

## BIOGRAPHICAL SKETCH

Provide the following information for the key personnel in the order listed on Form Page 2.  
Photocopy this page or follow this format for each person.

NAME Warren Strober Text		POSITION TITLE Chief, MIS, LHD, DIR, NIAID, NIH	
EDUCATION/TRAINING ( <i>Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training</i> ).			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
Brooklyn College University of Rochester	B.S. M.D.	1958 1962	Biology Medicine

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past three years and to representative earlier publications pertinent to this application. If the list of publications in the last three years exceeds two pages, select the most pertinent publications. **DO NOT EXCEED TWO PAGES.**

### PROFESSIONAL EXPERIENCE:

1962 - 1963	Internship, Strong Memorial Hospital, Rochester, New York
1963 - 1964	Assistant Resident, Strong Memorial Hospital, Rochester, New York
1964 - 1967	Clinical Associate, Metabolism Branch, NCI, National Institutes of Health, Bethesda, Maryland
1967 - 1973	Senior Investigator, Metabolism Branch, NCI, National Institutes of Health, Bethesda, Maryland
1977 - 1982	Chief, Immunophysiology Section, Metabolism Branch, NCI, National Institutes of Health, Bethesda, Maryland
1982 - 2004	Chief, Section on Mucosal Immunity, Laboratory of Clinical Investigation, NIAID, National Institutes of Health Bethesda, Maryland
2004-present	Chief, Section on Mucosal Immunity, Laboratory of Host Defenses, NIAID, National Institutes of Health Bethesda, MD
1991 - 1995	Deputy Director, Division of Intramural Research, NIAID, National Institutes of Health, Bethesda, Maryland
1998 - 1999	Acting Scientific Director, NIAMS, National Institutes of Health, Bethesda, Maryland
1999-2003	Deputy Director, Laboratory of Clinical Investigation, NIAID, National Institutes of Health, Bethesda, Maryland

### AWARDS AND HONORS:

Salk Scholarship, 1958; State-of-the-Art Lecture: The Pathogenesis of Gluten-Sensitive Enteropathy, Induction into the American Society for Clinical Research, 1973; Induction into the Association of American Physicians, 1985; American Gastroenterological Association, 1978; PHS Distinguished Service Award, 1979; Distinguished Achievement Award, American Gastroenterological Association, 1981; Leo H. Crip Alumni Lectureship, 38<sup>th</sup> Annual Meeting, American Academy of Allergy, 1982; Merrill Lectureship, Medical College of Virginia, 1982; PHS Outstanding Service Medal, 1984; Medicine for the Layman Lecture, NIH, 1985; PHS Meritorious Service Award, 1988; State-of-the-Art Lecture: The Mucosal Immune System, German Gastroenterological Society, 1989; Honorary Member, Swedish Immunological Society, 1995; Batterello Medal of Brazil, 1996; PHS Distinguished Service Medal, 1997; Nelson Prize, University of California at Davis, 2000; Doctor of Medicine, Honoris Causa, Charite Hospital - Humboldt University, Berlin, Germany, 2007; Outstanding Mentor Award, 2007; NIH Merit Award (Laboratory Group Award), 2007; Ismar Boas Medal, German Society of Digestive Diseases and Metabolic Diseases, 2008; Scientific Achievement Award for Basic Science, Crohn's and Colitis Foundation, 2008; William Beaumont Award, American Gastroenterological Association, 2009; Lifetime Achievement Award, Society of Mucosal Immunology, 2009.

