BIOGRAPHICAL SKETCH

NAME SAMUEL STROBER
eRA COMMONS USER NAME

POSITION TITLE **PROFESSOR OF MEDICINE**

Strober.Samuel

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
Columbia College, New York, New York	B.A.	1960	Liberal Arts
Harvard Medical School, Boston, MA	M.D.	1966	Medicine

A. Positions and Honors

Positions

- 1962-63 Research Fellow (part-time), Surgical Research Laboratory, Peter Bent Brigham Hospital, Boston, Massachusetts (Head: Professor J.E. Murray)
- 1963-64 Research Fellow, Cellular Immunology Research Unit, Oxford University, Oxford, England (Head: Professor J.L. Gowans)
- 12/65-6/66 Research Fellow, Surgical Research Laboratory, Peter Bent Brigham Hospital, Boston, Massachusetts
- 1966-67 Intern in Medicine, Massachusetts General Hospital, Boston, Massachusetts (Professor Alexander Leaf, Head of the Department of Medicine)
- Research Associate, Laboratory of Cell Biology, National Cancer Institute, NIH, Bethesda, • 1967-70 Maryland (Head: Dr. L.W. Law)
- 1970-71 Senior Assistant Resident, Department of Medicine, Stanford University School of Medicine, Stanford, California
- 1971-72 Instructor in Medicine, Department of Medicine, Stanford University School of Medicine, Stanford, California
- 1972-78 Assistant Professor of Medicine, Department of Medicine, Division of Immunology, Stanford University School of Medicine, Stanford, California
- 1976-81 Investigator, Howard Hughes Medical Institute, Miami, Florida
- 1978-82 Associate Professor of Medicine, Department of Medicine, Division of Immunology, Stanford University School of Medicine, Stanford, California
- 1978-97 Chief, Division of Immunology and Rheumatology, Department of Medicine, Stanford University School of Medicine, Stanford, California
- 1982-Present Professor of Medicine, Department of Medicine, Division of Immunology and Rheumatology, Stanford University School of Medicine, Stanford, California

2005-Present Chairman, Board of Directors, La Jolla Institute for Allergy and Immunology, La Jolla, CA **Honors**

- Leon Reznick Memorial Research Prize, Harvard Medical School
- Alpha Omega Honorary Society ٠
- Career Development Award from NIAID
- John Putnam Merrill Memorial Lecture, Harvard Medical School •
- E. Donnell Thomas Annual Lecture, Fred Hutchinson Cancer Research Center
- Councilor, Transplantation Society •
- President, Clinical Immunology Society

B. Selected peer-reviewed publications (-selected from 315 peer-reviewed articles)

Lan, F., Hayamizu, K., and Strober, S. Cyclosporine facilitates chimeric and inhibits non-chimeric tolerance after posttransplant total lymphoid irradiation (TLI). Transplantation 69:649-655, 2000

Strober, S. Benike, C., Krishnaswamy, S., Engleman, E.G., Grumet, F.K. Clinical transplantation tolerance twelve years after prospective withdrawal of immunosuppressive drugs: Studies of chimerism and anti-donor reactivity. Transplantation. 69:1549-1554, 2000

