

BIOGRAPHICAL SKETCH

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NAME Lena Al-Harhi	POSITION TITLE Professor		
eRA COMMONS USER NAME lalharhi			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
The American University	B.S.	1986-1989	Biology
The American University	M.S.	1989-1992	Biology
The George Washington University	PhD	1992-1996	Microbiology

A. Personal Statement

I am a Professor in the Dept. of Immunology/Microbiology at Rush University Medical Center in Chicago, IL. My research over the past 16 years has focused on HIV/host interactions, with a special emphasis on bridging basic and clinical science in the HIV/AIDS field. Because of my experience in HIV molecular biology, immunology, and for the past nine years in NeuroAIDS, I have been able to probe mechanistic questions that are clinically relevant to HIV/AIDS. I have over 60 peer-reviewed publications and invited reviews/book chapters. Recently, my group has identified the β -catenin signaling pathway as an important regulator of HIV replication in multiple compartments, including the central nervous system. Through multiple NIH funded studies, I am investigating the molecular pathway by which β -catenin inhibits HIV replication, its impacts on HIV neuropathogenesis, and the role of host and viral factors in modulating β -catenin interaction with HIV. I hold a pending patent to develop small molecules that will interface with the β -catenin pathway to modulate HIV replication and/or latency. We also defined β -catenin as a key regulator of key functions of astrocytes (e.g glutamate transport). As such, β -catenin -based therapeutic strategies may also be employed to treat HIV associated neurocognitive disorder (HAND). As PI or co-investigator, I have collaborated in numerous nationally funded large cohort studies, such as the Women's Interagency HIV Study (WIHS) and the AIDS Clinical Trial Group (ACTG).

B. Positions and Honors**Positions and Employment**

1990-1992	Intern in the laboratory of Dr. Rita Colwell, Department of Microbiology, the University of Maryland (College Park, MD)
1992-1996	Graduate Fellow, Department of Microbiology/Immunology, the George Washington University (Washington, DC).
1994-1996	Pre-doctoral Intramural Research Fellow (IRTA), Laboratory of Tumor Cell Biology under the direction of Dr. Robert Gallo, National Cancer Institute, NIH (Bethesda, MD).

1996-1998	Mark Weiss Fellow of Infectious Diseases, Department of Immunology/Microbiology in the laboratory of Dr. Alan Landay, Rush Medical College (Chicago, IL).
1998-1999	Instructor, Department of Immunology/Microbiology, Rush Medical College (Chicago, IL).
2000-2004	Assistant Professor, Department of Immunology/Microbiology, Rush Medical College (Chicago, IL).
2002-2008	Director of the Graduate Program, Division of Immunology/Microbiology, Rush Graduate College (Chicago, IL).
2004-2010	Associate Professor, Department of Immunology/Microbiology, Rush Medical College (Chicago, IL).
2010-present	Professor, Department of Immunology/Microbiology, Rush Medical College (Chicago, IL).

Other Experience and Professional Memberships:

2008-present	Member, International Society of Neurovirology
2010	Member, Society of Neuroimmunopharmacology
2010-present	Associate Editor, Journal of NeuroVirology
2011-2012	Guest Editor, Journal of neuroimmunopharmacology

Honors:

1989-1991	Graduate Fellowship Award, The American University
1990	Hemlinge Scholar Award, The American University
1991	Graduate Student Council Outstanding Service Award
1994-1996	Pre-doctoral Intramural Research Training Award (IRTA), NCI/NIH
1992-1996	Graduate Fellowship Award, the George Washington University.
2002	Nominated for the Exceptional Research Mentoring Award, Rush Graduate College (Chicago, IL).

