BIOGRAPHICAL SKETCH

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NAME	POSITION TITLE
Garcia-Martinez, J. Victor	Professor of Internal Medicine
eRA COMMONS USER NAME (credential, e.g., agency login) VGARCI	

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
Instituto Technologico y de Estudios, Superiores de Monterray, Mexico	B.Sc.	1979	Chemistry
Georgetown University, Washington, D.C.	Ph.D.	1984	Chemistry/Biochemistry
National Cancer Institute, NIH	Fellow	1984-85	Biology/Immunology
Massachusetts Institute of Tech., Boston, MA	Fellow	1985-87	Cell Biology
Fred Hutchinson Cancer Ctr., Seattle, WA	Res. Assoc.	1987-92	Human Gene Therapy

A. Positions and Honors:

1992 – 1999 **Assistant Member**, **Associate Member,** Department of Virology and Molecular Biology, St. Jude Children's Research Hospital, Memphis, TN

1999 – 2002 **Associate Professor (Tenured)**, Departments of Internal Medicine and Microbiology, Division of Infectious Diseases, UT Southwestern Medical Center at Dallas, Dallas, TX

2002 – 2009 **Professor (Tenured)**, Departments of Internal Medicine and Microbiology, Division of Infectious Diseases, UT Southwestern Medical Center at Dallas, Dallas, TX

2009 – Present **Professor**, Department of Medicine, The University of North Carolina at Chapel Hill, Chapel Hill, NC

Other Professional Activities:

1996-1999 Medical Biochemistry Study Section, NIH, Member

2001 Chair, ZRGI AARR-5 03 M Special Review Panel

1999-2005 AARC-1 Study Section, NIH, Member

2009-Present National Board of Directors SACNAS

B. Selected Publications:

Garcia JV and Miller AD. Nef induces cell surface CD4 downregulation by a serine phosphorylation independent pathway. Nature 350:508-511, 1991.

Anderson SJ, Lenburg M, Landau NR, **Garcia JV**. The cytoplasmic domain of CD4 is sufficient for its down-regulation from the cell surface by HIV-1 Nef. J Virol 68:3092-3101, 1994.

Adams M, Sharmeen L, Kimpton J, Romeo JR, **Garcia JV**, Peterlin BM, Groudine M, Emerman M. Cellular latency in HIV-infected individuals with high CD4 levels can be detected by the presence of promoter-proximal transcription. Proc Natl Acad Sci USA 91:3862-3866, 1994.

Constantinescu SN, Croze E, Murti A, Wang C, Basu L, Hollander D, Russell-Harde D, Betts M, **Garcia JV**, Mullersman JE, Pfeffer LM. Expression of signaling specificity of the IFNR-1 chain of the type I IFN receptor complex. Proc Natl Acad Sci 92:10487-10491, 1995.

Luo T, Anderson SJ, **Garcia JV**. Inhibition of Nef- and phorbol ester-induced CD4 degradation by macrolide antibiotics. J Virol 70:1527-1534, 1996.

Luo T, Downing JR, and **Garcia JV**. Induction of phophorylation of human immunodeficiency virus type 1 Nef and enhancement of CD4 downregulation by phorbol myristate acetate. J. Virology 71:2535-2539, 1997.

O'Neill E, Douglas JL, Chien M, and **Garcia JV**. Open Reading Frame 26 of Human Herpesvirus 8 Encodes a TPA- and Butyrate-Inducible 32 kDa Protein Expressed in a Body Cavity-Based Lymphoma Cell Line. J. Virol. 71:4791-4797, 1997.

Chien M, Foster JL, Douglas, JL, and **Garcia, JV**. The Amphotropic murine leukemia virus receptor gene encodes a 71-Kilodalton protein that is induced by phosphate depletion. J. Virol. 71:4564-4570, 1997.

Luo L, Douglas JL, Livingston, RL, and **Garcia JV**. Infectivity enhancement by HIV-1 Nef is dependent on the pathway of virus entry: implications for HIV-based gene transfer systems. Virology 241:224-233, 1998.

Douglas J, Kelly P, Evans JT and **Garcia JV**. Efficient Transduction of Human Lymphocytes and $CD34^+$ Cells Via HIV-Based Gene Transfer Vectors. Human Gene Therapy 10:935-945, 1999.