### SELECTED PUBLICATIONS: (from more than 400 original publications)

1. **Strober W**, Wochner RD, Carbone PP, Waldmann TA. Intestinal lymphangectasia: a protein-losing enteropathy with hypogammaglobulinemia, lymphocytopenia and impaired homograft rejection. *J Clin Invest* 46: 1643-1656, 1967.
2. Wochner, RD, **Strober W**, Waldman TA. The role of the kidney in the catabolism of Bence Jones proteins and immunoglobulin fragments. *J Exp Med* 126: 206-221, 1967.
3. Elson, CO, Heck JA, **Strober W**. T cell regulation of murine IgA synthesis. *J Exp Med* 149: 632-643, 1979.
4. Kawanishi H, Saltzman LE, **Strober W**. Mechanisms regulating IgA class-specific immunoglobulin production in murine gut-associated lymphoid tissues. I. T cells derived from Peyer's patches with switch sIgM B cells to sIgA B cells in vitro. *J Exp Med* 157: 433-450, 1983.
5. Elson CO, James SP, Graeff AS, Berendson RA, **Strober W**. Hypogammaglobulinemia due to abnormal suppressor T-cell activity in Crohn's disease. *Gastroenterology* 86: 569-576, 1984.
6. Harriman GR, Kunimoto DY, Elliott JF, Paetkau V, **Strober W**. The role of IL-5 in IgA B cell differentiation. *J Immunol* 140: 3033-3039, 1988.
7. Ehrhardt RO, **W Strober**, Harriman GR. Effect of transforming growth factor TGF- $\beta_1$  on IgA isotype expression. *J Immunol* 148:3830-3836, 1992.

