

BIOGRAPHICAL SKETCH

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NAME Michael M. Lederman, M.D.		POSITION TITLE Scott R. Inkley Professor of Medicine Professor of Microbiology/Molecular Biology and Pathology, Director, CWRU Center for AIDS Research	
eRA COMMONS USER NAME MLEDERMAN			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
Brandeis University, Waltham, MA	B.A.	1970	Biology
Mount Sinai School of Medicine, New York, NY	M.D.	1974	Medicine

A. Positions.

1974-1978 Residency, Chief Residency in Med, Univ Hospitals of Cleveland, Cleveland VA Med Center
1978-1980 Fellow in Infectious Diseases, CWRU, University Hospitals of Cleveland
1980-2002 Asst Professor, Assoc Professor, Professor, Department of Medicine, CWRU/UHC
1985-1989 Founding Director, Special Immunology Unit, University Hospitals of Cleveland.
1987 - Present Director, CWRU/UHC AIDS Clinical Trials Unit
1999-Present Director, CWRU/UHC Center for AIDS Research
2002- Present Scott R. Inkley Professor of Medicine, CWRU/UHC

Current External Committees, Study Sections, Advisories:

NIH, ACTG Executive Committee and Scientific Agenda Steering Committee; IDSA, Annual Meeting Program Committee; U. Capetown/U. Witwatersrand CIPRA External Advisory Committee. Forum for Collaborative HIV Research Executive Committee; NIAID, ACE Study Section (Chair 2006-2008); AMFAR Scientific Advisory Committee; CFAR External Advisory Boards: U Penn, UNC, UC Davis, UCSF, University of Washington; Agence Nationale de Recherches sur le Sida (ANRS), Scientific Advisory Board: NIH Office of AIDS Research – Chair Microbicides FY 2006, 2007 Planning Committee; Keystone HIV Pathogenesis Meeting Chairman (Banff) 2005; Wellcome Trust Tropical and Clinical Immunology and Infectious Diseases Funding Committee.

B. Peer-reviewed publications (selected from more than 220).

1. **Lederman MM**, Ratnoff OD, Scillian J, Jones PK, Schacter B. Impaired Cell Mediated Immunity in Patients with Classic Impaired Cell Mediated Immunity in Patients with Classic Hemophilia (Factor VIII Deficiency) N Engl J Med 308:79-83, 1983.
2. Ratnoff OD, Menitove JE, Aster RH, **Lederman MM**. Coincident Classic Hemophilia and "Idiopathic" Thrombocytopenic Purpura in Patients Under Treatment with Concentrates of Antihemophilic Factor (Factor VIII) N Engl J Med 308:439-442, 1983.
3. **Lederman MM**, Ratnoff OD, Evatt BL, McDougal JS. Acquisition of Antibody to Lymphadenopathy-Associated Virus (LAV) in Patients With Classic Hemophilia (Factor VIII Deficiency). Ann Intern Med 102:753-757, 1985.
4. Katzman M, **Lederman MM**. Defective Postbinding Lysis Underlies the Impaired Natural Killer Activity in Factor VIII-Treated, HTLV-III Seropositive Hemophiliacs. J Clin Invest 77:1057-1062, 1986.
5. **Lederman MM**, Purvis S, Walter EI, Carey JT, Medof ME. Heightened Complement Sensitivity of Acquired Immunodeficiency Syndrome Lymphocytes Related to Diminished Expression of Decay-Accelerating Factor. Proc Nat Acad Sci 86:4205-4209, 1989.
6. Patki AH, Quiñones-Mateu ME, Dorazio D, Yen-Lieberman B, Boom WH, Thomas EK, **Lederman MM**. Activation of Antigen-Induced Lymphocyte Proliferation by Interleukin-15 Without the Mitogenic Effect of Interleukin-2 That May Induce Human Immunodeficiency Virus-1 Expression. J Clin Invest 98:3:616-21, 1996.
7. **Lederman MM**, Connick E, Landay A, Kuritzkes DR, Spritzler J, St. Clair M, Kotzin BL, Fox L, Heath Chiozzi M, Leonard JM, Rousseau F, Wade M, D'Arc Roe J, Martinez A, Kessler H. Immunologic Responses Associated with 12 Weeks of Combination Antiretroviral Therapy Consisting of Zidovudine, Lamivudine and Ritonavir: Results of AIDS Clinical Trials Group Protocol 315. J Inf Dis 178:70-79, 1998.