- Lan, F., Zeng, D., Huie, P., Higgins, J.P., and **Strober, S.** Allogeneic bone marrow cells that facilitate complete chimerism and eliminate tumor cells express both CD8 and TCRab Blood 97:3458-3465, 2001.
- Lan, F., Zeng, D., Huie, P., Higgins, J.P., and Strober, S. Predominance of NK.K1⁺TCRαβ or DX5⁺TCRαβ⁺T Cells in Mice Conditioned with Fractionated Lymphoid Irradiation Protects Against Graft Versus Host Disease. J. Immunol. 167: 2087-2096, 2001.
- Dejbakhsh-Jones, S. Garcia-Ojeda, M.E., Chatterjea-Matthes, D., Zeng, D., and **Strober, S.** Clonable progenitors committed to the T Lymphocyte lineage in the mouse bone marrow; use of an extrathymic pathway. Proc. Nat. Acad. Science USA 98:7455-7460, 2001.
- Zeng, D., Hoffman, P., Lan, F., Huie, P., Higgins, J., and **Strober, S.** Unique patterns of surface receptors, cytokine secretion, and immune functions distinguish T cells in the bone marrow from those in the periphery: impact on allogeneic bone marrow transplantation. Blood. 99:1449-1457, 2002.
- Millan, M.T., Shizuru, J.A., Hoffmann, P., Dejbakhsh-Jones, J.D., Scandling, J.D., Grumet, F.C., Tan, J.C., Salvatierra, O., and Strober, S. Mixed Chimerism without graft versus host disease after HLA-mismatched kidney and hematopoietic progenitor transplantation. Transplantation 73:1386-1391, 2002.
- Hoffmann, P., Erman, J., Fathman, C.G., and **Strober, S**. Donor Type CD4⁺CD25⁺ regulatory T cells suppress lethal acute graft-versus-host disease after allogeneic bone marrow transplantation. J. Exp. Med 196:389-399, 2002.
- Higuchi, M., Zeng, D., Shizuru, J., Gworek, J., Dejbakhsh-Jones, S., Taniguchi, M., and **Strober, S.** Immune Tolerance to combined Organ and Bone Marrow Transplants after Fractionated Lymphoid Irradiation Involves Regulatory NK T Cells and Clonal Deletion. J Immunol 169: 5564-5570, 2002.
- Hoffmann, P., Erman, J., Fathman, C.G., and **Strober, S**. Donor Type CD4⁺CD25⁺ regulatory T cells suppress lethal acute graft-versus-host disease after allogeneic bone marrow transplantation. J. Exp. Med 196:389-399, 2002.
- Higuchi, M., Zeng, D., Shizuru, J., Gworek, J., Dejbakhsh-Jones, S., Taniguchi, M., and **Strober, S.** Immune Tolerance to combined Organ and Bone Marrow Transplants after Fractionated Lymphoid Irradiation Involves Regulatory NK T Cells and Clonal Deletion. J Immunol 169: 5564-5570, 2002.
- Lan, F., Zeng, D., Higuchi, M., Higgins, J.P., and **Strober, S**. Host conditioning with total lymphoid irradiation and antithymocyte globulin prevents graft-versus-host disease: the role of CD1-reactive natural killer T cells. Biol Blood Marrow Transplant 9:355-364, 2003
- Edinger, M., Hoffmann, P., Ermann, J., Drago, K., Fathman, C.G., **Strober, S.**, and Negrin R.S. CD4⁺CD25⁺ regulatory T cells preserve graft-versus-tumor activity while inhibiting graft-versus-host disease after bone marrow transplantation. Nature Med. 9:1144-1150, 2003.
- Zeng, D., Lan, F., Hoffmann, P., and **Strober, S**., Suppression of graft-versus-host disease by naturally occurring regulatory T Cells. Transplantation 77(1):S9-S11, 2004
- Merad, M., Hoffmann, P., Ranheim, E., Slaymaker, S., Manz, M.G., Lira, S. A., Charo, I., Cook, D.N., Weissman, I.L., Strober, S. and Engleman, E.G. Depletion of host Langerhans cells prior to transplantation of donor alloreactive T cells prevents skin graft versus host disease. Nature Med. 10(5):510-517, 2004
- Ojeda-Garcia, M.E., Dejbakhsh-Jones, S., Chatterjea, D., Mukhopadhyay, A., BitMansour, A., Brown, J.M.Y., and **Strober, S**. Stepwise development of committed progenitors in the bone marrow that generate functional T cells in the absence of the thymus. J. Immunol. 175: 4363-4373, 2005
- Dutt, S., Ermann, J., Tseng, D., Liu, Y.P., George, T.I., Fathman, C.G., and **Strober, S**. L-selectin and β7 integrin on donor CD4 T cells are required for the early migration to host mesenteric lymph nodes and acute colitis of graft versus host disease. Blood. 106:4009-4015, 2005
- Ermann, J., Hoffmann, P., Edinger, M., Dutt, S., Blankenberg, F.G., Higgins, J.P., Negrin, R., Fathman, C.G., and **Strober, S.** Only the CD62L subpopulation of CD4⁺CD25⁺ regulatory T cells protects from lethal acute GVHD. Blood.105(5):2220-2226, 2005
- Lowsky, R., Takahashi, T. Liu, Y.P., Dejbakhsh-Jones, S., Grumet, F.C., Shizuru, J.A., Laport, G.G. Stockerl-Goldstein, K.E., Johnston, L.J., Hoppe, R.T., Bloch, D.A., Blume, K.A., Negrin, R.S., and **Strober, S**. Protective Conditioning for Acute Graft-versus-Host Disease. New Eng. J. Med. 353:1321-1331, 2005.
- Takahashi, T., Dejbakhsh-Jones, S. and **Strober, S**. Expression of CD161 (NKR-P1A) defines subsets of human CD4 and CD8 T cells with different functional activities. J. Immunol. 176: 211-216. 2006
- Zhang, C., Todorov, I., Zhang, A., Liu, Y., Kandeel, F., Forman, S., **Strober, S**., and Zeng, D. Donor CD4⁺ T and B cells in transplants induce chronic graft versus host disease with autoimmune manifestations. Blood: 107: 2993-3001. 2006