8. **Strober W.** and Ehrhardt RO. Chronic intestinal inflammation: An unexpected outcome in cytokine or T cell receptor mutant mice. *Cell* 75: 1, 1993.
9. Wakatsuki Y, **Strober W.** Effect of downregulation of germline transcripts on immunoglobulin A isotype differentiation. *J Exp Med* 178: 129-138, 1993.
10. Jaffe JS, **Strober W.**, Sneller MC. Functional abnormalities of CD8+ T cells define a unique subset of patients with common variable immunodeficiency. *Blood* 82 : 192-201, 1993.
11. Eisenstein EM, Chua K, **Strober W.** B cell differentiation defects in common variable immunodeficiency are ameliorated after stimulation with anti-CD40 antibody and IL-10. *J Immunol* 152 : 5957-5968, 1994.
12. Holland SM, Eisenstein EM, Kuhns DB, Turner ML, Fleisher TA, **Strober W.**, Gallin JI. Treatment of refractory disseminated nontuberculous mycobacterial infection with interferon gamma. A preliminary report. *N Engl J Med* 330 : 1348-1355, 1994.
13. Neurath MF, Fuss I, Kelsall BL, Stüber E, **Strober W.** Antibodies to interleukin 12 abrogate established experimental colitis in mice. *J Exp Med* 182 : 1281-1290, 1995.
14. Stüber E, **Strober W.**, Neurath M. Blocking the CD40L-CD40 interaction in vivo specifically prevents the priming of T helper 1 cells through the inhibition of interleukin 12 secretion. *J Exp Med* 183 : 693-698, 1996.
15. Neurath MF, Fuss I, Kelsall BL, Presky DH, Waegell W, **Strober W.** Experimental granulomatous colitis in mice is abrogated by induction of TGF- $\beta$ -mediated oral tolerance. *J Exp Med* 183 : 2605-2616, 1996.
16. Neurath MF, Fuss I, Pasparakis M, Alexopoulou L, Haralambous S, Meyer zum Buschenfelde KH, **Strober W.**, Kollias G. Predominant pathogenic role of tumor necrosis factor in experimental colitis in mice. *Eur J Immunol* 27 : 1743-1750, 1997.
17. Neurath MF, Pettersson S, Meyer zum Büschenfelde KH, **Strober W.** Local administration of antisense phosphorothioate oligonucleotides to the 065 subunit of NF- $\kappa$ B abrogates established experimental colitis in mice. *Nat Med* 2 : 998-1004, 1996.
18. **Strober W.**, Kelsall B, Marth T. Oral tolerance. *J Clin Immunol* 18(1):1-30, 1998.
19. Fuss IJ, **Strober W.**, Cuccherini BA, Pearlstein GR, Bossuyt X, Brown M, Fleisher TA, Horgan K. Intestinal lymphangectasia, a disease characterized by selective loss of naïve CD45RA+ lymphocytes into the gastrointestinal tract. *Eur J Immunol* 28: 4275-4285, 1998.
20. Boirivant M, Fuss IJ, Chu A, **Strober W.** Oxazolone colitis: A murine model of T helper cell type 2 colitis treatable with antibodies to interleukin 4. *J Exp Med* 188: 1929-1939, 1998.
21. Fuss IJ, Marth T, Neurath MF, Pearlstein GR, Jain A, **Strober W.** Anti-interleukin 12 treatment regulates apoptosis of Th1 T cells in experimental colitis in mice. *Gastroenterology* 117 : 1078-1088, 1999.
22. Ludviksson BR, **Strober W.**, Nishikomori R, Hasan SK, Ehrhardt RO. Administration of mAb against alpha E beta 7 prevents and ameliorates immunization-induced colitis in IL-2<sup>-/-</sup> mice. *J Immunol* 162 : 4975-4982, 1999.
