BIOGRAPHICAL SKETCH				
NAME David M. Margolis	POSITION TITL Professor o	POSITION TITLE Professor of Medicine, Microbiology & Immunology,		
eRA COMMONS USER NAME Margolis	and Epidem	nology		
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	
Harvard University, Cambridge, MA	AB	1981	Biology	
Tufts Univ. School of Medicine, Boston, MA	MD	1985	Medicine	

A. Personal Statement

Dr. Margolis and his laboratory have a long history of translational HIV research involving samples donated by HIV-infected volunteers to investigate basic molecular, virological, and immunological phenomenon, and leveraging insights to develop new interventions in HIV disease. He has studied molecular mechanisms in HIV replication and infection of HIV proviral latency, and defined the role of epigenetic factors in the repression of HIV transcription. Dr. Margolis also has along history of leading diverse, multidisciplinary collaborations that result in the discovery and publication of high-impact work.

More recently, priorities in HIV therapeutics have led Dr. Margolis and his group to revive the study of translational approaches to attack persistent HIV infection. This application represents the next step in the development of an expanding collaboration with many leaders in various aspects of HIV biology and persistent infection, and an attempt to establish the foundation the address key obstacles to progress in the understanding of HIV persistence and ways to defeat it.

In addition to directing the Collaboratory, Dr. Margolis will leverage his work with the UNC/Duke Acute HIV Infection cohort for the past 5 years, to study mechanisms of proviral latency and approaches to disrupt it in a spectrum of CD4+ T cell memory populations in patients treated in chronic or acute HIV infection. These studies may define new and important therapeutic directions and provide important insights into HIV persistence that may contribute to efforts to eradicate HIV infection.

B. Positions and Honors

1985-88:	Tufts-New England Medical Center, Boston, Mass: Residency in Internal Medicine	
1988-91:	National Institute of Allergy & Infectious Diseases, NIH, Bethesda, MD:	
	Medical Staff Fellow, Laboratory of Clinical Investigation (Stephen E. Straus), 1988-89	
	Clinical Associate, Medical Virology Section, 1989-91	
1991-94:	University of Massachusetts Medical Center, Worcester, MA:	
	Program in Molecular Medicine: postdoctoral fellowship (Michael R. Green, M.D., Ph.D.)	
1994-99:	University of Maryland, Baltimore, MD:	
	Assistant Professor: Institute of Human Virology and School of Medicine	
1999-2005:	University of Texas Southwestern Medical Center at Dallas, Dallas, TX:	
	Associate Professor, Department of Medicine, Division of Infectious Diseases	
	Section Chief, Infectious Diseases, Dallas VA Medical Center	
2005-present:	The University of North Carolina at Chapel Hill, Chapel Hill, NC:	
Professor of Medicine, Microbiology and Immunology, and Epidemiology		

Honors and Awards:

Magna Cum Laude, Harvard College, 1981 Clinical Associates award, Am. Coll. Phys., 1988 NIH Physician-Scientist award (K-11), 1991-94 Fellow, American College of Physicians, 1996 Nat'l Found. Infect. Dis. young investigator, 1996 IDSA young investigator, 1997 Fellow, Infectious Dis. Society of America, 2000 amfAR Basic Science award, 2001 Am. Society for Clinical Investigation, 2005 WJ Way Visiting Professor, Duke CFAR, 2005 Editorial Board, *AIDS* (2006-), *J Virology* (2008-) **Selected National Advisory and Review Committees:** NIAID AIDS Research Advisory Committee 2004-2008; AIDS Clinical Trials Strategic Working Group 2006-2008; IDSA Research Committee 2008-2011; NIAID ACTG Research Agenda Committees 1999-present; V.A. Merit Review 2000-04; NIAID AIDS Clinical Studies and Epidemiology Study Section 2010-14; amfAR Scientific Advisory board (since 2002).

