



# RETRO-ACTIVE NEWS

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

## 2017 Highlights

### Dr. Li Wu awarded NIH R01 to study how RNA modifications modulate retroviral infection



Dr. Li Wu has been awarded a new \$1.42 million R01 grant from NIH to investigate how HIV-1 RNA modifications modulate viral infection.

In this project, Dr. Wu and his collaborators will study the molecular mechanisms by which N<sup>6</sup>-methyladenosine (m<sup>6</sup>A) modification of HIV-1 RNA regulates

viral replication in CD4<sup>+</sup> T-cells. They hypothesize that reversible m<sup>6</sup>A modification of HIV-1 RNA regulates viral

replication in CD4<sup>+</sup> T-cells by affecting the structure, stability, splicing, and/or trafficking of HIV-1 RNA.

Investigations of the HIV-1 RNA m<sup>6</sup>A modification and interactions with host proteins represent a new area of HIV-1 RNA biology which can potentially facilitate therapeutic development against HIV-1 infection.

Dr. Wu's collaborators in this project include Dr. Chuan He at University of Chicago and Howard Hughes Medical Institute, Drs. Karin Musier-Forsyth and Mark Foster at The Ohio State University, and Dr. Mamuka Kvaratskhelia at the University of Colorado.

### Dr. Namal Liyanage, PhD joins the Ohio State faculty and the CRR



Dr. Namal Liyanage was recruited to join the Departments of Microbial Infection and Immunity and Veterinary Biosciences, and the Center for Retrovirus Research (CRR), as part of the university's Discovery Themes initiative.

Dr. Liyanage received his postdoctoral training with Dr. Genoveffa Franchini at the NIH, followed by a research fellow position in the laboratory of Immune Biology and Retroviral section under Dr. Marjorie Robert-Guroff in the Vaccine Branch at NCI. During his post-doctoral training, Dr. Liyanage studied the role of NK and mucosal innate lymphoid cells (ILCs) in HIV/SIV pathogenesis and vaccines.

Dr. Liyanage was a member of the team that recapitulated the RV144 clinical trial, the first human vaccine trial to show limited but significant protection from HIV acquisition in rhesus macaques. In a separate study, he investigated the innate gene regulation

during the ALVAC-SIV prime boost vaccination strategy in collaboration with Dr. Rafick-Pierre Sekaly, at Case Western Reserve University.

Dr. Liyanage is the recipient of a 2016 NIH career transition grant (K22 Award). Dr. Liyanage's lab at Ohio State mainly focuses on understanding the role of the innate and adaptive immune systems during chronic viral infections and development of novel strategies to prevent and control chronic viral infections, such as HIV. His lab currently is conducting studies to understand the role of NK/ILCs and innate memory in the RV144 HIV vaccine strategy, exploring the regulatory role of NK/ILCs on B and T cells during vaccines and discovery of novel adjuvants that enhance HIV vaccine efficacy.

His laboratory is also conducting research on understanding the immunopathology of HIV/TB, HIV/HCV and HIV/Zika co-infections and Dengue infection by collaborating with several national and international academic and industrial partners. Welcome Namal!



## Dr. Li Wu was elected fellow of the American Association for the Advancement of Science (AAAS)

Center member, Dr. Li Wu, Professor in the Department of Veterinary Biosciences, has been elected as a Fellow of the AAAS for his distinguished contributions to the field of molecular virology, particularly for the mechanisms of HIV replication and the virus interactions with host cells.

Election as an AAAS Fellow is a prestigious honor bestowed upon AAAS members by their peers. New fellows will be presented with an official certificate and a gold and blue rosette pin at the 2018 AAAS Annual Meeting in Austin, TX in February 2018. Members receive

the honor of Fellow in recognition of their scientific or socially distinguished efforts to advance science or its applications. Four Ohio State faculty members were among 396 AAAS members who received the prestigious honor this year. [vet.osu.edu/about-us/news/dr-wu-receives-prestigious-science-honor](http://vet.osu.edu/about-us/news/dr-wu-receives-prestigious-science-honor)

Other Center Members that are AAAS Fellows include; Patrick Green, Karin Musier-Forsyth, Michael Oglesbee, Christopher Walker, and Caroline Whitacre.