23. Jain A, Atkinson TP, Lipsky PE, Slater JE, Nelson DL, **Strober W.** Defects of T-cell effector function and post-thymic maturation in X-linked hyper-IgM syndrome. *J Clin Invest* 103(8): 1151-8, 1999.
24. Belyakov IM, Moss B, **Strober W.**, Berzofsky JA. Mucosal vaccination overcomes the barrier to recombinant vaccinia immunization caused by preexisting poxvirus immunity. *Proc Natl Acad Sci USA* 96: 4512-4517, 1999.
25. Blumberg RS, Saubermann LJ, **Strober W.** Animal models of mucosal inflammation and their relation to human inflammatory bowel disease. *Curr Opin Immunol* 11(6): 648-56, 1999.
26. Kitani A, Fuss IJ, Nakamura K, Schwartz OM, Usui T, **Strober W.** Treatment of experimental (Trinitrobenzene sulfonic acid) coli intranasal administration of transforming growth factor (TGF)-beta1 plasmid: TGF-beta1-mediated suppression of T helper cell type 1 response occurs by interleukin (IL)-10 induction and IL-12 receptor beta2 chain downregulation. *J Exp Med* 192: 41-52, 2000.
27. Nishikomori R, Ehrhardt RO, **Strober W.** T helper type 2 cell differentiation occurs in the presence of interleukin 12 receptor beta2 chain expression and signaling. *J Exp Med* 191: 847-858, 2000.
28. Neurath M, Fuss I, **Strober W.** TNBS-colitis. *Int Rev Immunol* 19: 51-62, 2001.
29. Neurath MF, Finotto S, Fuss I, Boirivant M, Galle PR, **Strober W.** Regulation of T-cell apoptosis in inflammatory bowel disease: to die or not to die, that is the mucosal question. *Trends Immunol* 22: 21-26, 2001.
30. Jain A, Ma CA, Liu S, Brown M, Cohen J, **Strober W.** Specific missense mutations in NEMO result in hyper-IgM syndrome with Hypohydrotic ectodermal dysplasia. *Nat Immunol* 2: 223-228, 2001.
31. Boirivant M, Fuss IJ, Ferroni L, De Pascale M, **Strober W.** Oral administration of recombinant cholera toxin subunit B inhibits IL-12-mediated murine experimental (trinitrobenzene sulfonic acid) colitis. *J Immunol* 166: 3522-3532, 2001.
32. Fleisher TA, Puck JM, **Strober W.**, Dale JK, Lenardo MJ, Siegel RM, Straus SE, Bleesing JJ. The autoimmune lymphoproliferative syndrome. A disorder of human lymphocyte apoptosis. *Clin Rev Allergy Immunol* 20: 109-120, 2001.
33. Tarr PE, Sneller MC, Mechanic LJ, Economides A, Eger CM, **Strober W.**, Cunningham-Rundles C, Lucey DR. Infections in patients with immunodeficiency with thymoma (Good syndrome). Report of 5 cases and review of the literature. *Medicine (Baltimore)* 80: 123-133, 2001.
34. **Strober W.**, Nakamura K, Kitani A. The SAMP1/Yit mouse: another step closer to modeling human inflammatory bowel disease. *J Clin Invest* 107: 667-670, 2001.
35. Nakamura K, Kitani A, **Strober W.** Cell contact-dependent immunosuppression by CD4+CD25+ regulatory T cells is mediated by cell surface-bound transforming growth factor beta. *J Exp Med* 194: 629-644, 2001.
36. Blumberg R, **Strober W.** Prospects for research in inflammatory bowel disease. *JAMA* 285: 643-647, 2001.
37. Fuss IJ, Boirivant M, Lacy B, **Strober W.** The interrelated roles of TGF- $\beta$  and IL-10 in the regulation of experimental colitis. *J Immunol* 168: 900-908, 2002.

