Program for HIV Satellite Symposium
“HIV, NeuroAIDS, Drug Abuse & EVs”
April 23, 2015
Forest Glen Room, Bethesda Marriott, Maryland
Chairs: Drs. Jeymohan Joseph and John Satterlee

8:00 - 8:05 a.m.: Introduction by Ken Witwer, Ph.D., Assistant Professor, Department of Molecular and Comparative Pathobiology, Johns Hopkins University

Kenneth Witwer is an assistant professor in the Department of Molecular and Comparative Pathobiology at the Johns Hopkins University. The Witwer lab investigates extracellular vesicles and RNA in the context of HIV infection and inflammatory diseases. Related research interests include retrovirus restriction factors and therapeutic delivery of RNA.

8:05 - 8:15 a.m.: Jeymohan Joseph, Ph.D., Chief, HIV Neuropathogenesis, Genetics and Therapeutics Branch, NIMH, NIH

NIMH priorities in NeuroAIDS and Exosome Research

Dr. Jeymohan Joseph is currently Chief of the HIV Neuropathogenesis, Genetics and Therapeutics Branch within the Division of AIDS Research at the National Institute of Mental Health (NIMH). He received his Ph.D. in Immunology from the University of Wisconsin-Madison. Before joining NIMH in 1999, Dr. Joseph served on the faculty at Jefferson Medical College and also at Hahnemann University in Philadelphia. His research interests include studies of the role of blood-brain barrier in regulating trafficking of immune cells and neurotropic viruses into the central nervous system (CNS), both in the context of autoimmune diseases such as multiple sclerosis, and also in relation to HIV infection of the brain. In his current position at NIMH, Dr. Joseph oversees a portfolio of grants worth approximately $45 million dollars that cover research on pathophysiology of HIV-associated neurocognitive disorders, viral and host genetic factors regulating HIV neuropathogenesis, and novel neuroprotective and delivery strategies for treating HIV-induced neurodegenerative processes. The NIMH NeuroAIDS program also has an interest in understanding the mechanisms of HIV latency and developing strategies for eradicating HIV from the CNS compartment. Dr. Joseph has served as guest editor on several special issues of the Journal of Neurovirology and Journal of Neuroimmunology. An important new priority area that Dr. Joseph is promoting is the role of exosomes in HIV neuropathogenesis, biomarkers for HAND or as delivery vehicles for CNS targeted therapeutics.
8:15 - 8:25 a.m.: John Satterlee, Ph.D., Program Director: Epigenetics, Model Organism Genetics & Functional Genomics, NIDA, NIH

**Extracellular Vesicles: NIDA and the Common Fund Extracellular RNA Communication Program**

Dr. Satterlee is the Program Director of Epigenetics, Model Organism Genetics & Functional Genomics at the National Institute on Drug Abuse (NIDA), NIH. He earned a B.S. in Biology from Cornell University and a M.S. in Science Education from Syracuse University. He completed a Ph.D at the University of Wisconsin-Madison in plant molecular biology. His post-doctoral work at Brandeis University was in behavioral genetics. In 2003, Dr. Satterlee became co-director of the C. elegans Core facility at Massachusetts General Hospital where he identified new genes involved in a variety of developmental processes. In 2005, he began work at NIDA. He has been co-coordinator of the Roadmap Epigenomics Program since its inception and is involved with other Common Fund programs including the 4D Nucleome and exRNA Communication Programs.

8:25 - 8:45 a.m.: Vincent C. Bond, Ph.D., Professor and Acting Chair of Microbiology, Biochemistry & Immunology, Morehouse School of Medicine

**Cytokines Associated with Exosomes in HIV-infected Individuals**

Dr. Bond has studied HIV pathogenesis for more than 20 years. His lab has developed evidence that exosomes significantly contribute to immune activation, bystander CD4 T cell depletion and HIV propagation via bystander cell activation during HIV infection. His group has shown this to occur through release of exosomes from HIV-infected cells that induce apoptosis in bystander uninfected CD4+ T cells. In HIV infected, viremic patients, exosomes circulating in the plasma were found to be enriched for a host of pro-inflammatory cytokines that induce immune activation in naive and central memory CD4 and CD8 T cells, one of the hallmarks of HIV infection and well established as one of the strongest predictors of HIV disease progression. This work has uniquely positioned his group to decipher the mechanisms underlying HIV disease. Out of this evidence, he identified new targets for AIDS therapy, as well as a potential therapeutic antagonist against those targets. This work has been instrumental in development of his lab expertise in microvesicle research, including isolation and analysis of the same. He leveraged this expertise to develop a Microvesicle Lab at MSM, which helps other researchers studying microvesicles’ role in aspects of their own research.
Dr. Haughey has developed a distinctive disease-oriented research program that addresses questions in basic neurobiology and in clinical neurology. His primary interests are: 1) To identify biomarkers for neurodegenerative diseases including HIV-Associated Neuro-cognitive Disorder, Alzheimer’s disease and Multiple Sclerosis. In these studies, blood and cerebral spinal fluid samples obtained from ongoing clinical studies (often longitudinal) are analyzed for metabolite profiles through a variety of mass spectrometry and bioinformatic techniques. These biomarkers may then be used in the diagnosis of disease, as prognostic indicators for disease trajectory, or as surrogate markers to track the effectiveness of disease modifying interventions; 2) To better understand the lipid components of cellular membranes and how these components interact with proteins to regulate signaling associated with cellular functions such as differentiation, motility, inflammatory signaling and survival (primarily in neurons and astrocytes); and 3) To develop small molecule therapeutics to regulate the activity of enzymes involved with lipid metabolism as a neuroprotective strategy.

