



RETRO-ACTIVE NEWS

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

2010 Highlights

The Center for Retrovirus Research 2010 Distinguished Research Career Award

Dr. Stephen P. Goff, PhD. Higgins Professor of Biochemistry and Molecular Biophysics and Microbiology, Investigator, Howard Hughes Medical Institute, Columbia University College of Physicians and Surgeons was the 11th recipient of the annual award for his seminal contributions to retrovirology.

Throughout his distinguished career, Dr. Goff has strategically and cleverly leveraged viruses to decipher how normal cells enable virus replication, yet defend against pathogenic infection, or are co-opted to drive malignant transformation or fatal immunodeficiency.

Dr. Goff developed the first methods to deliver recombinant DNA molecules into mammalian cells by employing SV40 virus, and was among the first to prepare molecular clones of retroviruses. He isolated the Abelson murine leukemia virus; identified the v-abl oncogene that is the cause of the viral cancer; and discovered the c-abl proto-oncogene in the normal mouse chromosome. Dr. Goff defined the functional domains of viral pol gene products, which are separable into the RNA/DNA polymerase and RNase H domains, and integrase. Dr. Goff identified the integrase function that inserts proviral DNA into the host chromosome, which is the basis for retroviral vector transduction and a major target of successful anti-HIV-1 drugs. Dr. Goff has discovered several host gene products that interact with retroviral protein or RNA and modulate infectivity and escape from host restriction by distinct mechanisms. For example, cyclophilin A, a host prolyl isomerase, binds specifically to HIV-1 Gag, and regulates both infectivity and escape from host restrictions; the novel zinc-finger antiviral protein (ZAP) binds specific sequences in viral RNAs and directs their degradation; TRIM28 mediates primer binding site-targeted silencing of retroviruses that utilize Lys1,2 tRNA in embryonic cells; and eIF3f affects 3' end processing of HIV-1 and can inhibit viral replication.

Dr. Goff's visit was sponsored jointly by the Center for Retrovirus Research and the Department of Veterinary Biosciences, Department of Molecular Virology, Immunology and Medical Genetics, and the Comprehensive Cancer Center Viral Oncology Program.

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



Dr. Stephen Goff received the engraved crystal award sculpture from Center for Retrovirus Research Associate Director Dr. Kathleen Boris-Lawrie and presented the special lecture "Innate Immunity against Infectious Diseases: New Paradigms from Host Restriction of Retrovirus Replication".



Dr. Goff presented a second lecture entitled "RNA Structures Regulating Retrovirus Replication" at the Center for Retrovirus Research weekly scientific group meeting.

Lawrence Mathes Honored with 40+ Years of University Service



Center for Retrovirus Research Member and Professor, Dr. Lawrence Mathes, retired in 2010 after more than 40 years of service to The Ohio State University and College of Veterinary Medicine. During his tenure, Dr. Mathes was a founding member and served as Director of the Center for Retrovirus Research for 12 years; he led the Comprehensive Cancer Center's Viral Oncogenesis Program for 17 years and served as the Associate Dean for Research and Graduate Studies in the College of Veterinary Medicine for the last 5 years. He has been honored with the SmithKline Beecham Award for Research Excellence (1994), the Dean's Teaching Excellence Award for Graduate Education (2000), American

Association for the Advancement of Science (AAAS) Fellow (2004), and the OSU Distinguished Scholar Award (2005).

As a graduate student and subsequently as a young faculty member in the Department of Veterinary Pathobiology, Dr. Mathes played a major role in the development of the first commercial feline leukemia virus vaccine, Leukocell, which resulted in royalties of over \$20M. Over the years Dr. Mathes's research has provided critical knowledge of immunosuppressive factors in retrovirus infections and neoplastic disease. His research program focused on the treatment and prevention of retrovirus disease utilizing feline leukemia virus and feline immunodeficiency virus as model systems. Dr. Mathes had over 25 years of continuous extramural funding as a Principal Investigator from the National Institutes of Health and other agencies to the tune of \$12M. During that time, he trained numerous PhD and MS students as well as many undergraduate and veterinary students in his laboratory. Dr. Mathes has authored or coauthored more than 130 peer-reviewed publications.