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39. **Strober W**, Fuss IJ, Blumberg RS. The immunology of mucosal models of inflammation. *Annu Rev Immunol* 20: 495-549, 2002.
40. Heller F, Fuss IJ, Nieuwenhuis EE, Blumberg RS, **Strober W**. Oxazolone colitis, a Th2 colitis model resembling ulcerative colitis, is mediated by IL-13-producing NK-T cells. *J Immunity* 17: 629-638, 2002.
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43. **Strober W**, Fuss IJ, Nakamura K, Kitani A. Recent advances in the understanding of the induction and regulation of mucosal inflammation. *J Gastroenterol* 38 Suppl 15: 55-58, 2003.
44. Kitani A, Fuss I, Nakamura K, Kumaki F, Usui T, **Strober W**. Transforming growth factor (TGF)- $\beta$ 1-producing regulatory T cells induce Smad-mediated interleukin 10 secretion that facilitates coordinated immunoregulatory activity and amelioration of TGF- $\beta$ 1-mediated fibrosis. *J Exp Med* 198: 1179-1188, 2003.
45. Nakamura K, Kitani A, Fuss I, Pedersen A, Harada N, Nawata H, **Strober W**. TGF- $\beta$ 1 plays an important role in the mechanism of CD4+CD25+ regulatory T cell activity in both humans and mice. *J Immunol* 172: 834-842, 2004.
46. Watanabe T, Kitani A, Murray PJ, **Strober W**. NOD2 is a negative regulator of Toll-like receptor 2-mediated T helper type 1 responses. *Nat Immunol* 5: 800-8, 2004.
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48. Kaser A, Nieuwenhuis EE, **Strober W**, Fuss I, Colgan S, Blumberg RS. CD1d-restricted T cell pathways at the epithelial-lymphocyte-luminal interface. *J Pediatr Gastroenterol Nutr* 39 Suppl 3: S719-S722, 2004.
49. Stevceva L, **Strober W**. Mucosal HIV vaccines: where are we now? *Curr HIV Res* 2: 1-10, 2004.
50. Kaser A, Nieuwenhuis EE, **Strober W**, Mayer L, Fuss I, Colgan S, Blumberg RS. Natural killer T cells in mucosal homeostasis. *Ann NY Acad Sci* 1029: 154-168, 2004.
51. Fuss IJ, Heller F, Boirivant M, Leon F, Yoshida M, Fichtner-Feigl S, Yang Z, Exley M, Kitani A, Blumberg RS, Mannon P, **Strober W**. Nonclassical CD1d-restricted NK T cells that produce IL-13 characterize an atypical Th2 response in ulcerative colitis. *J Clin Invest* 113: 1490-1497, 2004.
52. Fichtner-Feigl S, Fuss IJ, Preiss JC, **Strober W**, Kitani A. Treatment of murine Th1- and Th2-mediated inflammatory bowel disease with NF- $\kappa$ B decoy oligonucleotides. 115: 3057-3071, 2005.
53. Watanabe T, Kitani A, **Strober W**. NOD2 regulation of Toll-like receptor responses and the pathogenesis of Crohn's disease. *Gut* 54: 1515-1518, 2005.
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55. Mannon PJ, Fuss IJ, Mayer L, Elson CO, Sandborn WJ, Present D, Dolin B, Goodman N, Groden C, Hornung RL, Quezado M, Yang Z, Neurath MF, Salfeld J, Veldman GM, Schwertschlag U, **Strober W**, Anti-IL-12 Crohn's Disease Study Group. Anti-interleukin-12 antibody for active Crohn's disease. *N Engl J Med* 351: 2069-2079, 2004.
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57. Leon F, Contractor N, Fuss I, Marth T, Lahey E, Iwaki S, la Sala A, Hoffman V, **Strober W**, Kelsall BL. Antibodies to complement receptor 3 treat established inflammation in murine models of colitis and a novel model of psoriasisform dermatitis. *J Immunol* 177: 6974-6982, 2006.
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60. **Strober W**, Murray PJ, Kitani A, Watanabe T. Signalling pathways and molecular interactions of NOD1 and NOD2. *Nat Rev Immunol* 6: 9-20, 2006.
61. Watanabe T, Kitani A, Murray PJ, Wakatsuki Y, Fuss IJ, **Strober W**. Nucleotide binding oligomerization domain 2 deficiency leads to dysregulated TLR2 signaling and induction of antigen-specific colitis. *Immunity* 25: 473-485, 2006.
62. Xu L, Kitani A, Fuss I, **Strober W**. Cutting edge: regulatory T cells induce CD4+CD25-Foxp3- T cells or are self-induced to become Th17 cells in the absence of exogenous TGF- $\beta$ . *J Immunol* 178: 6725-6729, 2007.
63. Yang Z, Fuss IJ, Watanabe T, Asano N, Davey MP, Rosenbaum JT, **Strober W**, Kitani A. NOD2 transgenic mice exhibit enhanced MDP-mediated down-regulation of TLR2 responses and resistance to colitis induction. *Gastroenterology* 133: 1510-1521, 2007.
64. Boirivant M, **Strober W**. The mechanism of action of probiotics. *Curr Opin Gastroenterol* 23: 679-792, 2007.
65. **Strober W**, Fuss I, Mannon P. The fundamental basis of inflammatory bowel disease. *J Clin Invest* 117: 514-521, 2007.
66. Watanabe T, Asano N, Murray PJ, Ozato K, Tailor P, Fuss IJ, Kitani A, **Strober W**. Muramyl dipeptide activation of nucleotide-binding oligomerization domain 2 protects mice from experimental colitis. *J Clin Invest* 118: 545-559, 2008.
67. Boirivant M, Amendola A, Butera A, Sanchez M, Xu L, Marinaro M, Kitani A, Di Giacinto C, **Strober W**, Fuss IJ. A transient

