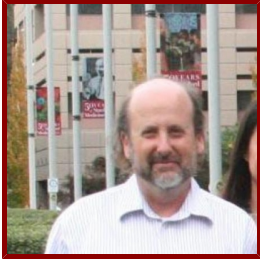


# Stanford

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## David B. Lewis M.D.

Professor of Pediatrics (Immunology) at the Lucile Salter Packard Children's Hospital  
Pediatrics - Immunology and Allergy

 NIH Biosketch available Online

### CLINICAL OFFICES

- **Pediatric Allergy and Immunology**

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### ACADEMIC CONTACT INFORMATION

- **Alternate Contact**

Elena Infeld - Administrative Assistant

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### Bio

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#### CLINICAL FOCUS

- Primary Immunodeficiency
- Pediatrics

#### ACADEMIC APPOINTMENTS

- Professor - Med Center Line, Pediatrics - Immunology and Allergy
- Member, Child Health Research Institute
- Member, Stanford Cancer Institute

#### ADMINISTRATIVE APPOINTMENTS

- Acting Associate Professor, Stanford University, Department of Pediatrics, (1997-1997)
- Associate Professor, Stanford University, Department of Pediatrics, (1997-2005)
- Director of the Jeffrey Modell Primary Immunodeficiency Center at Stanford, Supported by the Jeffrey Modell Foundation and the Lucile Packard Fund of Children's Health, (2002- present)
- Professor, Stanford University, Department of Pediatrics, (2005- present)
- Chief, Stanford Department of Pediatrics, Division of Immunology and Allergy, (2008- present)

#### HONORS AND AWARDS

- Henry J. Kaiser Award for Excellence in Preclinical Teaching (Immunology), Kaiser Foundation (2001)
- Henry J. Kaiser Award for Excellence in Preclinical Teaching (Immunology), Kaiser Foundation (2005)

#### PROFESSIONAL EDUCATION

- Fellowship: Childrens Hospital and Regional Medical Center Fellowships (1988) WA
- Internship: Childrens Hospital and Regional Medical Center Fellowships (1982) WA
- Board Certification: Pediatrics, American Board of Pediatrics (1986)

- Residency: UCSF Medical Center (1984) CA
- Medical Education: UCSF Medical Center (1981) CA
- M.D., Univ.Calif at San Francisco , Medicine (1981)
- B.S., Yale University , Biology (1976)

## LINKS

- Lewis Lab Website: <http://dblewislab.stanford.edu>

## Research & Scholarship

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### CURRENT RESEARCH AND SCHOLARLY INTERESTS

A long-standing interest is to understand the cellular and molecular basis for this vulnerability of the human neonate to infection with intracellular pathogens that require T helper 1 (Th1) cells [CD4 T cell producing interferon-gamma (IFN-gamma)] for effective immune control. We have previously shown that CD4 T cells of the newborn have a unique limitation in the ability to produce certain effector molecules, such as CD40-ligand (CD154) and IFN-gamma compared to these cells in adults due to both reduced gene transcriptional and impaired signals that lead to gene transcription. Recently, we have shown that these limitations apply to physiological T-cell activation, e.g., using allogeneic dendritic cells. Defining the molecular mechanisms for decreased IFN-gamma production by neonatal CD4 T cells is a current focus.

We have also found that recent thymic emigrants, which predominate in the newborn and young infant, are less able to differentiate into T helper 1 cells, which produce IFN-gamma. These studies required the development of a novel marker for recent thymic emigrants (RTEs) of the CD4 T-cell lineage in humans. Using a combination of approaches, we have identified protein tyrosine kinase 7 (PTK7) as such a marker. In progress are to studies to define the role of PTK7, an orphan member (no known ligand) of the receptor tyrosine kinase family, in T-cell development and immunity, and to determine how this marker can be used to follow the output of recent thymic emigrants in health and disease. We are also interested in determining the molecular mechanisms for the reduced RTE function and to what extent these mechanisms are shared by neonatal CD4 T cells and CD4+CD8-CD3+ thymocytes, the immediate precursors of antigenically naive CD4 T cells.

We have also found that limitations in T-cell immunogenicity to viruses and viral vaccines extend beyond the neonatal period to childhood. These studies highlight a need to develop more potent vaccines to overcome developmental and other factors, such as genetic inheritance, in mounting adaptive immunity. With this as an ultimate goal, we are examining the ability of a novel adjuvant, cationic liposome DNA complexes (CLDC)(Juvaris Biotherapeutics), to induce durable CD4 and CD8 T-cell immunity and humoral immunity to influenza A. The molecular and cellular components of the innate immune system that are required for immunogenicity are of particular interest. Our preliminary results in mice suggest that the CLDC adjuvant will be substantially more robust than any adjuvants currently approved for clinical use or in clinical trials.

