CURRICULUM VITAE FOR
CWRU SCHOOL OF MEDICINE
12/15/15

PERSONAL INFORMATION

BIOGRAPHY

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Date of Birth:	November 17, 1972

EDUCATION

1991-1995	B.A. in Molecular Biology, Princeton University
1996-2001	M.D., Yale School of Medicine
2001	M.D. Thesis. *Mutagenesis of the NK cell receptor 2B4*. Thesis committee: Eric Long, Ph.D., Charles Janeway, M.D.

POST-GRADUATE TRAINING

2001-2006	Clinical Research Fellow, Clinical and Molecular Retrovirology Section, NIAID, NIH, Bethesda, MD
2006-2010	Senior Research Investigator, Department of Microbiology, University of Pennsylvania, Philadelphia, PA

PROFESSIONAL APPOINTMENTS

Nov 1, 2010-present	Assistant Professor, Center for Proteomics & Bioinformatics, Case Western Reserve University, Cleveland, OH
2012-present	Director of Immunobiology, Center for Proteomics & Bioinformatics, Case Western Reserve University, Cleveland, OH
2014-present	Assistant Professor, Molecular Biology & Microbiology, Case Western Reserve University, Cleveland, OH
2015-present	Assistant Professor, Department of Nutrition, Case Western Reserve University, Cleveland, OH

HONORS, AWARDS, AND FELLOWSHIPS

1995	Magna Cum Laude, Princeton University
1995	Sigma Xi Scientific Research Society, Princeton University
1998	Winternitz Prize in Pathology, Yale School of Medicine

1999-2000	Howard Hughes Medical Institute-National Institutes of Health Cloisters Research Scholar
2002-2005	National Institutes of Health Special Act Award
2007-2010	Ruth L. Kirschstein National Research Service Award (NRSA)
2008	Postdoctoral Speaking Award, University of Pennsylvania

MEMBERSHIPS IN PROFESSIONAL SOCIETIES

2013-Present	American Society for Microbiology (ASM)
2014-Present	American Association for the Advancement of Science (AAAS)

PROFESSIONAL SERVICE

STUDY SECTIONS

NATIONAL AND INTERNATIONAL

2014	Deutsche Forschungsgemeinschaft Grant Reviewer (German equivalent of the National Institutes of Health)
2015	National Institutes of Allergy and Infectious Diseases (NIAID) Reviewer, Ad Hoc study section ZAI1-JRR-A-M1 (RFA-AI-14-020 'Innovative Assays to Quantify the Latent HIV Reservoir (R01)'
2015	National Institutes of Allergy and Infectious Diseases (NIAID) Reviewer, AIDS Discovery and Development of Therapeutics (ADDT) study section.
2015	National Institute of Dental and Craniofacial Research (NIDCR) Special Grants Review Committee (DCR) study section.

UNIVERSITY AND DEPARTMENT

2014-2015	Clinical and Translational Science Collaborative (CTSC) Pilot Grant reviewer
2014	Center for AIDS Research (CFAR) Developmental Grant reviewer

MANUSCRIPT REVIEWS

Chemistry & Biology, Cell Press
JAIDS-Journal of Acquired Immune Deficiency Syndromes
Journal of Immunology
Journal of Infectious Diseases
Journal of Translation Medicine
Journal of Virology
PLoS One
PLoS Pathogens
Retrovirology

COMMITTEE SERVICE

UNIVERSITY LEVEL

2011-Present	Interviewer, Biological Sciences Training Program (Ph.D. program)
2012-2013	Member, Climate Survey Task Force
2013-Present	Center for AIDS Research (CFAR) Virology and Cure Working Group leader
2014-Present	Member, Faculty Development Council
2015-Present	Member, Department of Nutrition and Systems Biology Committee on Advancement, Promotion and Tenure (CAPT)

DEPARTMENT LEVEL

2011-2012	Strategic Direction Committee, Center for Proteomics & Bioinformatics
2012-Present	Director of Immunobiology, Center for Proteomics & Bioinformatics
2014-Present	Working Group member for merger of the Center for Proteomics & Bioinformatics with the Department of Nutrition
2015-Present	Chair, committee for Departmental Metrics, Department of Nutrition
2015-Present	Departmental Research Committee, Department of Nutrition

TEACHING ACTIVITIES

Please refer to the accompanying *Teaching Portfolio Narrative* for details on my teaching philosophy, teaching methods, evidence of teaching success, and list of students taught in the laboratory and the classroom.

