

ISNV

International Society for NeuroVirology

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2012 ISNV Symposium New York, New York

Brian Wigdahl



The 11th International Symposium on NeuroVirology will be held in concert with the 2012 Conference on HIV in the Nervous System at the Grand Hyatt in New York, New York from May 29 to June 2, 2012. Major sponsorship for the jointly held meeting will be provided by ISNV and the National Institute for Mental Health with a number of sponsors providing funding for specific lectureships, sessions, or workshops. The 11th Symposium and 2012 Conference will be guided by a Local Organizing Committee chaired by David Volsky and comprised of Joan Berman, Susan Morgello, David Simpson, Kamel Khalili, Avindra Nath, Lynn Pulliam, and Brian Wigdahl. Additional guidance will be provided by the ISNV Meetings Committee chaired by Brian Wigdahl and comprised of Steven Jacobson, Pasquale Ferrante, Robert Fujinami, Jennifer Gordon, Lynn Pulliam, David Volsky, Walter Royal, III, and Israel Steiner.

The overall goal of this jointly held meeting is to provide investigators working in the field of neurovirology and related areas with leading edge information so that important gaps in knowledge can continue to be identified. Armed with this information, attendees of both the Symposium and Conference will work toward formulating questions and experimental directions that will enhance the development of new preventative and therapeutic strategies effective against neurologic diseases associated with prions, HIV, and other viral and non-viral nervous system pathogens. The jointly held meeting will be highly integrated and divided into 12 scientific sessions, 4 interdisciplinary and translational workshops, and 5 special lectureships. The 11th ISNV Symposium and 2012 Conference on HIV in the Nervous System will be capped by a banquet and the announcement of the 2012 Pioneer in NeuroVirology. *Continued on page 7*

ISNV congratulates Shilpa Buch

Please join the ISNV in congratulating Dr. Shilpa Buch on receiving the University of Nebraska Medical Center (UNMC) Distinguished Scientist Award. Dr. Buch, Professor and Vice Chair for Research in the Department of Pharmacology and Experimental Neuroscience, was recognized on May

2, 2011 in a ceremony honoring 24 scientists for outstanding research achievements and sustained contributions to UNMC's research mission.



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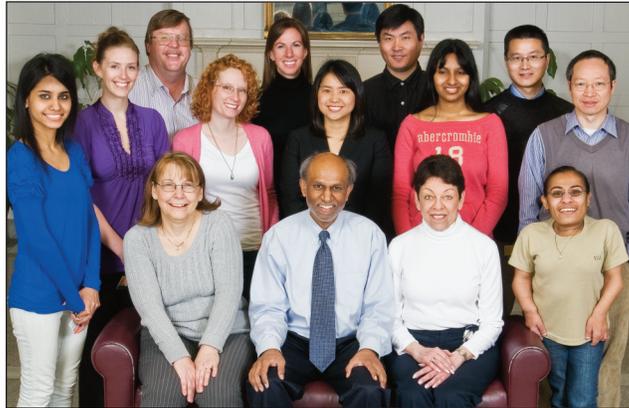
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NIH News

Avindra Nath moves to the NINDS/NIH

Dianne Langford

As of February 1, 2011, Dr. Avindra Nath joined the National Institute of Neurological Disorders and Stroke (NINDS) in Bethesda, Maryland as the Clinical Director of the intramural program. His goals are to build the clinical program through recruitment of new faculty and the development of a Translational Neuroscience Center. This center will provide support for all aspects of preclinical drug development and for conducting early phase clinical trials for a wide variety of neurological diseases. The center will have a drug development unit and a clinical trials unit. The directors of each of these units are being recruited. The center will closely interact with other efforts at the National Institutes of Health (NIH) to develop programs in translational medicine. The NIH also has a 250-bed hospital for research studies only. Large numbers of patients admitted to the hospital are on research protocols that use a variety of immune suppressive drugs or stem cell transplants for a number of systemic diseases or cancer. These patients often develop a wide spectrum of central nervous system (CNS) infections. The NIH also has an undiagnosed disease program, which investigates patients referred from institutions all over the country, who have had extensive work ups, but no conclusive diagnoses. Interestingly, most of these conditions are neurological in nature. Many of these patients have immune-mediated syndromes with the possibility of an underlying infection. Dr. Nath



and his team work closely with both these programs to provide necessary clinical and research support. The NINDS also has a large clinical fellowship program in several neurological sub-specialties. For the academic year 2011-12, there will be 20 clinical fellows at NINDS of which 4 will be in Neuroimmunology and Neurovirology. The fellowship program is coordinated through the Clinical Director's office. An important ongoing effort is to develop new interdisciplinary fellowship programs, including one in collaboration with the FDA.

