

**BIOGRAPHICAL SKETCH**

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NAME David Bram Lewis	POSITION TITLE Professor of Pediatrics		
eRA COMMONS USER NAME LEWIS.DAVID			
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
Yale University, New Haven, CT	B.S.	1976	Biology
University of California, San Francisco, CA	M.D.	1981	Medicine

**Academic Positions:**

1981-1982 Pediatric Internship, Children's Hospital and Medical Center, Seattle, WA  
 1982-1984 Pediatric Resident, University of California, San Francisco, CA  
 1985-1988 Fellow, Pediatric Infectious Disease, University of Washington, Seattle, WA  
 1988-1989 Instructor of Pediatrics, University of Washington, Seattle, WA  
 1989-1994 Assistant Professor of Pediatrics, University of Washington, Seattle, WA  
 1992-1994 Adjunct Assistant Professor of Immunology, University of Washington, Seattle, WA  
 1994-1997 Associate Professor of Pediatrics, University of Washington, Seattle, WA  
 1994-1997 Adjunct Associate Professor of Immunology, University of Washington, Seattle, WA  
 1997-2005 Associate Professor of Pediatrics, Stanford University, Stanford, CA  
 2005- Professor of Pediatrics, Stanford University, Stanford, CA  
 2008- Chief of Division of Immunology and Allergy, Stanford University

**Honors:**

B.S., *Summa cum laude* in Biology (1976)  
 Phi Beta Kappa (1976)  
 Alpha Omega Alpha, University of California (1981)  
 March of Dimes Basil O'Connor Scholar Research Award (1990-93)  
 Ross Young Investigator Award, Society for Pediatric Research (1993)  
 Science in Medicine Investigator Award, University Of Washington (1996)  
 Kaiser Award for Excellence in Medical Student Teaching (2001 and 2005)  
 Director, Jeffrey Modell Foundation Primary Immunodeficiency Center at Stanford (2002-present).

**Public and Professional Service:**

NIH Ad Hoc Reviewer – NHLBI Special Emphasis – 7/01  
 Pediatric Infectious Disease Sub-Board Panel Member - 10/01-10/08  
 Immune Deficiency Foundation, Medical Advisory Committee Member – 11-03-present  
 US Primary Immunodeficiency Network Grant Review Committee – 11/03-present  
 Faculty Member, AAI Advanced Course in Immunology 8/04  
 Society for Pediatric Research Nominating Committee 7/04-7/05  
 NIH NICHD Study Section – CHDDA 10/01-6/03; Pediatrics 6/03 to 6/06  
 NIH Ad Hoc Reviewer – CBJ(3) Study Section – Flow Cytometry (S10) Applications - 7/09

