouse models of multiple sclerosis. *Nature Med. 11:335-339.*

***Croxford, J. L., J. K. Olson*, H. A. Anger, and S. D. Miller.** 2005. Initiation and exacerbation of CNS autoimmune demyelination via virus-induced molecular mimicry: Implications for MS pathogenesis. *J. Virol. 79:8581-8590.* (*Co-first authors)

Smith, C. E., T. N. Eagar, J. Strominger, and S. D. Miller. 2005. Differential induction of IgE-mediated anaphylaxis after soluble vs. cell-bound tolerogenic peptide therapy of autoimmune encephalomyelitis. *Proc. Natl. Acad. Sci. USA. 102:9595-9600.*

Melvold, R. W. and S. D. Miller. 2005. Immunogenetics/resistance/susceptibility to Theiler's virus infection. In: *Experimental Models of Multiple Sclerosis* (E. Lavi and S. Constantinescu, eds.). Kulwer Academic Publishers, London. *Pp. 629-644*.

Kohm, A. P., J. S. Williams, A. L. Bickford, J. S. McMahon, L. Chatenoud, J. F. Bach, J. A. Bluestone, and S. D. Miller. 2005. Treatment with non-mitogenic anti-CD3 antibody induces $CD4^+$ T cell unresponsiveness and functional reversal of established autoimmune disease. *J. Immunol*. *174:4525-4534*

Kohm, A. P., J. S. McMahon, J. R. Podojil, W. Smith Begolka, M. Degutes, D. J. Kasprowicz, S. F. Ziegler, and S. D. Miller. 2006. ***Cutting Edge:*** Anti-CD25 monoclonal antibody injection results in the functional inactivation, not depletion, of $CD4^+CD25^+$ T regulatory cells. *J. Immunol. 176:3301-3305.**)***

Bailey, S. L., P. A. Carpentier, E. J. McMahon, W.S. Begolka, and S. D. Miller. 2006. Innate and adaptive immune responses of the central nervous system. *Crit. Rev. Immunol. 26:149-188.*

Ercolini, A. M. and S. D. Miller. 2006. ***Brief Review:*** Mechanisms of immunopathology in murine models of CNS demyelinating disease. *J. Immunol. 176:3293-3298.*

Lin, W., S. L. Bailey, H. Ho, H. P. Harding, D. Ron, S. D. Miller, and B. Popko. 2007. The integrated stress response protects oligodendrocytes against immune-mediated demyelination. *J. Clin. Invest. 117:448-456.*

Balabanov, R., K. Strand, R. Goswami, E. McMahon, W. Smith Begolka, S. D. Miller, and B. Popko. 2007. Interferon-gamma-oligodendrocyte interactions in the regulation of EAE. *J. Neurosci. 27:2013-2024.*

Carpentier, P. A., B. R. Williams, and S. D. Miller. 2007. Distinct roles of PKR and TLR3 in the activation of astrocytes by viral stimuli. *Glia. 55:239-252*.

Schreiner, B., S. M. Bailey, and S. D. Miller. 2007. T cell response dynamics in animal models of multiple sclerosis: Implications for immunotherapies*. Expert Rev. Clin. Immunol. 3:57-72.*

Turley, D. M. and S. D. Miller. 2007. Peripheral tolerance induction using ECDI-fixed APCs uses both direct and indirect mechanisms of antigen presentation for prevention of EAE. *J. Immunol. 178:2212-2220.*

Bailey, S. L., B. Schreiner, E. J. McMahon, and S. D. Miller. 2007. CNS myeloid dendritic cells presenting endogenous myelin peptides preferentially polarize $CD4^+$ Th17 cells in relapsing EAE. *Nat. Immunol. 8:172-180.*

Teague Getts, M. T., B. S. Kim, and S. D. Miller. 2007. Differential outcome of tolerance induction in naïve vs. activated Theiler's virus epitope-specific $CD8^+$ cytotoxic T cells. *J. Virol. 81:6584-6593.*

