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ISNV

International Society for NeuroVirology

Editor: Dianne Langford, Ph.D.
Associate Editor: Michael Nonnemacher, Ph.D.

Message from the President

The 12th International Symposium on NeuroVirology and the 2013 Conference on HIV and the Nervous System was held in October 2013 in the Capital Hilton, Washington, DC. This meeting was a tremendous success. Just two blocks from the White House, this venue was in the heart of the political district. Taking advantage of this venue, the meeting had a strong presence of attendees and speakers from the National Institutes of Health, the Federal Drug Agency and the Centers for Disease Control and Prevention. Over 250 scientists and students from 10 different countries attended the meeting. The meeting consisted of 200 poster presentations, 12 scientific sessions, 12 plenary speakers, 6 lectureships and 4 workshops; all over a span of 4 ½ days. A total of 87 speakers took the platform to present their work.

The National Institutes of Health provided support for the meeting through several mechanisms. The National Institute of Mental Health (NIMH) provided for the Conference on HIV and the Nervous System, and conducted a satellite meeting on "Eradication of HIV-CNS Reservoirs: Current strategies and future priorities". Additionally NIMH supported a trainee workshop on Neuro-AIDS. Special sessions on "CNS immunity and alcohol abuse" and "Consequences of substance abuse addiction in Neuro-AIDS" were held as well. Financial support was also provided by the Journal of Neurovirology, Drexel University, Temple University, Seton Hall University, Genentech, Janssen Pharmaceuticals and Biogen. I am grateful to the fund raising committee for their assistance in securing this financial support.

This year the meeting expanded its electronic footprint. A "twitter account" for rapid communication between attendees and a mobile device "app" that had the meeting agenda, an electronic feedback link and information about the local venue, restaurants, etc. were both launched at the 2013 meeting. The Society also established a Wikipedia page.

The Pioneer Award was presented to Dr. Brian Wigdahl and the Society hosted a reception and a gala dinner in his honor. Several of the past Pioneer awardees attended the dinner and named awards were given to students honoring the Pioneers (see page 8).

An important aspect of the meeting was the emphasis on trainees. The meeting included two platform sessions devoted to posters and presentations by trainees and awards for best presentations (7 investigators-in-training awards; 4 outstanding postdoctoral awards, and 3 poster awards), an NRSA trainee workshop and a Junior Scientist/Mentor luncheon (see page 3).

The success of this meeting is attributed to the hard work by many key individuals. While it is impossible to name everyone, a special thanks go out to Sandy Weiss and Betty Condran who played roles in every aspect of the meeting, and to Fred Krebs, Michael Nonnemacher and Vanessa Pirrone, who handled all the electronic and audiovisual aspects of the meeting. I would also like to thank Dr. Walter Royal and the local organizing committee for setting up the venue.

Most importantly, I am most grateful to all those who attended the meeting, made presentations and engaged in discussions making the ISNV the major venue for advancing the field of NeuroVirology as together, we face the challenges in diagnosing and treating these devastating disorders.

I look forward to seeing everyone at our next gathering in the spring of 2015.

Avindra Nath

National NeuroAIDS Tissue Consortium

Dianne Langford

The wealth of information that we have acquired as investigators focused on the impact of HIV on the central and peripheral nervous systems can be attributed in large part to the excellent and comprehensive human brain, blood and cerebral spinal fluid and data banks of the National NeuroAIDS Tissue Consortium (NNTC). In the field of HIV research, both clinical and basic scientists rely on translational evidence for studies aimed at improving quality of life, increasing lifespan and increasing the effectiveness of anti-viral therapies. Numerous relevant and powerful animal models for HIV infection exist and studies from these models have added immensely to our understanding of HIV infection and related disease. Likewise, studies using in vitro models have increased our understanding of cellular and biochemical events that occur during HIV infection. The NNTC, or the Consortium, provides high-quality, well-characterized tissue specimens from patients who died with HIV infection, and for whom comprehensive neuromedical and neuropsychiatric data have been gathered antemortem, in order to foster understanding of HIV disease.

As a long time user of the NNTC resources, I am still amazed at the ease and quick turnaround time for each tissue and data request. While the registration process and tissue request is straightforward, the amount of work that goes into building and maintaining this extensive bank is largely unrecognized. We hope to give a glimpse "behind the scenes" of how the Consortium works and the level of coordination required to make the NNTC so successful.