## Miguel Lopez selected for prestigious career development opportunity



Miguel A. Lopez Jr., a PhD graduate student in Dr. Kristine Yoder's lab, has been accepted to the Yale Ciencia Academy (YCA) 2018 career development cohort. He is one of only 40 doctoral students nationwide selected.

The YCA is a year-long NIH funded program aimed to develop traditionally underrepresented graduate students through direct mentoring, peer support and networking. It utilizes STEM networks to enhance the

engagement and participation of people from diverse backgrounds.

The program includes several components that are designed to train participants to be successful, productive and culturally conscientious scientists. Training culminates with a capstone project where students lead science outreach initiatives in their own communities. This opportunity will allow Miguel to develop as a scientist and learn how to further aid other minority scientists to thrive here at Ohio State.

Miguel is looking forward to making the most of this exciting opportunity. Good luck Miguel!

## Dr. Shan-Lu Liu named as Co-Director of the Viruses and Emerging Pathogens Program of The Ohio State University's Infectious Diseases Institute (IDI)



Dr. Shan-Lu Liu, a center investigator and Professor of the Departments of Veterinary Biosciences, Microbiology, and Microbial Infection and Immunity has been selected, along with Dr. Linda Saif, as Co-Director of the Viruses and Emerging Pathogens Program (VEP) of the Ohio State IDI.

The IDI was established by the university in 2017 in order to accelerate infectious disease research and education across campuses. VEP is one of the six thematic programs within the institute, the mission of which is to facilitate research, training and educational outreach focused on viruses and emerging pathogens. Scientists

in this program collaborate with campus, regional, national and international colleagues and leaders to better understand the etiology, transmission, immunity and pathogenesis of viruses and emerging pathogens, with an ultimate goal of developing innovative and highly effective strategies for diagnosis, prevention and treatment.

VEP scientists actively work on HIV, HTLV, coronaviruses (PEDV, MERS, SARS), Ebola virus, noroviruses, rotaviruses, hepatitis viruses, Zika virus, influenza viruses, sea viruses, and more, as well as on animal and plant pathogens that are possible sources of transmission to humans. The research topics in this program cover the basic virology, immunity, microbiome, nutrition, pathogenesis, diagnosis, animal models, vaccine development, treatment, and more.

## Dr. Kristine Yoder awarded NIH R01 to investigate the mechanics of retroviral integration in real-time.



Dr. Kristine Yoder, Assistant Professor, Department of Cancer Biology and Genetics and member of the Center for Retrovirus Research, has received a five-year multi-PI (R. Fishel) grant of \$1.95M from the National Institutes of Health.

Dr. Yoder is utilizing the non-pathogenic prototype foamy virus (PFV), an unsurpassed biophysical model for retrovirus

integration analysis, and novel single molecule imaging techniques to visualize the retroviral integration process in real-time.

The specific aims are to 1) detail the target site selection process of the PFV intasome, 2) examine the dynamics of retroviral IN protein and viral cDNA following integration, and 3) determine the influence of defined chromatin on retroviral intasome dynamics and target site selection. These studies are designed to interrogate the animated processes associated with PFV integration to provide a quantitative biophysical foundation for retroviral intasome progressions.

## Drs. Musier-Forsyth and Kvaratskhelia receive funding as part of the NIH U54 Collaborative HIV Interaction in Viral Evolution (HIVE) Center



The HIVE Center, which was recently renewed for a second 5-year term, comprises a group of highly collaborative investigators with deep experience in HIV research and well established expertise in structural, biophysical, biochemical, and computational biology, as well as synthetic chemistry, and virology. The Center is aimed at understanding the system

interdependency of interacting HIV macromolecules and their assemblies, which shape the HIV life cycle.