In collaboration with Dr. Neal Boerkoel, University of British Columbia, we are defining the mechanism of T-cell lymphopenia in genetic deficiency of SMARCAL1, a protein that may play a novel role in PolII gene transcription using T cells from patients with SMARCAL1 deficiency (Schimke immuno-osseous dysplasia) as well as SMARCAL1 knockout mice. We hypothesize that the peripheral T-cell lymphopenia is due to attenuation of transcriptional efficiency for multiple genes required for T-cell development and peripheral homeostasis, e.g., cytokines and cytokine receptors.

## Teaching

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### COURSES

#### 2018-19

- Immunology in Health and Disease: IMMUNOL 205 (Win)

#### 2017-18

- Immunology in Health and Disease: IMMUNOL 205 (Win)

#### 2016-17

- Immunology in Health and Disease: IMMUNOL 205 (Win)

#### 2015-16

- Immunology in Health and Disease: IMMUNOL 205 (Win)

### STANFORD ADVISEES

#### Postdoctoral Faculty Sponsor

Elizabeth Lippner

### GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

- Immunology (Phd Program)
- Infectious Diseases (Fellowship Program)

## Publications

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### PUBLICATIONS

- **Mapping the Fetomaternal Peripheral Immune System at Term Pregnancy.** *Journal of immunology*  
Fragiadakis, G. K., Baca, Q. J., Gherardini, P. F., Ganio, E. A., Gaudilliere, D. K., Tingle, M., Lancero, H. L., McNeil, L. S., Spitzer, M. H., Wong, R. J., Shaw, G. M., Darmstadt, G. L., Sylvester, et al  
2016
- **A cationic liposome-DNA complexes adjuvant (JVRS-100) enhances the immunogenicity and cross-protective efficacy of pre-pandemic influenza A (H5N1) vaccine in ferrets** *VIROLOGY*  
Liu, F., Sun, X., Fairman, J., Lewis, D. B., Katz, J. M., Levine, M., Tumpey, T. M., Lu, X.  
2016; 492: 197-203
- **Lack of IL7Ra expression in T cells is a hallmark of T-cell immunodeficiency in Schimke immuno-osseous dysplasia (SIOD).** *Clinical immunology*  
Sanyal, M., Morimoto, M., Baradaran-Heravi, A., Choi, K., Kambham, N., Jensen, K., Dutt, S., Dionis-Petersen, K. Y., Liu, L. X., Felix, K., Mayfield, C., Dekel, B., Bokenkamp, et al  
2015; 161 (2): 355-365
- **Single-cell systems-level analysis of human Toll-like receptor activation defines a chemokine signature in patients with systemic lupus erythematosus** *JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY*  
O'Gorman, W. E., Hsieh, E. W., Savig, E. S., Gherardini, P. F., Hernandez, J. D., Hansmann, L., Balboni, I. M., Utz, P. J., Bendall, S. C., Fantl, W. J., Lewis, D. B., Nolan, G. P., Davis, et al  
2015; 136 (5): 1326-1336
- **Heightened risk of preterm birth and growth restriction after a first-born son** *ANNALS OF EPIDEMIOLOGY*  
Bruckner, T. A., Mayo, J. A., Gould, J. B., Stevenson, D. K., Lewis, D. B., Shaw, G. M., Carmichael, S. L.  
2015; 25 (10): 743-747
- **Implementing Mass Cytometry at the Bedside to Study the Immunological Basis of Human Diseases: Distinctive Immune Features in Patients with a History of Term or Preterm Birth** *CYTOMETRY PART A*  
Gaudilliere, B., Ganio, E. A., Tingle, M., Lancero, H. L., Fragiadakis, G. K., Baca, Q. J., Aghaeepour, N., Wong, R. J., Quintance, C., El-Sayed, Y. Y., Shaw, G. M., Lewis, D. B., Stevenson, et al  
2015; 87A (9): 817-829
- **Heme oxygenase and the immune system in normal and pathological pregnancies.** *Frontiers in pharmacology*  
Ozen, M., Zhao, H., Lewis, D. B., Wong, R. J., Stevenson, D. K.  
2015; 6: 84-?
- **Bayesian immunological model development from the literature: Example investigation of recent thymic emigrants.** *Journal of immunological methods*  
Holmes, T. H., Lewis, D. B.  
2014; 414: 32-50