Miller, S. D., D. M. Turley, and J. R. Podojil. 2007. Antigen-specific tolerance strategies for the prevention and treatment of autoimmune disease. *Nat. Rev. Immunol. 7:665-677.*

Ercolini, A. M. and S. D. Miller. 2007. Molecular mimics can induce novel self peptide-reactive $CD4^+$ T clonotypes in autoimmune disease. *J. Immunol. 179:6604-6612*

***Carpentier, P. A., D. S. Duncan*, and S. D. Miller.** 2008. Glial Toll-like receptor signaling in central nervous system infection and autoimmunity. *Brain Behav. Immun. 22:140-147.* (*co-first authors)

Carpentier, P. A. and S. D. Miller. 2008. Pro-inflammatory functions of astrocytes correlate with viral clearance and strain-dependent protection from TMEV-induced demyelinating disease. *Virology. In press.*

Bailey-Bucktrout, S. L., S. Caulkins, G. Goings, J. A. Fischer, A. Dzionek, and S. D. Miller. 2008. ***Cutting Edge:*** CNS plasmacytoid dendritic cells regulate the severity of relapsing experimental autoimmune encephalomyelitis. *J. Immunol. In press*

C. Research Support:

ONGOING RESEARCH SUPPORT

R01 NS-030871-14	07/08/06-05/31/11
NIH/NINDS (S. D. Miller, P. I.)	
Pathogenesis and Immunoregulation of PLP-Induced R-EAE	
Examines: (1) temporal progression, effector role, TCR repertoire, and epitope spreading of peripheral and CNS Th1/Th2 responses in mice with relapsing, chronic and acute EAE; and (2) peripheral and CNS-resident APC population involved in presenting endogenous myelin epitopes to naïve and activated T cells in EAE	

RG 3793-A-7	04/01/06-03/31/09
National Multiple Sclerosis Society (S. D. Miller, P. I.)	
Pathogenesis and Immunoregulation of PLP-Induced R-EAE	
80% overlap with NIH NS-030871-14 above - provides a supplement to support 75% of a research tech.	

R01 NS-026543-18	05/01/07-04/30/12
NIH (S.D. Miller, P.I.)	
Immunoregulation and Pathology of Chronic-Relapsing EAE	
Examines: (1) *in vivo* mechanisms responsible for Ag-SP tolerance induced by peptide-pulsed, ECDI-fixed APCs; (2) direct effects of *in vitro* tolerogenic vs. immunogenic encounter on Th1/Th2/Th17 cytokine production and induction of $CD^+CD25^+Foxp3^+$ Treg cells; and (3) effects of Ag-SP tolerance on signaling events in APCs and tolerized T cells.	

RG 3965-A-8	04/01/07-03/31/10
NMSS (S.D. Miller, P.I.)	
Immunoregulation and Pathology of Chronic-Relapsing EAE	
90% overlap with NIH R01 NS-026543-18 above – provides supplement to support a postdoctoral fellow.	

R01NS-048411-04	12/01/04-11/30/08
NIH/NINDS (S. D. Miller, P. I.)	
Mechanisms of $CD4^+CD25^+$ T Regulatory Cells in EAE	

Examines: (1) role of $CD4^+CD25^+$ Treg cells in modulating the initiation and progression of EAE; (2) contribution of $CD4^+CD25^+$ Tregs to age-, gender-, and strain-associated susceptibility to EAE; and (3) mechanism by which $CD4^+CD25^+$ Tregs influence T cell activation, expansion and/or effector function.

RO1 NS-040460-08	08/03/05-05/31/09
NIH/NINDS (S. D. Miller, P. I.)	
A Virus-Induced Molecular Mimicry Model of MS	
Examines: (1) efficiency of autoreactive T cell activation, T cell repertoire, and induction of demyelinating disease following infection with TMEV and non-neurotropic viruses encoding molecular mimics of $PLP_{139-151}$; (2) activation/regulation of autoimmune responses and clinical disease in humanized HLA-$DR2^b$/MBP_{85-99}-specific TcR Tg mice with TMEV encoding mimics of MBP_{85-99}; and (3) activation of autoimmune responses and clinical disease in SJL mice following infection with *H. influenzae* expressing a natural mimic of $PLP_{139-151}$.	