Dr. Nath's laboratory also relocated with him from Johns Hopkins University and is now called the Section of Infections of the Nervous System. His laboratory will continue to conduct research on the neuropathogenesis of HIV infection and endogenous retroviruses. A major emphasis will be to study the HIV reservoirs in the brain and understand the underlying mechanisms of neuronal injury. His laboratory thus joins a group of other neurovirologists at NINDS that includes, Dr. Eugene Major, who studies JC virus, Dr. Steve Jacobson, whose laboratory studies HTLV-I and HHV-6 infection of the CNS, and Dr. Dorian McGavern, who studies lymphochoriomeningitis virus. Dr. Nath will also interact closely with other HIV researchers at NIH that follow large cohorts of well-characterized patients with HIV infection. The intramural program at NINDS thus has very strong clinical and bench research programs in neurological infections.

Summary of the Colorado Alphaherpesvirus Latency Society (CALS) Symposium

Don Gilden and Randall Cohrs

The inaugural symposium of the Colorado Alphaherpesvirus Latency Society (CALS) convened May 11-13, 2011 at the Christiania Lodge in Vail, Colorado. Human alphaherpesviruses include herpes simplex virus (HSV) types 1 and 2 and varicella zoster virus (VZV) and are characterized by their ability to establish latency in cranial nerve ganglia (HSV-1 and VZV), dorsal root ganglia (VZV), sacral ganglia (VZV and HSV-2) and autonomic ganglia (VZV). Along with these neurotropic human pathogens, alphaherpesviruses are significant pathogens of nonhuman primates (simian varicella virus) and domestic animals (bovine herpesvirus and Marek's disease virus). The CALS mission is to convene researchers active in alphaherpesvirus latency to discuss current advances in a relaxed venue. The mission was a success on both fronts: 47 senior researchers traveled over 79,000 miles to discuss their ongoing work concerning all facets of alphaherpesvirus latency in a quiet town in the heart of Colorado's Rocky Mountains. The CALS symposium was the first meeting specifically dedicated to understanding alphaherpesvirus latency.

The participants account for more than 2600 PubMed cited publications in the field. The success of this first symposium promises that future meetings will be of the same high caliber.



Sawtell, Don Gilden, Maria Nagel, Subbiah Pugazhenth, Michael Gershon, Anne Gershon, Greg Smith, Chandrasen Soans; (Ilhem Messaoudi, Christine Meyer; not pictured).

Top left to right: Barbara Hill, Linda van Dyk, David Koelle, Benedikt Kaufer, John Blaho, Scott Schmid, David Bloom, Tobias Derfuss, Nigel Fraser, Dale Carpenter, Marius Birlea, Jim Hill, Georges Verjans, Werner Ouwendijk, Clinton Jones, Bernard Roizman, Monique van Velzen, Kip Kinchington, Joel Rovnak, Caroline Kulesza, Nicole Giordani, Stephanie James, Jason Chen, Christopher Abraham, Charles Grose, Robert Hendricks, Andrea Bertke, Ravi Mahalingam, Stacey Efstathiou, Peter Kennedy, Vicki Traina-Dorge, Randy Cohrs, Marieke Verweij, Sandy Weiss, Leigh Zerbini, Ann Arvin, Igor Jurak, Richard Thompson, Nancy

Science News

Puerto Rico Scientists Highlight

Loyda M. Meléndez

Dianne Langford

Dr. Loyda M. Meléndez is a Professor in the Department of Microbiology, University of Puerto Rico School of Medicine (<http://www.md.rcm.upr.edu/micro/faculty/melendez.php>). She directs the Research Centers in Minority Institutions (RCMI) and Translational Proteomics Center at the University of Puerto Rico Medical Sciences Campus (UPR-MSC) (<http://rcmi.rcm.upr.edu/research/proteomics.html>) that provides clinical and basic researchers with proteomics instrumentation and services to determine biomarkers for diseases that involve health disparities. Dr. Meléndez received her Ph.D. in Experimental Pathology & Immunology cum laude from Emory University School of Medicine in 1990, where she also completed post-doctoral training in Hematology and Pediatric Infectious Diseases in collaboration with the Centers for Disease Control. She also received an M.S. degree magna cum laude in Microbiology from the University of Georgia, Athens in 1981, and a Medical Technology degree magna cum laude from the University of Puerto Rico Medical Sciences Campus in 1979. She has been Professor of Virology since 1992 and was the Director of the Biosafety Committee with the Department of Microbiology and Medical Zoology of the School of Medicine at the UPR-MSC for 6 years. She is currently a Principal Investigator of an NIH-funded study to understand the mechanisms of macrophage-induced HIV



From left to right: Marínes Plaud, M.S. (Research Associate), Linda Rivera, Ph.D. (post-doc), Yolanda Rodríguez (Research Associate), Dr. Meléndez, and four doctoral students: Frances Zenon, Krystal Colon, Yisel Cantres, and Eillen Rodríguez.

neuropathogenesis using proteomics approaches.