Gatlin J, Douglas J, Evans JT, Collins RH, Wendel GD and **Garcia JV.** In vitro Selection of Lentivirus Vector Transduced Human CD34+ Cells. Human Gene Therapy 11,1949-1957, 2000.

Evans JT and **Garcia JV**. Lentivirus Vector Mobilization and Spread by the Human Immunodeficiency Virus. Human Gene Therapy 11,2331-2339, 2000.

Evans JT, Cravens P., Lipsky PE and **Garcia JV**. Differentiation and Expansion of Lentivirus-Vector Marked Dendritic Cells Derived from Human CD34+ Cells. Human Gene Therapy 11, 2483-2492, 2000.

Gatlin J, Padgett A, Melkus MW, Kelly PF and **Garcia JV**. Long-Term Engraftment of NOD/SCID Mice with Human $CD34^+$ Cells Transduced by a Self-Inactivating HIV-1 Vector. Human Gene Ther. 12, 1079-1089, 2001.

Gatlin J, Melkus MW, Padgett A, Kelly PF and **Garcia JV**. Engraftment of NOD/SCID mice with human $CD34^+$ cells transduced by concentrated oncoretroviral vector particles pseudotyped with the feline endogenous virus (RD114) envelope glycoprotein. J. Virol. 75, 9995-9999, 2001. PMCID: PMC114573.

Evans JT, Cravens P, Gatlin J, Kelly P, Lipsky PE and **Garcia JV**. Pre-Clinical Evaluation of an In Vitro Selection Protocol for the Enrichment of Transduced CD34+ Cell Derived Human Dendritic Cells. Gene Therapy 8, 1427-1435, 2001.

Arora VA, Molina RP, Foster JL, Blakemore JL, Chernoff J, Fredericksen BL and **Garcia JV**. Lentivirus Nef Specifically Activates Pak2. J. Virol. 74, 11081-11087, 2000. PMCID: PMC113188.

Luo T, Fredericksen, BL, Hasumi, K, Endo A, and **Garcia JV**. Human immunodeficiency Virus Type-1 Nef-Induced CD4 Cell Surface Downregulation Is Inhibited by Ikarugamycin. J Virology 75, 2488-2492, 2001. PMCID: PMC114835.

Foster JF, Molina RP, Luo T, Arora VK, Huang Y, Ho D and **Garcia JV.** Genetic and Functional Diversity Amongst HIV-1 Subtype B Nef Primary Isolates. J. Virology 75, 1672-1680, 2001. PMCID: PMC114076.

Arora, VK, Fredericksen BL, and **Garcia JV**. Nef: agent of cell subversion. Microbes and Infection 4m 189-199, 2002.

Fredericksen BL, Yao J, Luo T and **Garcia JV.** Inhibition of Endosomal/Lysosomal Degradation Increases the Infectivity of the Human Immunodeficiency Virus. J. Virology. 76, 11440-11446, 2002. PMCID: PMC136743.

Wilund KR, Yi M, Champagna F, Arca M, Zuliana G, Fellin R, Ho YK, **Garcia JV,** Hobbs HH, Cohen JC. Molecular Mechanisms of Autosomal Recessive Hypercholesterolemia. Human Mol. Genetics. 11, 3019-30,2002.

Hamra FK, Gatlin JE, Chapman KM, Grellhesl DM, **Garcia JV**, Hammer RE and Garbers DL. Production of Transgenic Rats by Direct Germline Transmission. Proc. Nat. Acad. Sci. USA 99, 14931-14936, 2002. PMCID: PMC137522.

Gatlin J, Melkus MW, Padgett A, Petroll WM, Cavanaugh D, **Garcia JV** and Jester JV. In Vivo Fluorescent Labeling of Corneal Wound Healing Fibroblasts. Exp. Eye Res. 76, 361-71, 2003.

Palucka AK, Gatlin JE, Blanck JP, Melkus MW, Clayton S, Ueno H, Kraus ET, Cravens P, Bennett L, Padgett-Thomas A, Marches F, Islas-Ohlmayer M, **Garcia JV** and Banchereau J. Human Dendritic Cell Subsets in NOD/SCID Mice Engrafted with $CD34^+$ Hematopoietic Progenitors. Blood. 102, 3302-3310, 2003.