To accomplish this goal, the program will explore the structural and biophysical interactions of HIV Gag and Gag-Pol polyproteins, capsid, reverse transcriptase, and integrase and their evolutionary relationships.

The Center's research focus also extends to cellular factors that inform the structural and macromolecular dynamics of events in reverse transcription, assembly, and integration and includes studies on how APOBEC3 proteins suppress reverse transcription, and the role of LEDGF in guiding viral integration and its contribution to latency in conjunction with CPSF6.

The HIVE Center is directed by Drs. Stefan Sarafianos (Emory University) and Bruce Torbett (The Scripps Research Institute).

[www.scripps.edu/hive\\_center/index.html](http://www.scripps.edu/hive_center/index.html)

## Congratulations!



Professor Mamuka Kvarastkhelia departed Ohio State in August, 2017 to join the University of Colorado School of Medicine, Division of Infectious Diseases.

Congratulations Mamuka and we wish you the best in your new position.

# The Center for Retrovirus Research 2017 Distinguished Research Career Award

**Dr. Stephen H. Hughes**, Senior Investigator, Acting Chief of Host-Virus Interaction Branch, and Head of the Vector Design and Replication Section at the Center for Cancer Research, National Cancer Institute was the 18th recipient of the annual award for his seminal contributions to the field of retroviruses with emphasis on the roles of reverse transcriptase and integrase in HIV-1 replication.

Dr. Hughes received his Ph.D. from Harvard University under the direction of Dr. Mario Capecchi and performed postdoctoral research under the direction of Drs. J. Michael Bishop and Harold Varmus at the University of California, San Francisco. From 1979 until 1984, Dr. Hughes was a Senior Staff Investigator at Cold Spring Harbor Laboratory. In 1984, he established the Gene Expression in Eukaryotes Section at the National Cancer Institute (NCI)-Frederick. He became Deputy Director of the ABL-Basic Research Program in 1988 and Director of the Molecular Basis of Carcinogenesis Laboratory at the NCI-Frederick in 1995.

In 1999, Dr. Hughes joined the HIV Drug Resistance Program (HIV DRP) at the NCI as Chief of the Retroviral Replication Laboratory. In 2005, he was appointed Acting Director of the HIV DRP and Acting Chief of the Host-Virus Interaction Branch. He was Director of the HIV DRP from 2006 to 2015. He has successfully trained many junior scientists.

Dr. Hughes is an Organizer of the Annual HIV DRP Conference and David Derse Memorial Lecture and Award, and has served as an Organizer of the Retroviruses and Viral Vectors Meetings at Cold

Spring Harbor Laboratory and the Annual Meeting on Oncogenes. He has been invited to present his cutting-edge research at numerous national and international conferences and seminars at leading research institutions worldwide.

Dr. Hughes and his colleagues have published over 323 research articles and 41 invited book chapters, reviews, and commentaries. He was named one of the most frequently cited AIDS researchers by Science Watch in 1996. Dr. Hughes holds eight issued and two pending U.S. patents derived from his innovative retrovirus research and antiviral drug development.

Dr. Hughes was elected to the American Academy of Microbiology in 2007. He also has received numerous prestigious awards, including an NCI Technology Transfer Award, NIH Intramural AIDS Targeted Antiviral Program Research Awards, an NCI Director's Award, and an NCI Special Act or Service Award for Groundbreaking Advances.

Dr. Hughes has served as the Editor of Technique and as an editorial board member of Journal of Virology, Molecular and Cellular Biology, Virology, and Antimicrobial Agents and Chemotherapy. Dr. Hughes also serves as a member of many national and international committees and boards, such as the FDA Vaccines and Related Biological Products Advisory Committee, NCI-Frederick Institutional Biosafety Committee, and the World Health Organization Study Group on Cell Substrates for Production of Biologicals.

