



Raymond A. Sobel, M.D.

Professor of Pathology

 NIH Biosketch available Online

 Curriculum Vitae available Online

Bio

BIO

Dr. Sobel is a Board Certified neuropathologist who has practiced academic neuropathology service and teaching for 40 years. His research interests are primarily in immune responses in the central nervous system as they relate to the pathogenesis of multiple sclerosis.

ACADEMIC APPOINTMENTS

- Professor, Pathology
- Member, Wu Tsai Neurosciences Institute

HONORS AND AWARDS

- Associate Editor, Journal of Neuropathology and Experimental Neurology (2005-2007)
- Editor-in-Chief, Journal of Neuropathology and Experimental Neurology (2007-2016)
- President, American Association of Neuropathologists (2011-2012)
- Award for Meritorious Contributions to Neuropathology, American Association of Neuropathologists (June 8 2019)

PROFESSIONAL EDUCATION

- M.D., UCSF , Medicine (1976)

Research & Scholarship

CURRENT RESEARCH AND SCHOLARLY INTERESTS

The lab is concerned with mechanisms of cellular immune reactions and tissue injury in the central nervous system (CNS) as they occur in human multiple sclerosis (MS). CNS tissue samples from animals with experimental autoimmune encephalomyelitis (EAE), a model of MS, and from patients with MS and other CNS diseases are studied using histology and immunohistochemistry at the light microscopic and ultrastructural levels to visualize directly the locations of molecules that are involved in immune-mediated injury and the failure of tissue repair.

We are currently focusing on cross-recognition of neurons and neuronal precursors by anti-myelin proteolipid protein antibodies, which may result in neuronal dysfunction and the failure of neuronal repair in CNS injury and on an oligodendrogliaopathy induced by the environmental agent azetidine.

Teaching

GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

- Immunology (Phd Program)

- Neurosciences (Phd Program)

Publications

PUBLICATIONS

- **Parkinson Disease and Amyotrophic Lateral Sclerosis in a Machinist-Welder: Reconsideration of an Archival Case**
Sobel, R.
OXFORD UNIV PRESS INC.2020: 697
- **Mechanisms of Azetidine-2-carboxylic Acid (Aze)-Induced Oligodendroglial Pathy In Vivo and In Vitro**
Sobel, R., Albertelli, M., Hinojoza, J., Eaton, M., Grimes, K., Rubenstein, E.
OXFORD UNIV PRESS INC.2020: 661
- **Checkpoint Receptor TIGIT Expressed on Tim-1+ B Cells Regulates Tissue Inflammation.** *Cell reports*
Xiao, S., Bod, L., Pochet, N., Kota, S. B., Hu, D., Madi, A., Kilpatrick, J., Shi, J., Ho, A., Zhang, H., Sobel, R., Weiner, H. L., Strom, et al
2020; 32 (2): 107892