- **Somatic reversion in dedicator of cytokinesis 8 immunodeficiency modulates disease phenotype.** *journal of allergy and clinical immunology*  
Jing, H., Zhang, Q., Zhang, Y., Hill, B. J., Dove, C. G., Gelfand, E. W., Atkinson, T. P., Uzel, G., Matthews, H. F., Mustillo, P. J., Lewis, D. B., Kavadas, F. D., Hanson, et al  
2014; 133 (6): 1667-1675
- **ICOS Regulates the Generation and Function of Human CD4(+) Treg in a CTLA-4 Dependent Manner** *PLOS ONE*  
Zheng, J., Chan, P., Liu, Y., Qin, G., Xiang, Z., Lam, K., Lewis, D. B., Lau, Y., Tu, W.  
2013; 8 (12)
- **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
- **Newborn screening for severe combined immunodeficiency and T-cell lymphopenia in California: Results of the first 2 years** *JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY*  
Kwan, A., Church, J. A., Cowan, M. J., Agarwal, R., Kapoor, N., Kohn, D. B., Lewis, D. B., McGhee, S. A., Moore, T. B., Stiehm, E. R., Porteus, M., Aznar, C. P., Currier, et al  
2013; 132 (1): 140-U245
- **Retinoic Acid Hypersensitivity Promotes Peripheral Tolerance in Recent Thymic Emigrants** *JOURNAL OF IMMUNOLOGY*  
Bhaumik, S., Giffon, T., Bolinger, D., Kirkman, R., Lewis, D. B., Weaver, C. T., Randolph, D. A.  
2013; 190 (6): 2603-2613
- **Human Neonatal Naive CD4(+) T Cells Have Enhanced Activation-Dependent Signaling Regulated by the MicroRNA miR-181a** *JOURNAL OF IMMUNOLOGY*  
Palin, A. C., Ramachandran, V., Acharya, S., Lewis, D. B.  
2013; 190 (6): 2682-2691
- **Human CD8(+) Regulatory T Cells Inhibit GVHD and Preserve General Immunity in Humanized Mice** *SCIENCE TRANSLATIONAL MEDICINE*  
Zheng, J., Liu, Y., Liu, Y., Liu, M., Xiang, Z., Lam, K., Lewis, D. B., Lau, Y., Tu, W.  
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- **Reduced elastogenesis: a clue to the arteriosclerosis and emphysematous changes in Schimke immuno-osseous dysplasia?** *ORPHANET JOURNAL OF RARE DISEASES*  
Morimoto, M., Yu, Z., Stenzel, P., Clewing, J. M., Najafian, B., Mayfield, C., Henderson, G., Weinkauff, J. G., Gormley, A. K., Parham, D. M., Ponniah, U., Andre, J., Asakura, et al  
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- **ICOS-ICOSL regulates the generation and function of CD4(+) Treg in a CTLA-4 dependent manner** *European Congress of Immunology*  
Zheng, J., Chan, P. L., Liu, Y., Qin, G., Xiang, Z., Lam, K. T., Lewis, D. B., Lau, Y. L., Tu, W.  
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- **Dental Abnormalities in Schimke Immuno-osseous Dysplasia** *JOURNAL OF DENTAL RESEARCH*  
Morimoto, M., Kerouedan, O., Gendronneau, M., Shuen, C., Baradaran-Heravi, A., Asakura, Y., Basiratnia, M., Bogdanovic, R., Bonneau, D., Buck, A., Charrow, J., Cochat, P., DeHaai, et al  
2012; 91 (7): S29-S37
- **Dental abnormalities in Schimke immuno-osseous dysplasia.** *Journal of dental research*  
Morimoto, M., K erour edan, O., Gendronneau, M., Shuen, C., Baradaran-Heravi, A., Asakura, Y., Basiratnia, M., Bogdanovic, R., Bonneau, D., Buck, A., Charrow, J., Cochat, P., DeHaai, et al  
2012; 91 (7): 29S-37S
- **Genotype, phenotype, and outcomes of nine patients with T-B plus NK plus SCID** *PEDIATRIC TRANSPLANTATION*  
Yu, G. P., Nadeau, K. C., Berk, D. R., de Saint Basile, G., Lambert, N., Knapnougel, P., Roberts, J., Kavanau, K., Dunn, E., Stiehm, E. R., Lewis, D. B., Umetsu, D. T., Puck, et al  
2011; 15 (7): 733-741
- **Protein tyrosine kinase 7: a novel surface marker for human recent thymic emigrants with potential clinical utility** *JOURNAL OF PERINATOLOGY*  
Lewis, D. B., Haines, C., Ross, D.  
2011; 31: S72-S81