**B. Selected peer-reviewed publications (in chronological order).**

1. **Lewis, DB**, Larsen, A, and Wilson CB. Reduced interferon gamma mRNA levels in neonates: Evidence for an intrinsic T-cell deficiency independent of other genes involved in T-cell activation. *J. Exp. Med.* 163:1018-1023, 1986.
2. Ziegler, SF, Marth JD, **Lewis DB**, and Perlmutter RM. Novel protein-tyrosine kinase gene (*hck*) preferentially expressed in cells of hematopoietic origin. *Mol. Cell. Biol.* 7:2276-2285, 1987.  
Marth, JD, **Lewis DB**, Wilson, CB, Gearn ME, Krebs EG, and Perlmutter RM. Regulation of *pp56lck* during T cell activation. *Eur. Mol. Biol. Org. J.* 6:2727-2734, 1987.
3. deVillartay J-P, **Lewis DB**, Hockett R, Korsmeyer S, Waldmann T, and Cohen D. A new type of rearrangement involving the human TCR- $\alpha$  gene. *Proc. Natl. Acad. Sci. USA* 84:8608-8612, 1987.
4. **Lewis DB**, Prickett K, Larsen A, Grabstein K, Weaver M, and Wilson CB. Restricted production of interleukin-4 by activated human T cells. *Proc. Natl. Acad. Sci. USA* 85:9743-9747, 1988.
5. **Lewis DB**, Yu, CC, Forbush, KA, Carpenter J, Sato TA, Grossmann A, Liggitt DA, and Perlmutter RM. IL-4 expressed *in situ* selectively alters thymocyte development. *J. Exp. Med.* 173:89-100, 1991.
6. **Lewis DB**, Yu CC, Meyer J, English BK, Kahn SJ, Wilson CB. Cellular and molecular mechanisms for reduced interleukin-4 and interferon- $\gamma$  production by neonatal T cells. *J Clin Invest* 87:194-202, 1991.
7. Wildin RS, Garvin AM, Pawar S, **Lewis DB**, Abraham KM, Forbush KA, Perlmutter RM. Developmental regulation of *lck* gene expression in T lymphocytes. *J Exp Med* 173:383-393, 1991.
8. **Lewis DB**, Liggitt HD, Effmann EL, Motley ST, Teitelbaum SL, Jepsen KJ, Bonadio J, Goldstein SA, Carpenter J, and Perlmutter RM. Osteoporosis induced in mice by overproduction of interleukin-4. *Proc Natl Acad Sci USA* 90:11618-11622, 1993.
9. Young HA, Ghosh P, Ye J, Lederer J, Lichtman A, Gerard JR, Penix L, Wilson CB, Melvin AJ, McGurn ME, **Lewis DB**, Taub D. Differentiation of the T helper phenotypes by analysis of the methylation state of the interferon-gamma gene. *J Immunol* 153:3603-3610, 1994.
10. Melvin AJ, McGurn ME, Bort SJ, Gibson C, **Lewis DB**. Hypomethylation of the IFN- $\gamma$  gene correlates with its expression by primary T-lineage cells. *Eur J Immunol* 25:426-430, 1995.
11. Nonoyama S, Penix L, Edwards CP, Aruffo A, **Lewis DB**, Wilson CB, Ochs HD. Diminished expression of CD40 ligand (gp39) by activated neonatal T cells: Effect on immunoglobulin production and class switching. *J Clin Invest* 95:66-75, 1995.
12. Schubert LA, King G, Cron RQ, **Lewis DB**, Aruffo A, Hollenbaugh D. The human gp39 promoter: Two distinct nuclear factor of activated T-cell protein binding elements contribute independently to transcriptional activation. *J Biol Chem* 279:29624-29627, 1995.
13. Dolganov, G, Bort S, Lovett M, Burr J, Schubert L, Short D, McGurn M, Gibson C, **Lewis DB**. Co-expression of the interleukin-13 and interleukin-4 genes correlates with their physical linkage in the cytokine gene cluster on human chromosome 5q23-31. *Blood* 87:3316-3326, 1996.
14. Zhang Y, Rogers KH, **Lewis DB**.  $\beta$ 2-Microglobulin-dependent T cells are dispensable for allergen-induced Th2 responses. *J Exp Med* 184:1507-1512, 1996.
15. Henderson WR Jr, **Lewis DB**, Albert RK, Zhang Y, Lamm WJE, Eriksen P, Jonas M, Chi EY. The importance of leukotrienes in an airway inflammation mouse model of asthma. *J Exp Med* 184:1483-1494, 1996.
16. Cron RQ, Bort SJ, Wang Y, Brunvand M, **Lewis DB**. T Cell Priming Enhances IL-4 Gene Expression by Increasing NFAT. *J Immunol* 162:860-870, 1999.
17. Zheng D, **Lewis DB**, Dejbaksh-Jones S, Lan F, Garcia-Ojeda M, Sibley R, Strober S. Bone marrow NK1.1- and NK1.1+ T cells reciprocally regulate lethal graft-versus-host-disease. *J Exp Med* 189:1073-1082, 1999.
18. Alizadeh A, Eisen MB, Davis RE, Ma C, Lossos IS, Rosenwald A, Boldrick JC, Sabet H, Tran T, Yu X, Powell JI, Liming Y, Marti GE, Moore T, Hudson Jr, J, Lu L, **Lewis DB**, Tibshirani R, Sherlock G, Chan WC, Greiner TC, Weisenburger DD, Armitage JO, Warnke R, Levy R, Wilson W, Grever MR, Byrd JC, Botstein D, Brown PO, Staudt LM. Distinct types of diffuse large B-cell lymphoma identified by gene expression profiling. *Nature* 403:503-511, 2000.
19. Cron RQ, Bartz SR, Clausell A, Bort SJ, Klebanoff SJ, **Lewis DB**. NFAT1 enhances HIV-1 gene expression in normal human CD4 T cells. *Clin Immunol* 94:179-191, 2000.
20. Tsitoura DC, Kim S, Dabbagh K, Berry G, **Lewis DB**, Umetsu DT. Respiratory infection with influenza A virus interferes with the induction of tolerance to aeroallergens, *J Immunol*, 165:3484-91, 2000.
21. Dabbagh K, Xiao Y, Smith C, Stepick-Biek P, Kim SG, Lamm W, Liggitt HD, **Lewis DB**. Local blockade of asthmatic airway hyperreactivity and inflammation by the poxvirus-derived pan-CC-chemokine inhibitor vCCI, *J Immunol*, 165:3418-22, 2000.
22. Cron RQ, Brunvand MW, **Lewis DB**. Octamer proteins inhibit IL-4 gene transcription in normal human CD4 T cells, *Genes and Immunity* 2:464-8, 2001.