- **Anti-Myelin Proteolipid Protein Peptide Monoclonal Antibodies Recognize Cell Surface Proteins on Developing Neurons and Inhibit Their Differentiation.** *Journal of neuropathology and experimental neurology*
Sobel, R. A., Eaton, M. J., Jaju, P. D., Lowry, E., Hinojoza, J. R.
2019
- **Glioneuronal Tumor With Features of Ganglioglioma and Neurocytoma Arising in the Fourth Ventricle: A Report of 2 Unusual Cases and a Review of Infratentorial Gangliogliomas.** *Journal of neuropathology and experimental neurology*
Harrison, W., Elsamadicy, A. A., McMahon, J. T., Chagoya, G., Sobel, R. A., McLendon, R. E., Adamson, C.
2019
- **IL-11 Induces Encephalitogenic Th17 Cells in Multiple Sclerosis and Experimental Autoimmune Encephalomyelitis.** *Journal of immunology (Baltimore, Md. : 1950)*
Zhang, X., Kiapour, N., Kapoor, S., Khan, T., Thamilarasan, M., Tao, Y., Cohen, S., Miller, R., Sobel, R. A., Markovic-Plese, S.
2019
- **Liver-specific knockdown of long-chain acyl-CoA synthetase 4 reveals its key role in VLDL-TG metabolism and phospholipid synthesis in mice fed a high-fat diet** *AMERICAN JOURNAL OF PHYSIOLOGY-ENDOCRINOLOGY AND METABOLISM*
Singh, A. B., Kan, C. K., Kraemer, F. B., Sobel, R. A., Liu, J.
2019; 316 (5): E880–E894
- **DGAT1 inhibits retinol-dependent regulatory T cell formation and mediates autoimmune encephalomyelitis.** *Proceedings of the National Academy of Sciences of the United States of America*
Graham, K. L., Werner, B. J., Moyer, K. M., Patton, A. K., Krois, C. R., Yoo, H. S., Tverskoy, M., LaJevic, M., Napoli, J. L., Sobel, R. A., Zabel, B. A., Butcher, E. C.
2019
- **Dendritic Cell PD-L1 Limits Autoimmunity and Follicular T Cell Differentiation and Function** *JOURNAL OF IMMUNOLOGY*
Sage, P. T., Schildberg, F. A., Sobel, R. A., Kuchroo, V. K., Freeman, G. J., Sharpe, A. H.
2018; 200 (8): 2592–2602
- **Functional Anti-TIGIT Antibodies Regulate Development of Autoimmunity and Antitumor Immunity** *JOURNAL OF IMMUNOLOGY*
Dixon, K. O., Schorer, M., Nevin, J., Etminan, Y., Amoozgar, Z., Kondo, T., Kurtulus, S., Kassam, N., Sobel, R. A., Fukumura, D., Jain, R. K., Anderson, A. C., Kuchroo, et al
2018; 200 (8): 3000–3007
- **Fas Promotes T Helper 17 Cell Differentiation and Inhibits T Helper 1 Cell Development by Binding and Sequestering Transcription Factor STAT1** *IMMUNITY*
zu Horste, G., Przybylski, D., Schramm, M. A., Wang, C., Schnell, A., Lee, Y., Sobel, R., Regev, A., Kuchroo, V. K.
2018; 48 (3): 556+
- **Epitope Mapping of SERCA2a Identifies an Antigenic Determinant That Induces Mainly Atrial Myocarditis in A/J Mice** *JOURNAL OF IMMUNOLOGY*
Krishnan, B., Massilamany, C., Basavalingappa, R. H., Gangaplara, A., Rajasekaran, R. A., Afzal, M. Z., Khalilzad-Sharghi, V., Zhou, Y., Riethoven, J., Nandi, S. S., Mishra, P. K., Sobel, R. A., Strande, et al