C. Selected Publications (of 83 and 4 manuscripts in review)

- 1. Romerio, F., Gabriel, M., **Margolis, D.M.** Repression of HIV-1 through the novel cooperation of the human factors YY1 and LSF. J. Virol. 1997, 71:9375-9382.
- Flamand, L., Crowley, R.W., Lusso, P., Columbini-Hatch, S., Margolis, D.M., Gallo, R.C: Activation of CD8+ T lymphocytes through the T cell receptor turns on CD4 gene expression: implications for HIV pathogenesis. Proc. Natl. Acad. Sci. USA 1998, 95:3111-3116.
- Coull, J., Romerio, F., Sun, J.-M., Volker, J.M., Galvin, K.M., Davie, J.R., Shi, Y., Hansen, U., Margolis, D.M. The human factors YY1 and LSF repress the human immunodeficiency virus type-1 long terminal repeat via recruitment of histone deacetylase 1. J. Virology, 2000; 74:6790–6799.
- He, G. and Margolis, D.M. Counter-regulation of Chromatin Acetylation and Histone Deacetylase Occupancy at the Integrated Promoter of Human Immunodeficiency Virus Type 1 by the HIV-1 Activator Tat and the HIV-1 Repressor YY1. Molecular Cell. Biol. 2002; 22:2965-2973.
- Ylisastigui L., Archin, N.M., Lehrman, G., Bosch, R.J., and Margolis, D.M. Coaxing Human Immunodeficiency Virus Type 1 from Resting CD4+ T Cells: can the reservoir of HIV be purged? AIDS. 2004; 18:1101-1108
- Lehrman, G., Hogue, I.B., Palmer, S., Jennings, C., Spina, C.A., Wiegand, A., Landay, A.L., Coombs, R.W., Richman, D.D., Mellors, J.W., Coffin, J.M., Bosch, R.J., Margolis, D.M. Depletion of latent HIV infection in vivo. Lancet 2005; 36:549-555. PMCID: PMC1894952
- Klichko, V., Kaur, R.J., Archin, N., Lehrman, G, and Margolis, D.M. Hexamethylbisacetamide remodels the Human Immunodeficiency Virus type 1 promoter and induces Tat-independent HIV-1 expression without cellular activation. J. Virology, 2006; 80:4570–4579. PMCID: PMC1472000
- 8. Bowman MC, Ballard TE, Ackerson CJ, Feldheim DL, **Margolis DM**, Melander C. Inhibition of HIV Fusion with Multivalent Gold Nanoparticles. J Am Chem Soc 2008; 130:6896-7. PMCID: PMC2916654
- Jiang G, Espeseth A, Hazuda DJ, and Margolis DM. c-Myc and Sp1 Contribute to Proviral Latency by Recruiting Histone Deacetylase 1 to the Human Immunodeficiency Virus Type 1 Promoter. J Virol. 2007; 81: 10914-10923. PMCID: PMC2045540
- Archin NM, Espeseth A, Parker D, Cheema C, Hazuda DJ, Margolis DM. Expression of Latent HIV Induced by the Potent HDAC Inhibitor Suberoylanilide Hydroxamic Acid. AIDS Res Hum Retro. 2009; 25:207-212. PMID: 19239360; PMCID: PMC2853863
- Keedy KS, Archin NM, Gates AT, Espeseth AS, Hazuda DJ, and Margolis DM. A limited group of class I histone deacetylases act to repress human immunodeficiency virus type-1 expression. J Virol. 2009; 88:4749–4756. PMID: 19279091; PMCID: PMC2682072
- Choudhary S.K., Rezk M.L., Kashuba A.D.M., Ince W.L., Zhang L., Su L., Swanstrom R., Margolis DM. Suppression of HIV-1 viremia with reverse transcriptase and integrase inhibitors, immune recovery, and viral rebound upon therapy interruption in a new model for HIV treatment in the humanized Rag^{-/-} γ_c^{-/-} mice. J. Virol 2009. 83:8254–8258. PMID: 19494021; PMCID: PMC2715775
- Archin NM, Keedy KS, Espeseth AS, Dang H, Hazuda DJ, and Margolis DM. Expression of Latent Human Immunodeficiency Type-1 is Induced by Novel and Selective Histone Deacetylase Inhibitors. AIDS 2009; 23:1799-806. PMID: 19590405; PMCID: PMC2853863
- 14. Levesque MC, Moody AM, Hwang KK, Marshall D, Whitesides J, Amos J, Gurley T, Allgood S, Kuraoka M, Haynes BB, Parker DC, Shaheen NJ, Plonk S, Cohen MS, Tomaras G, Goepfert P, Shaw G, Eron J, Hicks CB, Liao HX, Markowitz M, Kelsoe G, Margolis DM, and Haynes BF. Transmitted/Founder HIV-1 Induces B Cell Polyclonal Differentiation and Apoptosis With Massive Gastrointestinal Tract Germinal Center Loss In the Earliest Stages of Infection. PLoS Med. 6:e1000107. PMCID: PMC2702159
- 15. Archin NA, Cheema M, Parker D, Wiegand A, Bosch R, Coffin J, Eron J, Cohen M, and **Margolis DM.** Antiretroviral intensification and valproic acid have limited effect on residual HIV-1 viremia or resting CD4+ cell infection. PLoS One 2010; 5:e9390. PMCID: PMC2826423