Islas-Ohlmayer M, Padgett-Thomas A, Domiati-Saad R, Melkus MW, Cravens PD, Martin M del P, Netto G, and **Garcia JV**. Experimental Infection of NOD/SCID Mice Reconstituted with Human CD34+ Cells with Epstein-Barr Virus. J. Virol. 78, 13891-13900, 2004. PMCID: PMC533956.

Cravens PD, Melkus MW, Padgett-Thomas A, Islas-Ohlmayer M, Martin MP and **Garcia JV**. *In vivo* modeling of human dendritic cell development, differentiation and function: phenotypic and functional analysis during the steady state and acute response to endotoxin. Stem Cells. 23, 264-278, 2005.

Wei, B.L., P.W. Denton, E. O'Neill, T. Luo, J. L. Foster, and **Garcia JV**. Inhibition of Lysosome and proteasome function enhances human immunodeficiency virus type I infection. J. Virol. 79: 5705-5712, 2005. PMCID: PMC1082736.

Raney A, Kuo LS, Baugh LL, Foster JL and **Garcia JV**. Reconstitution and molecular analysis of an active Nef/PAK-2 complex. J. Virology. 79, 12732-12741, 2005. PMCID: PMC1235864.

Wei B, Arora VK, Raney A, Kuo L, Xiao G-H, O'Neill E, Testa JR, Foster JL and **Garcia JV**. Activation of p21-activated kinase by human immunodeficiency virus type-1 Nef induces merlin phosphorylation. J. Virology. 79, 14976-14980, 2005. PMCID: PMC1287594.

O'Neill E, Kuo LS, Krisko JF,Tomchick DR, **Garcia JV**, and Foster JL. Dynamic evolution of the human immunodeficiency virus type 1 pathogenic factor, Nef. J. Virology. 80, 1311-1320, 2006. PMCID: PMC1346962.

Agopian J, Wei BL, **Garcia JV**, and Gabuzda D. A Hydrophobic Binding Surface on the Human Immunodeficiency Virus Type 1 Nef Core Is Critical for Association with p21-Activated Kinase 2. J. Virology. 80, 3050-3061, 2006. PMCID: PMC1395437.

Foster, JL and **Garcia JV**. HIV Pathogenesis: Nef loses control. Cell. 125, 1034-1035, 2006.

Melkus MW, Estes JD, Padgett-Thomas A, Gatlin J, Denton PW, Othieno F, Wege AK, Hasse AT, and **Garcia JV**. Humanized mice mount specific adaptive and innate immune response to EBV and TSST-1. Nature Medicine. 12:1316-1322, 2006.

O'Neill E, Baugh LL, Novitsky VA, Essex ME and **Garcia JV**. 2006. Itra- and intersubtype alternative Pak2-activating structural motifs of HIV-1 Nef. J. Virology. 80: 8824-8829, 2006. PMCID: PMC1563850.

Sun Z, Denton PW, Estes JD, Othieno F, Wei B, Wege AK, Melkus MW, Padgett-Thomas A, Zupancic M, Haase AT and **Garcia JV**. Intrarectal transmission, systemic infection and CD4 T cell depletion in humanized mice infected with HIV-1. J. Exp. Med. 204: 705-714, 2007. PMCID: PMC2118553.

Raney A, Shaw AY, Foster JL and **Garcia JV**. Structural constraints on human immunodeficiency virus type 1 Nef function. Virology. 368, 7-16, 2007.

Wege A, Denton PD, Estes JD and **Garcia JV**. Functional and phenotypic characterization of the humanized BLT mouse model. Current Topics in Microbiology and Immunology. 324:149-165, 2008.

Denton PW, Estes JD, Sun Z, Othieno F, Wei B, Wege AK, Powell DA, Payne D, Haase AT and **Garcia JV**. Antiretroviral Pre-exposure Prophylaxis Prevents Vaginal Transmission of HIV-1 in Humanized BLT Mice. PLoS Medicine Vol. 5, No. 1, e16 doi:10.1371, 2008. PMCID: PMC2194746.