Numerous publications on CSF and monocyte protein biomarkers in NeuroAIDS from her group were instrumental in obtaining funding for an RCMI Core in Proteomics at UPR-MSC and subsequent R01 funding from the National Institute of Mental Health for the study entitled, Cystatins and Cathepsins in HIV Neuropathogenesis (Meléndez et al., *Journal of Neuroimmune Pharmacology* 2011, 6:89-106). In this exciting work, a graduate student in her laboratory (Ms. Eillen Rodríguez) *Continued on page 7*

Linda Rivera

Dianne Langford

Dr. Linda Rivera is a post-doctoral fellow in the Department of Microbiology, School of Medicine, University of Puerto Rico. She completed both master's and doctoral studies at the University of Puerto Rico, Medical Sciences Campus, with specific training in biochemistry, molecular biology and medical microbiology. During her pre-doctoral training, Linda received a summer internship from the NIH-National Human Genome Research Institute. This allowed her to integrate her research at several interdisciplinary areas by investigating the *in vitro* development of zebrafish hematopoietic cells induced by zSCF and zEPO with Dr. David Bodine, Chief & Senior Investigator of the Genetics and Molecular Biology Branch. They proved that zebrafish primitive hematopoietic cells provided with stem cell factor and erythropoietin could generate colonies with morphologic characteristics similar to those observed during the development of mouse and human cells. This novel *in vitro* differentiation system may prove important for genetic modifier screens.

After completing her Ph.D. in Biochemistry, Linda began a postdoctoral fellowship in Dr. Loyda Meléndez' laboratory. Currently, she is working to identify cellular mechanisms, protein complexes and signaling pathways that impact different aspects of HIV replication. These studies show that cystatin B expression is positively correlated with HIV replication and decreased levels of



STAT-1 phosphorylation in monocyte-derived macrophages (MDM). However, the mechanisms by which this occurs are unknown. Linda's research further demonstrated that cystatin B inhibits IFN- β mediated signaling suggesting that this protein may contribute to decreased host defense against HIV-1 allowing increased viral replication in macrophage reservoirs. She hypothesizes that cystatin B inhibits the IFN response and *Continued on page 7*

Highlights

from the 2010 ISNV meeting in Milan

Rosemarie Booze

Dianne Langford



Neurodevelopmental disorders in the pediatric population in the context of maternal HIV infection and intravenous drug abuse are the main focus of Dr. Rosemarie Booze's laboratory. The differential effects of stimulants on the developing brain in males versus females, the biological basis for attention deficiency and hyperactivity disorder, and the long-term consequences of early brain injury are just some of the main questions addressed by the Booze laboratory at the University of South Carolina.

Dr. Booze described recent studies from her laboratory at the ISNV meeting in Milan in October 2010. Studies from her laboratory show that 17β -estradiol is protective against the neurotoxic effects of HIV-Tat via modulating the apoptotic signaling cascade (Adams et al., 2010, *Synapse* 64: 829-838). More specifically, estrogen receptor (ER) α and β antagonists showed that the effects of estrogen on caspase 3 may be mediated by both ER subtypes, whereas ER β was more involved in estrogen's effects

on pro-apoptotic signaling. Other more recent studies addressed the effects of Tat on dopamine transporter function and her results indicate that Tat allosterically modulates dopamine transporter activity (Zhu et al, 2011, *Synapse*, in press).

In the future, Dr. Booze plans to explore the hypothesis that estrogenic compounds may serve as protective agents against synaptic impairments in the nucleus accumbens (NA) caused by cocaine and HIV proteins. The NA is a critical brain region involved in HIV-1-associated neurocognitive disorder (HAND) and is recognized as the main target of the mesotelencephalic dopamine system and the main striatal weigh-station for circuits of prefrontal origin. In this context, estrogen will be used to modulate cognition and dopamine markers following cocaine and HIV-1 exposure in both an animal model and *in vitro*. These studies will provide insight into potential neuroprotective mechanisms and therapeutic strategies for HAND. Investigations will also focus on quantifying spine density changes with respect to regulators of NA medium spiny neurons and prefrontal cortical neuronal plasticity. The ultimate goal of this research is to identify sensitive targets and unique pharmacological interventions (estrogen β -receptor modulators for preventing HAND following cocaine abuse in HIV-1+ populations).

Dr. Booze received her Ph.D. from *Continued on page 8*

Philippe Gasque

Dianne Langford

A wide variety of emerging and re-emerging viruses (e.g. arboviruses, 'arthropod-borne viruses') contribute to neurological diseases. Infections can be associated with new viral variants that are more efficiently transmitted. In turn, massive outbreaks and increased reports of complicated cases involving the CNS may occur. It is also possible that previously non-neurotropic viruses may have acquired increased neurovirulence. Viruses that appear to have recently become more neurovirulent include the West Nile flavivirus, Chikungunya α -virus (CHIKV) and the enterovirus 71. CHIKV, an α -virus of the Togaviridae family, is transmitted by mosquitoes of the *Aedes* (Ae) genus and has rapidly spread worldwide. The α -virus group includes 29 viruses, (six of which form the 'Old World' Africa group) and can cause human joint disorders (arthralgia evolving to arthritis). These include CHIKV, o'nyong-nyong virus (ONNV), Semliki forest virus (SFV), Ross River (RRV), Sindbis virus (SINV), Mayaro virus (MAYV). The so-called 'New World' viruses such as Eastern equine encephalitis virus (EEEV) and Venezuelan equine encephalitis virus (VEEV) can also cause severe brain damage. Interestingly, CHIKV-associated neuropathology was first described in the 1960s but it is the unprecedented incidence rate in the Indian Ocean with efficient clinical facilities that has allowed a better description of cases with severe encephalitis, meningoencephalitis, peripheral neuropathies and deaths among newborns (mother-to-child infection), infants and elderly patients.