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- breach in the epithelial barrier leads to regulatory T-cell generation and resistance to experimental colitis. *Gastroenterology* 135: 1612-1623, 2008.
68. Pesu M, Watford W, Wei L, Xu L, Fuss I, **Strober W**, Andersson J, Shevach E, Quezado M, Bouladoux N, Roebroek A, Belkaid Y, Creemers J, O'Shea J. T-cell-expressed proprotein convertase furin is essential for maintenance of peripheral immune tolerance. *Nature* 455: 246-250, 2008.
  69. Boirivant M, Amendola A, Butera A, Sanchez M, Xu L, Marinaro M, Kitani A, Di Giacinto C, **Strober W**, Fuss IJ. A transient breach in the epithelial barrier leads to regulatory T-cell generation and resistance to experimental colitis. *Gastroenterology* 135: 1612-1623, 2008.
  70. Zhang F, Meng G, **Strober W**. Interactions among the transcription factors Runx1, ROR $\gamma$  and Foxp3 regulate the differentiation of interleukin 17-producing T cells. *Nat Immunol* 9: 1297-1306, 2008.
  71. Meng G, Zhang F, Fuss I, Kitani A, **Strober W**. A mutation in the Nirp3 gene causing inflammasome hyperactivation potentiates Th17 cell-dominant immune responses. *Immunity* 30: 860-874, 2009.
  72. Watanabe T, Asano N, Fichtner-Feigl S, Forelick P, Tsuji Y, Matsumoto Y, Chiba T, Fuss I, Kitani A, **Strober W**. NOD1 contributes to mouse host defense against *Helicobacter pylori* via induction of type 1 IFN and activation at the ISGF3 signaling pathway. *J Clin Invest* 120: 1645-1662, 2010.
  73. **Strober W**. Adherent-invasive *E. coli* in Crohn's disease: bacterial "agent provocateur." *J Clin Invest* 121: 841-844, 2011.
  74. Zwiers A, Fuss IJ, Seegers D, Konijn T, Garcia-Vallejo JJ, Samsom JN, **Strober W**, Kraal G, Bouma G. A polymorphism in the coding region of Il12b promotes IL-12p70 and IL-23 heterodimer formation. *J Immunol* 186: 3572-3580, 2011.
  75. Schiechl G, Bauer B, Fuss I, Lang SA, Moser C, Ruemmele P, Rose-John S, Neurath MF, Geissler EK, Schlitt HJ, **Strober W**, Fichtner-Feigl S. Tumor development in murine ulcerative colitis depends on MyD88 signaling of colonic F4/80+CD11b(high)Gr(low) macrophages. *J Clin Invest* 121: 1692-708, 2011.
  76. Tsuji Y, Watanabe T, Kudo M, Arai H, **Strober W**, Chiba T. Sensing of commensal organisms by the intracellular sensor NOD1 mediates experimental pancreatitis. *Immunity* 37: 326-338, 2012.
  77. Fuss I.J., Friend J., Yang Z., He J.P., Hooda L., Boyer J., Xi L., Raffeld M., Kleiner D.E., Heller T., **Strober W**. Nodular regenerative hyperplasia in common variable immunodeficiency. *J Clin Immunol* 33: 748-758, 2013.
  78. Amendola A., Butera A., Sanchez M., **Strober W**., Boirivant M. Nod2 deficiency is associated with an increased mucosal immunoregulatory response to commensal microorganisms. *Mucosal Immunol* 7: 391-404, 2014.
  79. Fichtner-Feigl S., Kesselring R., Martin M., Obermeier F., Ruemmele P., Kitani A., Brunner S.M., Haimerl M., Geissler E.K., **Strober W**., Schlitt H.J. IL-13 orchestrates resolution of chronic intestinal inflammation via phosphorylation of glycogen synthase kinase-3 $\beta$ . *J Immunol* 192: 3969-3980, 2014.
  80. Zhang F., Fuss I.J., Yang Z., **Strober W**. Transcription of ROR $\gamma$ t in developing Th17 cells is regulated by E-proteins. *Mucosal Immunol* 7: 521-532, 2014.
  81. **Strober W**., Asano N., Fuss I., Kitani A., Watanabe T. Cellular and molecular mechanisms underlying NOD2 risk-associated polymorphisms in Crohn's disease. *Immunol Rev* 260: 249-260, 2014.
  82. Fuss I.J., Joshi B., Yang Z., Deheidy H., Fichtner-Feigl S., de Souza H., Rieder F., Scalfaferrri F., Schirbel A., Scarpa M., West G., Yi C., Xu L., Leland P., Yao M., Mannon P., Puri R.K., Fiocchi C., **Strober W**. IL-13R $\alpha$ 2-bearing, type II NK T cells reactive to sulfatide self-antigen populate the mucosa of ulcerative colitis. *Gut* 63: 1728-1736, 2014.
  83. Watanabe T., Asano N., Meng G., Yamashita K., Arai Y., Sakurai T., Kudo M., Fuss I.J., Kitani A., Shimosegawa T., Chiba T., **Strober W**. NOD2 downregulates colonic inflammation by IRF4-mediated inhibition of K63-linked polyubiquitination of RICK and TRAF6. *Mucosal Immunol* 7: 1312-1325, 2014.
  84. Gao P., Han X., Zhang Q., Yang Z., Fuss I.J., Myers T.G., Gardina P.J., Zhang F., **Strober W**. Dynamic changes in E-protein activity regulate T reg cell development. *J Exp Med* 211: 2651-2668, 2014.
  85. Kiesler P., Fuss I.J., **Strober W**. Experimental Models of Inflammatory Bowel Disease. *Cell Mol Gastroenterol Hepatol* 1: 154-170, 2015.