Dr. Mathes' vision brought the technology of flow cytometry to the OSU campus. Since 1985, he has pursued cutting edge technologies in flow cytometry and confocal microscopy and was the driving force behind the purchase of state-of-the-art instrumentation that eventually developed into the CVM Imaging Core, which has become a campus-wide resource.

Currently Dr. Mathes holds the position of Emeritus Professor in the College of Veterinary Medicine. He continues to conduct basic research relating to the pathogenesis of retrovirus disease. The focus of his current studies is on factors contributing to the development of drug resistance by human immunodeficiency virus. Most of this work utilizes the feline immunodeficiency virus animal model for AIDS. Dr. Mathes is also engaged in helping the College develop its translational research program as it relates to securing intellectual property rights and licensing agreements. This program is directed at assuring the greatest impact from research by preparing discoveries and inventions for the market place.

Selected Invited Presentations and Other Recognitions

Li Wu: AIDS Institute, Li Ka Shing Faculty of Medicine, The University of Hong Kong, China. "New insights into HIV interactions with dendritic cells".

Li Wu: Aaron Diamond AIDS Research Center, Rockefeller University, NY "HIV exploitation of dendritic cells: infection and viral dissemination"

Patrick Green: NIH Workshop on Novel Viruses Associated with Human Cancer, Syria, Virginia. "The HTLV-1 HBZ gene, a key player in oncogenesis"

Patrick Green: Editor, AIDS Research and Human Retroviruses

Dr. Michael D. Lairmore Elected into the Institute of Medicine

Dr. Michael Lairmore, Associate Dean of Research and Graduate Studies and Associate Director for Basic Sciences at the Ohio State Comprehensive Cancer Center, was elected to the prestigious Institute of Medicine of the National Academies of Science. Dr. Lairmore was recognized as a renowned scientist and leader who bridges multiple disciplines to address basic questions of viral causes of cancer. Dr. Lairmore has been continuously funded by the National Institutes of Health for nearly 20 years (totaling nearly \$30 million in direct costs) and has authored or co-authored over 170 scientific publications. He has been appointed to numerous National Institutes of Health Study Sections and scientific panels in addition to directing a National Cancer Institute Program Project Grant and post doctoral NIH T-32 training grant. Dr. Lairmore is the recipient of numerous academic awards including the Hero of Hope Award by the American Cancer Society, is a fellow of the American Association for the Advancement of Science (AAAS), and is an Ohio State University Distinguished Scholar.

Link to full press release:

researchnews.osu.edu/archive/iomlairmore.htm



Dr. Michael Lairmore is congratulated by Dean Lonnie King at a University reception honoring his election to the Institute of Medicine (IOM).



Selected Publications

Using a simplified human immunodeficiency virus type 1 p24 antigen assay to diagnose pediatric HIV-infection in Malawi. Mwapasa V, Cachafeiro A, Makuta Y, Beckstead DJ, Pennell ML, Chilima B, Mwangomba B, Fiscus SA, Kwiek JJ. (2010) *J Clin Virol*, 49(4):299-302.

Identification of host proteins associated with HIV-1 preintegration complexes isolated from infected CD4+ cells. Raghavendra NK, Shkriabai N, Graham RLJ, Hess S, Kvaratskhelia M, Wu L. (2010) *Retrovirology*, 7:66.

HIV-1 transmission by DC-SIGN is regulated by determinants in the carbohydrate recognition domain that are absent in L-SIGN. Chung NP, Breun SK, Bashirova A, Baumann JG, Martin TD, Karamchandani JM, Rausch JW, Le Grice SF, Wu L, Carrington M, Kewalramani VN. (2010) *J Biol Chem*, 285(3):2100-2112.

Human immunodeficiency virus-1 inhibition of immunoamphisomes in dendritic cells impairs early innate and adaptive immune responses. Blanchet FP, Moris A, Nikolic DS, Lehmann M, Cardinaud S, Stalder R, Garcia E, Dinkins C, Leuba F, Wu L, Schwartz O, Deretic V, Piguet V. (2010) *Immunity*, 32:654-669.

