HIV, Neurodegenerative Disorders and Aging: Mitochondria - from basic mechanisms to disease

5th Annual Colloquium

Wednesday, May 20, 2015
8 am - 3:30 pm (CDT)

University of Nebraska Medical Center
Durham Research Center, 1002
550 South 45th Street
Omaha, NE 68198

Also, presented via a FREE interactive webinar

Webinar register:
https://pen-unmc.adobeconnect.com/e1swxx1ocux/event/registration.html
Mitochondria are key in normal and pathological processes in the body. Their physiological role, including the well-known generation of energy, also includes cellular signaling, differentiation and death as well as other important physiological roles. Recent work unraveling the complex interplay between the mitochondria’s regulation of cellular function and cellular processes that regulate mitochondria themselves have lead to key advances in our knowledge as well as pointed out gaps in our understanding.

This colloquium will address the roles mitochondria play in current disorders afflicting those with HIV, with a focus on the brain. Lessons from the biology and physiology of mitochondrial, aging, neurodegenerative diseases, the effects of therapeutic agents and more will bring together leaders in the field enabling the communication of state of the art knowledge. This forum will enable the communication of state of the art knowledge and how cross-fertilization of overlapping expertise allows us to find ways to address ongoing issues.

**Program Sponsors**

- Chronic HIV Infection and Aging in NeuroAIDS (CHAIN) Center
  (PI: Howard S. Fox, M.D., Ph.D.)
- University of Nebraska Medical Center Development Fund
  (PI: Shilpa Buch, Ph.D.)
- Department of Pharmacology and Experimental Neuroscience
  University of Nebraska Medical Center, Omaha, NE
  (Howard E. Gendelman, M.D., Chair)
- University of Nebraska Medical Center
  Tobacco Settlement Funds
  (Jennifer Larsen, M.D., Vice Chancellor for Research)
- Seahorse Bioscience

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The National Institute of Mental Health, National Institutes of Health for its support of the CHAIN Center.
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<td>Session 1: Regulation of mitochondrial fission in the nervous system</td>
<td>Stefan Strack, Ph.D., University of Iowa</td>
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<td>NRTIs and Pol gamma hypothesis: continuing controversy or closed case?</td>
<td>William Lewis, M.D., Emory University School of Medicine</td>
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<td>Mitochondrial DNA variation and neurologic disorders during HIV infection</td>
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<td>10:15 a.m.</td>
<td>Session 2: Mitochondrial function, proteins and metabolites in the aging brain</td>
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<td>10:50 a.m.</td>
<td>Brain aging, Alzheimer’s and mitochondria</td>
<td>Russell H. Swerdlow, M.D., University of Kansas Medical Center</td>
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<td>Session 3: Unexpected relationships between mitochondrial dysfunction, apoptotic signals and aging</td>
<td>Siegfried Hekimi, Ph.D., F.R.S.C., McGill University</td>
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<td>The tale of mitochondria in Parkinson’s disease</td>
<td>Serge Przedborski, M.D., Ph.D., Columbia University</td>
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<td>2:00 p.m.</td>
<td>Panel Discussion: All presenters and participants</td>
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Dr. Howard Fox received his B.A. and M.A. in biophysics from The Johns Hopkins University and his M.D. and Ph.D. from the University of California, San Francisco (UCSF). Following post-doctoral work at Cold Spring Harbor Labs and anatomic pathology residency at UCSF, he began his independent research career in 1990 in the department of immunology at The Scripps Research Institute, moving to the Department of Neuropharmacology (later renamed Molecula and Integrative Neuroscience) to pursue his work on the effects of HIV on the brain. In 2008, he moved to the department of Pharmacology and Experimental Neuroscience (PEN) at the University of Nebraska Medical Center (UNMC) to further expand the basic and translational aspects of this work.

He has served as long-term chair of the Center for Scientific Review Study Section on NeuroAIDS and Co-morbidity Factors in AIDS, the University of California University-Wide Taskforce on AIDS, on multiple extramural NIH grant external advisory boards, is principal investigator of the Data Coordinating Center and leads the Scientific Advisory Group for the National NeuroAIDS Tissue Consortium. He is currently Professor and Executive Vice-Chair in the PEN department and Senior Associate Dean for Research and Development for the College of Medicine at UNMC. He directs the Chronic HIV Infection and Aging in NeuroAIDS (CHAIN) Center (P30, NIMH) and the University of Nebraska Center for Integrative and Translational Neuroscience (CITN), as well as NIH R01 grants.

Dr. Fox’s work has focused on knowledge learned from the SIV/ nonhuman primate model of neuroAIDS. In addition to functional, neuropathologic and neuroimmune findings, he has integrated high-density data acquisition and analysis through transcriptomic, proteomic and metabolomic technologies with a systems biology approach. Recent findings have led to a new focus on brain mitochondria. His lab is now probing the role of mitochondria in normal physiological functions, aging and neurodegenerative diseases.