Dr. Hughes's visit was sponsored by the Center for Retrovirus Research, Department of Veterinary Biosciences, Infectious Diseases Discovery Theme, Infectious Disease Institute, and the Comprehensive Cancer Center.



Dr. Hughes receives Career Award crystal from members of the Center for Retrovirus Research. Shown from left are Drs. David Symer, Sanggu Kim, Karin Musier-Forsyth, Li Wu, Steven Hughes, Kristine Yoder, Mamuka Kvaratskhelia, Patrick Green, Shan-Lu Liu, Ross LaRue and Jesse Kwiek. Dr. Hughes's distinguished award lecture was entitled "Why Study HIV Reverse Transcription and Integration".

## Selected Grant Awards

### Kristine Yoder

Campbell Foundation “A self-limiting CRISPR vector to treat HIV-1 infection” (2017-2018)

### Kristine Yoder

NIH R01AI126742 “Mechanics of retroviral integration” (2017-2021)

### Li Wu

NIH R01GM128212 “Mechanisms of HIV-1 RNA methylation in regulating viral replication” (2017-2021)

### Li Wu

NIH/NCI P30 CA016058 supplemental grant  
“Administrative supplement to stimulate research in non-AIDS defining cancers in aging population” (2017-2018)

### Li Wu

Global Gateways (Shanghai) and Ohio State Office of International Affairs, “Travel grant to foster virology collaborative research and education” (2017-2018)

### Karin Musier-Forsyth and Mamuka Kvarastkhelia

NIH U54 GM103368 “HIV interactions in viral evolution” (2017-2022)

### Namal Liyanage

NIH K22 “Retooling NK and mucosal ILCs for an effective HIV vaccine” (2017-2019)

### Shan-Lu Liu

NIH R01AI112381 “IFITM-mediated Inhibition of HIV Infection and viral countermeasures” (2017-2019)

### Shan-Lu Liu

NIH R21AI109464 “Inhibition of *Ebolavirus* entry by IFITM2 protein” (2017-2018)

### Patrick Green

NIH/NCI P01 CA100730 supplement “Role of HTLV-1 Hbz in Transformation and Disease” (2017-2019)

### Patrick Green and Lee Ratner

NIH R21AI126652 “Role of CTCF in HTLV-1 Pathogenesis” (2017-2018)

## Student, Post-doc, Research Scientist and Visiting Scholar Awards

**Miguel Lopez** (PhD student; Yoder Lab) - Selected for the Yale Ciencia Academy

**Jonathan Kitzrow** (PhD student; Musier-Forsyth Lab), NIH Molecular Biophysics Training Grant Fellowship (2017-2018)

**Madhavkarthik Kodigepalli** (Postdoctoral Researcher; Wu Lab) - Outstanding Poster Award –basic science category Ohio State Annual Comprehensive Cancer Center Scientific Meeting (2017)

**Madhavkarthik Kodigepalli** (Postdoctoral Researcher; Wu Lab) - Winner Oral Platform Presentation, College of Veterinary Medicine Research Day (2017)

**Madhavkarthik Kodigepalli** (Postdoctoral Researcher; Wu Lab) Accepted a position as a Research Scientist at the Nationwide Children’s Hospital, Columbus, OH.

**Amanda Panfil** (Research Scientist; Green Lab) - PLOS Pathogens Oral Platform Award at the 29th International Workshop on Retroviral Pathogenesis, Prague- Czech Republic (Aug 2017)

**Corine St. Gelais** (Senior Research Associate; Wu lab) - College of Veterinary Medicine Outstanding Staff Service Award (2017)

**Corine St. Gelais** (Senior Research Associate; Wu lab) - Recipient of The Ohio State University Staff Career Development Grant (2017)

## 2017 Graduation and Candidacy Exam

**Alice Duchon**, PhD (Musier Forsyth Lab) “Noncanonical function of cellular translational machinery in human immunodeficiency virus type-1 assembly and primer packaging”. Accepted a postdoctoral fellowship at NIH/NCI Frederick (Dr. Wei-Shau Hu’s lab).