RESEARCH ACTIVITIES

ONGOING RESEARCH PROJECTS

1R01HD077886-01 (Tilton) 9/30/13-6/30/18
NICHD/NIAID RFA-HD-13-008
Total Award: $2,438,125 ($1,538,250 Direct Costs)
"*Enhancement of HIV transmission by hormones and bacterial metabolites*."
This study is investigating the role of hormones and bacterial byproducts, specifically short chain fatty acids, in regulating the susceptibility of cervical CD4+ T cells to infection by HIV.

1R01DE025464 (Karn) 7/1/15-6/30/20
NIDCR RFA-DE-15-003
Project Role: Co-investigator
Total Award: $3,936,569 ($2,483,640 Direct Costs)
"Identification and elimination of HIV reservoirs in oral lymphoid tissues by engineered NK cells."
This study seeks to identify latent reservoirs in tonsillar tissues through flow cytometric and imaging techniques in both human lymphoid aggregate cultures (HLACs) and tonsillar block histoculture. Strategies to eliminate the reservoirs using NK cells engineered to home to oral tissues and express chimeric antigen receptors will be assessed.

COMPLETED RESEARCH PROJECTS

1R21AI113148-01 (Tilton) 7/1/14–6/30/16
NIAID RFA-HD-13-038 (R21)

Total Award: $435,875 ($275,000 Direct Costs)
"Detection of latent HIV infection using selective reaction monitoring mass spectrometry."
This project is investigating the feasibility of using targeted mass spectrometry as an approach to monitor the latent reservoir in infected patients, a pre-requisite for clinical trials designed to purge and eliminate reservoirs and cure HIV infection. A paper describing this assay is current in preparation.

CTSC Core Pilot Utilization Award (Tilton) 6/30/15-12/31/15
Direct Costs: $10,000
"Characterizing the Acetylome of CD4+ T cells to Identify Anti-HIV Targets"
This study employed global phosphoproteomics of acetylated proteins to identify targets of the lysine acetyltransferases garcinol, curcumin, and anacardic acid. Garcinol and curcumin reduce HIV infection of primary CD4+ T cells, whereas anacardic acid has no effect. The goal of this project is to identify novel host proteins or protein modifications that regulate HIV infectivity for use in pre-exposure prophylaxis (PrEP) strategies.

CTSC Core Pilot Utilization Award (Tilton) 6/30/14-12/31/14
Direct Costs: $10,000
"Monitoring Viral Induction of CCR5 Signaling in Memory CD4+ T cells"
This study employed phosphoproteomics to determine signal transduction following stimulation of memory CD4+ T cells with HIV in the presence or absence of maraviroc compared to a microvesicle control.

Australian Centre for HIV and Hepatitis Virology Research (ACH2) (Ryan) 7/1/12-6/30/13
Direct Costs: $109,000
"*Characterisation of novel CCR5 genotypes influencing the emerging and unique HIV-1 epidemic in Papua New Guinea*."
This study proposed to characterize *CCR5* genotypes in Papua New Guinean (PNG) blood samples, determine whether these genotypes increase expression of CCR5 on peripheral blood mononuclear cells, and whether the surface expression of CCR5 correlates with magnitude of *in vitro* viral replication.

