

**BIOGRAPHICAL SKETCH**

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NAME OF SPONSOR (CO-SPONSOR) John M. Coffin		POSITION TITLE American Cancer Society Research Professor	
eRA COMMONS USER NAME jcoffin1			
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
Wesleyan University, Middletown CT	BA	1967	Biology
University of Wisconsin, Madison WI	Ph.D.	1972	Molecular Biology
Institut für Molekularbiologie, University of Zürich		1972-1975	Molecular Virology

**A. Personal Statement**

I have closely followed the HIV field ever since discovery of the virus in 1983, although I did not take an active role until I founded the HIV Drug Resistance Program in 1997. In 1995, I published an essay in which I pointed out that HIV must have a uniquely dynamic mechanism of persistence in the infected human host, and argued that drug resistance must arise during replication, and are then selected from the highly diverse population, often leading to therapeutic failure. The invitation to start a new research program within the NCI dedicated to the study of HIV-host interaction allowed me to put together a group to develop a set of uniquely sensitive and specific assays to quantitatively assess viral diversity, persistence, and evolution of resistance in infected patients. All of these assays have become the gold standard in the field for studying HIV-host interaction, and their use has provided significant insight into mechanisms of its replication, persistence, and evolution. At the same time, I have continued to delve into important theoretical aspects of HIV infection, such as the roles of immune selection and recombination in evolution in vivo.

**B. Positions and Honors**Professional Experience:

1972-1975 Postdoctoral Fellow, Institut für Molekularbiologie, Universität Zürich  
 1975-1978 Assistant Professor, Molecular Biology and Microbiology, Tufts University School of Medicine  
 1978-1982 Associate Professor, Molecular Biology and Microbiology, Tufts University School of Medicine  
 1982-present Professor, Molecular Biology and Microbiology, Tufts University School of Medicine  
 1985-1994 American Cancer Society, Massachusetts Division, Professor of Molecular Biology  
 1994-present American Cancer Society Research Professor of Molecular Biology and Microbiology  
 2002-present Distinguished Professor, Tufts University  
 1997-2005 Director, HIV Drug Resistance Program, National Cancer Institute, Frederick MD

Honors and Service

Fellow, Jane Coffin Childs Memorial Fund for Medical Research, 1972-74  
 Editorial Boards: J. Virol. 1978-1991, Virology, 1980-1993, Genes and Development, 1991-1994, PNAS, 2000-  
 Editor, Journal of Virology, 1991-1997  
 Virology Study Section, 1980-1984  
 Organizer, Cold Spring Harbor meeting on RNA Tumor Viruses, 1981, 1991, 1997  
 Member, Retrovirus subsection, International Committee on the Taxonomy of Viruses, 1982-1987, Chair, 1987-95  
 Member, California AIDS Task Force, Basic Science Review Group, 1986-97, Chair 1993-97  
 Member, Leukemia Society of America, Grant Review Subcommittee, 1987-1991; 1992-2000, Chair 1997-2000  
 Member, Leukemia Society of America, National Board of Trustees, 1987-1991, 1992-2004  
 Member, National Cancer Institute Manpower Initial Review Group, 1987-1991

Outstanding Investigator Award, National Institutes of Health, 1987-1994; 1994-2001

Reviewing Editor, Science, 1987- 1996

American Society for Microbiology Foundation Lecturer, 1988-1989

Member, Institute of Medicine Committee to Study the AIDS Research Program of the NIH, 1989-1991

Milton and Natalie Zucker Award for Research, 1989, 1997

Member, National Cancer Institute-Frederick Cancer Research & Development Center Advisory Committee, 1993-1999

Fellow, American Academy of Microbiology, 1993-present

Member, Panel to Assess the NIH Investment in Gene Therapy, 1995

Distinguished Faculty Award, Tufts University, 1997

Member, National Academy of Sciences, 1999-

Massachusetts Columbus Quincentennial Discovery Award, 2006

Member, Massachusetts Academy of Sciences, 2008-

### **C. Selected Publications (out of about 150 total)**

#### **5 Most relevant Publications:**

Coffin, J.M. 1995. HIV population dynamics in vivo: Implications for genetic variation, pathogenesis, and therapy. *Science* 267: 483-488.

Rouzine, I.M., Wakely, J., and Coffin, J.M. 2003. The solitary wave of asexual evolution. *Proc. Natl. Acad. Sci. USA* 100: 587-592.