D. Research Support (Ongoing)

NIH NIAID U19AI082608 (Margolis) 09/02/09 – 08/31/11: *Innovative therapies to eliminate persistent HIV Infection:* A collaboration of scientists at UNC, Case, and Merck Research Laboratories will test novel candidate molecules in human cells, a humanized mouse model, and HIV+ patient's cells for their ability to disrupt latent HIV infection.

NIH NIMH R01 MH085597 (Margolis) 04/01/09-01/31/14: *Nanocrystal delivery to the CNS to improve HIV Therapy:* We will test delivery of novel nanotherapeutics across the blood-brain barrier to treat HIV infection.

NIH NIAID R34 AI084553 (Margolis) 05/01/09-04/30/10: The in vivo effect of HDAC inhibitors on HIV gene expression in resting CD4+ T cells. This is a planning grant for a clinical study to directly assess the effect of HDAC inhibitors on HIV latency *in vivo*.

NIH NIAID R21 Al81613 (Choudhary) 04/01/09-03/31/11: *Modeling HIV-1 Eradication Therapies in the hu-Rag2-/- gamma c-/- Mouse Model*. We will establish suppressive ART in an alternative humanized murine model and validate persistent infection of human CD4+ T cells despite ART, thus providing a model system to study HIV-1 latency and test approaches to deplete persistent HIV infection.

NIH NIAID U01-AI067854 (Haynes) 07/01/07-06/30/12: Center for HIV/AIDS Vaccine Immunology: *Acute HIV-1 Infection Prospective Cohort Study* – to collect biological specimens in acutely HIV-infected patients to study the HIV-1 virus, the host response, the factors that determine HIV transmission.

NIH NIAID U01 AI069423 (Eron) 02/01/07-11/30/13: UNC AIDS Clinical Trials Unit: The major goals of this project are to provide an effective and efficient system to evaluate the safety and efficacy of the therapeutic interventions against HIV infection, AIDS, and its associated conditions.

NIH NIDA 1R01 DA030156 (Margolis) 07/15/10-02/28/15: HIV Latency, Epigenetics, and Therapeutics: To overcome HIV latency in a broad population of infected individuals, it is also important to assess the effect of environmental exposures, such as those to drugs of abuse, on persistent HIV infection. Therefore a more detailed understanding is needed of the epigenetic mechanisms behind persistent infection.

Completed Research Support

Trimeris/Roche Pharmaceuticals Investigator-initiated program (Margolis) 07/01/06-12/31/09: The Effect of HDAC inhibition and Intensified ART Therapy on the Frequency of HIV in Resting CD4 Cells. This project will explore the effect of intensified antiretroviral therapy on persistent HIV infection

Merck Research Laboratories Investigator-initiated Study Program (Margolis) 05/01/09-04/30/10: Assay development to measure the effect of HDAC inhibitors on HIV infection in vivo. This grant supports assay development and validation for the pending U19 project.

NIH/NIAID 5-RO1-AI45297-10 (Margolis) 07/01/99-08/14/07, 2-R56-AI045297-11A1 (Margolis) 08/15/07-07/31/09: Repression of HIV Transcription: from mechanism to anti-latency therapies The major goal of this project is to define cellular factors that downregulate HIV gene expression, the mechanism of this inhibition, and the role of these factors in the establishment of long-term viral reservoirs.

amfAR 107168-44-RGRL (Margolis) 07/01/08-06/30/09: HDAC Inhibition and chromatin remodeling to disrupt proviral latency. We wish to test the effect of HDACi with improved selectivity for the Class I HDAC1 on HIV gene expression.

Bristol-Myers Squibb Company BMS Fellows Training Program (Margolis/Bowman) 07/01/08-06/30/09: Gold Nanoparticle Therapeutics in the Treatment of HIV-1. To test the ability of targeted gold nanoparticles to delivery antiretrovirals to the CNS.