

RETRO-ACTIVE NEWS

Newsletter of the Center for Retrovirus Research
at The Ohio State University College of Veterinary Medicine

2012 Highlights

The Center for Retrovirus Research 2012 Distinguished Research Career Award

Warner C. Greene, MD, PhD, Director, Gladstone Institute of Virology and Immunology (GIVI), Nick and Sue Hellmann Distinguished Professor of Translational Medicine, Professor of Medicine, Microbiology and Immunology, Co-Director, University of California, San Francisco (UCSF)-GIVI Center for AIDS Research was the 13th recipient of the annual award for his seminal contributions to the understanding of the molecular and cellular biology of HIV and HTLV.



Dr. Warner C. Greene (center) receives Career Award crystal from Center for Retrovirus Research Director Dr. Patrick L. Green (right) and Center member Dr. Li Wu (left). Distinguished award lecture entitled "Murder on the HIV express: New insights into how CD4 T cells die"

Dr. Greene received his BA degree with great distinction from Stanford University and his MD and PhD degrees with honors from Washington University School of Medicine. He then completed his residency training in Internal Medicine at the Massachusetts General Hospital at Harvard University. From 1979-1986, he served as a senior investigator at the National Cancer Institute, where he established his research laboratory. In 1987, he became professor of medicine at Duke University and an Investigator in the Howard Hughes Medical Institute. In 1992, Dr. Greene became the founding director and a senior investigator of the GIVI and was also appointed a professor of medicine, microbiology, and immunology at UCSF.

Dr. Greene's basic and translation studies of HIV and HTLV have fundamentally contributed to our understanding of human retroviruses and viral pathogenesis. His current research focuses on the pathogenic interplay between human retroviruses and

immune cells to define the mechanisms underlying viral replication and transmission. Dr. Greene's laboratory also pursues basic studies on important transcription factors to better understand their roles in HIV latency. Dr. Greene is the author of more than 350 scientific papers and has been recognized as one of the 100 Most Cited Scientists in the world. He has been invited for many distinguished lectures worldwide. Dr. Greene is a member of the Institute of Medicine of the National Academies, a fellow of the American Academy for the Advancement of Science, and President-Elect of the American Association of Physicians. Dr. Greene has mentored more than 120 students and fellows during his over 30 year career in science. Many of his trainees have become independent researchers.

In addition to his distinguished research contributions, Dr. Greene also dedicates his time and effort to community service to enhance public health. Since 2007, he has served as President of the Accordia Global Health Foundation, whose mission is to overcome the burden of infectious diseases in Africa by creating innovative health models, building centers of excellence, and strengthening medical institutions.

Dr. Greene's visit was sponsored by the Center for Retrovirus Research, Departments of Veterinary Biosciences and Molecular Virology, Immunology and Medical Genetics, Public Health Preparedness for Infectious Diseases Program, and the Comprehensive Cancer Center Viral Oncology Program.

See a summary of previous award winners:
vet.osu.edu/retrovirus-research/award

Dr. Kathleen Boris-Lawrie and a multi-institution team of scientists launch the NIH Center for HIV RNA Studies (CRNA)



The NIH CRNA will receive up to \$21.5 million in funding over five years to unlock the secrets of RNA-based diseases. An example of interdisciplinary research across university campuses, the CRNA will study the structural biology of viral RNA and its interactions with viral and host proteins. Because RNA is less amenable to structural analysis than proteins are, the researchers will develop approaches to overcome this technical challenge. The new technology will be applied by the Boris-Lawrie lab to their previous discovery of the positive-acting translational control element in the 5'-leader of HIV-1 overlapping TAR-polyA. Structural investigations will define the necessary interactions with host effectors proteins, including host RNA helicase proteins. This work could help identify RNA-based targets for HIV treatments as well as shed light on application of the RNA-based target for other diseases

More at <http://sitemaker.umich.edu/crna/home>

Dr. Kristine Yoder, PhD has been promoted to assistant professor in the Department of Molecular Virology, Immunology, and Medical Genetics



