



Pharmacological
Sciences

Stony Brook University School of Medicine



Summer | 2012 | Issue 2

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Department of Pharmacological
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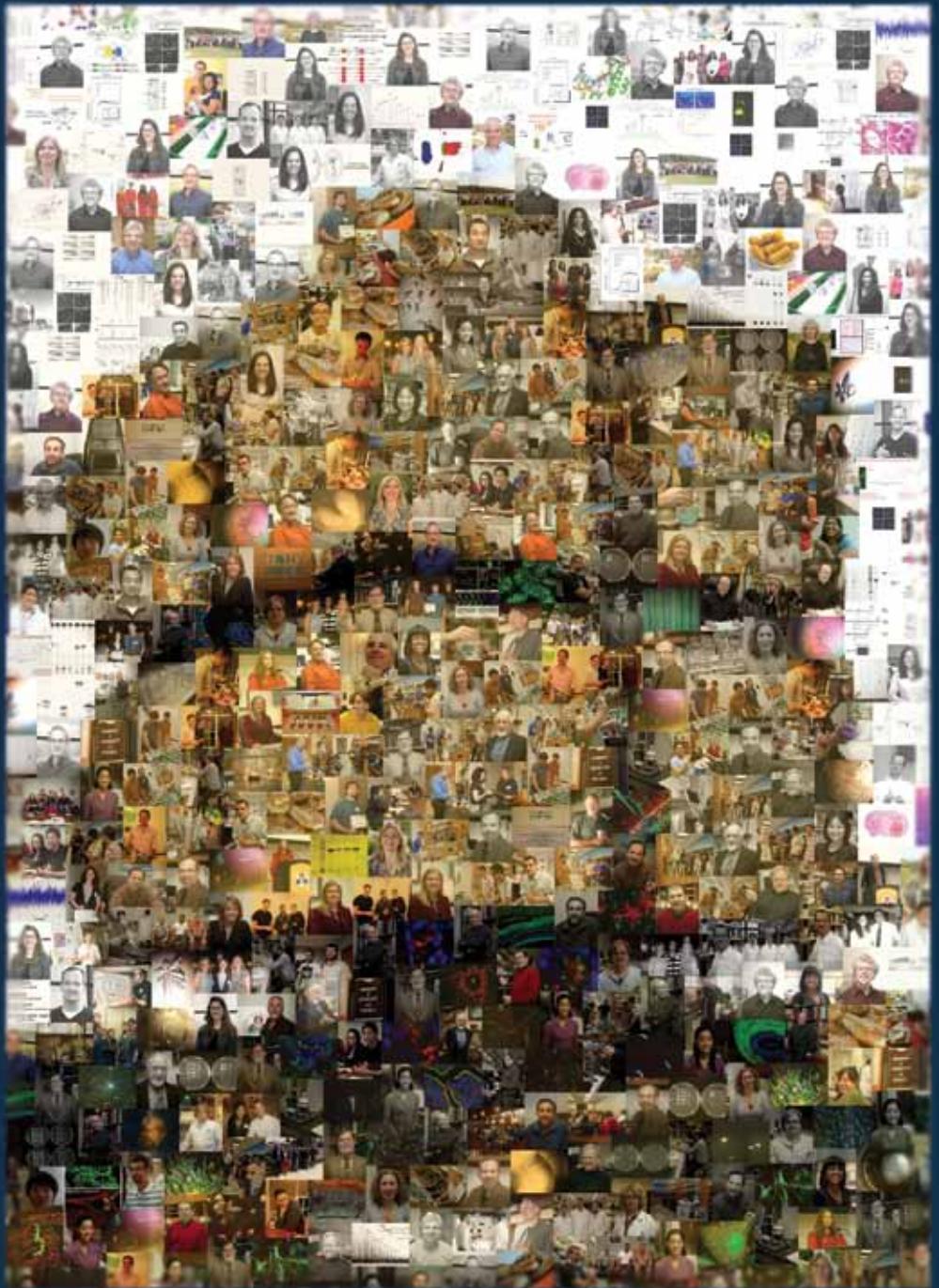
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Stony Brook
University

Department of Pharmacological Sciences
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School of Medicine Health Sciences Center

Faculty Awards



Congratulations to Dr. Arthur Grollman, who received the EMS Award from the Environmental Mutagen Society in October 2011.

Dr. Grollman was recognized for his “fundamental studies on the mechanisms of mutagenesis and DNA repair, including public health investigations linking environmental mutagens to human diseases.” He is the 39th recipient of this annual award.

In addition, related work from Drs. Moriya and Grollman was highlighted by the National Institute of Environmental Health Sciences in their November 2011 selection of notable papers:

Moriya M., et al. TP53 Mutational signature for aristolochic acid: an environmental carcinogen (2011) *Int. J. Cancer*. 129, 1532-1536.