Dr. Philippe Gasque and his team at the University and Hospital of la Réunion Immunopathology and Infection Research Center are studying the pathology of CHIKV. In 2005-2006, over 270,000 people were infected by the CHIKV and Dr. Gasque's group

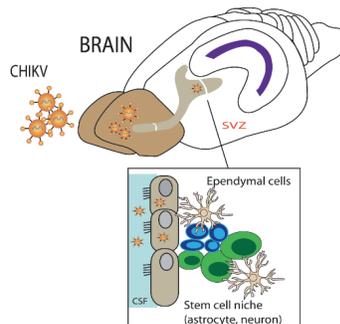


Figure 1. Chikungunya alphavirus (CHIKV) targets the leptomeninges, the choroid plexus and ependymal cells lining the subventricular zone (SVZ), also known as the neural stem cell niche.

has incorporated data from this large cohort into their research. The follow-up of the neonates affected by CHIKV clearly indicates poor outcomes and neurodevelopment defects at 5 years post-infection. Neurological manifestations described in adults requiring hospitalization included cases of encephalopathy, encephalitis, Guillain-Barre like syndrome, encephalomyelorradiculitis and in some cases, death. CHIKV infection in adults is associated with white matter lesions, focal perivascular lymphocytic infiltrates in areas of active demyelination and to some degree, microglial activation, which may contribute to bystander neuronal loss. Although data are still scarce, the numbers of cases with CNS involvement appears to support the neurotropic/neuroinfectious activity of CHIKV. Several teams have confirmed this unique CNS infection experimentally and the virus was shown to infect mouse and macaque brains and to replicate in cultures of glial and neuronal cells. In mice, CHIKV targets the leptomeninges, the choroid plexus and ependymal cells lining the subventricular zone (SVZ) also known as the neural stem cell niche (Fig. 1). Receptor(s)-mediated cell attachment and infection remains to be characterized, but the role of apoptotic blebs carrying the virus from cell to cell *Continued on page 8*

Adriano Boasso

Leslie Marshall

Dr. Adriano Boasso recently presented his work on the “Chronic innate immune activation in the immunopathogenesis of HIV infection” at the ISNV symposium last Fall in Milan. He is an associate faculty member of the Department of Medicine at the Imperial College in London, where he conducts a research program to identify the key features that render HIV pathogenic for the immune system. He joined the faculty at Imperial College London in 2008 first under the Wellcome Trust VIP Award, and soon after under a Wellcome Trust Research Career Development Fellowship. Dr. Boasso has authored thirty-six scientific publications and serves as a mentor for several Ph.D. students. Adriano received his BSc/MSc and Ph.D. from the Department of Immunology at the University of Milan where he studied molecular medicine of immune and inflammatory reactions. He completed post-doctoral training in the laboratory of Dr. Gene M. Shearer in the Experimental Immunology Branch at the National Cancer Institute (NCI) at NIH. While at the NIH, he was recognized with the distinguished Norman P. Salzman Memorial Award in Virology in 2007. At the NCI, Dr. Boasso’s research contributions included establishing a role of indoleamine 2,3 dioxygenase (IDO) in HIV-mediated blockage of T-cell responses and understanding the role of interferon signalling in the activation of T-cells during HIV infection (Boasso et al., *Blood*, 2007; 109(8): 3351-9; Boasso et al., *PLoS ONE*, 2008 Aug 13; 3(8): e2961).

In his current research program, in collaboration with Prof. David Graham (Johns Hopkins University) and Prof. Mario Clerici (University of Milan), he manipulated HIV by depleting envelope-associated cholesterol and generated virions with reduced ability to activate plasmacytoid dendritic cells (pDC). Cholesterol is a critical component of biological membranes, including the HIV envelope, and is necessary to maintain the organization of the membrane into functionally distinct subdomains. Modified HIV virions were used to show that upregulation of co-stimulatory molecules and partial activation of