Siegfried Hekimi obtained his undergraduate degree in biology at the University of Geneva. He did not immediately pursue graduate studies but instead engaged in a full-time career as a cyclist, first as a member of the Swiss National Team and then as a professional in various teams in Switzerland and Italy. He was selected four times for the World Championships and participated in such well-known races as the Tour de France and the Giro d’Italia.

In 1988, he renewed his true calling by completing a Ph.D. in neurobiology with Professor Michael O’Shea, again at the University of Geneva, focusing on the biosynthesis of neuropeptides. It was to tackle this problem that he first developed an interest in using invertebrate models to study evolutionarily conserved processes. He then moved to the Laboratory of Molecular Biology (LMB) of the Medical Research Council in Cambridge, UK, to collaborate with Dr. J.J. White. It is at the LMB that Sydney Brenner developed the nematode Caenorhabditis elegans as one of the premier research tools in genetics, and where Hekimi developed his interest for using ‘the worm’ for translational studies in the biology of aging. It is also in Cambridge that he identified the first mutants that helped to demonstrate that aging could be manipulated genetically and that mitochondrial dysfunction could in fact slow down the aging process of animals.

After Cambridge, Hekimi joined the Department of Biology at McGill University in Montreal, where he is a full professor since 2004, and where he extended his research interest to mouse models and projects in drug discovery. In 2010 he became a Fellow of the Royal Society of Canada (RSC), and two years later was awarded the Flavelle Medal of the RSC for outstanding contribution to biological science.
Dr. Hulgan completed an undergraduate degree at the University of South Alabama, and obtained an MD from the University Of Alabama School Of Medicine at UAB in 1996. After Internal Medicine residency and a chief residency at Wake Forest University-Baptist Medical Center, he moved to Vanderbilt for Fellowship in Infectious Diseases and an MPH, and has been on faculty at Vanderbilt since 2004.

The primary goal of Dr. Hulgan’s research is to improve the health of HIV-infected persons by better understanding, predicting, preventing, and treating complications of HIV infection and antiretroviral therapy. Dr. Hulgan has pursued this goal through observational cohort studies- both large multi-site and targeted local cohorts- and prospective clinical trials of HIV-infected persons. This work includes collaborations with the CNS HIV Antiretroviral Therapy Effects Research (CHARTER) study group, the AIDS Clinical Trials Group (ACTG), and the Multicenter AIDS Cohort Study (MACS).

An area of primary focus includes the field of translational mitochondrial genomics in HIV. He has been PI of multiple collaborative multi-disciplinary projects funded through NIMH, NINDS, and NIDDK to expand our understanding of the role of genetic variation in mitochondrial DNA (mtDNA) in diverse outcomes of HIV infection and treatment. Current phenotypes of interest are neurocognition and neuroinflammation. The ultimate vision for this work is to provide new knowledge and tools (genomic and/or biological markers) that inform a “precision-medicine” approach to improve treatment and management decisions for clinical care- and thus the length and quality of life- of an aging population of HIV infected persons.

Dr. Hulgan maintains an active clinical and teaching program, having cared for HIV-infected patients for almost 15 years, and mentoring four to five Infectious Diseases fellows each year at both the Nashville VA and Vanderbilt Comprehensive Care Clinic, and attending regularly on inpatient ID consult and HIV services.

todd.hulgan@vanderbilt.edu
Dr. Serge Przedborski is the Page and William Black Professor of Neurology. He holds a joint appointment in the Departments of Neurology, Pathology and Cell Biology and is the Director of the Columbia Translational Neuroscience Initiative, the Co-Director of the Center for Motor Neuron Biology and Disease, the Vice-Chair of Neurology, and a faculty member of the graduate program in Neurobiology and Behavior at Columbia University.

Dr. Przedborski attended medical school at the Université Libre de Bruxelles (ULB), Belgium, and did his internship and residency in Neurology and Psychiatry at the ULB-Erasme Academic Medical Center, Belgium. He obtained both his MD degree (1983) and then a PhD degree in neurological sciences (1991) from the ULB. He then did a fellowship in movement disorders with Dr. Stanley Fahn at Columbia University, where he became Assistant Professor in 1991.

The research conducted in Dr. Przedborski’s laboratory is geared toward unraveling the molecular basis of neurodegeneration and devising therapeutic strategies to hamper the processes that cause neuronal death, the source of many debilitating disorders. In keeping with this goal, to what extent and by which mechanisms do cell-autonomous and non-cell autonomous deleterious processes contribute to the demise of specific subpopulation of neurons in neurodegenerative disorders, such as Parkinson’s disease, represent a main line of research in his laboratory. These research efforts are supported by federal grants from both NIH and the DoD and by private agencies including the Parkinson’s Disease Foundation, MDA, ALSA, Project-ALS, and P2ALS/Target-ALS.