The NNTC is comprised of four Clinical Sites and one Data Coordinating Center:

Manhattan Brain Bank
Mount Sinai Medical Center
Dr. Susan Morgello
U24MH100931-01

National Neurological AIDS Bank
University of California,
Los Angeles
Dr. Elyse Singer
U24MH100929-01

Data Coordinating Center
University of Nebraska
Medical Center
Dr. Howard Fox
U24MH100925-01

Texas NeuroAIDS Research Center
University of Texas Medical Branch,
Galveston
Dr. Benjamin Gelman
U24MH100930-01

California NeuroAIDS Tissue Network
University of California,
San Diego
Dr. Igor Grant
U24MH100928-01

The NNTC has served the research community since 1998 as an NIH-sponsored multi-site repository that distributes antemortem and postmortem samples with clinical and serological data from HIV-infected individuals. Over 13,500 specimens of various tissue types have been distributed between 1999 and 2014. The NNTC has recently evolved its tissue bank processes, clinical data, and web resources to meet the changing needs of the research community it serves. Participants are recruited from diverse populations of HIV-infected individuals including women and minorities in addition to control cases. Sites assess a variety of conditions that are thought to be good predictors of subsequent near-term demise. Most enrolled participants are characterized as being in the late-stages of HIV infection. Occasionally, participants are enrolled upon death and ante-mortem clinical data is then abstracted from medical records and/or acquired through family reports. Participants are seen on a 6-month visit schedule. Based on the health of the participant or other circumstances, however, the schedule may be altered accordingly and participants may be moved into a different tiering assignment (1-year, 2-year, phone-only). There are basically three levels of assessment:

Standard Visit Assessments: Anti-retroviral medication history, concomitant medication use, laboratory results, blood and CSF collection and testing, urine toxicology, neuromedical evaluation, neuropsychological testing, neuropsychiatric assessment (currently the Composite International Diagnostic Interview), anthropomorphic measurements, and comorbid medical illnesses. At baseline, dates and risks for HIV acquisition, and reading assessment (the Wide Range Achievement Test-3).

Phone call Assessments: Updates on all medications, medical illnesses and encounters, and verbal report of CD4 count and viral load (not laboratory confirmed).

Assessments after death: Chart review for terminal medical conditions, brain and spinal cord pathology, HIV-related organ pathology, and organ pathology that is non-HIV related.

To request and acquire these tissues, a web-based user-friendly guide can be found at: www.nntc.org. Using the "Specimen Query Tool," researchers can quickly search and select from over 20 NNTC specimen types to support their research projects. To enlist the assistance of the DCC staff for all requests for information, tissue, and data, the NNTC researchers need only go to the "Contact Us" tab to fill out the form and submit such requests or they may call/email the DCC at the contact information below. All requests are required to go through the DCC which presents the request to the NNTC Steering Committee for discussion and approval. When approved by

Continued on page 3

National NeuroAIDS Tissue Consortium - continued from page 2

the Steering Committee, specimens are shipped from the individual clinical sites which house them while data are sent to researchers from the DCC. Researchers can request tissues and clinical data from participants who have been characterized by:

- history of drug use
- antiretroviral treatments
- blood and CSF viral load
- neuropathological diagnosis
- degree of neurobehavioral impairment
- neurological and other clinical diagnoses

There are 2,149 HIV+ and 88 HIV- participants enrolled in the NNTC with at least one antemortem visit, with 542 HIV+ and 36 HIV- participants currently active. Among the HIV+ participants with baseline neurocognitive diagnoses, 20% are normal, 13% have asymptomatic neurocognitive impairment, 21% have mild cognitive motor disorder, 12% suffer from HIV dementia, and 34% have neurocognitive impairment due to other causes. Of those evaluated, 71% have a history of substance abuse, with alcohol, cocaine and cannabis being the top three, followed by stimulants and opioids. Sixty-six percent of HIV+ patients suffer from at least one co-morbidity including viral hepatitis, hypertension, hyperlipidemia and smoking.