Wang J, Shackelford JM, Selliah N, Shivers DK, O'Neill E, **Garcia JV,** Karuppiah M, Weiner D, Yu X-F, Gabuzda D and.Finkel TH. The HIV-1 Vif Protein Mediates degradation of Vpr and Reduces Vpr-Induced Cell

Cycle Arrest. DNA and Cell Biology. 27(5):267-77, 2008.

Buzina A, Lo M, Moffett A, Hotta A, Fussner E, Bharadwaj R, Pasceri P, **Garcia JV**, Bazett-Jones D, and Ellis J. β-globin LCR and intron elements cooperate and direct spatial reorganization for gene therapy. PLoS Genetics. 4(4):e1000051.doi:1.1371/journal.pgen.1000051, 2008.

Baugh LL, **Garcia JV**, Foster JL. Functional Characterization of the Human Immunodeficiency Type 1 Nef Acidic Domain. J. Virology. 82(19):9657-67. PMCID: PMC2546962, 2008.

Foster JL, **Garcia JV.** HIV-1 Nef: at the crossroads. Retrovirology 5:84, doi:10.1186/1742-4690-5-84 (2008).

Denton PW and **Garcia JV.** Novel humanized murine models for HIV research. Curr HIV/AIDS Rep 6(1):13-9 (2009).

C. Research Support: <u>Ongoing</u>

NIAID 5 R01 AI033331, "Nef Function," 06/01/07 – 05/31/11. J. Victor Garcia-Martinez, Ph.D., Principal Investigator. The focus of this competitive renewal grant is to implement a novel in vivo system of HIV infection developed in our laboratory to begin to dissect the individual contributions of the different *in vitro* activities of HIV-1 Nef to pathogenesis and disease progression.

NIH R01 AI073146-01A2, "Vaginal/Rectal HIV Transmission Model," 08/01/07 – 07/31/11. J. Victor Garcia-Martinez, Ph.D., Principal Investigator. The long-term goal of our laboratory is to investigate novel approaches to prevent HIV transmission by the use of antivirals and microbicides.

NIH NIAID 4R33 AI071940-3, "Implementation of a vaginal/rectal HIV transmission model to evaluate microbicides," 09/20/08 – 08/31/11. J. Victor Garcia-Martinez, Ph. D. Principal Investigator. The long term goal of this project is to study HIV transmission in a xenograft model of infection.

NIAID 5 R01 AI39416, "Gene Transfer System for AIDS Therapy," 12/01/03 – 11/30/09. J. Victor Garcia-Martinez, Ph.D., Principal Investigator. The long-term goal of this proposal is to develop gene therapy approaches to treat HIV disease.

NIH 1R21-AI068527-01, "Structural Plasticity of an HIV-1 Nef/Pak-2 Activating Surface," 08/01/06 – 07/31/09. J. Victor Garcia-Martinez, Ph.D., Principal Investigator. The studies proposed here will help elucidate the structural requirements for the activation of Pak-2 by Nef and will serve as the basis for future in vivo experiments aimed at characterizing its functional significance.

<u>Pending</u>

NIH 1R01AI079607-01A1 "Molecular Basis of Mucosal HIV Transmission," 07/01/09 – 06/31/13. J. Victor Garcia-Martinez, Ph.D., Principal Investigator. The long term-goal of our laboratory is to investigate novel approaches to prevent HIV transmission.

NIH "Modeling eradication of HIV infection in BLT mice," 03/01/2009 – 02/28/2014. J. Victor Garcia-Martinez, Ph.D., Principal Investigator (David M. Margolis, M.D., PI, University of N. Carolina Consortium). The long term goal of our project is to develop and implement an in vivo animal model in which novel protocols for HIV-1 eradication can be evaluated.

NIH "Topical antiretrovirals to prevent rectal HIV infection," 03/01/2009 – 02/28/2014. J. Victor Garcia-Martinez, Ph.D. (Ian McGowan, M.D., PI, Magee Womens Research Institute and Foundation Consortium). Our long term-goal is to investigate novel approaches to prevent HIV transmission by the use of topical microbicides.