Immunization with synthetic VEGF peptides in ovarian cancer. Wang B, Kaumaya PT, Cohn DE. (2010) *Gynecol Oncol*. 119(3):564-70.

Mouse models of human T lymphotropic virus type-1 associated adult T-cell leukemia/lymphoma. Zimmerman B, Niewiesk S, Lairmore MD. (2010) *Vet Path*, 47:677-89.

C-terminal domain regulates the nucleic acid chaperone activity of human T-cell leukemia virus type 1 (HTLV-1) nucleocapsid protein (NC) via an electrostatic mechanism. Qualley DF, Stewart-Maynard KM, Wang F, Mitra M, Gorelick RJ, Rouzina I, Williams MC, Musier-Forsyth K. (2010) *J Biol Chem*, 285:295-307.

A comparative analysis of RNA/protein dynamics for the arginine-rich-binding-motif (ARM) and zinc-finger-binding-motif proteins encoded by HIV-1. Wang H, Yeh Y-S, Ma X, Zhu Y, Daugherty MD, Frankel AD, Musier-Forsyth K, Barbara PF. (2010) *Biophysical J*, 99(10):3454-3462.

Formation of the tRNALys packaging complex in HIV-1. Kleiman L, Jones C, Musier-Forsyth K. (2010) *FEBS Letters*, 584:359-365.

Role of HIV-1 nucleocapsid protein in HIV-1 reverse transcription. Levin JG, Mitra M, Mascarenhas A, Musier-Forsyth K. (2010) *RNA Biology*, 7:6, 754-774.

Cloaked virus slips between cells. Jones KS, Green PL. (2010) *Nature Med*, 16(1):25-27.

RNA helicase A modulates translation of HIV-1 and infectivity of progeny virions. Bolinger C, Sharma A, Singh D, Yu L, Boris-Lawrie K. (2010) *Nucleic Acids Res*, Mar;38(5):1686-96.

Human T lymphotropic virus type 1 (HTLV-1): Molecular biology and oncogenesis. Kannian P, Green PL. (2010) *Viruses*, 2(9):2037-2077.

RNA helicases: Emerging roles in viral replication and the host innate response. Ranji A, Boris-Lawrie K. (2010) *RNA Biol*, Nov 1;7(6).

Features of double-stranded RNA-binding domains of RNA helicase A are necessary for selective recognition and translation of complex mRNAs. Ranji A, Shkriabai N, Kvaratskhelia M, Musier-Forsyth K, Boris-Lawrie K. (2010) *J Biol Chem*, 18;286(7):5328-37.

Selected Grant Awards

Jesse Kwiek: R01AI090644, "A method to stop HIV replication: Inhibition of human purine utilizing proteins" (2010-2014)

Mamuka Kvaratskhelia: R01 AI062520, "Structural studies of HIV integration" (2010-2015)

Karin Musier-Forsyth: Southern Research Institute contract) "In vitro testing resources for AIDS therapeutic development"

Christopher Jones (Musier-Forsyth mentor) was awarded an RNA Center Fellowship for his work on Retroviral Assembly

Geoff Bennett (Yoder mentor), OSU Undergraduate Research Award from the SOLAR Foundation Research Fund "The Role of Base Excision Repair Proteins During HIV Infection".

Amit Sharma (Boris-Lawrie mentor) was awarded a Pelotonia Graduate Fellowship "Novel translation control strategy of junD protooncogene, a modulator of neoplastic transformation".

Doctoral Graduates

Surender Kumar "Studies to understand the mechanism of horizontal and vertical transmission of human immunodeficiency virus".

Current position: Post-doctoral fellow OSU

Cecilia Machado-Parrula "Measles Virotherapy in Adult T cell Leukemia"

Current position: Staff Clinical Pathologist, Pfizer Inc, UK

Master's Graduates

Laurie Millward "Yeast Two-Hybrid Analysis of Cellular Proteins interacting with HTLV-1p30"

Current position: Clinical Assistant Professor, Dept VBS

Rebecca Urbiztondo "Studies of Gut-associated lymphoid tissues and other secondary lymphoid tissues in 12 week old New Zealand white specific pathogen free rabbits"

Current position: Clinical Assistant Professor, Dept VBS