Pillai, A., George, T., Dutt, S., Teo, P. and Strober, S. Host NKT cells can prevent graft-versus-host disease and permit graft anti-tumor activity after bone marrow transplantation. J. Immunol 178:6241-6251. 2007

Pillai, A., Teo, P., George. T.I., Mukhopadhyay, A., Dejbakhsh-Jones, S., and Strober, S. Alloantigen recognition is critical for CD8 T cell-mediated graft anti-tumor activity against murine BCL1 lymphoma after myeloablative bone marrow transplantation. Bone Marrow Transplant 40:487-497. 2007

Dutt, S., Tseng, D., Ermann, J., George, T.I., Liu, Y-P., Davis, C., Fathman, C.G., and Strober, S. Naïve And Memory T Cells Induce Different Types Of Graft Versus Host Disease. J. Immunol 179:6547-6554 2007

Scandling, J.D., Busque, S., Dejbakhsh-Jones, S. Benike, C., Millan, M.T., Shizuru, J.A., Hoppe R.T., Lowsky, R. Engleman, E.G., and Strober, S. Combined kidney and Hematopoietic cell transplantation with persistent mixed chimerism and tolerance. New Eng. J. Med, 4: 362-368. 2008

Yao, Z., Liu, Y., Jones, J., and Strober S. Differences in Bcl-2 expression by T Cell subsets alter their balance after In vivo Irradiation to favor CD4⁺Bcl-2^{hi} NKT Cells. Eur. J. Immunol. 39:1-13 2009.

Pillai, A., George, T.I., Dutt, S., and Strober, S. Host natural killer T cells induce an interleukin-4-dependent expansion of donor CD4⁺ CD25⁺ Foxp3⁺ T regulatory cells that protects against graft-versus-host disease. Blood 113(18):4458-4467 2009.

Kohrt, H.E., Turnbull, B.B., Heydari, K., Shizuru, J., Laport, G.G., Miklos, D.B., Johnston, L.J., Arai, S., Weng, W-K., Hoppe, R.T., Lavori, P.W., Blume, K.G., Negrin, R.S., Strober, S., and Lowsky, R. TLI and ATG Conditioning with Low risk of GVHD Retains Anti-Tumor Reactions after Allogeneic Hematopoietic Cell Transplantation from Related and Unrelated Donors. Blood 2009 (PMID 19423725, in press).