23. Schubert LA, Cron RQ, Song A, Lu Li-Sheng, Jullien P, Krensky AM, **Lewis DB**: A T- cell-specific enhancer of the human CD40 ligand gene. *J Biol Chem* 277:7386-7395 2002.
24. Dabbagh K, Dahl ME, Stepick-Biek P, **Lewis DB**. Toll-Like receptor 4 activation enhances T helper 2 responses to non-microbial antigens, *J Immunol* 168:4524-4530, 2002.
25. Dunn HS, Haney DJ, Ghanekar SA, Stepick-Biek P, **Lewis DB**, Maecker HT. Dynamics of CD4 and CD8 T cell responses to cytomegalovirus in healthy human donors. *J Infect Dis* 186:15-22, 2002.
26. Schmidlin, F, Amadesi, S, Dabbagh, K, **Lewis, DB**, Knott, P, Bunnett, NW, Gater, PR, Pierangelo, G, Bertrand, C Stevens, ME. Protease-activated receptor 2 mediates eosinophil infiltration and hyperreactivity in allergic inflammation of the airway, *J Immunol* 169:5315-5321, 2002.
27. Cleary AM, Tu W, Enright A, Giffon T, De Waal-Malefyt R, Gutierrez K, **Lewis DB**. Impaired accumulation and function of memory CD4 T cells in human IL-12R $\beta$ 1 deficiency. *J Immunol* 170:597-603, 2003.
28. Jullien P, Cron RQ, Dabbagh K, Tran P, Stepick-Biek P, **Lewis DB**. Mechanisms for decreased CD40-ligand (CD154) expression by human neonatal CD4 T cells, *Int Immunol*, 15:1461-72, 2003.
29. Tu W, Chen S, Sharp M, Dekker C, Adler S, Manganello AM, Maecker HT, Holmes TH, Wang Z, Kemble G, Arvin A, **Lewis DB**. Persistent deficiency of CD4 T cell immunity to cytomegalovirus in immunocompetent young children, *J Immunol*, 172:3260-67, 2004.
30. Dahl ME, Dabbagh K, Kim S, Liggitt DH, and **Lewis DB**. Viral-induced T<sub>H</sub>1 responses enhance allergic disease by effects on lung dendritic cells. *Nat Immunol* 5:337-43, 2004.
31. Chen SF, Tu W-W, Sharp MA, Tongson EC, He X-S, Greenberg HB, Holmes TH, Wang Z, Kemble G, Manganello AM, Adler SP, Dekker CL, **Lewis DB**, Arvin AM. Antiviral CD8 T cells in the control of primary human cytomegalovirus infection in early childhood. *J Infect Dis*, 189:1619-27, 2004.
32. Zhou B, Comeau MR, De Smedt T, Liggitt HD, Dahl ME, **Lewis DB**, Byarmati D, Aye T, Campbell D, Ziegler SF. Thymic stromal lymphopoietin as a key initiator of allergic airway inflammation in mice. *Nat Immunol*, 6:1047-53, 2005.
33. Chen, L, Cleary, AM, **Lewis, DB**. Impaired allogeneic activation and T helper 1 differentiation of human cord blood naïve CD4 T cells, *Biol. Blood Marrow Transplant*, 12:160-171, 2006.
34. Debes, G.F., Dahl, M.E., Mahiny, A.J., Bonhagen, K., Campbell, D.J., Siegmund, K., Erb, KJ, **Lewis, DB**, Kamradt, T, Hamann, A. Chemotactic responses of IL-4-, IL-10- and IFN- $\gamma$ -producing CD4<sup>+</sup> T cells depend on tissue origin and microbial stimulus. *J. Immunol*, 176:557-66, 2006.