For more information, please contact:
National NeuroAIDS Tissue Consortium Data Coordinating Center

401 N. Washington St., Suite 700
Rockville, MD 20850

Email: nntc@emmes.com
Website: www.nntc.org

Toll free: 866-668-2272
(1-866-NNTC-BRAIN)

First ISNV Junior Scientist Mentor Luncheon

Lynn Pulliam

In 2013, a Junior Investigator subcommittee of the ISNV was established. The aim of the subcommittee is to address issues facing junior scientists including working relationships, discrimination issues, administrative duties and research and juggling science demands with family. The first luncheon for Junior Investigators was held at the 12th ISNV meeting in Washington DC in Fall 2013 and was hosted by Dr. Don Gilden, an ISNV Pioneer awardee. The purpose of the gathering was to facilitate conversation between young investigators and senior scientists on topics related to careers in science. There were 10 roundtables, each with 2 senior scientist co-Chairs and five to six junior investigators. Each table was assigned a theme and 80 junior scientists signed up at registration for a table hosting a topic of their interest. Topics included: Physician scientists, Transition from postdoc to faculty, Academic promotion and tenure, Government positions/NIH, Publishing your data and FDA/CDC positions. Co-Chairs introduced the topic and welcomed questions on that topic or on any other issues related to a career in science. One highlight of the luncheon was Dr. Dick Johnson's remarks about his memorable experiences as a young investigator. His remarks included an overview of the history of neurovirology including how the term "neurovirology" was coined. The feedback was extremely positive as illustrated by comments from several attendees below. We look forward to organizing another forum for Junior Investigators at our next ISNV meeting!

"I really enjoyed the junior scientist luncheon. It was a great way to meet and chat with some of the biggest "names" in neurovirology. The set-up was very conducive to an informal question and answer session, and I think we all got very helpful career advice from the mentors. It really highlights one of the best aspects of ISNV meetings - the extensive opportunities for students to interact with and ask questions of the top scientists in our field." **Colleen Kovacsics, PhD graduate student, UPENN**

"My conversation with the mentors at the junior scientist luncheon actually changed the way I think about my future career as a physician scientist. Although I came to the event with clear and specific objectives for what I wanted to accomplish in translational medicine, I realized that hadn't yet considered how these objectives meshed with the real world and, specifically, the current health care system. Drawing from their own experiences, speaking with the mentors helped me develop a feasible plan for achieving my career goals!" **Lindsey Gerngross, MD/PhD graduate program, Temple University**

"The ISNV luncheon was a unique opportunity to speak with leaders in the field and ask for career development advice. I found the suggestions and guidance encouraging and applicable. In addition, the small group setting made me feel comfortable to ask questions that I would not have done in a larger group." **Tory Johnson, Post-doc, SINS, NINDS, NIH**

"The event was very unique and provided advice from the senior mentors regarding career transition from postdoc to faculty. Mentors were well prepared to give valuable tips along with the handouts provided by the ISNV on making a career transition in the current funding environment. Please do consider such events in the future ISNV meetings." **Manohar Mutnal, Postdoctoral Research Associate, University of Minnesota**

"The mentors shared very helpful insights on how to find a balance between clinical responsibilities and scientific research as a physician scientist." **Natalie Chen, MD/PhD graduate program, Drexel University**

Interview with Eugene O. Major, PhD at the National Institute of Neurological Diseases and Stroke, National Institutes of Health, Bethesda, MD

Avindra Nath

Reflecting on his career of 40 years in virology, 33 years of which were at the NIH, Dr. Major sat down with Avi Nath to answer a few questions.

How did you get interested in virology?

My father was a physician in 'general practice' who made rounds at the hospital on Sundays. I went with him but stayed in laboratories and not on the patient wards. I loved seeing all the equipment in a lab, fascinating since I wanted to know what all those things did. My father and grandfather, also a physician, were both students of medicine and medical history so I was aware of Pasteur, Fleming, Osler and Semmelweiss long before any of my classmates. I still have many of my father's books in my library at home. I worked for several years after college as a lab assistant in the Department of Biophysics and Biochemistry on DNA structure, a brand new science then in the late 60s. The Microbiology Department was down the hall with projects on viruses that caused cancer, a new finding then, the mouse mammary tumor virus or MMTV. I got interested in that since I usually did experiments in biophysics using analytical ultracentrifugation and moving boundry electrophoresis, the forerunners of optical based laser sensors today. I would make a few analytical runs over one week and then calculate data using a number 2 pencil and yellow pads for maybe 3 weeks. So when I saw that experimental animals developed large tumors in a few months that were caused by an infectious agent like a virus, I gravitated to that work, remembering some early reading of those medical history books.