8. Badley AD, Dockrell DH, Ziesmer S, Landay A, **Lederman MM**, Connick E, Kessler H, Kuritzkes D, Lynch DH, Roche P, Yagita H, Paya CV. In vivo Analysis of Fas/FasL Interactions in HIV-Infected Patients. J Clin Invest 102:79-87, 1998.
9. Fry TJ, Connick E, Falloon J, **Lederman MM**, Liewehr, Spritzler J, Steinberg SM, Wood LV, Yarchoan R, Zuckerman J, Landay A, Mackall CL. A potential role of IL-7 in T cell homeostasis. Blood 97:2983-2990, 2001.
10. Teixeira L, Valdez H, McCune JM, Koup RA, Badley AD, Hellerstein MK, Napolitano LA, Douek DC, Mbisa G, Deeks S, Harris JM, Barbour JD, Gross BH, Francis IR, Halvorsen R, Asaad R, **Lederman MM**. Poor CD4+ T-cell restoration after suppression of HIV-1 replication may reflect lower thymic function. AIDS 15:1749-56, 2001.
11. Sieg SF, Bazdar DA, Harding CV, **Lederman MM**. Differential expression of interleukin-2 and interferon gamma in HIV disease J. Virology 75:9983-5, 2001
12. Sieg SF, Harding CV, **Lederman MM**. HIV-1 infection impairs cell cycle progression of CD4+ T cells without affecting early activation responses. J Clin Invest 108:757-64, 2001.
13. Sieg SF, Mitchem JB, Bazdar D, **Lederman MM**. Close Link between CD4+ and CD8+ T Cell Proliferation Defects in Patients with Human Immunodeficiency Virus Disease and Relationship to Extended Periods of CD4+ Lymphopenia. J. Infect Dis. 185(10):1401-8, 2002.
14. Zhang D, Shankar P, Harnisch B, Xu Z, Chen G, Lange C, Lee SJ, Valdez H, **Lederman MM**, Lieberman J. Most anti- viral CD8 T cells during chronic viral infection do not express perforin and are not cytotoxic. Blood 101:226-235, 2003.
15. Valdez H, Mitsuyasu R, Landay A, Sevin AD, Chan ES, Spritzler J, Kalams S, Pollard RB, Fahey J, Namkung A, Estep S, Moss R, Sahner D, **Lederman MM**. Interleukin-2 increases CD4+ lymphocyte numbers but does not enhance responses to immunization: results of ACTG 5046s. J Inf Dis 187:320-325, 2003.
16. Kalayjian RC, Landay A, Pollard RB, Taub RB, Gross BH, Francis IR, Sevin A, Pu M, Spritzler J, Chernoff M, Namkung A, Fox L, Martinez A, Waterman K, Fiscus SA, Rousseau F, **Lederman MM**. Age-Related Immune Dysfunction in Health and in HIV-Disease: Both Age and HIV are Associated with Naïve CD8⁺ Cell Depletion and Reduced Expression of CD28 on CD8⁺ Cells. J. Inf Dis 187:1924-33, 2003.
17. Quinones-Mateu M, **Lederman MM**, Feng Z, Chakraborty B, Weber J, Rangel HR, Marotta ML, Mirza M, Jang B, Kiser P, Medvik K, Sieg S, Weinberg A. Human epithelial beta-defensins 2 and 3 inhibit HIV-1 replication. AIDS 17: F39-48, 2003.
18. Lange CG, **Lederman MM**, Medvik K, Asaad R, Wild M, Kalayjian R, Valdez H. Functional immune reconstitution is impaired when initiation of HAART is delayed in chronic HIV-1 infection. AIDS 17: 2015-23, 2003.
19. Kawamura T, Gulden FO, Sugaya M, McNamara DT, Borris DL, **Lederman MM**, Orenstein JM, Zimmerman PA, Blauvelt A. R5 HIV productively infects Langerhans cells and infection levels are regulated by compound *CCR5* polymorphisms. Proc Nat'l Acad Sci (USA) 100:8401-8406, 2003.
20. Landay AL, Spritzler J, Kessler H, Mildvan D, Pu M, Fox L, O'Neil D, Schock B, Kuritzkes D, **Lederman MM**. Immune Reconstitution Is Comparable in Antiretroviral (ARV) Naïve Subjects after 1 Year of Successful Therapy with a Nucleoside Reverse Transcriptase Inhibitor or Protease Inhibitor- Containing Antiretroviral Regimen J Inf Dis 188:1444-54, 2003.
21. Sieg SF, Bazdar DA, **Lederman MM**. Impaired T cell receptor-mediated induction of Ki67 by naïve CD4+ T cells is only occasionally corrected by exogenous interleukin-2 in HIV-1 infection. J Immunology 171:5208-14, 2003.
22. Burton DR, Desrosiers RC, Doms RW, Feinberg MB, Gallo RC, Hahn B, Hoxie JA, Hunter E, Korber B, Landay A, **Lederman MM**, Lieberman J, McCune JM, Moore JP, Nathanson N, Picker L, Richman D, Rinaldo C, Stevenson M, Watkins DI, Wolinsky SA, Zack JA. A sound rationale is needed to justify phase III HIV-1 vaccine trials. Science 303:316, 2004.
23. Salkowitz JR, Sieg SF, Harding CV, **Lederman MM**. *In vitro* human memory CD8 T cell expansion in response to cytomegalovirus requires CD4+ T cell help. J Inf Dis 204:971-83, 2004.
24. Anthony DD, Yonkers NL, Post AB, Asaad R, Heinzl FP, **Lederman MM**, Lehmann PV, Valdez H. Selective impairments in dendritic cell function distinguish HCV and HIV infection. J. Immunology 172:4907-16, 2004.
25. **Lederman MM**, Veazey R, Hartley O, Mosier D, Dufour J, Mefford M, Piatak M Jr, Salkowitz JR, Rodriguez B, Blauvelt A, Offord R. Prevention of vaginal SHIV transmission in rhesus macaques through inhibition of *CCR5*. Science 306:485-7, 2004.