International Study Section Service:

2001	Dr. Hadwen Trust for Humane Research, England
2002	Associazione Italiana per la Ricerca sul Cancro (AIRC), Italy
2012	Netherlands AIDS Fond

National Study Section Service

2006-2012	Study section member, The Campbell Foundation (Ft. Lauderdale, FL)
2004-2009	NIH Study Section Ad hoc reviewer, AIDS and Related Research, Small Business Research Initiatives (SBRI)
2003	NIH Center for Scientific Review and Special Emphasis Panel, reviewer of General Clinical Research Center (GCRC)
2003	NIH Study Section Ad hoc reviewer, AIDS and Related Research, Vaccines Grant Applications, ZRG1 VACC 03
2004	NIH Study Section Ad hoc reviewer, HIV Vaccine Research and Design Program, ZAI1 CL-A M4
2005, 2008, 2010	NIH, Center for Scientific Review, ZRG1-AARR-H, NeuroAIDS and other end organ diseases (NAED) study section, ad hoc reviewer
2006- 2010	NIH, AIDS F30, F31, F32 fellowship reviewer.

- 2009 NIH, NIAID Special Emphasis Panel/ HIV microbicides and prevention ZA11 EL-A (C1).
- 2010-2014 NeuroAIDS and End-Organ Disease (NAED) Study Section, Standing member
- 2013-2015 Chair NAED study Section (Starting in summer 2013)

C. Selected Peer-reviewed Publications (Selected from 60 publications)

Most relevant to the current application

1. Carroll-Anzinger, D., **Al-Harathi, L.** (2006) Gamma interferon primes productive human immunodeficiency virus infection in astrocytes. *J Virol* **80**, 541-4.
2. Carroll-Anzinger, D., Kumar, A., Adarichev, V., Kashanchi, F., **Al-Harathi, L.** (2007) HIV restricted replication in astrocytes and the ability of IFN γ to modulate this restriction is regulated by a downstream effector of the Wnt signaling pathway. *J. Virol* **81**, 5864-71.
3. Kumar, A., Zloza, A., Moon, R.T., Watts, J., Tenorio, A.R., **Al-Harathi, L.** (2008) Active β -catenin signaling is an inhibitory pathway of HIV replication in peripheral blood mononuclear cells. *J Virol* **82**, 2813-20.
4. Li, W., Henderson, L.J., Major, E.O., **Al-Harathi, L.** (2011) IFN- γ Mediates Enhancement of HIV Replication in Astrocytes by Inducing an Antagonist of the β -Catenin Pathway (DKK1) in a STAT 3-Dependent Manner. *J Immunol* **186**, 6771-8.
5. Narasipura, S.D., Henderson, L.J., Fu, S.W., Chen, L., Kashanchi, F., **Al-Harathi, L.** (2012) Role of beta-catenin and TCF/LEF family members in transcriptional activity of HIV in astrocytes. *J Virol* **86**, 1911-21.
6. Henderson, L.J., **Al-Harathi, L.** (2011) Role of beta-Catenin/TCF-4 Signaling in HIV Replication and Pathogenesis: Insights to Informing Novel Anti-HIV Molecular Therapeutics. *J Neuroimmune Pharmacol* **6**, 247-59.
7. Henderson, L.J., Narasipura, S.D., Adarichev, V., Kashanchi, F., **Al-Harathi, L.** (2012) Identification of Novel T Cell Factor 4 (TCF-4) Binding Sites on the HIV Long Terminal Repeat Which Associate with TCF-4, beta-Catenin, and SMAR1 To Repress HIV Transcription. *J Virol* **86**, 9495-503.
9. Henderson, L.J., Sharma, A., Monaco-Kushner, M.C., Major, E.O., **Al-Harathi, L.** (2012) HIV Tat through its intact core and cysteine-rich domains inhibits Wnt/beta-catenin signaling in astrocytes: Relevance to HIV neuropathogenesis. *J Neurosci* **46**, 16306-13.
10. **Al-Harathi, L.** (2012) Wnt/beta-catenin and its Diverse Physiological Cell Signaling Pathways in Neurodegenerative and Neuropsychiatric Disorders. *J Neuroimmune Pharmacol*.
11. **Al-Harathi, L.** (2012) Interplay Between Wnt/beta-Catenin Signaling and HIV: Virologic and Biologic Consequences in the CNS. *J Neuroimmune Pharmacol*.