- **CROSS-REACTIVE NEUTRALIZING ANTIBODY AGAINST PANDEMIC 2009 H1N1 INFLUENZA A VIRUS IN INTRAVENOUS IMMUNOGLOBULIN PREPARATIONS** *PEDIATRIC INFECTIOUS DISEASE JOURNAL*  
Hong, D. K., Tremoulet, A. H., Burns, J. C., Lewis, D. B.  
2011; 30 (1): 67-69
- **Generation of human Th1-like regulatory CD4(+) T cells by an intrinsic IFN-gamma- and T-bet-dependent pathway** *EUROPEAN JOURNAL OF IMMUNOLOGY*  
Zheng, J., Liu, Y., Qin, G., Lam, K., Guan, J., Xiang, Z., Lewis, D. B., Lau, Y., Tu, W.  
2011; 41 (1): 128-139
- **Cationic Lipid/DNA Complex-Adjuvanted Influenza A Virus Vaccination Induces Robust Cross-Protective Immunity** *JOURNAL OF VIROLOGY*  
Hong, D. K., Chang, S., Botham, C. M., Giffon, T. D., Fairman, J., Lewis, D. B.  
2010; 84 (24): 12691-12702
- **Revisiting Human IL-12R beta 1 Deficiency A Survey of 141 Patients From 30 Countries** *MEDICINE*  
de Beaucoudrey, L., Samarina, A., Bustamante, J., Cobat, A., Boisson-Dupuis, S., Feinberg, J., Al-Muhsen, S., Janniere, L., Rose, Y., de Suremain, M., Kong, X., Filipe-Santos, O., Chappier, et al  
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- **Alternate Mechanisms of Initial Pattern Recognition Drive Differential Immune Responses to Related Poxviruses** *CELL HOST & MICROBE*  
O'Gorman, W. E., Sampath, P., Simonds, E. F., Sikorski, R., O'Malley, M., Krutzik, P. O., Chen, H., Panchanathan, V., Chaudhri, G., Karupiah, G., Lewis, D. B., Thorne, S. H., Nolan, et al  
2010; 8 (2): 174-185
- **Adult-onset presentations of genetic immunodeficiencies: genes can throw slow curves** *CURRENT OPINION IN INFECTIOUS DISEASES*  
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- **A new genetic subgroup of chronic granulomatous disease with autosomal recessive mutations in p40(phox) and selective defects in neutrophil NADPH oxidase activity** *BLOOD*  
Matute, J. D., Arias, A. A., Wright, N. A., Wrobel, I., Waterhouse, C. C., Li, X. J., Marchal, C. C., Stull, N. D., Lewis, D. B., Steele, M., Kellner, J. D., Yu, W., Meroueh, et al  
2009; 114 (15): 3309-3315
- **Efficient Induction and Expansion of Human Alloantigen-Specific CD8 Regulatory T Cells from Naive Precursors by CD40-Activated B Cells** *JOURNAL OF IMMUNOLOGY*  
Zheng, J., Liu, Y., Qin, G., Chan, P., Mao, H., Lam, K., Lewis, D. B., Lau, Y., Tu, W.  
2009; 183 (6): 3742-3750
- **Cationic lipid/DNA complexes (JVRS-100) combined with influenza vaccine (Fluzone (R)) increases antibody response, cellular immunity, and antigenically drifted protection** *VACCINE*  
Lay, M., Callejo, B., Chang, S., Hong, D. K., Lewis, D. B., Carroll, T. D., Matzinger, S., Fritts, L., Miller, C. J., Warner, J. F., Liang, L., Fairman, J.  
2009; 27 (29): 3811-3820
- **Human CD4(+) T cell recent thymic emigrants are identified by protein tyrosine kinase 7 and have reduced immune function** *JOURNAL OF EXPERIMENTAL MEDICINE*  
Haines, C. J., Giffon, T. D., Lu, L., Lu, X., Tessier-Lavigne, M., Ross, D. T., Lewis, D. B.  
2009; 206 (2): 275-285
- **Efficient generation of human alloantigen-specific CD4(+) regulatory T cells from naive precursors by CD40-activated B cells** *BLOOD*  
Tu, W., Lau, Y., Zheng, J., Liu, Y., Chan, P., Mao, H., Dionis, K., Schneider, P., Lewis, D. B.  
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- **Focus on FOCIS: The continuing diagnostic challenge of autosomal recessive chronic granulomatous disease** *CLINICAL IMMUNOLOGY*  
Yu, G., Hong, D. K., Dionis, K. Y., Rae, J., Heyworth, P. G., Curnutte, J. T., Lewis, D. B.  
2008; 128 (2): 117-126
- **Maternal T-cell engraftment associated with severe hemophagocytosis of the bone marrow in untreated X-linked severe combined immunodeficiency** *JOURNAL OF PEDIATRIC HEMATOLOGY ONCOLOGY*  
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- **Asymmetric dimethylarginine and cardiac allograft vasculopathy progression: Modulation by sirolimus** *TRANSPLANTATION*  