When did you come to NIH and what brought you here?

What brought me here were owl monkeys who had intracranial injections of this new human polyomavirus, JC virus and then developed gliomas not progressive multifocal leukoencephalopathy (PML). I worked with BK virus as a postdoctoral fellow and helped establish the Tumor Virus Genetics Group at the University of Illinois Medical Center. Dr. John Sever was the Chief of the Infectious Diseases Branch (IDB) at NINDS and knew that I was in Chicago, now at Loyola University Medical School faculty and that I described the oncogenic potential of BK virus in PNAS 1974. So he invited me to do a sabbatical for one year in 1981 at the IDB and put together a working group for JC virus. After the year ended, I was given the opportunity to stay at NINDS. That was a difficult decision both professionally and personally since I was tenured in Chicago. The position in Chicago and Bethesda could not have more different. So I like to say that I have had a more than a three decade sabbatical here.

How has science evolved over the years at NIH and in the academic community?

There are several differences in the way we do our work today compared with even 10 years ago. First, the accessibility of research materials is much greater from common lab reagents to more sophisticated gene clones, molecular techniques, and contract companies to do the tedious work. Many components come in kits these days, it's the 'lego world' so we only need to piece things together. Second is the increasing number of opportunities to publish with so many journals available to send in manuscripts. Certainly not all journals are equal in quality but with such rapid publication and PubMed reaching so many scientists globally, the emphasis seems more on getting something out, incrementally, and not on substantial results. Third is the sense of competition among labs and scientists. There should be more collaboration and less competition. But at times of resource restrictions, it is inevitable that competition takes the lead. But that creates an environment of mistrust; and a healthy science community relies heavily on the opposite, a trust based, honor system.

What are your major accomplishments?

I'll keep to the work on PML to answer that. As a lab chief here and before, I have always taken the approach of identifying the problem first and then looking for answers to solve the problem. I have often told the NINDS that working in human virology requires research to be disease oriented. So when asked in 1981 to tackle PML as a rare, viral induced demyelinating disease caused by JC virus, I knew we had to create new tools to get answers and then focus on the disease pathways. So we had to build new tools, new techniques to get answers. To summarize a list of 'big results':

1. Making the SVG cell lines from human fetal brain to allow more available relevant host cells.
2. Isolating human neural stem cells from the developing brain.
3. Making the unique anti-nestin antibody that the NIH now has licensed to commercial companies contributing to stem cell biology.
4. Developing in situ DNA hybridization methods for JC virus DNA detection.
5. Identification of immune system cells as a primary site of infection and the link between cells of the immune system and the brain at the transcriptional, molecular level
6. Involvement of hematopoietic stem cells and similarities to neural stem cells.
7. The development of quantitative specific measurement of viral DNA in clinical samples, qPCR, that were validated and certified as a diagnostic for PML that has made the LMMN a global focal point for studies on JC virus and PML.

What is the next major challenge in PML research?

The current emphasis is on determining which patients with underlying immune deficiencies are at greatest risk for developing PML. The use of biological therapies, mostly monoclonal antibodies,

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Interview with Eugene O. Major, PhD - continued from page 4

that modulate the immune system like the α 4 integrin inhibitors such as natalizumab for MS patients has focused attention on PML as much as HIV infection. Actually the highest incidence of PML as a percentage of patients treated occurs in MS patients treated with natalizumab. That has always impressed me since we never see two neurological diseases occur in the brain of a single patient much less two demyelinating diseases. The emphasis is now on what is called 'risk stratification', driven a great deal by the FDA that requires biotech and pharma companies to include metrics for assessment of PML, as well as education programs for treating physicians and their patients. Of course, there is a critical need to treat PML patients or patients on therapies or have underlying diseases that place them at greatest risk for PML. Of course to do this requires more fundamental knowledge of basic biology of JCV at the cell and molecular levels.