Dr. Przedborski is the current president of the World Parkinson Coalition, a nonprofit organization dedicated to providing an international forum to learn about the latest scientific discoveries, medical practices, caregiver initiatives and advocacy work related to Parkinson’s disease.

Dr. Stefan Strack is a Professor and Associate Chair in the Department of Pharmacology at the University of Iowa. Born and raised in Germany, he received his Ph.D. at the State University of New York at Albany and his postdoctoral training at Vanderbilt University before joining the faculty at the University of Iowa in 2000.

Dr. Strack has authored over 60 publications. His research is supported by several NIH grants and he directs a NIGMS-funded pre-doctoral training grant (T32) in Pharmacological Sciences. He is currently a chartered member of the NIH study section Clinical Neuroplasticity and Neurotransmitters (CNNT) and serves on the editorial board of the Journal of Biological Chemistry.

His current research focuses on the regulation of mitochondrial dynamics by protein kinases and phosphatases in normal brain function and neurological diseases and injury. His group discovered a conserved inhibitory phosphorylation site in the mitochondrial fission enzyme dynamin-related protein 1 (Drp1), which determines not only neuronal responses to ischemia, excitotoxicity, and other insults, but also critically regulates dendrite development and synaptogenesis. More recent work centers on mitochondrial fission factor (Mff), a protein that recruits Drp1 to the outer mitochondrial membrane.

In 2014, Dr. Strack was named a winner of the GlaxoSmithKline Discovery Fast Track Challenge. This challenge is designed to encourage the translation of academic research into novel therapies. Dr. Strack works with scientists in GSK’s Discovery Partnerships with Academia (DPac) and the Molecular Discovery Research teams to develop high throughput assays in order to screen mitochondrial targets against GSK’s 2 million compound collection. The ultimate goal of this partnership is to find better drugs to treat peripheral neuropathy associated with diabetes and chemotherapy.
Dr. Russell Swerdlow is a physician-scientist at the University of Kansas. He directs the NIH-funded University of Kansas Alzheimer’s Disease Center, serves as an attending physician at the Kansas University Medical Center’s Memory Disorders Clinic, directs the Kansas University Medical Center’s Neurodegenerative Disorders Program, and is a professor in the Departments of Neurology, Molecular and Integrative Physiology, and Biochemistry and Molecular Biology at the University of Kansas School of Medicine.

Dr. Swerdlow received his undergraduate and doctor of medicine degrees from New York University, and trained as a neurologist and Alzheimer’s disease specialist at the University of Virginia. He currently holds the Gene and Marge Sweeney Chair at the University of Kansas and is a recipient of an S. Weir Mitchell Award from the American Academy of Neurology, a Cotzias Award from the American Parkinson’s Disease Association, a Scholarly Research Award from the University of Kansas, and multiple grant awards from the National Institutes of Health and neurodegenerative disease-related foundations. He has served as the Research Committee Chair of the CurePSP Foundation; Chaired the Commonwealth of Virginia’s Alzheimer’s Disease Commission; is on the editorial board of several research journals including Neurology and the Journal of Alzheimer’s Disease; and frequently sits on NIH, Veteran’s Administration, and non-profit research foundation study sections.

Dr. Swerdlow’s research currently focuses on brain energy metabolism, the role brain energy metabolism plays in Alzheimer’s disease and other neurodegenerative diseases, and how to manipulate brain energy metabolism.

Dr. Shilpa Buch is a professor and vice chair in the department of pharmacology and experimental neuroscience at the University of Nebraska Medical Center. She is also the Director of the Nebraska Center for Substance Abuse Research at UNMC. Her primary research focus is aimed at understanding the molecular mechanism(s) by which drugs of abuse, such as cocaine and morphine, co-operate with HIV-1/HIV proteins to enhance progression of HIV-1 associated neurological disorders (HAND). Specifically, her research involves a multipronged approach comprising of in vitro cell systems, complementary rodent models, the higher more relevant macaque model of SIV pathogenesis, and archival human tissue, to dissect the signaling pathways crucial in CNS pathogenesis that is triggered by the host-virus interplay. More recently, her research is centered on exploring the molecular pathways by which microRNAs, small noncoding RNAs that shuttle in extracellular vesicle cargos, regulate gene expression and cellular cross-talk. Work from her group has also shed light on novel therapeutic strategies, such as delivery of platelet-derived growth factor-C chain in mitigating neuroinflammation and associated synaptodendritic injury observed in HAND.

Dr. Gendelman joined UNMC in 1993 and is the Margaret R. Larson Professor of Internal Medicine and Infectious Diseases and chair of the pharmacology and experimental neuroscience department at the UNMC. Dr. Gendelman’s research contributed to the understanding of how alterations in mononuclear phagocyte function induce metabolic changes in the brain and ultimately lead to neural cell damage. He created the field of cell based drug delivery that has broad implications in developing the means to prevent, slow or reverse infectious, metabolic and degenerative disorders of the nervous system.
Acknowledgments:

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Administrative Staff
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