Potena, L., Fearon, W. F., Sydow, K., Holweg, C., Luikart, H., Chin, C., Weisshaar, D., Mocarski, E. S., Lewis, D. B., Valantine, H. A., Cooke, J. P.  
2008; 85 (6): 827-833
- **A novel mutation associated with autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy** *ANNALS OF ALLERGY ASTHMA & IMMUNOLOGY*  
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2008; 100 (2): 169-169
- **Influenza A virus elevates active cathepsin B in primary murine DC** *INTERNATIONAL IMMUNOLOGY*  
Burster, T., Giffon, T., Dahl, M. E., Bjorck, P., Bogy, M., Weber, E., Mahmood, K., Lewis, D. B., Mellins, E. D.  
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- **[Coronary allograft vasculopathy: pathophysiological interaction between the immune system, infections and metabolic syndrome].** *Giornale italiano di cardiologia (2006)*  
Potena, L., Ferrara, R., Mocarski, E. S., Lewis, D. B., Cooke, J. P., Grigioni, F., Coccolo, F., Magnani, G., Fallani, F., Magelli, C., Valantine, H. A., Branzi, A.  
2007; 8 (2): 73-82
- **Humoral and cellular immune responses in children given annual immunization with trivalent inactivated influenza vaccine** *PEDIATRIC INFECTIOUS DISEASE JOURNAL*  
Zeman, A. M., Holmes, T. H., Stamatis, S., Tu, W., He, X., Bouvier, N., Kemble, G., Greenberg, H. B., Lewis, D. B., Arvin, A. M., Dekker, C. L.  
2007; 26 (2): 107-115
- **A novel missense mutation in CYBB gene in chronic granulomatous disease** *63rd Annual Meeting of the American-Academy-of-Allergy-Asthma-and-Immunology*  
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- **Cellular immune responses in children and adults receiving inactivated or live attenuated influenza vaccines** *JOURNAL OF VIROLOGY*  
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- **T-cell immunity to subclinical cytomegalovirus infection reduces cardiac allograft disease** *CIRCULATION*  
Tu, W., Potena, L., Stepick-Biek, P., Liu, L., Dionis, K. Y., Luikart, H., Fearon, W. F., Holmes, T. H., Chin, C., Cooke, J. P., Valantine, H. A., Mocarski, E. S., Lewis, et al  
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- **Cutting edge: Decreased accumulation and regulatory function of CD4(+)CD25(high) T cells in human STAT 5b deficiency** *JOURNAL OF IMMUNOLOGY*  
Cohen, A. C., Nadeau, K. C., Tu, W., Hwa, V., Dionis, K., Bezrodnik, L., Teper, A., Gaillard, M., Heinrich, J., Krensky, A. M., Rosenfeld, R. G., Lewis, D. B.  
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- **Acute rejection and cardiac allograft vascular disease is reduced by suppression of subclinical cytomegalovirus infection** *TRANSPLANTATION*  
Potena, L., Holweg, C. T., Chin, C., Luikart, H., Weisshaar, D., Narasimhan, B., Fearon, W. F., Lewis, D. B., Cooke, J. P., Mocarski, E. S., Valantine, H. A.  
2006; 82 (3): 398-405
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Lewis, D. B., Gern, J. E., Hill, H. R., Friedlander, S. L., La Pine, T. R., Lemanske, R. F., Stiehm, E. R.  
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- **Impaired allogeneic activation and T-helper differentiation of human cord blood naive CD4 T cells** *BIOLOGY OF BLOOD AND MARROW TRANSPLANTATION*  
Chen, L., Cohen, A. C., Lewis, D. B.  
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- **Prevention of subclinical CMV infection reduces cardiac allograft disease progression by positively affecting coronary remodeling**  
Potena, L., Fearon, W., Holweg, C., Luikart, H., Chin, C., Cooke, J., Lewis, D., Mocarski, E., Valantine, H.  
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- **Chemotactic responses of IL-4-, IL-10-, and IFN-gamma-producing CD4(+) T cells depend on tissue origin and microbial stimulus** *JOURNAL OF IMMUNOLOGY*  
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