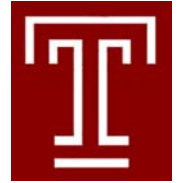




DEPARTMENT OF NEUROSCIENCE

Newsletter



No. 1, Issue 2

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Temple University School of Medicine Philadelphia, Pennsylvania USA

MESSAGE FROM THE CHAIR



Each of us has had mentors in our careers; those individuals who have provided guidance, encouragement, and criticism when needed during the early stages of our careers. Mentorship is an important and integral component of developing as a scientist. It picks up where textbooks leave off. As graduate students we

had formal mentors in the form of thesis advisors, committees, etc. However, it is critical to career development to have good leadership as postdocs and junior faculty. It is equally important, at some point, to assume the role of mentor to others. I have been fortunate in my career to have had dedicated and influential mentors, perhaps that is the reason that I have felt so strongly committed to mentoring young scientists for the past twenty years.

Here in the Department of Neuroscience we have been very fortunate to have had several talented, eager, and hardworking students, postdocs, and junior faculty who graciously allowed us to serve as their mentors. Many of them now hold top positions at academic institutions such as Johns Hopkins, the University of Pennsylvania, and the University of Texas. Others decided to stay with the department to establish their own independent programs. Those individuals have become collaborators, and indeed, assist in developing new programs as well as strengthening our existing programs. As a measure of successful mentorship, our mentees become our collaborators and, in turn, mentors for others. With the momentum that has been built at TUSM and the Department of Neuroscience, we will maximally capitalize on our extensive experience in mentorship and continue to train first rate, highly competitive scientists and educators.

Kamel Khalili

FEATURED INVESTIGATOR

Nune Darbinian, Ph.D.

Nune Darbinian joined our group in 1998 as a postdoctoral fellow. She received her Ph.D. training at the Moscow Institute of Molecular Genetics/Yerevan State University (Armenia) in 1993. She currently holds the position of Associate Scientist in the Department of Neuroscience. Her research has focused on the biology of Pura, a multifunctional cellular protein whose presence is essential for neuronal cell development. Her work has revealed several important functions of Pura related to its interaction with neurotropic proteins and its impact on viral replication and neuronal cell function. She has also begun a project to investigate the role of Pura in DNA damage as related to neurodegenerative disorders such as Alzheimer's disease. In an alternative study, she has identified p27SJ, a novel protein from a callus culture of St. John's Wort whose expression modulates transcription of the HIV-1 promoter in several mammalian cells. These results support the utility of p27SJ in suppressing transcription and replication of HIV-1 by interfering with the function of cellular proteins such as C/EBP β and viral activators including Tat.



Dr. Darbinian is a talented and knowledgeable scientist. She has assumed a leadership role in the laboratory and readily imparts her knowledge and expertise to others. She is an excellent teacher and routinely instructs and supervises junior scientists and support personnel on the performance of various techniques. She has taken on the role of mentor to high school students over the past few summers and has done an outstanding job of guiding these students through a project. In fact, some of her students have received awards for the work performed under her tutelage. Dr. Darbinian is an up and coming scientist and an asset to our department.

NEW FACULTY

Wenhui Hu, M.D., Ph.D. joined the Department of Neuroscience as an Assistant Professor on April 1, 2008. Previously, Dr. Hu held a similar rank in the Department of Physiology at Virginia Commonwealth University School of Medicine. Dr. Hu is an experienced scientist whose research focuses on the molecular mechanisms of inflammation, NF κ B signaling and G-protein-coupled receptors. He is currently the Principal Investigator on an R01 grant from NIH that focuses on the regulation of smooth muscle contraction/relaxation by cytokines. With extensive experience in molecular neurobiology, Dr. Hu will develop an active program to study NF κ B signaling in the development of the nervous system. In addition, Dr. Hu will take an active role in teaching and mentoring postdocs and students of our graduate program.



TRAINING PROGRAM IN NEUROAIDS

In a unique collaborative arrangement, **Dr. Rappaport** (Professor, Department of Neuroscience) and **Dr. Khalili** (Professor and Chair, Department of Neuroscience) along with **Drs. Brian Wigdahl** and **Olimpia Meucci** (Department of Microbiology and Immunology, Drexel University College of Medicine) and **Dr. Dennis Kolson** (Department of Neurology, University of Pennsylvania) have developed an interdisciplinary research training program for predoctoral students in NeuroAIDS. The unique aspect of this proposal is that it is a joint training program between Temple University and Drexel University, and will also integrate teaching activities and resources available through a graduate and clinical training program in the Department of Neurology at the University of Pennsylvania. This initiative would create a city-wide predoctoral training program with shared resources and activities such as journal clubs, seminar series, thesis mentoring, etc. The curricula at both Temple and Drexel will provide a broad-based scientific foundation in biomedical science including neuroscience, immunology, microbiology, pharmacology, and physiology. Investigators at Temple and Drexel have built productive and well-funded NeuroAIDS research programs capable of supporting the proposed training. By combining the complementary research and educational resources, this will establish a premier training experience that will serve as a benchmark for future training programs.