What advice do you have for young investigators?
Be committed to what you want to do, move your career in a direction that is aligned to what you are passionate about, be strategic in planning, and just plain work at it. It's always good to remember there is lots of competition for resources and that competition is working at goals 7 days a week, in the lab, the clinic, and on line. And don't be afraid to move into new areas or take on new challenges if that is consistent with your goals. I would never have made the switch from viral oncology to neuroviology unless I saw that I could take all the tools I had, the interest in infectious agents, and background in DNA structure and apply those to working in the brain. I've never formally studied neuroscience or neurology but have had 'on the job training' for more than 3 decades now. It's been fascinating and challenging and very rewarding. It all fits from various approaches to a single focus. I would also suggest reading two books that are not in the medical lexicon of bibliography. One is Thomas Freidman's 'The Lexus and the Olive Tree' that describes the influence of history and culture that has deep roots in behavior symbolized by the olive tree rubbing up against the fast paced and technical precision of modern life represented by the Lexus luxury automobile. The other book is Jim Collins, 'Good to Great', describing what factors make for successful organizations, the characteristics of leadership, and what are the best motivators for success. Both books emphasize the importance of self awareness, how you might measure your own success, and what drives your work ethic.

What are your future plans?
I had decided to step aside from public service after 33 years at NIH in January of this year, add another 8 years from times in Chicago and you have over 40 years since I was awarded my Ph.D. degree. I am now a Senior Advisor to NINDS so have a different role but still in the discovery business with PML and all its challenges in the lab and in the clinics helping to support patient oriented work. I do have time to continue to work with academics and industry but as an independent person with insights and ideas that I think need expansion in a different environment. The nice thing about future plans at this stage in my career is that trying new things is the accomplishment. Whether success comes later is important and needed but that can be managed more easily; success is measured differently now. And of course there are the 5 grandchildren; they are the ones with the future plans.

For the full interview, please visit http://isnv.org/newsletter/em2014.php

Eradication of HIV-CNS Reservoirs: Current Strategies and Future Priorities

Jeymohan Joseph

The Division of AIDS Research at the National Institute for Mental Health (NIMH) organized a satellite session entitled, "Eradication of HIV-CNS Reservoirs: Current Strategies and Future Priorities" on October 29, 2013 in conjunction with the 12th International Symposium on NeuroVirology at the Capital Hilton in Washington D.C. The goal of this meeting was to review the current knowledge related to HIV CNS reservoirs and the use of in vitro and in vivo model systems to facilitate research on viral latency and eradication strategies in the brain.

The first session opened with Dr. Steven Deeks (University of California-San Francisco) providing an overview of the HIV eradication field and the critical knowledge gaps with regard to the role of brain as a reservoir and source of rebound virus after cessation of anti-retroviral therapy. Dr. David Margolis (University of North Carolina-Chapel Hill) discussed the translational challenges in targeting latent HIV Infection. Dr. Avindra Nath (National Institute of Neurological Disorders and Stroke) discussed the challenges of HIV eradication from the brain and potential neuronal toxicity associated with current viral reactivation strategies.

The second session which focused on in vitro model systems to study viral persistence was led by Dr. Ronald Swanstrom (University of North Carolina-Chapel Hill) who provided an overview of viral compartmentalization in CNS with a specific focus on myeloid cells. Dr. Mario Stevenson (University of Miami) discussed in vitro model systems to study HIV persistence which was followed by Dr. Jonathan Karn (Case Western Reserve University-Cleveland) describing a novel microglial model system to assess HIV latency. Dr. Ruth Brack-Werner (German Research Center for Environmental Health, Munich) described similarities between HIV-1 latency in the brain and immune system using a novel model for proviral latency in neural cells.

The third session focused on in vivo models was led by Dr. Janice Clements (Johns Hopkins University, Baltimore) who provided an overview of an SIV model to identify and eradicate latent viral reservoirs in both T-cells and macrophages. Dr. Victor Garcia-Martinez (University of North Carolina-Chapel Hill) described a novel mouse model system to study HIV-latency in the myeloid compartment.

The next session of the meeting was focused on novel technologies for achieving HIV CNS Eradication. Dr. Kamel Khalili (Temple University, Philadelphia) described an RNA assisted gene surgery approach for removal of integrated HIV DNA from the host genome in the brain.

The last session of the meeting was a discussion led by Drs. Mario Stevenson and Avindra Nath on future research needs and priorities for HIV Eradication research. Several novel ideas and needs for the field were identified and NIMH is in the process of developing approaches to facilitate the further development of this emerging research area.