26. Martin MP, **Lederman MM**, Hutcheson H, Nelson GW, Goedert JJ, Detels R, Buchbinder S, Hoots K, Vlahov D, O'Brien DJ, Carrington M. Association of *DC-SIGN* promoter polymorphisms with increased risk for parenteral but not mucosal acquisition of HIV-1 infection. *J. Virol* 78:14053-56, 2004.
27. Sieg SF, Rodriguez B, Asaad R, Jiang W, Bazdar DA, **Lederman MM**. S phase lymphocytes in HIV disease have a central memory phenotype and rarely have evidence for recent T cell receptor engagement. *J. Inf Dis* 192:62-70, 2005.
28. Jiang W, **Lederman MM**, Salkowitz JR, Rodriguez B, Harding CV, Sieg SF. Impaired monocyte maturation in response to CpG oligodeoxynucleotide is related to viral RNA levels in HIV disease and is at least partially mediated by deficiencies in Type I interferon responsiveness and production. *J. Virol* 79:4109-19, 2005.
29. Kalayjian RC, Spritzler J, Pu, M, Landay A, Pollard RB, Spritzler J, Stocker V, Al-Harthi L, Gross BH, Francis IR, Fox L, Martinez A, Fiscus SA, Tebas P, Bosch R, Valcour V, **Lederman MM**. Distinct mechanisms of T-cell reconstitution can be identified by estimating thymic volumes in adult HIV-1 disease. *J. Inf. Dis.* 192:1577-87, 2005.
30. Betts MR, Nason MC, West SM, DeRosa SC, Migueles S, Abraham J, **Lederman MM**, Benito JM, Goepfert PA, Connors M, Roederer M, Koup RA. HIV-infected nonprogressors preferentially retain highly functional HIV-specific CD8⁺ T cell responses *Blood* 107:4781-9, 2006.
31. **Lederman MM**, Offord RE, Hartley O. Microbicides and other topical strategies to prevent vaginal transmission of the human immunodeficiency virus. *Nature Reviews Immunology* 5:371-82, 2006.
32. Rodriguez B, **Lederman MM**, Jiang W, Bazdar D, Garate K, Harding CV, Sieg SF. Interferon-alpha differentially rescues CD4⁺ and CD8⁺ T cells from apoptosis in HIV infection. *AIDS* 20:1379-89, 2006.
- Feng Z, Dubyak G, **Lederman MM**, Weinberg A. Cutting Edge: Human beta defensin-3: a novel antagonist of the HIV-1 co-receptor CXCR4. *J Immunol* 177:782-6, 2006.
33. **Lederman MM**, Nicholson A, Cho M, Mosier D. Biology of CCR5 and its role in HIV infection and treatment. *JAMA* 296:815-26, 2006.
34. Rodriguez B, Sethi AK, Cheruvu V, Mackay W, Bosch RJ, Kitahata M, Boswell SL, Matthews C, Bangsberg D, Martin J, Whalen C, Yadavalli S, Sieg S, Deeks S, **Lederman MM**. Predictive value of plasma HIV RNA level on rate of CD4 T cell decline in untreated HIV infection. *JAMA* 296:1498-1506, 2006.