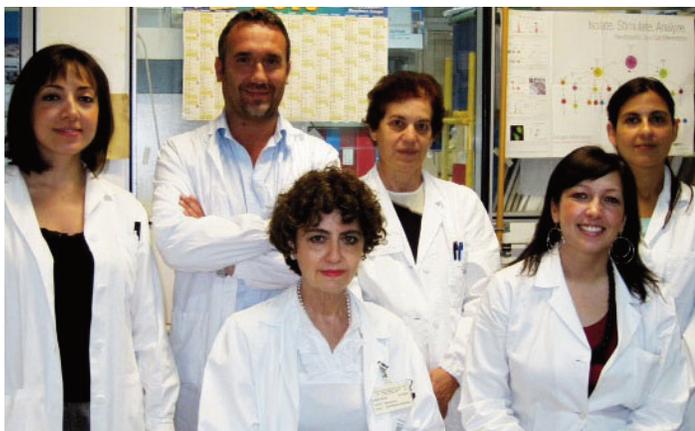
Dr. Adriano Boasso (middle), Ms Barbara Tavano (left) and Ms Caroline Royle (right).

antigen-presenting cells can be achieved even without the induction of pDC-mediated immunosuppression *in vitro*. Once deprived of its ability to activate pDC, cholesterol-depleted HIV was turned into a powerful recall antigen capable of stimulating memory CD8+ T-cell responses *in vitro*. These studies suggest that HIV can directly restrain HIV-specific T-cell responses by potentially activating immunopathogenic mechanisms associated with pDC activity (manuscript submitted). This immunological phenomenon may have important implications in determining whether the immune responses induced by an HIV vaccine will effectively block the spread of the infection or will succumb to the rapid induction of pDC-mediated immunopathogenesis. Vaccine-induced immune responses might be futile against intact HIV, which is capable of hijacking basic mechanisms of immune regulation and evading immune responses. The aims of Dr. Boasso’s research program in his own words are “to provide a comprehensive model of the pathogenic mechanisms which characterize HIV infection and identify the specific features that render HIV pathogenic for the immune system”.

Antonina Dolei

Dianne Langford

Dr. Antonina Dolei is a Professor of Virology in the Faculty of Medicine at the University of Sassari in Sardinia, Italy. Her main interest is the role of human endogenous retroviruses in the



From left to right: Elena Uler Ph.D. student, Giuseppe Mameli Ph.D., Antonina Dolei Ph.D., Caterina Serra Ph.D., Alessandra Mei Ph.D., Luciana Poddighe Ph.D.

pathogenesis of neurological diseases. For example, multiple sclerosis-associated retrovirus (MSRV), the founding member of the type W family of human endogenous retroviruses (HERVs), was first described in 1991 and repeatedly isolated from cells of multiple sclerosis (MS) patients. Dr. Dolei’s research has contributed significantly to our understanding of how retroviral infections interact with the host to affect disease progression and outcome. Because Sardinia has such a high incidence of MS, Dr. Dolei looked for evidence of environmental factors that may contribute to the unusually high number of cases. In this study of 39 MS patients and 39 healthy donors, all 39 (100%) of the MS patients were positive for MSRV, compared to only 5 (12%) of the healthy controls (Dolei et al., *Neurology* 2002 58(3): 471-473). In 2008, Dolei’s group reported that interferon- β therapy for MS correlated with a drop in MSRV viral load to undetectable levels and suggested that plasma levels of MSRV could serve as a biomarker to monitor disease progression and therapy outcome (Mameli et al., *JNV* 2008 14:73-77). More recent studies from her group have shown in a 10 year follow up study that the presence of MSRV in the cerebrospinal fluid of patients in the early stages of MS is associated with a significantly greater *Continued on page 8*

Ian Lipkin: From Microbe Hunter to Hollywood

Dianne Langford

In the run up to the tenth anniversary of 9/11 and the anthrax attacks that followed, Hollywood is drawing attention to our vulnerability to biological threats. In a recent video interview with the Mailman School of Public Health at Columbia University, Ian Lipkin states that the “vast majority” of infectious agents surfacing over the past several years have emerged naturally. He continues to point out that development of new and better vaccines and diagnostics is key to combating both deliberate and naturally emerging infectious pathogens.

The movie *Contagion*, directed by Steven Soderbergh, and written by Scott Z. Burns, is an action-thriller documenting the emergence and evolution of a pandemic. It stars Kate Winslet, Matt Damon, Laurence Fishburne, Jude Law, Marion Cotillard, and Gwyneth Paltrow. Lipkin began work on the project three years ago with Soderbergh and Burns. Initially reticent to participate due to concerns that he might be criticized by colleagues for promoting another *Outbreak* or *I Am Legend*, he was rapidly converted to active support by the commitment of Soderbergh and Burns to sound science. “They vetted everything from dialog to costumes, stage sets, laboratory equipment, props and action scenes. We created plausible sequence files, phylogenetic trees and 3D structures using real databases and common programs. The immunofluorescent and EM images represent bona fide homologs of the pandemic neurotropic virus.” Lipkin notes that, in preparing for their roles, actors trained at Columbia in extracting RNA, performing PCR, and tissue culture. “In the unlikely event they elect a career change we would happily recruit them to the lab.” He adds, “Everyone involved in this project has been clear that the real stars are the scientists and public health practitioners who work in discovery, diagnostics, epidemiology, pathogenesis and