**Minghua Li**, PhD (Liu Lab). “Restriction of HIV by TIM-family proteins and antagonism by Nef”. Accepted a postdoctoral fellowship at the University of Pennsylvania (Dr. Sara Cherry’s lab).

**Michael Martinez**, DVM (Green Lab) successfully passed his PhD candidacy exam

**Zhihua Qin** (Wu Lab) successfully passed her PhD candidacy exam

**Jingyou Yu** (Liu Lab) successfully passed his PhD candidacy exam

## Selected Upcoming Meetings

### Symposium on HIV/AIDS

March 1 – 4, 2018 Palm Springs, CA

### Cold Spring Harbor Laboratory “Retroviruses”

May 21-26, 2018, Cold Spring Harbor, NY  
The 2018 Andy Kaplan Prize Call for Applications:

<https://sites.google.com/a/umich.edu/the-andy-kaplan-prize/home>

### American Society for Virology

July 14-18, 2018, College Park, MD

### 30th Workshop on Retroviral Pathogenesis

October 8-12, 2018, Awaji City, Japan

## Selected Publications

- Al-Saleem J, **Kvaratskhelia M**, **Green PL**: Methods for identifying and examining HTLV-1 HBZ post-translational modifications. *Methods Mol Biol*, 2017 1582:111-126.
- Antonucci JM, St. Gelais C, **Wu L**. The dynamic interplay between HIV-1, SAMHD1, and the innate antiviral response. *Front Immunol*, 2017 8:1541.
- Buzovetsky O, Tang C, Knecht K, Antonucci JM, **Wu L**, Ji X, Xiong Y. The SAM domain of mouse SAMHD1 is critical for its activation and regulation. *Nat Commun*, 2017 In press.
- Cantara WA, Hatterschide J, Wu W, **Musier-Forsyth K**. RiboCAT: A new capillary electrophoresis data analysis tool for nucleic acid probing. *RNA*, 2017 23(2):240-249.
- Cantara WA, Olson ED, **Musier-Forsyth K**. Analysis of RNA structure using small-angle X-ray scattering. *Methods*, 2017 113:46-55.
- Comandur R, Olson ED, **Musier-Forsyth K**. Conservation of tRNA mimicry in the 5'-untranslated region of distinct HIV-1 subtypes. *RNA*, 2017 23(12):1850-1859.
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- Esser AK, Rauch DA, Xiang J, Harding JC, Kohart NA, Ross MH, Su X, Wu K, Huey D, Xu Y, Vij K, **Green PL**, **Rosol TJ**, **Niewiesk S**, Ratner L, Weillbaecher KN. HTLV-1 viral oncogene HBZ induces osteolytic bone disease in transgenic mice. *Oncotarget*, 2017 Aug 27;8(41):69250-69263.
- Huey D, Bolon B, La Perle KMD, Kannian P, Jacobson S, Ratner L, **Green PL**, **Niewiesk S**. Role of wild type and recombinant human T cell leukemia viruses in lymphoproliferative disease in humanized NSG mice. *Comparative Medicine* In press
- Khamaikawin W, Shimizu S, Kamata M, Cortado R, Jung Y, Lam J, Wen J, Kim P, Xie Y, **Kim S**, Arokium H, Presson AP, Chen ISY, An D-S. Modeling anti-HIV-1 HSPC based gene therapy in humanized mice previously infected with HIV-1. *Molecular Therapy-Methods & Clinical Development*, 2017 Dec 1, In Press.
- Kenny A, Dowdle JA, Bozzacco L, McMichael TM, St. Gelais C, Panfil AR, Sun Y, Anderson MZ, **Green PL**, López CB, Rosenberg BR, **Wu L**, Yount JS: Human genetic determinants of viral diseases. *annual reviews of genetics*, 2017 Nov 27;51:241-263.
- Kodigepalli KM, Li M, **Liu S-L**, and **Wu L**. Exogenous expression of SAMHD1 inhibits proliferation and induces apoptosis in cutaneous T-cell lymphoma-derived HuT78 cells. *Cell Cycle*. 2017 16(2):179-188.
- Kohnken R, Kodigepalli KM, Mishra A, Porcu P, and **Wu L**. MicroRNA-181 contributes to downregulation of SAMHD1 expression in CD4+ T-cells of Sèzary syndrome patients. *Leuk Res*, 2017 52: 58-66.
- Kulkarni MM, Ratcliff A, Bhat M, Alwarawrah Y, Hughes P, Arcos J, Loiselle D, Torrelles JB, Haystead TA, **Kwiek JJ**. Cellular fatty acid synthase is required for late stages of HIV-1 replication. *Retrovirology*, 2017 Sep 29;14(1):45.
- Liu Z, Chen S, Jin X, Wang Q, Yang K, Li C, Xiao Q, Hou P, Liu S, Wu S, Hou W, Xiong Y, Kong C, Zhao X, **Wu L**, Li C, Sun G, and Guo D. Genome editing of the HIV co-receptors CCR5 and CXCR4 by CRISPR-Cas9 protects CD4+ T cells from HIV-1 infection. *Cell Biosci*, 2017 7:47.
- Lopez MA, Mackler RM, Altman MP, **Yoder KE**. Detection and removal of nuclease contamination during purification of recombinant prototype foamy virus integrase. *J Vis Exp*, 2017 [www.jove.com/video/56605](http://www.jove.com/video/56605).
- Miller AD, de Las Heras M, Yu J, Zhang F, **Liu S-L**, Vaughan AE, Vaughan TL, Rosadio R, Rocca S, Palmieri G, Goedert JJ, Fujimoto J, Wistuba II. Evidence against a role for Jaagsiekte sheep retrovirus in human lung cancer. *Retrovirology* 2017 14(1):3.