CFAR Supplemental Grant (Tilton) 5/5/10-4/30/13
Funded through the University of North Carolina Centers for AIDS Research (CFAR) Grant
PI: Swanstrom
Direct Costs of Sub-Contract: $75,000
Mass Spectrometry Detection of Viral Peptides after in vitro *culture.*
This CFAR supplement administered through the UNC CFAR and the Martin Delaney Collaboratory will investigate the potential of stable isotope dilution mass spectrometry (SID-MS) to monitor the size of latent HIV reservoirs using peripheral blood from HIV-infected patients.

Research Grant #108257-51-RGRL (Tilton) 11/1/11-10/31/12
Foundation for AIDS Research (amfAR)
Direct Costs - $100,000
"*CD4+ T cell subsets: targets for HIV infection and latency*."
CD4+ T cells are the primary reservoir of HIV and can be divided into several subsets, whose contribution to viral persistence is incompletely understood. This study aims to characterize memory and lineage CD4+ T cell subsets to determine their susceptibility to abortive, latent, or productive infection following viral fusion.

CFAR Development Grant (Tilton) 5/1/11-4/30/12
CWRU CFAR
Direct Costs - $50,000
"*Effects of chronic immune activation on CD4+ T cell subset susceptibility to HIV infection*."

This study is investigating whether chronic HIV-associated immune activation alters the subsets of CD4+ T cells that are targets for viral fusion and productive infection.

NSRA F32 AI077370 (Tilton) 2/1/08-10/31/10
NIH – Ruth L. Kirschstein NRSA
Total Award: $150,000
"*Mechanisms of HIV Resistance to CCR5 Inhibitors and Consequences for Pathogenesis*."
This study examined how HIV developed resistance to the CCR5 antagonists maraviroc and aplaviroc in patients experiencing viral rebound while treated with these agents.

PRESENTATIONS

INTERNATIONAL MEETINGS

Invited Talks

"*HIV-specific CD4+ T cell replication is not associated with virologic control.*" July 2002
XIV International AIDS Conference, Barcelona, Spain

"*HIV-specific CD4+ T cell IL-2 production is diminished during viremia and accounts for reduced proliferation in response to HIV antigens*." July 2004
XV International AIDS Conference, Bangkok, Thailand

"CD4+ Memory Stem Cells (T_{SCM}) are Productively and Latently Infected by CCR5- and CXCR4-Tropic HIV." April 2013
Keystone Symposia. Immune Activation in HIV Infection: Basic Mechanisms and Clinical Implications (D2). Breckenridge, CO, USA

Poster Presentations

"CD4+ memory stem cells (Tscm) are productively and latently infected by CCR5- and CXCR4- Tropic HIV." April 2013
Keystone Symposia. Immune Activation in HIV Infection: Basic Mechanisms and Clinical Implications (D2). Breckenridge, CO, USA

"Detection of HIV peptides using SRM mass spectrometry." June 2013
American Society for Mass Spectrometry (ASMS) meeting, Minneapolis, MN, USA.

"The HDAC inhibitor vorinostat increases productive HIV-1 infection by enhancing the efficiency of post-entry viral events." March 2014
Keystone Symposia. HIV Pathogenesis – Virus vs. Host (X4). Banff, AL, Canada.

"HIV infection and its regulation by SAMHD1 in CD4+ T cell subsets in relation to memory stem cells (Tscm)." March 2014
Keystone Symposia. HIV Pathogenesis – Virus vs. Host (X4). Banff, AL, Canada.

"The vast majority of unstimulated primary CD4+ T cells are refractory to HIV infection regardless of viral concentration." March 2014
Keystone Symposia. HIV Pathogenesis – Virus vs. Host (X4). Banff, AL, Canada.

"Dynamic phosphoproteomics of HIV gp120 signaling through CD4 and CCR5." June 2015
American Society for Mass Spectrometry (ASMS) meeting, St. Louis, MO, USA.