vaccinology. I am grateful for their support of our community and optimistic that this movie will increase appreciation and understanding of what we do. It is important that we encourage people to see it.” The movie screens at the Venice Film Festival and premieres in New York City before opening in theaters on September 9. W. Ian Lipkin is the John Snow Professor of Epidemiology, Professor of Neurology and Pathology, and Director of the Center for Infection and Immunity, the Northeast Biodefense Center, and the WHO Collaborating Centre on Diagnostics, Surveillance and Immunotherapeutics for Emerging Infectious and Zoonotic Diseases. A graduate of Sarah Lawrence College, he obtained his MD at Rush Medical College, Medicine Residency at the University of Washington, Neurology Residency at the UCSF, and Fellowship in Neurovirology and

Neuroscience at The Scripps Research Institute. He has devoted his career to microbe hunting since the early 1980s with contributions that include the first use of purely molecular methods to identify an infectious agent; implication of West Nile virus as the cause of the encephalitis in North America in 1999; invention of MassTag PCR and the first panmicrobial microarray (GreeneChip); first use of deep sequencing in pathogen discovery; discovery or characterization of more than 400 viruses including Borna disease virus, rhinovirus C, Dandenong, LuJo, Lloviu and canine hepacivirus; and the largest prospective birth cohort focused on neurodevelopmental disorders. The Center for Infection and Immunity conducts basic and translational research in infectious disease epidemiology and pathogenesis in 25 countries in collaboration with the WHO, PAHO, CDC, USAID, NIH, Institut Pasteur, FAO, and OIE.

2011- 2012 Upcoming Conferences

2011

September

Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC): September 18-21, Chicago, Illinois

October

Infectious Diseases Society of America (IDSA): October 20-23, Boston, Massachusetts

November

Society for Neuroscience: November 12-16, Washington, DC

2012

March

Conference on Retroviruses and Opportunistic Infections : March 5-8, Seattle, Washington

April

American Academy of Neurology: April 21-28, New Orleans, Louisiana

Society on NeuroImmune Pharmacology (SNIP), 18th Scientific Conference : April 25-28, Honolulu, Hawaii

May

International Symposium on HIV and Emerging Infectious Diseases (ISHEID): May 23-25, Marseille, France
11th International Symposium on NeuroVirology held jointly with the Conference on HIV in the Nervous System: May 29-June 2, New York, New York

October

American Neurological Association: October 7-10, Boston, Massachusetts

Society for Neuroscience: October 13-17, New Orleans, Louisiana

2012 ISNV Symposium New York, New York (continued)

The 12 scientific sessions will include (1) Brain as a Reservoir for HIV, (2) Neuroimaging and Surrogate Markers in HAND, (3) Neurobehavioral Challenges and Therapeutic Advances, (4) Viral Latency and Molecular Pathogenesis, (5) Chronic Immune Reactivation and Leukocyte Trafficking, (6) Immunopathogenesis of Viral Infections, (7) Neuro-Restoration Following Virus-associated Injury, (8) Emerging CNS Infections, (9) Misfolding Diseases and Non-Inflammatory Viral Mechanisms, (10) Animal Models and Behavior, (11) HIV and Co-morbidity, and (12) Molecular Neurovirology. Integrated into the series of scientific sessions are four workshops with the first pair focused on substance abuse and CNS infections (HIV and non-HIV) and pathogenesis of multiple sclerosis and other demyelinating diseases, and the second pair of workshops focused on International NeuroAIDS and Polyomaviruses. The workshops have grown into a tradition of intense scientific interchange with each workshop taking on a different format guided by the directors of each workshop.

Over the past several years, the ISNV has developed a series of special lectureships created to recognize outstanding achievements in the area of neurovirology and related disciplines. The first four lectureships are the Neurological Infections Lectureship, Women in Neuroscience Lectureship (followed by a reception), Paradigm Builder Lectureship, and the Bill Narayan Lectureship. The fifth special lecture will be the Audrey Steinman Gilden Lectureship and will recognize investigators whose cutting-

edge research achievements have made important contributions to understanding the molecular pathogenesis of neurotropic virus infection. The lectureship was established by Dr. Don Gilden, who has contributed significantly to the disciplines of neuroscience and neurovirology through his groundbreaking work on lymphocytic choriomeningitis virus, varicella zoster virus and multiple sclerosis. A 2007 recipient of the ISNV Pioneer in NeuroVirology award, Dr. Gilden established this lectureship in honor of his wife, Audrey. This will be the first Audrey Steinman Gilden Lectureship to feature a leading investigator in the field of neurovirology.