## Selected Publications - continued

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Qiu X, Lei Y, Yang P, Gao Q, Wang N, Cao L, Huang X, Sun Y, Yuan S, Deng Y, Hu J, **Liu S-L**, Qin C, Wang X, Xu Z, Rao Z. Structural basis for neutralization of Japanese encephalitis virus by two therapeutic antibodies. *Nature Microbiology*, 2017 In press.

St. Gelais C, Kim SH, Maksimova VV, Buzovetsky B, Knecht K, Shepard C, Kim B, Xiong Y, and **Wu L**. A cyclin-binding motif in human SAMHD1 is required for its HIV-1 restriction, dNTPase activity, tetramer formation, and efficient phosphorylation. *J Virol*, 2017 In press.

Suryawanshi GW, Xum S, Xie Y, Chou T, Kim N, Chen ISY, **Kim S**: Bidirectional retroviral integration site PCR methodology and quantitative data analysis workflow. *J Vis Exp* 2017 Jun 14;(124).

Todd GC, Duchon A, Inlora J, Olson ED, **Musier-Forsyth K**, Ono A. Inhibition of HIV-1 Gag-membrane interactions by specific RNAs. *RNA*, 2017 23(3):395-405.

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Wang Y, Pan Q, Wang Z, Yu J, **Liu S-L**, Liang C. The V3-loop of HIV-1 Env determines viral susceptibility to IFITM3 impairment of viral infectivity. *J Virol*, 2017 91(7). pii: e02441-16.

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Yu J, Liang C, **Liu S-L**. Interferon-inducible LY6E protein promotes HIV infection. *J. Biol. Chem.* 2017 292(11):4674-4685.