Science News

Cellular miRNA is complicit in the pathogenesis of EEEV

Fred Krebs

North American eastern equine encephalitis virus (EEEV) is a virulent pathogen that infects humans with a 30-70% mortality rate. Transmitted by mosquitos, this alphavirus causes a high fever, myalgia, and arthralgia. After several days of systemic infection, the involvement of nervous system (in the form of encephalitis) can be signaled by headache, irritability, drowsiness, seizures, and coma. Even after the infection has been resolved, patients can be left with mild to severe mental and physical deficits.

EEEV infection before the onset of encephalitis is characterized by restricted replication in cells of myeloid origin and a limited type I interferon (IFN) immune response, suggesting that these aspects of infection contribute to EEEV-associated pathogenesis. Using experiments to examine the underlying mechanisms and consequences of limited EEEV infection in myeloid cell populations, investigators at the University of Pittsburgh (PA, USA), University of Texas Medical Branch (Galveston, TX, USA), and the Weizmann Institute of Science (Rehovot, Israel) discovered a unique role for cellular microRNA (miRNA) in regulating the replication of this RNA virus and contributing to its pathogenesis (Trobaugh *et al.*, *Nature*, 506(7487): 245-248, 2014).

During infection in the human (and murine) host, wild-type EEEV replicates ineffectively in macrophages and dendritic cells. The authors hypothesized that this restriction was due to the interaction of a cellular miRNA with an EEEV non-translated region (NTR), since (i) miRNAs function by binding specifically complementary sequences in the 3' NTRs of cellular messenger RNAs and (ii) other viruses, including vesicular stomatitis virus and hepatitis C virus, can be regulated by host miRNA expression. In support of this hypothesis, miRNA prediction algorithms applied to the EEEV 3' NTR revealed three canonical binding sites, which were conserved across multiple strains of EEEV, for the hematopoietic cell-specific miRNA miR-142-3p.

In a series of *in vitro* and *in vivo* experiments, the authors demonstrated that miR-142-3p was indeed responsible for potently restricting EEEV replication specifically in myeloid cells (Figure 1). This mechanism is unique to EEEV, since the replication of the closely related Venezuelan equine encephalitis virus (VEEV) is not similarly affected. Mice infected with recombinant EEEV lacking the three miR-142-3p binding sites were found to have greater levels of virus replication in the lymph nodes, more prominent prodromal (early) disease, significantly higher levels of serum IFN-α/β, and extended survival times. These results suggest that miR-142-3p-mediated restriction of EEEV replication dampens the immune response to infection and paves the way for virus-associated neuropathogenesis.

Interestingly, the binding sites for miR-142-3p appear to be conserved through mechanisms that operate outside the human host. In experiments using mosquito cells, replication of the recombinant virus lacking the miRNA binding sites was significantly reduced compared to the wild-type virus, suggesting the requirement of these sequences for efficient infection in the mosquito vector. As RNA viruses undergo rapid mutation during their replication, this mechanism may positively select for viruses that maintain functional miR-142-3p binding sites in the 3' NTR.

In yet another example of virus adaptation to host cell defenses, EEEV uses the regulatory activity of a host miRNA to restrict its replication and suppress the innate immune response to infection, thereby promoting virus-associated disease. These studies provide new insights into virus-host cell interactions, and the mechanisms by which viruses are able to circumvent normally effective antiviral immune responses.

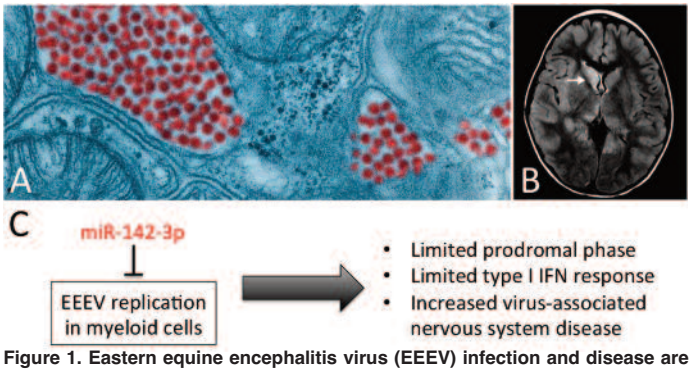

Figure 1. Eastern equine encephalitis virus (EEEV) infection and disease are regulated by miR-142-3p. (**A**) EEEV particles imaged by transmission electron microscopy (TEM) in the mosquito salivary gland (83,900x). (**B**) Lesion (indicated by arrow) visualized by magnetic resonance imaging (MRI) in the brain of a pediatric patient infected with EEEV. (**C**) Consequences of miR-142-3p down-regulation of EEEV replication.