STUDENTS AND POSTDOCS

Nana Merabova, M.D.

Nana joined our group as an assistant scientist in 2004. Her current research in our laboratory focuses on the role of LIX (CXCL5) chemokine in neuronal cell survival and differentiation of oligodendrocytes and the regulation of LIX (CXCL5) by JCV agnoprotein in oligodendrocytes. In a recent study she has used bipotential CG4 cells to examine the impact of agnoprotein on oligodendrocyte differentiation and survival in the absence of JCV lytic infection. She has demonstrated that expression of agnoprotein delayed the formation of complex outgrowth networks of the cells during oligodendrocytes differentiation. These alterations were accompanied by high levels of DNA damage, induction of pro-apoptotic proteins, and suppression of pro-survival signaling. Apoptosis was significantly increased upon induction of CG-4 cells toward differentiation in cells expressing agnoprotein. These observations demonstrate the possible involvement of agnoprotein in a series of biological events that may contribute to the pathologic features seen in PML lesions. This work has been published in the *Journal of Virology*.



Ilker Sariyer, D.V.M.

Ilker joined the graduate program in 2007 as a member of the inaugural class of the Biomedical Neuroscience degree program. Ilker received his veterinary degree in 2000 from Selcuk University in Konya, Turkey. His current research project focuses on understanding the molecular pathogenesis of viral-induced diseases in brain using in vitro cell culture and in vivo animal models. In this respect, he has successfully developed a cell culture system that permits replication of JCV and HIV-1 in glial cells. This is an important biological system that will help to investigate the interaction of these two human viruses with CNS cells in a culture system, and develop a fast assay for screening potential therapeutic compounds. Ilker has recently published his findings on the interaction of JCV early protein, t-antigen and PP2A in the journal *Virology*.

NEUROSCIENCE IN THE NEWS



Drs. Jay Rappaport and **Tracy Fischer-Smith** of the Department of Neuroscience in collaboration with **Dr. Ellen Tedaldi** (Department of Medicine) undertook a study to investigate whether an alteration in a subset of monocytes can serve as a biomarker for the progression of HIV disease. Their findings have been reported in a paper entitled "CD163/CD16 Coexpression by Circulating Monocytes/Macrophages in HIV: Potential Biomarkers for HIV Infection and AIDS Progression" that appeared in the March issue of *AIDS Research and Human Retroviruses* (www.liebertonline.com/aid).

In their study, they examined a cohort of 18 patients from the Comprehensive HIV Program at Temple University Hospital and seven individuals without HIV infection. They found that patients with detectable virus had an increase of this monocyte subset that correlated with the amount of virus they had in their blood. The investigators were surprised to find that in patients with CD4+ T cell counts of less than 450 cells per microliter [200 or less per microliter is defined as AIDS], the increase of this monocyte subset correlates inversely with the number of T cells.

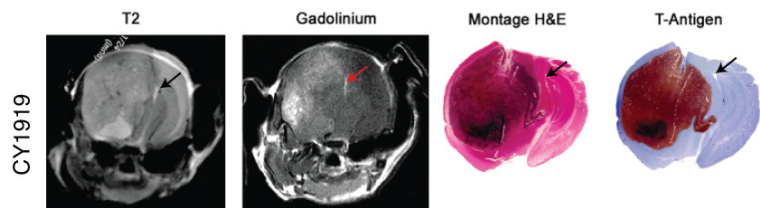
Dr. Fischer-Smith said this finding suggests that as the monocyte cells are increasing, these patients are losing CD4+ T cells, which are critical for the maintenance of immunological competence. **Dr. Rappaport** believes the CD163+/CD16+ monocyte subset is the first biomarker that correlates with both viral load and CD4+ count, which suggests it as a key cell type in the pathogenesis of AIDS.

The study was supported by the National Institute of Neurological Disorders and Strokes (NINDS) and the National Institute on Drug Abuse (NIDA). Their finding was reported by various news agencies including the Washington Post, ABC News, USA Today, and Genetic Engineering and Biotechnology News.