Dr. Yoder studied host co-factors of HIV integration as a graduate student with Dr. Frederic Bushman. Her postdoctoral studies evaluated the roles of DNA repair proteins during integration. She has shown that host DNA repair proteins may be either positive or negative regulators of retroviral infection. Proteins of the nucleotide excision repair pathway, XPB and XPD, are able to defend the host genome from retroviral integration by degrading the viral cDNA by an evolutionarily ancient mechanism. In contrast, base excision repair (BER) proteins enhance HIV integration. Her lab continues to focus on the mechanism of retroviral integration. They are using a combination of cellular and biochemical assays to determine how chromatin and DNA repair factors affect integration sites and efficiency.

Dr. Jesse Kwiek and colleagues lead an outreach effort to develop public health interventions to fight HIV

In Malawi, a peaceful country in sub-Saharan Africa, there are an estimated one million people living with HIV (out of a population of 14 million), one half of whom are women. Prevention of HIV infection and unwanted pregnancy is essential for the survival and well-being of women and families throughout the world. In a collaboration led by Dr. Alison Norris of the Ohio State University College of Public Health, Drs. Jesse Kwiek and Abigail Norris Turner of the Ohio State College of Medicine, Dr. John Casterline

from the Ohio State Institute of Population Research, Dr. Victor Mwapasa of Malawi College of Medicine, Dr. Michael Belfort of Baylor College of Medicine, and colleagues at Child Legacy International (CLI), the multidisciplinary team has designed a study to examine how decision making effects people's behavior around HIV testing and contraception use. With a better understanding of decision making, the team expects to develop public health interventions to improve reproductive health.



In the OH spirit, from L to R: Jeff Rogers (CLI), Dr. Jesse Kwiek (Ohio State), Dr. Alison Norris (Ohio State), Elly Kirupto (CLI)

Dr. Patrick Green receives the inaugural David Derse Memorial Lecture/Award

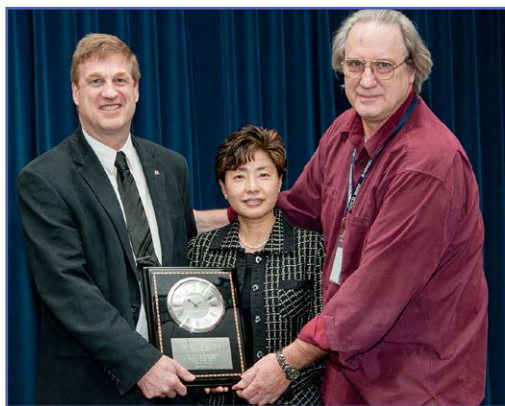


Dr. Patrick Green, PhD, Associate Dean for Research and Graduate Studies, Director of the Center for Retrovirus Research, and Leader of the CCC Viral Oncology Program at The Ohio State University, received the inaugural David Derse Memorial Lecture/Award on December 11, 2012 at the Frederick National Laboratory for Cancer Research. Dr. Green presented his memorial lecture entitled "HTLV-1 Transforming Genes: Tax versus Hbz".

Dr. Green has over 30 years of research experience in the field of murine and

human retroviral pathogenesis with more specific focus on human T-cell leukemia virus (HTLV). He has been appointed as a member of numerous NIH study sections and scientific panels, he currently serves as Editor of AIDS Research and Human Retroviruses, as well as a member of the editorial boards of Retrovirology and Journal of Virology. Dr. Green has been recognized with a number of honors that include the Pfizer Award for Research Excellence and the International Retrovirology Association Award, as well as designation as an American Cancer Society Fellow, Leukemia Society of America Scholar, American Association for the Advancement of Science (AAAS) Fellow, American Society for Microbiology Fellow, Ohio State University Distinguished Scholar, and member of the Board of Trustees of the Leukemia/Lymphoma Society.