35. Ahuja SK, Aiuti F, Berkout B, Biberfeld P, Burton D, Colizzi V, Deeks SG, Desrosiers RC, Dierich MP, Doms RW, Emerman M, Gallo RC*, Girard M, Greene WC, Hoxie JA, Hunter E, Klein G, Korber B, Kuritzkes DR, **Lederman MM**, Malim MH, Marx PA, McCune JM, McMichael A, Miller C, Miller V, Montagnier L, Motefiore DC, Moore JC, Nixon DF, Overbaugh J, Pauza D, Richman DC, Saag MS, Sattenau Q, Schooley RT, Shattock R, Shaw GM, Stevenson M, Trkola A, Wainberg MA, Weiss RA, Wolinsky S, Zack JA. A Plea for Justice for Jailed Medical Workers. *Science* 314:924-5, 2006
36. **Lederman MM**, Smeaton L, Smith K, Rodriguez B, Pu M, Wang H, Sevin A, Tebas P, Sieg SF, Medvik K, Margolis DM, Pollard R, Ertl HCJ, Valdez H. In chronic HIV-1 infection, Cyclosporine A provides no sustained immunologic benefit to persons starting suppressive antiretroviral therapies – results of a randomized controlled trial of the AIDS Clinical Trials Group: A5138. *J. Inf. Dis.* 194:1677-85, 2006.
37. Brenchley JM, Price DA, Schacker TW, Asher TE, Silvestri G, Rao S, Kazzaz Z, Lambotte O, Altman D, Blazar B, Rodriguez B, Teixeira-Johnson L, Landay A, Martin J, Hecht R, Picker LJ, **Lederman MM**, Deeks S, Douek DC. Microbial translocation is a cause of systemic immune activation in chronic HIV infection. *Nature Med* 12:1365-71, 2006.
38. Dion M-L, Bordi R, Zeidan J, Asaad R, Boulassel M-R, Routy J-P, **Lederman MM**, Sekaly R-P, Cheynier R. Slow disease progression and good immunological response to HAART are associated with efficient thymopoiesis during chronic HIV-1 infection *Blood* 109(7):2912-20, 2007.
39. Biancotto A, Grivel J-C, Igelhart SJ, Vanpouille C, Lisco A, Sieg SF, Debernardo R, Garate K, Rodriguez B, Margolis L, **Lederman MM**. Abnormal activation and cytokine spectra in lymph nodes of persons chronically infected with HIV-1. *Blood* 109(10):4272-9, 2007.
40. Mitsuyasu R, Gelman R, Weng Cherng D, Landay A, Fahey J, Reichman R, Erice A, Bucy P, Kilby JM, **Lederman MM**, Dukes-Hamilton C, Lertora J, Stephenson BL, Tebas P, Duliege A-M, Pollard R. The Virologic, Immunologic and Clinical Effects of Interleukin-2 with Potent Antiretroviral Therapy in Patients with moderately advanced HIV Infection: A Randomized Controlled Clinical Trial - ACTG 328. *Arch Int Med* 167:597-605, 2007
41. **Lederman MM**, Miller V, Weller I, Deeks S. A new approach for “deep salvage” trials in advanced HIV infection. *AIDS* 21:1503-1506, 2007
42. Jiang W, **Lederman MM**, Harding CV, Rodriguez B, Mohner RJ, Sieg SF. TLR9 ligation induces naïve B cell proliferation independent of B cell receptor activation *Eur J Immunol* (E pub ahead of press, 2007).