COLLABORATIONS

Recently, **Dr. Jennifer Gordon** (Department of Neuroscience) and **Dr. Feroze Mohamed** (Department of Radiology) have initiated a close collaboration on MR imaging techniques for brain tumors. Detecting the early signs of cancer has proved to be an elusive goal, particularly when it comes to tumors of the brain. They are working on novel ways to image transgenic mouse models of brain tumors developed in the Department of Neuroscience. In addition, **Drs. Gordon** and **Mohamed** are developing new molecular imaging techniques which rely on super paramagnetic iron-oxide nanoparticles conjugated to antibodies that bind specifically to tumor cells. The nanoparticles will then be visible by MRI at high field strength and will allow greater sensitivity for detecting smaller lesion and local recurrences, as well as metastases. Their collaborators on translational neuroimaging and molecular imaging include **Drs. Luis Del Valle** (Neuroscience) and **Linda Knight** (Radiology) at Temple and **Dr. Harvey Hensley** (Microimaging Core Facility) at the Fox Chase Cancer Center.

The figure illustrates co-registration of MR images and histological features of JCV T-antigen induced mouse brain tumor model.



In another study, **Dr. Bassel Sawaya** (Department of Neuroscience) and **Dr. Salim Merali** (Department of Biochemistry) are collaborating on the detection of HIV-1 protein in CNS infected cells as well as in CSF of AIDS patients with dementia using state-of-the-art proteomics and complementary electrophoresis. It is anticipated that the outcome of this study will assist as an early marker of neurologic complications in AIDS patients and will assist in deciphering the pathogenesis of the disease.

GRANTS AND AWARDS

During the last three months, several members have received good news regarding their grant applications from the National Institutes of Health. The following grants have recently been awarded to our faculty from the NIH.

- R01AI077460 entitled "Cytokine regulation of JC virus latency and reactivation" has been awarded to [Dr. Martyn White](#).
- R01NS063605 entitled "Role of monocytes/macrophages in CNS disease in the HAART era" has been awarded to [Dr. Tracy Fischer-Smith](#) for a period of five years.
- K01DA022147 entitled "Role of opioids and complements in AIDS pathogenesis" has been awarded to [Dr. Prasun Datta](#).

[Dr. Jennifer Gordon](#), in collaboration with [Dr. Linda Knight](#) of the Department of Radiology, received funding for one year from the Nanotechnology Institute for a project entitled "Targeted nanoparticles for intracellular cancer therapy."

In addition, several other faculty members have received very favorable scores and have a high probability of being funded.

- P01DA23860 entitled "Drugs of abuse affecting AIDS pathogenesis" received an outstanding score (priority score 148). [Dr. Jay Rappaport](#) is co-program director along with [Dr. Thomas Rogers](#) of the Fels Institute and Department of Pharmacology of this multidisciplinary, inter-departmental program project. This program will support [Dr. Rappaport's](#) project entitled "Opioids in AIDS progression and neuropathogenesis of SIV infected macaques", [Dr. Kamel Khalili's](#) and [Dr. Bassel Sawaya's](#) project entitled "Molecular events involved in HIV-1/morphine induced neuropathogenesis, and the Histopathology Core facility under the direction of [Dr. Tracy Fischer-Smith](#).
- R01CA095518 entitled "Nuclear IRS-1 DNA repair and mutagenesis in medulloblastoma" that was submitted by [Dr. Krzysztof Reiss](#) has also received an outstanding priority score of 119.

CONFERENCES AND SYMPOSIA

The International Society for Neurovirology held its 8th [International Symposium on Neurovirology](#) from October 29 to November 2, 2007 at the US Grant Hotel in San Diego, California. The Department of Neuroscience was well-represented. Drs. Khalili, Gordon and Rappaport chaired sessions, Drs. Langford, Peruzzi, and Sawaya gave oral presentations, and Dr. Georgina Perez-Liz gave an oral presentation as an Investigator in Training. In addition, other members of our department presented twenty posters.

UPCOMING EVENTS

2nd [International Conference on Viral Oncology](#)

Philadelphia, Pennsylvania USA.
September 2008

9th [International Symposium on Neurovirology](#)
Miami, Florida USA. Spring 2009

SPECIAL ACKNOWLEDGMENTS



The Department of Neuroscience recognizes the efforts of [Denise Hawkins](#), who joined our department in 2004 as a laboratory aide. Denise provides excellent service to each of the laboratories and is an integral component to the efficient and seamless operation of our Department.

NEW ADDITIONS

The Department of Neuroscience is pleased to welcome [Kristine Plegaria](#), Administrative Assistant, to our administrative staff. Kristine joined us just before the holidays and has quickly become a key member of our team.



For more information, please visit us at http://www.temple.edu/medicine/departments_centers/basic_science/neuroscience.htm