NATIONAL AND UNIVERSITY MEETINGS

"*CCR5 Antagonists: Viral resistance and implications for Patients*." December 2009
University of Pennsylvania CFAR Scientific Retreat

"*Viral fusion and productive infection of CD4+ T cell subsets: a novel explanation for reduced fitness of X4-tropic HIV*." February 2011
CWRU CFAR Scientific Retreat

"*Analysis of multiple stages of the HIV life cycle by flow cytometry*." August 2011
CWRU CFAR Scientific Retreat

"*Probing HIV infection of T cells with a combination reporter virus*." September 2012
Microbiology and Molecular Biology Departmental Retreat, CWRU

"*Viral outcomes following fusion with CD4+ T cell subsets*." January 2013
CWRU CFAR Scientific Retreat

"*The HDAC Inhibitor SAHA (vorinostat) increases the susceptibility of CD4+ T cells to productive infection by HIV*." August 2013
CWRU CFAR Scientific Retreat

"*Detection of Latent HIV using Selective Reaction Monitoring - Mass Spectrometry (SRM-MS)*." February 2014
CWRU CFAR Scientific Retreat

"*Stem Your Enthusiasm: Memory Stem Cells in HIV Infection.*" February 2014
Cleveland Immunopathogenesis Consortium Meeting

"*Histone deacetylase (HDAC) inhibitors enhance cellular susceptibility to HIV infection."* November 2014
National CFAR Directors Meeting. Providence, RI, USA.

"*Global phosphoproteomics of HIV gp120 signaling through CD4 and CCR5*." January 2015
CWRU CFAR Scientific Retreat

UNIVERSITY SEMINARS

"*Pre-existing resistance to CCR5 antagonists in a patient treated with Aplaviroc*." March 2008
Microbiology Departmental Seminar, University of Pennsylvania

"*HIV Resistance to CCR5 antagonists and implications for tropism*." February 2009
University of Colorado CFAR Seminar

"*New Drugs and Technologies to Examine Viral Tropism and Disease Progression*." January 2010

Microbiology Departmental Seminar, University of Pennsylvania

"*CD4+ T cell subsets: susceptibility to HIV fusion and productive infection*." May 2011
Microbiology and Molecular Biology Departmental Seminar, CWRU

"*HIV Replication and Pathogenesis: New insights from a multi-stage reporter*." November 2012
virus system."
World Health Interest Group Seminar, CWRU

"*HIV Replication and Pathogenesis: New insights from a multi-stage reporter*." January 2013
virus system."
Ohio State University Department of Microbiology Seminar, Ohio State University

"*The latent reservoir in HIV infection and the hope for a cure."* March 2014
Center for Proteomics and Bioinformatics Seminar.

"*HIV latency: defining and measuring the latent reservoirs and the hope for a cure*." April 2014
Microbiology and Molecular Biology Departmental Seminar, CWRU