Morshed, S.R., Takahashi, T., Savage, P.B., Kambham, N., Strober, S. β-galactosylceramide alters invariant natural killer T cell function and is effective treatment for lupus. 2009 Clin. Immunol. in press

C. <u>Research Support</u>

5 P01 HL -075462-05 A1

NIH/NHLBI- (Strober, S., P.I.)

Blood Stem Cell Transplantation as Immunotherapy

TLI and ATG Conditioning for Combined Kidney and Blood Stem Cell Transplantation

A central theme of the project is the use of allogeneic blood progenitor cell transplantation to induce host versus donor and donor versus host immune tolerance in patients after the development of chimerism without the development of graft versus host disease (GVHD). The role of regulatory T cells in the protection against GVHD will be studied as well as the immune competence of the protected hosts.

2 PO1 CA-49605-19 (Negrin, R., Director)

NIH/NCI – Project 4 (Strober, Project Leader)

Bone Marrow Grafting for Leukemia and Lymphoma Non-Myeloblative Host Conditioning with TLI/ATG.

The goal of the research plan is to use host regulatory natural killer (NK) T cells to prevent graft versus host disease (GVHD) and retain graft anti-lymphoma activity after MHC-mismatched bone marrow transplantation.

5 RO1 AI-37683-13

NIH/NIAID

Donor Cell Facilitation of Tolerance

The role of natural killer T cells in organ transplantation tolerance in mice after combined bone marrow and organ transplantation will be studied. Role: P.I.

1 RO1 HL087240

NIH/NHLBI (PI. Shizuru)

Barriers to Allogeneic Hematopoietic Stem Cell Engraftment

Goals: The overall goal is to utilize the experimental systems we have developed to further understand the biology of how hematopoietic cells are recognized and resisted. Based upon our understanding of the immune and non-immune barriers to engraftment, we have a long-term goal of making allogeneic HCT safer and more effective for the treatment of malignant and non-malignant disease. Role: Co-Investigator

7/01/04 - 6/30/09

no cost extension

3/01/07 - 2/29/12

5/10/07 - 4/30/11

3/01/07 - 2/29/12

The Leukemia and Lymphoma Society 1311 Mamaroneck Ave, White Plains, NY

Treatment of Lymphoma with Tumor Immune Marrow Transplants

Goals: The goal of the proposed research is to reduce the incidence of relapse by studying animal models that will increase the graft anti-lymphoma activity of immune cells in the transplant while maintaining the low incidence of graft versus host disease. Role: Pl

PENDING

NIH/NHLBI – Project 1 and Core A Strober (PI) Blood Stem Cell Transplantation as Immunotherapy

Project 1: TLI and ATG Conditioning for Combined Kidney and Blood Stem Cell Transplantation Goals: The goal of the research program is to develop immune tolerance to combined HLA haplotype matched living related kidney and hematopoietic cell transplants in order to remove the requirement for the lifelong use of maintenance immunosuppressive drugs and to improve long term graft survival.

NIH R01DK082537 Strober (PI)

Lupus Glomerulonephritis and NKT cells Goals: The goal of this proposed research is to elucidate the cellular and molecular mechanisms by which NKT cells promote lupus glomerulonephritis in mice and humans by studying immune cells in the spleen, blood, and diseased kidneys.

NIH/NIAID- AI-08-011 10160572 Strober (PI) Gene and Cytokine Expression in Tolerance and GVHD

Goals: To provide information about guidance of drug withdrawal and further insight into the cellular and molecular immune mechanisms of tolerance and GVHD protection.

4/1/10 - 3/31/15

4.8 calendar 40% effort

1.2 calendar 10% effort

10/01/08 - 9/30/11

7/1/09 - 6/30/14

7/1/09 - 6/30/13