The Annual David Derse Memorial Lecture and Award is supported by a gift fund established with the National Cancer Institute. This lecture series honors David Derse's outstanding accomplishments, remarkable generosity, and boundless passion for science and will help foster the scientific discourse and free exchange of ideas that were so much a part of his life.



Dr. Patrick Green (left) receives award from Hye-Kyung Derse and Dr. Stephen Hughes (Director, HIV Drug Resistance Program). Photo Courtesy of SAIC-Frederick Inc.

Doctoral Graduates

Rami Doueiri, PhD. "Characterization of the human T-cell leukemia virus type 2 p28 accessory protein". Molecular Cellular and Developmental Biology Graduate Program

Christopher Jones, Ph.D. "Primer tRNA annealing by human immunodeficiency virus type 1". Ohio State Biochemistry Graduate Program

Varun Dewan, Ph.D. "Lysyl-tRNA Synthetase-Capsid Interaction in Human Immunodeficiency Virus-1: Implications for the Priming of Reverse Transcription and Therapeutic Development". Ohio State Biochemistry Graduate Program

Meng Sun, Ph.D. "Retrovirus-Specific Differences in Matrix and Nucleocapsid Protein-Nucleic Acid Interactions: Implications for Genomic RNA Packaging". Chemistry Graduate Program

Sirena Coon, MS "Polymorphisms of the SAMHD1" Molecular Cellular and Developmental Biology Graduate Program