BIBLIOGRAPHY

1. Iyasere C, Tilton JC, Johnson AJ, Younes S, Yassine-Diab B, Sekaly RP, Kwok WW, Migueles SA, Laborico AC, Shupert WL, Hallahan CW, Davey RT Jr, Dybul M, Vogel S, Metcalf J, Connors M. "Diminished proliferation of human immunodeficiency virus-specific CD4+ T cells is associated with diminished interleukin-2 (IL-2) production and is recovered by exogenous IL-2." *J. Virol* **77**: 10900-10909 (2003).
2. Migueles SA, Tilton JC, Connors M. "Advances in understanding immunologic control of HIV infection." *Curr HIV/AIDS Reports* **1**: 12-17 (2004).
3. Eissmann P, Beauchamp L, Wooters J, Tilton JC, Long EO, Watzl C. "Molecular basis for positive and negative signaling by the NK cell receptor 2B4 (CD244)." *Blood* **105**: 4722-4729 (2005).
4. Migueles SA, Tilton JC, Connors M. "Qualitative host factors associated with immunological control of HIV infection by CD8 T cells." *Curr Opin HIV AIDS* **1**: 28-33 (2006)
5. Puig M, Mihalik K, Tilton JC, Williams O, Merchlinsky M, Connors M, Feinstone SM, Major ME. "CD4+ immune escape and subsequent T cell failure following chimpanzee immunization against hepatitis C virus." *Hepatology* **44**: 736-745 (2006).
6. Tilton JC, Johnson AJ, Luskin MR, Manion MM, Yang J, Adelsberger WJ, Lempicki RA, Hallahan CW, McLaughlin M, Mican JM, Metcalf JA, Iyasere C, Connors M. "Diminished production of monocyte proinflammatory cytokines during human immunodeficiency virus viermia is mediated by type I interferon. *J. Virol* **80**: 11486-11497 (2006).
7. Tilton JC, Luskin MR, Johnson AJ, Manion MM, Hallahan CW, Metcalf JA, McLaughlin M, Davey RT Jr, Connors M. "Changes in paracrine IL-2 requirement, CCR7 expression, frequency and cytokine secretion, of human immunodeficiency virus-specific CD4+ T cells are a consequence of antigen load." *J. Virol* **81**: 2713-2725 (2007).
8. Tilton JC and Doms RW. "Introduction to entry inhibitors in the management of HIV infection" in *Entry Inhibitors in HIV Therapy*, Jacqueline Reeves and Cynthia Derdeyn, Chapter 1, pps 1-15 (2007).
9. Tilton JC, Manion MM, Luskin MR, Johnson AJ, Patamawenu AA, Hallahan CW, Cogliano-Shutta NA, Mican JM, Davey RT Jr, Kotillil S, Lifson JD, Metcalf J, Lempicki RA, Connors M. "Human immunodeficiency virus viremia induces plasmacytoid dendritic cell activation *in vivo* and diminished interferon-alpha production *in vitro*." *J. Virol* **82**: 3997-4006 (2008).
10. Jagannathan P, Osborne CM, Royce C, Manion MM, Tilton JC, Li L, Fischer S, Hallahan CW, Metcalf JA, McLaughlin M, Pipeling M, McDyer JF, Manley TJ, Meier JL, Altman JD, Hertel L, Davey RT Jr, Connors

M. “Comparisons of CD8+ T cells specific for human immunodeficiency virus, hepatitis C virus, and cytomegalovirus reveal differences in frequency, immunodominance, phenotype, and interleukin-2.” *J. Virol* **83**: 2728-2742 (2009).

11. Tilton JC and Doms RW. “Entry Inhibitors in the treatment of HIV-1 infection.” *Antiviral Res* **85**: 91-100 (2010).

12. Tilton JC, Amrine-Madsen H, Miamidian JL, Kitrinos KM, Pfaff J, Demarest JF, Ray N, Leffrey JL, LaBranche CC, Doms RW. “HIV-1 from a patient with baseline resistance to CCR5 antagonists uses drug-bound receptor for entry.” *AIDS Res Hum Retroviruses* **26**:13-24 (2010).

13. Pfaff JM, Wilen CB, Harrison JE, Demarest JF, Lee B, Doms RW, Tilton JC. “HIV-1 resistance to CCR5 antagonists associated with highly efficient use of CCR5 and altered tropism on primary CD4+ T cells.” *J. Virol* **84**:6506-6514 (2010).

14. Tilton JC, Wilen CB, Didigu CA, Sinha R, Harrison JE, Agrawal-Gamse C, Henning EA, Bushman FD, Martin JN, Deeks SG, Doms RW. “A maraviroc-resistant HIV-1 with narrow cross-resistance to other CCR5 antagonists depends on both N-terminal and extracellular loop domains of drug-bound CCR5.” *J. Virol* **84:**10863-10876 (2010).

15. Wilen CB, Wang J, Tilton JC, Miller JC, Kim KA, Rebar EJ, Sherrill-Mix SA, Patro SC, Secreto AJ, Jordan AP, Lee G, Kahn J, Aye PP, Bunnell BA, Lackner AA, Hoxie JA, Danet-Desnoyers GA, Bushman FD, Riley JL, Gregory PD, June CH, Holmes MC, Doms RW. “Engineering HIV-resistant human CD4+ T cells with CXCR4-specific zinc-finger nucleases.” *PLoS Pathog* **7**:e1002020 (2011).