2018; 200 (2): 523–37

- **Microhemorrhage-associated tissue iron enhances the risk for *Aspergillus fumigatus* invasion in a mouse model of airway transplantation.** *Science translational medicine*
Hsu, J. L., Manouvakhova, O. V., Clemons, K. V., Inayathullah, M., Tu, A. B., Sobel, R. A., Tian, A., Nazik, H., Pothineni, V. R., Pasupneti, S., Jiang, X., Dhillon, G. S., Bedi, et al
2018; 10 (429)
- **Lack of Efficacy of Liposomal Amphotericin B Against Acute and Chronic *Trypanosoma cruzi* Infection in Mice** *AMERICAN JOURNAL OF TROPICAL MEDICINE AND HYGIENE*
Clemons, K. V., Sobel, R. A., Martinez, M., Correa-Oliveira, R., Stevens, D. A.
2017; 97 (4): 1141–46
- **Induction of Paralysis and Visual System Injury in Mice by T Cells Specific for Neuromyelitis Optica Autoantigen Aquaporin-4.** *Journal of visualized experiments : JoVE*
Sagan, S. A., Cruz-Herranz, A., Spencer, C. M., Ho, P. P., Steinman, L., Green, A. J., Sobel, R. A., Zamvil, S. S.
2017
- **T cells targeting neuromyelitis optica autoantigen aquaporin-4 cause paralysis and visual system injury.** *Journal of nature and science*
Cruz-Herranz, A., Sagan, S. A., Sobel, R. A., Green, A. J., Zamvil, S. S.
2017; 3 (5)
- **Tolerance checkpoint bypass permits emergence of pathogenic T cells to neuromyelitis optica autoantigen aquaporin-4** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*
Sagan, S. A., Winger, R. C., Cruz-Herranz, A., Nelson, P. A., Hagberg, S., Miller, C. N., Spencer, C. M., Ho, P. P., Bennett, J. L., Levy, M., Levin, M. H., Verkman, A. S., Steinman, et al
2016; 113 (51): 14781-14786
- **The central vein sign and its clinical evaluation for the diagnosis of multiple sclerosis: a consensus statement from the North American Imaging in Multiple Sclerosis Cooperative** *NATURE REVIEWS NEUROLOGY*
Sati, P., Oh, J., Constable, R. T., Evangelou, N., Guttmann, C. R., Henry, R. G., Klawiter, E. C., Mainero, C., Massacesi, L., McFarland, H., Nelson, F., Ontaneda, D., Rauscher, et al
2016; 12 (12): 714-722
- **Identification of an Epitope from Adenine Nucleotide Translocator 1 That Induces Inflammation in Heart in A/J Mice.** *American journal of pathology*
Basavalingappa, R. H., Massilamany, C., Krishnan, B., Gangaplara, A., Kang, G., Khalilzad-Sharghi, V., Han, Z., Othman, S., Li, Q., Riethoven, J., Sobel, R. A., Steffen, D., Reddy, et al
2016; 186 (12): 3160-3175
- **Anti-CD48 Monoclonal Antibody Attenuates Experimental Autoimmune Encephalomyelitis by Limiting the Number of Pathogenic CD4+ T Cells.** *Journal of immunology*
McArdel, S. L., Brown, D. R., Sobel, R. A., Sharpe, A. H.
2016; 197 (8): 3038-3048
- **Treatment of spontaneous EAE by laquinimod reduces Tfh, B cell aggregates, and disease progression.** *Neurology(R) neuroimmunology & neuroinflammation*
Varrin-Doyer, M., Pekarek, K. L., Spencer, C. M., Bernard, C. C., Sobel, R. A., Cree, B. A., Schulze-Topphoff, U., Zamvil, S. S.
2016; 3 (5)
- **IL-10-dependent Tr1 cells attenuate astrocyte activation and ameliorate chronic central nervous system inflammation** *BRAIN*
Mayo, L., da Cunha, A. P., Madi, A., Beynon, V., Yang, Z., Alvarez, J. I., Prat, A., Sobel, R. A., Kobzik, L., Lassmann, H., Quintana, F. J., Weiner, H. L.
2016; 139: 1939-1957
- **Dimethyl fumarate treatment induces adaptive and innate immune modulation independent of Nrf2** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*
Schulze-Topphoff, U., Varrin-Doyer, M., Pekarek, K., Spencer, C. M., Shetty, A., Sagan, S. A., Cree, B. A., Sobel, R. A., Wipke, B. T., Steinman, L., Scannevin, R. H., Zamvil, S. S.
2016; 113 (17): 4777-4782
- **CNS accumulation of regulatory B cells is VLA-4-dependent.** *Neurology® neuroimmunology & neuroinflammation*