Additional publications demonstrating expertise in HIV pathogenesis

12. Zloza, A., Kohlhapp, F.J., Lyons, G.E., Schenkel, J.M., Moore, T.V., Lacek, A.T., O'Sullivan, J.A., Varanasi, V., Williams, J.W., Jagoda, M.C., Bellavance, E.C., Marzo, A.L., Thomas, P.G., Zafirova, B., Polic, B., **Al-Harathi, L.**, Sperling, A.I., Guevara-Patino, J.A. (2012) NKG2D signaling on CD8(+) T cells represses T-bet and rescues CD4-unhelped CD8(+) T cell memory recall but not effector responses. *Nat Med* **18**, 422-8.
13. Zloza, A., Sullivan, Y.B., Connick, E., Landay, A.L., **Al-Harathi, L.** (2003) CD8+ T cells that express CD4 on their surface (CD4^{dim}CD8^{bright} T cells) recognize an antigen-specific target, are detected in vivo, and can be productively infected by T-tropic HIV. *Blood* **5**, 5.

14. Zloza, A., Schenkel, J.M., Tenorio, A.R., Martinson, J.A., Jeziorczak, P.M., **Al-Harathi, L.** (2009) Potent HIV-specific responses are enriched in a unique subset of CD8+ T cells that coexpresses CD4 on its surface. *Blood* **114**, 3841-53.
15. Wu, J., Richards, M.H., Huang, J., **Al-Harathi, L.**, Xu, X., Lin, R., Xie, F., Gibson, A.W., Edberg, J.C., Kimberly, R.P. (2011) Human FasL gene is a target of beta-catenin/T-cell factor pathway and complex FasL haplotypes alter promoter functions. *PLoS One* **6**, e26143.

Research Support

Ongoing Research Support

1 R01 DA033966-01A Al-Harathi, L (PI) 07/ 1/ 2012- 06/30/2017
 "Mechanisms of drugs of abuse and HIV neuropathogenesis": This project is focused on understanding the interplay between Meth, β -catenin, and HIV in astrocyte to define mechanism by which Meth and HIV through β -catenin can modulate key events in HIV pathogenesis in the CNS

R01 NIMH100628 Al-Harathi, L (PI) 03/15/2013-1/15/2018
 "HIV latency in astrocytes": The focus of this project is define epigenetic regulation of HIV latency in astrocytes

R01 NS060632-02 Al-Harathi, L (PI) 09/29/2008 – 07/31/2013
 "Interplay between neuroprotective pathways, HIV, and astrocytes": The goal of this application is to determine the biologic consequences of modulation of neuroprotective signaling pathways as they impact HIV-associated neurologic disease.

PO1 A1082971-01 Landay, A (PO, PI,) 09/30/2009-08/31/2014
 HIV susceptibility and pathogenesis in the female genital tract
 Dr. Al-Harathi is the PI of project IV, Title: Role of estrogen in HIV transmission and pathogenesis
 The goal of project IV is to understand the cross talk between estrogen, β -catenin, and HIV as they impact HIV transmission and pathogenesis in women.

1 R03 DA026723-01A1 Al-Harathi, L (PI) 03/15/2010 – 02/29/2013
 "Protective pathways against Meth abuse and HIV neuropathogenesis": The goal of this project is to determine the impact of HIV verotoxins and psychostimulants (Methamphetamine) on β -catenin activity and neuropathogenesis

Completed Research Support in past three years

R21 A1077324-02 Al-Harathi, L (PI) 09/24/08-08/31/2010
 Host signaling factors that repress HIV: The overall all goal of this application is to probe HIV/host interaction towards developing novel agents that suppress HIV replication in blood.

1 PO1 AI055356-01 Schooley, C (PI) 04/01/03 - 03/31/08
 Immunopathogenesis of Acute HIV-1 Infection: This is a multi-center study that is focused on examining HIV infection and treatment in acutely infected patients.