Palmer, S., Kearney, M., Maldarelli, F., Halvas, E.K., Bixby, C.J., Bazmi, H., Rock, D., Falloon, J., Davey, R.T. Jr., Dewar, R.L., Metcalf, J.A., Hammer, S., Mellors, J.W., and Coffin, J.M. 2005. Multiple, linked HIV-1 drug resistance mutations in treatment-experienced patients are missed by standard genotype analysis. *J. Clin. Microbiol.* 43: 406-413.

Palmer, S., Boltz, V., Martinson, N., Maldarelli, F., Gray, G., McIntyre, J., Mellors, J., Morris, L., and Coffin, J. 2006. Persistence of nevirapine-resistant HIV-1 in women after single-dose nevirapine for prevention of maternal to fetal transmission. *PNAS* 103: 7094-7099.

Palmer S, Maldarelli F, Wiegand A, Bernstein B, Hanna GJ, Brun SC, Kempf DJ, Mellors JW, Coffin JM, and King MS. 2008 Low-level viremia persists for at least seven years in patients on suppressive antiretroviral therapy. *PNAS*. 105: 3879-3884.

#### **Other Relevant Publications:**

Maldarelli, F., Palmer, S., King, M.S., Wiegand, A., Polis, M.A., Mican, J., Kovacs, J.A., Davey, R.T., Rock-Kress, D., Dewar, R., Liu, S, Metcalf, J.A., Rehm, C., Brun, S.C., Hanna, G.J., Kempf, D.J., Coffin, J.M., Mellors, J.W. 2007. Suppressive antiretroviral therapy lowers plasma HIV-1 RNA to stable set-point predicted by pretreatment viremia but not treatment regimen. *PloS Pathog*

Ambrose, Z., Palmer, S., Boltz, V.F., Kearney, M., Larsen, K., Polacino, P., Flanary, L., Oswald, K., Piatak, Jr., M., Smedley, J., Shao, W., Bischofberger N., Maldarelli, F., Kimata, J.T., Mellors, J.W., Hu, S.-L., Coffin, J.M., Lifson, J.D. and KewalRamani V.N. 2007 Suppression of viremia and evolution of human immunodeficiency virus type 1 drug resistance in a macaque model for antiretroviral therapy..

Kearney M, Maldarelli F, Shao W, Margolick JB, Daar ES, Mellors JW, Rao V, Coffin JM, Palmer S. 2009. HIV-1 Population Genetics and Adaptation in Newly Infected Individuals. *J. Virol.* **83**: 2715-2727

Dinso, J. B, Kim, S. Y, Wiegand, A. M., Palmer, S. E., Gange, S. J., Cranmer, L., O'Shea, A., Callender, M., Spivak, A., Brennan, T., Kearney, M. F., Proschan, M. A., Mican, J. M., Rehm, C. A., Coffin, J. M., Mellors, J. W., Siliciano, R. F., Maldarelli, F. 2009. Treatment Intensification Does Not Reduce Residual HIV-1 Viremia in Patients on highly Active Antiretroviral Therapy. *PNAS*. **106**: 9403-9408

Shao, W., Kearney, M., Maldarelli, F., Mellors, J. W., Stephens, R. M., Lifson, J. D., KewalRamani, V. N., Ambrose, Z., Coffin, J. M. and Palmer, S. E. 2009. RT-SHIV subpopulation dynamics in infected macaques during anti-HIV therapy. *Retrovirology* **6**: 101.

McMahon, D., Jones, J., Wiegand, A., Gange, S. J., Kearney, M., Palmer, S., McNulty, S., Metcalf, J. A., Acosta, E., Rehm, C., Coffin, J. M., Mellors, J. W. and Maldarelli, F. 2010. Short-course raltegravir intensification does not reduce persistent low-level viremia in patients with HIV-1 suppression during receipt of combination antiretroviral therapy. *Clin Infect Dis* **50**: 912-919.

Rouzine, I.M. and Coffin, J.M. 2010. Multi-Site Adaptation in the Presence of Infrequent recombination. *Theor Popul Biol* **77**: 189-204.

## C. Research Support

### Ongoing Research Support

R37 CA089441 Coffin (PI) (30%)

02/01/06 – 01/31/11

NIH/NCI

Retrovirus Evolution

Overall goals: To study important problems in retrovirus evolution, including roles of mutation, drift, recombination, and selection in short term evolution of viruses, evolution of *env* genes to use different receptors, and the long-term relationship of retroviruses and their hosts as revealed by analysis of endogenous proviruses.

PRD-94-037-13 Coffin (PI)

01/01/2008-4/30/2014

American Cancer Society

Research Professorship: Molecular Biology of Retroviruses

This award provides partial salary support for Dr. Coffin without supporting any specific projects