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- **CD5L/AIM Regulates Lipid Biosynthesis and Restrains Th17 Cell Pathogenicity** *CELL*
Wang, C., Yosef, N., Gaublot, J., Wu, C., Lee, Y., Clish, C. B., Kaminski, J., Xiao, S., Horste, G. M., Pawlak, M., Kishi, Y., Joller, N., Karwacz, et al
2015; 163 (6)
- **IL-21R signaling is critical for induction of spontaneous experimental autoimmune encephalomyelitis** *JOURNAL OF CLINICAL INVESTIGATION*
Lee, Y., Mitsdoerffer, M., Xiao, S., Gu, G., Sobel, R. A., Kuchroo, V. K.
2015; 125 (11): 4011-4020
- **Deletion of CTLA-4 on regulatory T cells during adulthood leads to resistance to autoimmunity** *JOURNAL OF EXPERIMENTAL MEDICINE*
Paterson, A. M., Lovitch, S. B., Sage, P. T., Juneja, V. R., Lee, Y., Trombly, J. D., Arancibia-Carcamo, C. V., Sobel, R. A., Rudensky, A. Y., Kuchroo, V. K., Freeman, G. J., Sharpe, A. H.
2015; 212 (10): 1603-1621
- **B-Cell Very Late Antigen-4 Deficiency Reduces Leukocyte Recruitment and Susceptibility to Central Nervous System Autoimmunity** *ANNALS OF NEUROLOGY*
Lehmann-Horn, K., Sagan, S. A., Bernard, C. C., Sobel, R. A., Zamvil, S. S.
2015; 77 (5): 902-908
- **Tim-1 Is Essential for Induction and Maintenance of IL-10 in Regulatory B Cells and Their Regulation of Tissue Inflammation** *JOURNAL OF IMMUNOLOGY*
Xiao, S., Brooks, C. R., Sobel, R. A., Kuchroo, V. K.
2015; 194 (4): 1602-1608
- **Podoplanin negatively regulates CD4(+) effector T cell responses** *JOURNAL OF CLINICAL INVESTIGATION*
Peters, A., Burkett, P. R., Sobel, R. A., Buckley, C. D., Watson, S. P., Bettelli, E., Kuchroo, V. K.
2015; 125 (1): 129-140
- **A Novel CMKLR1 Small Molecule Antagonist Suppresses CNS Autoimmune Inflammatory Disease** *PLOS ONE*
Graham, K. L., Zhang, J. V., Lewen, S., Burke, T. M., Dang, T., Zoudilova, M., Sobel, R. A., Butcher, E. C., Zabel, B. A.
2014; 9 (12)
- **Immunodominant T-cell epitopes of MOG reside in its transmembrane and cytoplasmic domains in EAE.** *Neurology® neuroimmunology & neuroinflammation*
Shetty, A., Gupta, S. G., Varrin-Doyer, M., Weber, M. S., Prod'homme, T., Molnarfi, N., Ji, N., Nelson, P. A., Patarroyo, J. C., Schulze-Topphoff, U., Fogal, S. E., Forsthuber, T., Sobel, et al
2014; 1 (2)
- **SJL Mice Infected with *Acanthamoeba castellanii* Develop Central Nervous System Autoimmunity through the Generation of Cross-Reactive T Cells for Myelin Antigens** *PLOS ONE*
Massilamany, C., Marciano-Cabral, F., da Rocha-Azevedo, B., Jamerson, M., Gangaplara, A., Steffen, D., Zabad, R., Illes, Z., Sobel, R. A., Reddy, J.
2014; 9 (5)
- **Uncovering Cryptic Glycan Markers in Multiple Sclerosis (MS) and Experimental Autoimmune Encephalomyelitis (EAE)** *DRUG DEVELOPMENT RESEARCH*
Wang, D., Bhat, R., Sobel, R. A., Huang, W., Wang, L., Olsson, T., Steinman, L.
2014; 75 (3): 172-188
- **A novel CMKLR1 small molecule antagonist suppresses CNS autoimmune inflammatory disease.** *PloS one*
Graham, K. L., Zhang, J. V., Lewén, S., Burke, T. M., Dang, T., Zoudilova, M., Sobel, R. A., Butcher, E. C., Zabel, B. A.
2014; 9 (12)
- **MHC class II-dependent B cell APC function is required for induction of CNS autoimmunity independent of myelin-specific antibodies** *JOURNAL OF EXPERIMENTAL MEDICINE*
Molnarfi, N., Schulze-Topphoff, U., Weber, M. S., Patarroyo, J. C., Prod'homme, T., Varrin-Doyer, M., Shetty, A., Linington, C., Slavina, A. J., Hidalgo, J., Jenne, D. E., Wekerle, H., Sobel, et al
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- **Defective sphingosine 1-phosphate receptor 1 (S1P1) phosphorylation exacerbates TH17-mediated autoimmune neuroinflammation.** *Nature immunology*
Garris, C. S., Wu, L., Acharya, S., Arac, A., Blaho, V. A., Huang, Y., Moon, B. S., Axtell, R. C., Ho, P. P., Steinberg, G. K., Lewis, D. B., Sobel, R. A., Han, et al
2013; 14 (11): 1166-1172