As in previous ISNV Symposia, the Investigators-in-Training sessions will highlight the research achievements of tomorrow's neurovirologists. Anticipation continues to build toward the 11th Symposium and the announcement of the 10th Pioneer in NeuroVirology at the banquet gala event. To date, additional financial backing has been obtained from Temple University School of Medicine and Drexel University College of Medicine Institute for Molecular Medicine and Infectious Disease with many additional opportunities for sponsorship available. We look forward to seeing everyone at the 11th International Symposium on NeuroVirology held in concert with the 2012 Conference on HIV in the Nervous System. We anticipate a record-breaking number of students, postdoctoral fellows, clinical fellows, along with new and established investigators from across the United States and around the world.

Loyda M. Meléndez (continued)

has found that dysregulation of the cystatins B/C: cathepsin B interaction in HIV-1 infected monocyte-derived macrophages with increased secretion of bioactive cathepsin B may contribute to neuropathogenesis. This bioactive cathepsin B is not secreted in HIV-1 infected microglia. These studies demonstrated important differences between two macrophage populations and suggest targets for prevention of HIV-associated neurocognitive disorder (HAND).

To address the roles of cystatin B/C, cathepsin B, and the proteins affected by their interactions in the progression to cognitive impairment in the presence of HAART, Dr. Meléndez' laboratory collaborated with Howard Gendelman's and Valerie Wojna's groups to study the proteome of blood-derived monocytes obtained from Hispanic women with the most severe form of HAND, HIV-associated dementia (HAD). These studies suggest that deficits in monocyte antioxidant proteins may lead to neuronal damage through the loss of hydrogen peroxide scavenging capabilities, thereby exposing neurons to apoptosis-inducing factors. Altered monocyte functions therefore may contribute to the development and/or progression of HAD (Kraft-Terry et al, *Proteomics Clin Appl* 2010, 4(8-9):706-14).

regulates STAT-1 phosphorylation by interacting with other proteins. She used a proteomics approach consisting of immunoprecipitation followed by LC-MS/MS to identify the proteins interacting with cystatin B to elucidate the relationship between cystatin B, STAT-1 and HIV persistence in macrophages. The findings confirmed that cystatin B interacts with proteins related to the regulation of STAT-1 phosphorylation and HIV replication, and elucidated the major vault protein (MVP) as an important signaling candidate. This is the first study to correlate the interactions of cystatin B, MVP and IFN responses with HIV persistence in MDM and suggests novel targets for HIV restriction in macrophages, the principal reservoirs for HIV in the CNS.

The Meléndez laboratory conducts immunohistochemical studies of cystatin B/C-cathepsin B interactions in perivascular macrophages and microglia using autopsy tissues collected by the PR Institute of Forensics Sciences and the National NeuroAIDS tissue consortium (NNTC). A battery of antibodies has been tested for distinguishing perivascular macrophages and microglia and this profile is expected to be ready soon for analyses of the samples from NNTC.

The significance of these studies is that by controlling the release of active cathepsins, novel translational targets could be developed to ameliorate HAND. Dr. Meléndez' laboratory plans to continue working to understand the exact mechanisms of HIV-induced cathepsin B secretion and the modulations induced by cystatin B and newly identified proteins. Dr. Meléndez is co-inventor on 3 patents, has written 2 book chapters, is an ad hoc reviewer for the National Institute on Drug Abuse (NIDA), National Institute of Allergy and Infectious Disease (NIAID), and the Journals of Leukocyte Biology, PlosOne, and Placenta. She has published more than 30 manuscripts in national and international journals in the areas of HIV and macrophages and NeuroAIDS.

Linda Rivera (continued)

Since she began working in the Meléndez laboratory, Linda presented 3 posters and won an award for her oral presentation at the ISNV meeting in Milan in October 2010. She completed a second publication from her doctoral studies, and coauthored a review article in the *Journal of Neuroimmune Pharmacology* entitled, "Proteomic analysis of HIV-infected macrophages". She plans to continue training in the neuroscience field while developing new techniques that she can apply to her research. Her areas of focus include understanding signaling pathways related to HIV persistence in the macrophage reservoir and their role in HAND. Dr. Rivera plans to apply this knowledge to advance drug therapeutics for HAND using a non-human primate model.

Rosemarie Booze (continued)

Johns Hopkins University and completed three years of post-doctoral training before accepting a position as an Assistant Professor of Pharmacology at Bowman Gray School of Medicine in North Carolina. In 1991, Dr. Booze joined the University of Kentucky, where she remained for over 10 years. In 2002, Dr. Booze accepted an appointment as Professor and Bicentennial Endowed Chair of Behavioral Neuroscience at the University of South Carolina in the Departments of Psychology and Physiology, Pharmacology and Neuroscience. Dr. Booze also serves as the

Director for the Brain and Behavior Institute at the University of South Carolina.

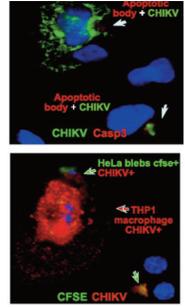
Her research program is supported by the NIH and the NSF and includes a recent R01 awarded to investigate mechanisms of pre-natal cocaine on the CNS. Dr. Booze has published over 100 peer-reviewed research articles, contributed to several books and serves on the editorial board of numerous scientific journals. She is a mentor to students at all academic levels and teaches a variety of graduate and medical school level courses.