35. Potena L, Holweg C, Chin C, Luikart S, Weisshaar HD, Narasimhan B, Fearon WF, **Lewis DB**, Cooke JP, Mocarski ES, Valentine HA; Acute rejection and cardiac allograft vascular disease is reduced by suppression of subclinical cytomegalovirus infection. *Transplantation*, 82:398-405, 2006.
36. Cohen AC, Nadeau KC, Tu W, Hwa V, Dionis K, Bezrodnik L, Teper A, Gaillard M, Heinrich JJ, Krensky AM, Rosenfeld RB, **Lewis, DB**. Decreased accumulation and function of CD4<sup>+</sup>CD25<sup>hi</sup> regulatory T cells in human STAT5b deficiency. *J Immunol*, 177:2770-7, 2006.
37. Tu W, Potena L, Stepick-Biek P, Liu L, Dionis KY, Luikart H, Fearon WF, Cooke JP, Holmes TH, Valentine HA, Mocarski ES, **Lewis DB**. T-cell immunity to subclinical cytomegalovirus infection limits cardiac allograft disease. *Circulation* 114:1608-15, 2006.
38. **Lewis, DB**. Avian flu to human influenzae. *Ann Rev Med*, 57:139-154, 2006.
39. He XS, Holmes TH, Zhang C, Mahmood K, Kemble GW, **Lewis DB**, Dekker CL, Greenberg HB, Arvin AM "Cellular immune responses in children and adults receiving inactivated or live attenuated influenza vaccines." *J Virol* 80:11756-11766, 2006.
40. Zeman AM, Holmes TH, Stamatis S, Tu W, He XS, Bouvier N, Kemble G, Greenberg HB, **Lewis DB**, Arvin AM, Dekker CL. Humoral and cellular immune responses in children given annual immunization with trivalent inactivated influenza vaccine. *Ped Infect Dis J* 26:107-115, 2007.
41. Burster T, Giffon T, Dahl ME, Bjorck P, Bogyo M, Weber E, Mahmood K, **Lewis DB**, Mellins ED. Influenza A virus elevates active cathepsin B in primary murine DC. *Int Immunol* 19:645-655, 2007
42. Dvorak CC, Sandford A, Fong A, Cowan MJ, George TI, **Lewis DB**. Maternal T-cell engraftment associated with severe hemophagocytosis of the bone marrow in untreated X-linked severe combined immunodeficiency. *J Pediatr Hem Onc*, 30:396-400, 2008.
43. Tu W, Lau YL, Zheng J, Liu Y, Chan PL, Mao H, Dionis K, Schneider P, **Lewis DB**. Efficient generation of human alloantigen-specific CD4<sup>+</sup> regulatory T cells from naive precursors by CD40-activated B cells. *Blood* 112:2554-2562, 2008.
44. Haines CJ, Giffon TD, Lu L-S, Lu X, Tessier-Lavigne M, Ross DT, **Lewis DB**. Human CD4<sup>+</sup> T-cell recent thymic emigrants are identified by protein tyrosine kinase 7 and have reduced immune function. *J Exp Med* 206:275-285, 2009.
45. Lay, M, Callejo B, Chang S, Hong DK, **Lewis DB**, Carroll TD, Matzinger S, Fritts L, Miller CJ, Warner JF, Liang L, Fairman J. Cationic lipid/DNA complexes combined with influenza vaccine increases antibody response, cellular immunity, and antigenically drifted protection. *Vaccine* 27:3811-3820, 2009.