- **Defective sphingosine 1-phosphate receptor 1 (S1P1) phosphorylation exacerbates TH17-mediated autoimmune neuroinflammation.** *Nature immunology*
Garris, C. S., Wu, L., Acharya, S., Arac, A., Blaho, V. A., Huang, Y., Moon, B. S., Axtell, R. C., Ho, P. P., Steinberg, G. K., Lewis, D. B., Sobel, R. A., Han, et al
2013; 14 (11): 1166-1172
- **Aspergillus fumigatus Invasion Increases with Progressive Airway Ischemia** *PLOS ONE*
Hsu, J. L., Khan, M. A., Sobel, R. A., Jiang, X., Clemons, K. V., Nguyen, T. T., Stevens, D. A., Martinez, M., Nicolls, M. R.
2013; 8 (10)
- **Tob1 plays a critical role in the activation of encephalitogenic T cells in CNS autoimmunity.** *journal of experimental medicine*
Schulze-Topphoff, U., Casazza, S., Varrin-Doyer, M., Pekarek, K., Sobel, R. A., Hauser, S. L., Oksenberg, J. R., Zamvil, S. S., Baranzini, S. E.
2013; 210 (7): 1301-1309
- **Amyloid Fibrils Composed of Hexameric Peptides Attenuate Neuroinflammation** *SCIENCE TRANSLATIONAL MEDICINE*
Kurnellas, M. P., Adams, C. M., Sobel, R. A., Steinman, L., Rothbard, J. B.
2013; 5 (179)
- **Novel dominant and subdominant T cell epitopes of the CNS autoantigen, myelin oligodendrocyte glycoprotein, in mice and MS patients** *11th International Congress of Neuroimmunology (ISNI)*
Shetty, A., Gupta, S., Varrin-Doyer, M., Weber, M., Ji, N., Molnarfi, N., Nelson, P., Sagan, S., Forstuber, T., Bernard, C., Slavin, A., Sobel, R., Zamvil, et al
ELSEVIER SCIENCE BV.2012: 147-47
- **Encephalitogenic potential of discrete T cell epitopes of aquaporin-4 (AQP4)** *11th International Congress of Neuroimmunology (ISNI)*
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ELSEVIER SCIENCE BV.2012: 49-49
- **Chaperone Activity of Small Heat Shock Proteins Underlies Therapeutic Efficacy in Experimental Autoimmune Encephalomyelitis** *JOURNAL OF BIOLOGICAL CHEMISTRY*
Kurnellas, M. P., Brownell, S. E., Su, L., Malkovskiy, A. V., Rajadas, J., Dolganov, G., Chopra, S., Schoolnik, G. K., Sobel, R. A., Webster, J., Ousman, S. S., Becker, R. A., Steinman, et al
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- **Induction and molecular signature of pathogenic T(H)17 cells** *NATURE IMMUNOLOGY*
Lee, Y., Awasthi, A., Yosef, N., Quintana, F. J., Xiao, S., Peters, A., Wu, C., Kleinewietfeld, M., Kunder, S., Hafler, D. A., Sobel, R. A., Regev, A., Kuchroo, et al
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- **Bat3 promotes T cell responses and autoimmunity by repressing Tim-3-mediated cell death and exhaustion** *NATURE MEDICINE*
Rangachari, M., Zhu, C., Sakuishi, K., Xiao, S., Karman, J., Chen, A., Angin, M., Wakeham, A., Greenfield, E. A., Sobel, R. A., Okada, H., McKinnon, P. J., Mak, et al
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- **Defect in regulatory B-cell function and development of systemic autoimmunity in T-cell Ig mucin 1 (Tim-1) mucin domain-mutant mice** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*
Xiao, S., Brooks, C. R., Zhu, C., Wu, C., Sweere, J. M., Petecka, S., Yeste, A., Quintana, F. J., Ichimura, T., Sobel, R. A., Bonventre, J. V., Kuchroo, V. K.
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- **Janus-like opposing roles of CD47 in autoimmune brain inflammation in humans and mice** *JOURNAL OF EXPERIMENTAL MEDICINE*
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- **Laquinimod Promotes T Cell Immune Modulation in Central Nervous System Autoimmunity Via Type II (M2) Myeloid APC** *64th Annual Meeting of the American-Academy-of-Neurology (AAN)*
Topphoff, U. S., Shetty, A., Varrin-Doyer, M., Molnarfi, N., Sagan, S., Sobel, R., Nelson, P., Zamvil, S.
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- **T Cell Epitope 119-132, but Not 35-55, Is the Immunodominant Encephalitogenic Determinant of the CNS Autoantigen, Myelin Oligodendrocyte Glycoprotein** *64th Annual Meeting of the American-Academy-of-Neurology (AAN)*
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- **Aquaporin-4 Peptide-Specific T Cells Induce CNS Inflammation** *64th Annual Meeting of the American-Academy-of-Neurology (AAN)*

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- **Aberrant mitochondrial fission in neurons induced by protein kinase C delta under oxidative stress conditions in vivo** *MOLECULAR BIOLOGY OF THE CELL*
Qi, X., Disatnik, M., Shen, N., Sobel, R. A., Mochly-Rosen, D.
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- **Peroxisome proliferator-activated receptor delta limits the expansion of pathogenic Th cells during central nervous system autoimmunity** *JOURNAL OF EXPERIMENTAL MEDICINE*
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- **Expression of Varicella-Zoster Virus Immediate-Early Regulatory Protein IE63 in Neurons of Latently Infected Human Sensory Ganglia** *JOURNAL OF VIROLOGY*
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 - **Opportunistic enteroviral meningoencephalitis: an unusual treatable complication of rituximab therapy** *LEUKEMIA & LYMPHOMA*
Ganjoo, K. N., Raman, R., Sobel, R. A., Pinto, H. A.
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