Philippe Gasque (continued)

has recently been established by Gasque's team as a Trojan-horse paradigm. His group is addressing the role of the local innate immune response which may control viral infection, but could also contribute to neuronal loss through the uncontrolled release of cytotoxic inflammatory cytokines, complement proteins or pro-apoptotic molecules (Fig. 2; Krejbich-Trotot et al, FASEB J 2011 25(1): 314-25). Moreover, the work is actively progressing to understand the pathology in the joint, which can lead to chronic arthritis reminiscent of rheumatoid arthritis. Dr. Gasque's team was the first to show that CHIKV can persist in macrophages (years after the initial insult) and collaborative work (consortium of 10 European labs) continues to investigate the mechanisms involved in chronic pathologies and to offer novel therapies toward a vaccine.

Dr. Philippe Gasque received his Ph.D. from the University of ROUEN in 1993 and he joined Université de la Réunion, Faculty of Sciences and Technologies in 2006. He is the director of the Groupe de Research sur le Innate Immunity and Infectious and Inflammatory Pathogenesis (GRII), a founding member of the International Association for NeuroInfection and numerous other societies that focus on neurotropic infectious diseases. Philippe

Figure 2. Engulfment of apoptotic blebs contributes to CHIKV infection of macrophages. Macrophages were labeled for cleaved caspase-3 (rabbit; red) and CHIKV E1 (mouse; green) to identify apoptotic blebs containing the virus (and/or viral proteins). Nuclei were counterstained with DAPI (blue). The white arrows show that apoptotic blebs stained for cleaved caspase-3 and CHIKV (E1 antigen) can interact with macrophages. To confirm that these blebs were originally from HeLa cells undergoing apoptosis, cells were pre-labeled with CFSE for cell membranes (green). The CFSE-labeled blebs were also associated with THP1 macrophages (at T 0) and led to the replication of the virus inside the phagocytic cells at 24 h PI. (Figure reprinted with permission from Krejbich-Trotot et al, FASEB J 2011).



has mentored many students at various levels of education, and has published over 75 peer-reviewed scientific articles and several book chapters. Dr. Gasque's program is funded by numerous agencies, including the Wellcome Trust Fund, Projet Européen ICRES towards the development of a CHIKV vaccine and CPER/FEDER Project INNOVOTOX to study the host's cellular and molecular responses to environmental toxins.

Antonina Dolei (continued)

rate of relapse-unrelated unremitting disability and secondary progression of the disease (Fig. 1) (Sotgiu et al., Multiple Sclerosis 2010 16(10): 1248-51). As pointed out in a 2009 review by Dolei and Perron, the connections between MSRV positivity, viral load, and MS could reflect the spreading of an infectious disease and may constitute an environmental risk factor for MS disease when later triggered by cofactors (Dolei and Perron, JNV 2009 15:4-13). Dr. Dolei suggests that if correlations between MSRV viral burden and disease evolution are confirmed in larger cohorts, modifications in interventions could be implemented before damage occurs, rather than in response to disability.

Dr. Dolei received her doctoral degree from the University of Rome in 1972 and completed specialization degrees in microbiology (Rome) and virology (Bologna) in 1975 and 1977, respectively. She became Assistant Professor of Virology, School of Medicine at La Sapienza University, Rome in 1981. After serving as Associate Professor of Pathology, Faculty of Sciences at the University of Camerino, Italy until 1985, Dr. Dolei joined the Faculty of Medicine as Professor of Virology at the University of Sassari. In 2001, Dr. Dolei co-founded the Italian Society of

Virology, and currently is Vice President. She serves as a Senior Editor for the Journal for NeuroVirology and as a reviewer for numerous scientific journals and research foundations including the Multiple Sclerosis Society of Great Britain & Northern Ireland and the Ministry of Health for Continuous Education in Medicine.

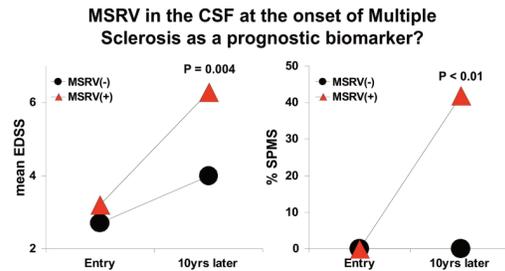


Figure 1: The presence of MSRV in the CSF of early multiple sclerosis patients is associated with a significantly greater rate of disability (Kurtzke's Expanded Disability Status Scale [EDSS] score, left), and predicts the conversion to secondary progressive multiple sclerosis (SPMS) course (right) upon a 10-year follow-up. (based on data from Sotgiu et al., Multiple Sclerosis 2010 16(10): 1248-51).

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ISNV Newsletter printed by the Center for Scientific Communication and Outreach: Director, Michael Nonnemacher, Ph.D.