**C. Research Support – Ongoing Research****ACTIVE**

U01 AI-074512 (Lewis DB, PI for Stanford) 8/01/07-7/30/12  
 NIH/NIAID \$272,000  
 Adjuvant Enhanced Antiviral Immunity

The major goal of this project is to develop and optimize subcutaneous vaccines for influenza A using cationic lipid/DNA/viral protein complexes. Both murine and non-human primate models will be evaluated.

Role: Co-investigator on overall U01

R56 AI083757-01 (Lewis, DB, PI) 7/21/09-6/30/10  
 NIH/NIAID \$277,250

Recent Thymic Emigrants of the CD4 T-cell Lineage

The major goal of this project is to define the function and phenotype CD4 recent thymic emigrants, as identified using a novel marker, protein tyrosine kinase 7, during normal post-natal development, immune reconstitution following hematopoietic stem cell reconstitution, and after thymectomy. **This is a stimulus-related bridge grant award that will allow the studies of the current proposal to be initiated.**

**PENDING**

1R01 AI-01 (Lewis, DB, PI) 4/01/10-3/31/15  
 NIH/NIAID \$308,097

Recent Thymic Emigrants of the CD4 T-cell Lineage

The major goal of this project is to define the function and phenotype CD4 recent thymic emigrants, as identified using a novel marker, protein tyrosine kinase 7, during normal post-natal development, immune reconstitution following hematopoietic stem cell reconstitution, and after thymectomy. This is the original grant application funded for one year by the R56 mechanism.

**COMPLETED (during the past three years)**

U19 AI057229 (Arvin, A) 9/30/03 - 03/31/09  
 NIH/NIAID \$180,000 (Project 1)

Program: Protective Mechanisms against Pandemic Respiratory Viruses

Subproject 1: CD4 T-cell immunity of influenza infection and vaccination

The major goal is to determine the CD4 T-cell responses to inactivated and live attenuated influenza vaccines.

Role: Subproject 1 Leader

R01 AI53589-01 (Dekker, C) 7/01/03 – 12/31/08  
 NIH/NIAID \$244,312

Health Impact of Congenital Cytomegalovirus Infection

The major goal is to prospectively define the risk of sensorineural deafness and immune sequelae of congenital cytomegalovirus infection.

Role: Co-Investigator

STTR PAS-02-149 NIH/NIAID (Lewis, DB for Stanford) 2/1/06-1/31/08  
 Lipid/DNA/Ag Complexes for Influenza A Viral Vaccination \$100,000

The major goal of this project is to use mouse models to test cationic lipid/DNA/viral protein complexes as a vaccine strategy for epidemic and pandemic influenza A infection.

The Dana Foundation (Lewis, DB) 1/01/05-12/31/07  
 \$100,000

Mechanism of T-cell immunodeficiency in Schmike immuno-osseous dysplasia

The goal is to the mechanisms of T-cell immunodeficiency in genetic deficiency of SMARCAL1.