Indo-US Symposium on Viral Infections of the CNS

Pankaj Seth

Severe morbidity and mortality associated with nervous system infections warrant global efforts to reduce the disease burden. Basic and clinical investigators are working closely together at national and international levels to address this issue. Along these lines, neurovirologists from India and the United States met during an Indo-US symposium on viral infections of the nervous system February 23-25, 2014 in Gurgaon, India. The symposium provided pioneers in the field of neurovirology from the US and India with a platform to encourage their research ideas and to explore potential collaborations. The symposium also provided young investigators working in the fields of neurovirology and related areas with cutting edge information to identify important gaps in knowledge and highlight interesting avenues for future research. This meeting included nearly 60 basic researchers, clinical scientists, students and trainees working in diverse areas of neurology, neuropathology, neuropathogenesis, neurobiology, neuroimmunology, neurochemistry and molecular virology of the CNS. Travel awards to attend the meeting were presented to two graduate students and three post-doctoral fellows.

The following are junior scientists who were selected from abstracts to receive travel awards from the Indo-US Science and Technology Forum (IUSSTF) who are partially sponsoring the Indo-US meeting on Viral Infections of the Nervous System.

Postdocs:	**Grad students:**
Debasis Nayak - NIH	Lu Yang - UNMC
Manohar Mutnal - U Minn	Archana Gupta - UCSF/Drexel
Michael Ferenczy - NIH	

The symposium was sponsored by Indo-US Science and Technology Forum (IUSSTF - http://www.indousstf.org/). The details of the symposium are available at: http://www.nbrc.ac.in/indous/IndoUS/

ISNV Highlights - Karin Peterson, Ph.D.

Amanda Brown

From left to right: Karin Peterson (PI), Clayton Winkler (post-doctoral fellow), Katherine Taylor (post-doctoral fellow) and Tyson Woods (microbiologist).

Dr. Karin Peterson is Chief of Neuroimmunology at the Laboratory of Persistent Viral Diseases at Rocky Mountain Laboratories (RML) in Hamilton, Montana. RML was established as a research site in the early 1900s to study Rocky Mountain spotted fever. Now a part of the National Institutes of Health's National Institute of Allergy and Infectious Diseases, RML scientists use state-of-the-art technology to investigate multiple bacterial and viral pathogens. Dr. Peterson's group studies neurovirulent viral infections, including La Crosse Virus (LACV), a bunyavirus that is a leading cause of pediatric viral encephalitis in the United States.

Dr. Peterson completed her doctoral degree in the laboratory of Dr. Helen Braley-Mullen at the University of Missouri. While there, she studied the mechanisms of T-cell activation in experimental autoimmune thyroiditis. She then completed a postdoctoral fellowship with Dr. Bruce Chesebro at RML, where she elucidated host immune responses to retrovirus infection, including those occurring in the central nervous system (CNS).

In 2004, she took a position as Assistant Professor in the Department of Pathobiological Sciences at the School of Veterinary Medicine at Louisiana State University (LSU) to continue studies on viral neuropathogenesis. At LSU, Dr. Peterson's group examined innate immune responses to murine retrovirus infection in the brain. The group generated recombinant viruses encoding portions of the envelope from neurovirulent retroviruses and inoculated these viruses into mice deficient in specific innate immune genes. These studies identified the neurovirulent determinants encoded in the envelope protein. Findings from these experiments also illustrated the complex relationship between neuroinflammation, viral replication and damage to the CNS.