Selected publications

- Anand A, Zhao H, Nagaraja T, Robinson LA, **Ganju RK**. N-terminal Slit2 inhibits HIV-1 replication by regulating the actin cytoskeleton. *Retrovirology* 2013 Jan 7;10(1):2. [Epub ahead of print].
- Coon S, Wang D, **Wu L**. Polymorphisms of the SAMHD1 gene are not associated with the infection and natural control of HIV-1 in Europeans and African Americans. *AIDS Res Hum Retroviruses*. 2012 28(12):1565-73.
- de Silva S, Planelles V, **Wu L**. Differential effects of Vpr on single-cycle and spreading HIV-1 infections in CD4+ T-cells and dendritic cells. *PLoS One*. 2012 7(5):e35385.
- Dewan D, Wei M, Kleiman L, **Musier-Forsyth K**. Dual Role for Motif 1 Residues of Human Lysyl-tRNA Synthetase in Dimerization and Packaging into HIV-1. *J Biol Chem* 2012 287: 41955-62.
- Doueiri R, Anupam R, **Kvaratskhelia M**, Green KB, Lairmore MD, Green PL. Comparative host protein interactions with HTLV-1 p30 and HTLV-2 p28: insights into difference in pathobiology of human retroviruses. *Retrovirology* 2012 9:64.
- Kannian P, Yin H, Doueiri R, Lairmore MD, Fernandez S, **Green PL**. Distinct transformation tropism exhibited by Human T lymphotropic virus type 1 (HTLV-1) and type 2 (HTLV-2) is the result of post-infection T cell clonal expansion. *J Virol* 2012 86(7):3757-66.
- Kessl JJ, Jena N, Koh Y, Taskent-Sezgin H, Slaughter A, Feng L, de Silva S, Wu L, Le Grice SF, Engelman A, Fuchs JR, **Kvaratskhelia M**. Multimode, cooperative mechanism of action of allosteric HIV-1 integrase inhibitors. *J Biol Chem* 2012 287(20):16801-11.
- Kumar, SB, Rice CE, Milner DA, Ramirez NC, Ackerman WE, Mwapasa V, Norris-Turner A, **Kwiek JJ**. Elevated Cytokine and Chemokine Levels in the Placenta Are Associated With *in utero* HIV-1 Mother-To-Child Transmission. *AIDS* 2012 26(6):685-94.
- Larue R, Gupta K, Wuensch C, Shkriabai N, Kessl JJ, Danhart E, Feng L, Taltynov O, Christ F, Van Duyne GD, Debyser Z, Foster MP, **Kvaratskhelia M**. Interaction of the HIV-1 intasome with transportin 3 protein (TNPO3 or TRN-SR2). *J Biol Chem* 2012 287(41):34044-58.
- Sharma A, **Boris-Lawrie K**. Determination of host RNA helicases activity in viral replication. *Methods Enzymol* 2012 511:405-35.
- Sharma A, Yilmaz A, Marsh K, Cochrane A, **Boris-Lawrie K**. Thriving under stress: selective translation of HIV-1 structural protein mRNA during Vpr-mediated impairment of eIF4E translation activity. *PLoS Pathog* 2012 8:e1002612.
- St Gelais C, Coleman CM, Wang JH, **Wu L**. HIV-1 Nef enhances dendritic cell-mediated viral transmission to CD4+ T cells and promotes T-cell activation. *PLoS One*. 2012; 7(3):e3452.
- St Gelais C, de Silva S, Amie SM, Coleman C, Hoy H, Hollenbaugh J, Kim B, **Wu L**. SAMHD1 restricts HIV-1 infection in dendritic cells (DCs) by dNTP depletion, but its expression in DCs and primary CD4+ T-lymphocytes cannot be upregulated by interferons. *Retrovirology*. 2012 9, 105.
- Tirumuru N, Anand AR, Zhao H, **Ganju RK**. SLP-76 regulates HIV-1 infection in T-cells through a Nef-dependent mechanism. *J Immunol*. 2012 15;188(6):2769-77.
- Walton JR, Frey HA, Vandre DD, **Kwiek JJ**, Ishikawa T, Takizawa T, Robinson JM, Ackerman WE 4th. "Expression of flotillins in the human placenta: potential implications for placental transcytosis." *Histochemistry and Cell Biology*, 2012 Oct 14. [Epub ahead of print].
- Wang H, Jurado KA, Wu X, Shun MC, Li X, Ferris AL, Smith SJ, Patel PA, Fuchs JR, Cherepanov P, **Kvaratskhelia M**, Hughes SH, Engelman A. HRP2 determines the efficiency and specificity of HIV-1 integration in LEDGF/p75 knockout cells but does not contribute to the antiviral activity of a potent LEDGF/p75-binding site integrase inhibitor. *Nucleic Acids Res* 2012 40(22):11518-11530.
- Yin H, Kannian P, Disinger N, Haynes R, **Green PL**. Human T-cell leukemia virus type 2 antisense protein 2 is dispensible for *in vitro* immortalization but functions to repress early viral replication *in vivo*. *J Virol* 2012 86(16):8412-21.
- Zhang C, de Silva S, Wang J, **Wu L**. Co-evolution of primate SAMHD1 and lentivirus Vpx leads to the loss of the vpx gene in HIV-1 ancestor. *PLoS One*. 2012 7(5):e37477

Selected grant awards

Li Wu, NIH R21AI098524 "The Role of UBE2V1 in HIV-1 Restriction in Primary Monocytes" (2012-2014)

Patrick Green R21GRT00025015 "Role of viral APH-2 in HTLV-2 replication and persistence (2012-2014)

Mamuka Kvaratskhelia NIH P50GM103368 (PI:Olson) "HIV Macromolecular Interactions and Viral Evolution Center" (2012-2017)

Jesse Kwiek R24HD058484 (PI:Norris) "Choices and constraints in reproductive health decisions making among Malawian women" (2012-2013)

Kristine Yoder, NIH R21AI099854, "Studies of the molecular mechanism of retroviral infection" (2013-2015)

Li Wu, NIH R21AI102822 "Novel Host Proteins in the HIV-1 Pre-integration Complexes" (2012-2014)

Kathleen Boris-Lawrie NIH P50GM103297 (PI:Telesnitsky) "Center for HIV RNA studies" (2012-2017)

Li Wu, UNESCO-ASM (American Society for Microbiology) Travel Award, Visiting Resource Person Program (2012)