P01 NS-023349-21	02/15/03-11/30/08 **No-Cost Ext.**
NIH/NINDS (S.D. Miller, Program Director and PI Project 1 + Admin. Core A + Histopathology Core C)	
CNS Damage from Theiler's Virus Persistence: MS Model	
PPG examines the molecular pathogenesis and immunopathogenesis of TMEV-induced demyelinating disease. Project 1 aims are (1) to examine the effector role, T cell receptor repertoire usage, and fine antigenic specificity of peripheral virus- and neuroantigen-specific immune responses at varying times following TMEV infection (2) analysis of T cell specificity and APC function of CNS-infiltrating T cells in TMEV-infected mice (3) efficacy, specificity and molecular mechanisms of regulation of virus-induced demyelination using specific tolerance and antagonists of B7/CD28-mediated costimulation.	

SM MRF0104	07/01/04-06/30/11
Myelin Repair Foundation (S. D. Miller, P. I.)	
Promotion of Oligodendrocyte Regeneration and CNS Remyelination	
Examines: (1) the temporal expression of myelin genes during R-EAE and TMEV-IDD; (2) temporal and spatial expression of molecules important in directing and/or regulating myelination/re-myelination (*e.g.,* Notch family members, Jagged, Serrate, Sonic hedgehog, BMP4, CxCL1, CxCR2) during R-EAE and TMEV-IDD; (3) the effect of γ-secretase (Notch) inhibitors on the course of EAE and TMEV-induced demyelinating disease; and (4) treatment of EAE combining immunoregulation with drugs enhancing myelin repair.	

SM FF-02	04/01/06-03/31/09 **No-Cost Ext.**
Fidelity Foundation (S. D. Miller, P. I.)	
Role of Specific Immunoregulation and Oligodendrocyte Stem Cell Transfer in Promoting Clinical Disease Amelioration and Remyelination in EAE	
Examines: (1) immunological and (2) neurobiological effects of GFP-labeled neurospheres in mice with R-EAE and C-EAE; and (3) combined effects of immunoregulation and stem cell therapy in R-EAE and C-EAE.	

200511934	09/01/06-07/31/08
CombinatoRx, Inc. (S. D. Miller, P. I.)	
Combination Therapy of R-EAE with Nortiptyline and Desloratadine	
Examines effects of combination therapy of R-EAE with nortiptyline and desloratadine on R-EAE.	

RG-3546-A-1	04/01/04-03/31/08 **No Cost Ext.**
National Multiple Sclerosis Society (S. D. Miller, P. I.)	
Understanding the Role of Gamma/Delta T Cells in Relapsing EAE	
Examines: (1) peripheral $\gamma\delta$ T cell responses in EAE and their migration to and function in the CNS; (2) influence of $\gamma\delta$ T cells on encephalitogenic T cell responses and EAE induction; and (3) mechanisms by with $\gamma\delta$ T cells modulate $\alpha\beta$ $CD4^+$ encephalitogenic T cells.	

1-2007-1055	09/01/07-08/31/10
Juvenile Diabetes Res. Foundation (S. D. Miller, P. I.)	
Creating an Immune Privileged Site for Islet Transplantation	
Examines: (1) efficacy of ECDI-fixed cell tolerance for islet and allo-antigens for the treatment of T1D in NOD mice and for induction of tolerance to allogeneic islets; (2) role of *ex vivo*-induced Tregs in allogeneic islet cell transplantation	

2 T32 AI-0007476-09-11A1	09/01/07-08/31/12
NIH/NIAID (S. D. Miller, P. I.)	
Immunology and Molecular Pathogenesis Training Program	