In 2008, Dr. Peterson returned to RML as Chief of the Neuroimmunology Unit. Her group continues to study the influence of the immune system on viral pathogenesis in the CNS. She uses both the retrovirus model, which induces damage indirectly through activation of glial cells, as well as an LACV model, where virus directly infects and induces apoptosis of neurons. Exciting new work from Dr. Peterson's laboratory reveals for the first time that LACV induces apoptosis of neurons by activating an innate pattern recognition sensor, RNA helicase (RIG-1). RIG-1 signaling leads to the activation of the mitochondrial antiviral signaling protein (MAVS). This in turn, stimulates the expression of sterile alpha and Toll/interleukin-1 receptor (TIR) motif-containing 1 protein (SARM1), an adapter molecule that binds to mitochondria and can trigger cell death. SARM1 deficient mice had reduced incidence of LACV-induced neurological disease, which was associated with decreased apoptosis of infected neurons (Figure 1). In addition, Dr. Peterson's group showed through immunoprecipitation analyses and mass spectrometry that MAVS and SARM1 form a protein-protein interaction. Moreover, in neurons deficient in MAVS, SARM1 expression is not upregulated and LACV-induced neuronal apoptosis is also reduced.

In contrast to immune-mediated neuronal damage, other studies from Dr. Peterson's lab have shown that the innate response to viral infection can be protective to neurons. For example, Dr. Peterson's group identified neuropeptide Y (NPY) as a key factor released from injured neurons that protects against virus-mediated damage in the retrovirus model. They are now investigating the mechanisms by which NPY suppresses this damage.

These new insights into the regulation of neuronal damage by the innate immune response hold promise for the development of novel approaches to protect neurons from cell death, not only during virus infection, but possibly in other neurodegenerative disorders that may occur through similar pathways.

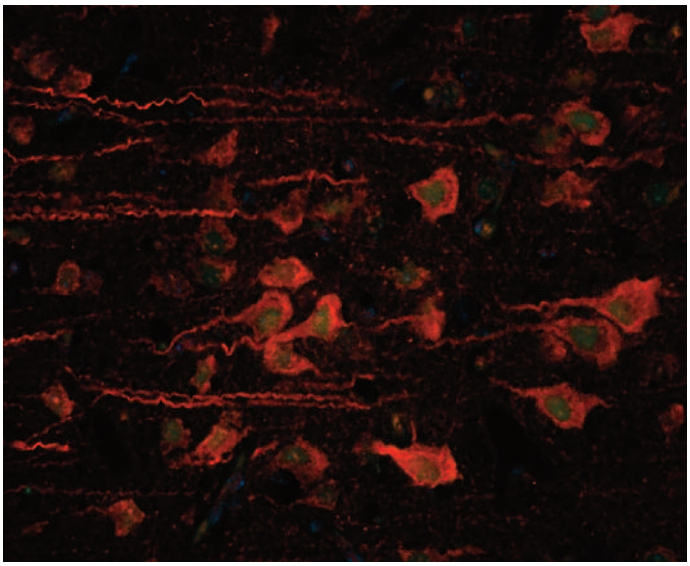

Figure 1. Axonal localization of SARM1 (red fluorescence) in neurons from La Crosse virus infected mice. SARM1 is normally found in the cell body of neurons, however, during La Crosse virus infection, SARM1 is observed in the axons of neurons in the cortex of the CNS. This correlates with localization of SARM1 to mitochondria in the axons in virus infected neuronal cultures. SARM1 mediates neuronal death during La Crosse virus infection through induction of reactive oxygen species and mitochondrial damage. SARM1 labeling is shown with red fluorescence. The neuronal nuclear marker NeuN - is shown with green fluorescence.

2013 Investigator-in-Training Awardees

Top row from the left: Alexander Gill, UPENN; Dionna Williams, AECOM; Tijana Knezevic, Temple; Nicholas Baird, University of Colorado School of Medicine. **Bottom row from the left:** Jessica Rotschafer, University of Minnesota; Raissa Menendez, University of Puerto Rico Medical Sciences Campus; Archana Gupta, UCSF, DUCM; Colleen Kovacsics, UPENN; Jennifer Campbell, Boston College and Gokul Swaminathan, Drexel University College of Medicine. **Pioneers in NeuroVirology pictured in top row left to right:** Kamel Khalili, Brian Wigdahl, Richard Johnson, Donald Gilden, Avindra Nath.

Contact the ISNV Administrative office at:

Tel: (215) 707-9788 **@joinISNV**

Email: mail@isnv.org **www.isnv.org**

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