C. Current Research Support

AI-36219

04/01/2004 – 03/31/2009

NIH

Center for AIDS Research (CFAR)

Promote increased collaboration between basic and clinical researchers through a central administrative structure, development of appropriate forums for sharing and exchange of ideas and pilot funding for interdisciplinary research. Also to enhance the depth and breadth of AIDS research by coordinated development of core activities and recruitment of new investigators.

Principal Investigator

AI-68636

07/26/2006 - 05/03/2013

NIH

AACTG Support Laboratory Solicitation (ISL)

Adult AIDS Clinical Trials Group advanced technology laboratory to monitor the immunologic determinants of disease progression among clinical trials participants.

Principal Investigator

AI51649-04

09/30/2002 – 06/30/2007

NIH/NIAID/NICHD

NCE – 6/30/08

Integrated Preclinical/Clinical Program for HIV Topical Microbicides

Multicenter Collaborative studies to design and test fusion inhibitors to prevent sexual transmission of HIV-1.

Principal Investigator

AI-069501

10/01/87 – 11/30/2013

NIH/NIAID

Case AIDS Clinical Trials Unit

Develop, implement, and analyze results of clinical treatment trials for HIV infection and its complications

Role: Principal Investigator

AI067039-01 (Saag)

09/30/06-08/31/08

NIH/NIAID

CFAR Network of Integrated Clinical Systems (CNICS)

Build a infrastructure for exchange, storage and retrieval of real-time clinical care data on HIV-infected patients receiving care at teaching institutions of excellence across the United States. To develop mechanisms for enrollment of further CFARs across the Nation. To conduct high-quality observational longitudinal research in the clinical course of HIV infection.

Role: Investigator

DE017335-02

07/15/2005 - 05/31/2008

NIH

Oral Defensins Bridge Innate and Adaptive Immunity(Sieg)

To test the hypothesis that responses to beta defensins are impaired in HIV disease, we will evaluate antigen presenting cells from HIV-infected persons for their phenotypic and functional responses to beta defensins.

Investigator

AI-071944

9/15/06-8/31/11

NIH

Topical Immune modulatory strategies to prevent HIV transmission.

A series of high-risk, exploratory studies to test the rationale for combination microbicide strategies.

Role: Principal Investigator

AI69918-1 (Moore)

7/01/06-6/30/11

NIAID

NA-ACCORD

North American AIDS Cohort Collaboration on Research and Design

Role: Investigator