16. Wilen CB, Parrish NF, Pfaff JM, Decker JM, Henning EA, Haim H, Petersen JE, Wojcechowskyj JA, Sodroski J, Haynes BF, Montefiori DC, Tilton JC, Shaw GM, Hahn BH, Doms RW. “Phenotypic and immunologic comparison of clade B transmitted/founder and chronic HIV-1 envelope glycoproteins.” *J Virol.* **85**:8514-27 (2011).

17. Jiang C, Parrish NF, Wilen CB, Li H, Chen Y, Pavlicek JW, Berg A, Lu X, Song H, Tilton JC, Pfaff JM, Henning EA, Decker JM, Moody MA, Drinker MS, Schutte R, Freel S, Tomaras GD, Nedellec R, Mosier DE, Haynes BF, Shaw GM, Hahn BH, Doms RW, Gao F. “Primary infection by a human immunodeficiency virus with atypical coreceptor tropism.” *J Virol*. **85**: 10669-10681 (2011).

18. Wilen CB, Tilton JC, Doms RW. “Molecular mechanisms of HIV Entry.” *Adv Exp Med Biol* **2012**:223-242 (2012).

19. Wilen CB, Tilton JC, Doms RW. “HIV Binding and Entry.” *Cold Spring Harbor Perspectives in Medicine.* 2(8). pii: a006866 (2012).

20. Parrish, N, Wilen C, Banks L, Iyer S, Pfaff J, Salazar-Gonzalez J, Salazar M, Decker J, Parrish E, Berg A, Hopper J, Hora B, Kumar A, Mahlokozera T, Yuan S, Coleman C, Vermeulen M, Ding H, Ochsenbauer C, Tilton J**,** Permar S, Kappes J, Betts M, Busch M, Gao F, Montefiori D, Haynes B, Shaw G, Hahn B, Doms R. “Transmitted/Founder and Chronic Subtype C HIV-1 use CD4 and CCR5 receptors with equal efficiency and are not inhibited by blocking the integrin $\alpha 4\beta 7$.” *PLoS Pathog*. May 8(5): e1002686. (2012).

21. Lobritz MA, Ratcliff AN, Marozsan AJ, Dudley DM, Tilton JC, Arts EJ. “Multifaceted mechanisms of HIV inhibition and resistance to CCR5 inhibitors PSC-RANTES and Maraviroc.” *Antimicrob Agents Chemother*. **57**:2640-2650 (2013).

22. Haqqani AA, Tilton JC. “Entry inhibitors and their use in the treatment of HIV-1 infection.” *Antiviral Res*. **98**:158-170 (2013).

23. Tilton CA, Tabler CO, Lucera MB, Tilton JC. “A combination HIV reporter virus system form measuring post-entry event efficiency and viral outcome in primary CD4+ T cell subsets” *J Virol Methods*. Jan; 195: 164-169 (2014).

24. Tabler CO, Lucera MB, Haqqani AA, McDonald DJ, Migueles SA, Connors M, Tilton JC. “CD4+ Memory stem cells are infected by HIV-1 in a manner regulated in part by SAMHD1 expression.” *J Virol*. 88(9):4976-86 (2014).

25. Lucera MB, Tilton CA, Mao H, Dobrowolski C, Tabler CO, Haqqani AA, Karn J, Tilton JC. “The histone deacetylase inhibitor vorinostat (SAHA) increases the susceptibility of uninfected CD4+ T cells to HIV by increasing the kinetics and efficiency of postentry viral events.” *J Virol*. 88(18):10803-12 (2014).

26. Haqqani AA, Marek SL, Kumar J, Davenport M, Wang H, and Tilton JC. “Central memory CD4+ T cells are preferential targets of double infection by HIV-1”. *Virol J.* 12(1):184 (2015).