In 2009, Shilpa Buch moved from Kansas to University of Nebraska Medical Center, Omaha, Nebraska as a Professor in the Department of Pharmacology and Experimental Neuroscience. Her research is focused on understanding the neuropathogenesis of HIV/SIV infection using cell culture, rodents and macaques as model systems. Her work has contributed to identification of the role of platelet-derived growth factor as a neuroprotective agent against viral (Tat & gp120), cellular (cytokines/chemokines) toxins. In recent years, she also developed her research program to examine the molecular mechanisms by which drugs of abuse such as cocaine and morphine, synergize with HIV-1/HIV proteins to enhance progression of HIV-1 associated neurological disorders. Specifically, using a multipronged approach comprising of in vitro cell systems, complemented with rodent models and the higher more relevant macaque model of SIV pathogenesis, and archival human tissue, her research aims to dissect the mechanism(s) of CNS pathology triggered by the host-virus interplay. Her newer areas of research include studying miRNAs as mediators of gene regulation, extracellular vesicles as cargos for cellular cross-talk and autophagy. She is also directing the Nebraska Center for Substance Abuse Research, the mission of which is to promote and enhance drug abuse research and mentor trainees in this area.
9:09 - 9:21 a.m.: Fatah Kashanchi, Ph.D., Professor, Laboratory of Molecular Virology, George Mason University

**Exosomes from latent HIV infections:**
**Spreading the message beyond infection**

For the past twenty years, Dr. Kashanchi’s has been interested in understanding the mechanism of viral gene expression in human viruses and how the virus and the host control the dynamics of fundamental machineries needed for viral replication and/or host survival. His group also has ample experience with biochemical pathways that lead to transcription and chromatin remodeling using *in vitro* reconstituted machineries. These complexes with epigenetic modifications utilize host signaling events that his group has used as therapeutic targets that control viral replication. His group has also started focusing on HIV mouse models using humanized animals for many of their studies. This includes both Rag and NSG animals. These animal studies have identified dynamics of viral replication in various tissues and organs. Finally, his lab was the first to describe the effect of exosomes from virally infected cells including HIV and HTLV infected cell lines and primary cells. The exosomes have been linked to the spread of information needed for subsequent virus homing and related pathogenesis. The exosomes from infected cells are normally purified using multi-step centrifugations followed by opti-prep gradients. He has further used CD63 and CD81 affinity to purify up to 90% of these exosomes. In case of patient samples, his group has used nanoparticles to purify exosomes for further physical and functional characterizations. His team is also trying to purify the exosomes from the NSG humanized mice tissues infected with HIV (R5 and X4 clinical strains).

9:21 - 9:33 a.m.: Lynn Pulliam, M.S., Ph.D., Professor, Departments of Pathology & Laboratory Medicine, University of California, San Francisco

**Monocyte immune activation in HIV can alter end organ function via Exosomes**

For over two decades, Dr. Pulliam’s laboratory has been focused on monocyte/macrophage activation in HIV infection, markers of disease progression and the effect on cognitive and neural cell function. She has reported several important markers on monocytes that correlate with activation as well as characterizing the monocyte phenotype in HIV and co-infection with hepatitis C virus (HCV) in the era of antiretroviral therapy (ART) showing correlation with cognitive impairment. The lab recently reported that peripheral monocyte activation might impact cardiovascular disease by increasing lipid uptake in subjects with HIV infection. Dr. Pulliam began studying monocyte-derived exosomes and the influence of miRNAs within exosomes in neural cell dysfunction and has expanded these studies to determine the influence on endothelial cell activation. In both cases, the impact of immune activated monocyte/macrophages and their exosomes influence end organ cellular function.

9:33 - 9:50 a.m.: Questions and Answers

9:55 a.m.: Wrap Up