Chair's Message

2012 ushers in change for the Department. We bid farewell last year to Dr. Howard Crawford, our local pancreatic cancer maven, as an excellent opportunity beckoned to him from the Mayo Clinic, and we now look forward to recruiting new cancer biologists, happily in collaboration with the freshly supercharged SBU Cancer Center.

The Cancer Center, directed by Dr. Yusuf Hannun, will be housed in a new Cancer Center research building, accompanied by space for a Center for Bioimaging and a new Children's Hospital. Dr. Hannun, and his spouse, Dr. Lina Obeid, both experts in lipid signaling in the context of cancer, bring to SBU a strong research program developed at the Medical University of South Carolina that complements signaling and lipid biology programs in Pharmacology.

We welcome Dr. Obeid to the Department as a joint faculty member and to the Graduate Program in Molecular and Cellular Pharmacology, along with the MD-PhD, MD, and PhD students and faculty that are accompanying her and Dr. Hannun to SBU.

The Graduate Program is strengthened by other great additions this year, including Dr. Ken Shroyer, MD, PhD, a cancer biologist and the Chair of Pathology, Dr. Shaoyu Ge, an expert on neuronal stem cells in the Department of Neurobiology and Behavior, and Dr. Leemor Joshua-Tor, Ph.D, HHMI, a structural biologist with current interests in RNAi pathway proteins, from CSHL.

The Department physical infrastructure continues to improve with completion of the long-awaited quadrant for Structural Biology on the 7th floor of the Basic Sciences Tower. The Structural Biology space houses the labs of Drs. Markus Seeliger and Miguel Garcia-Diaz, and we look forward to recruiting a third investigator with synergistic interests to complete the lab.

The Structural Biology quadrant was specially designed to contain facilities for computational biology and crystallography experiments, making it a core of expertise and technology that creates opportunities for collaboration with many other faculty and research groups in the School of Medicine.



With best wishes,

Michael A. Frohman

Department of Pharmacological Sciences

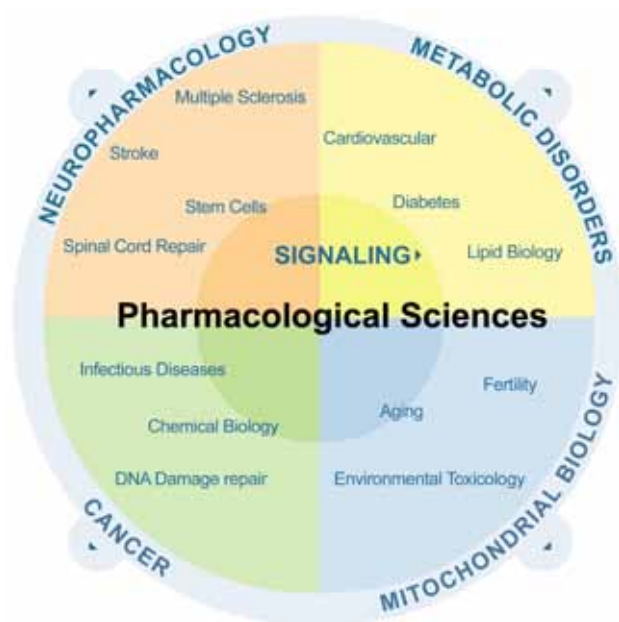
Research Highlights

Neurobiology of Disease & Development

D. TALMAGE. S. J. Canetta, et al. (2011) Type III Nrg1 back signaling enhances functional TRPV1 along sensory axons contributing to thermal pain sensation and hyperalgesia. *PLoS One.* 6, e25108. [PMID: 21949864]

S. TSIRKA. N. Bukhari, et al. (2011) Axonal Regrowth after Spinal Cord Injury via Chondroitinase and the Tissue Plasminogen Activator (tPA)/Plasmin System. *J. Neurosci.* 31, 14931. [PMID: 22016526]

S. TSIRKA. H. Zhai, et al. (2011) Annexin A2 promotes glioma cell invasion and tumor progression. *J. Neurosci.* 31, 14346. [PMID: 21976520]



Molecular Mechanisms of Signaling

C. MALBON. S. Gao S, et al. (2011) AKAP12 and AKAP5 form higher-order hetero-oligomers. *J. Mol. Signal.* 6, 8. [PMID: 21831305]

C. MALBON. R. K. Bikkavilli, C. C. Malbon (2011) Arginine methylation of G3BP1 in response to Wnt3a regulates β -catenin mRNA. *J. Cell Sci.* 124, 2310-20. [PMID: 21652632]

Genome Stability and the Environment

C. DE LOS SANTOS. M. Lukin, et al. (2011) Novel post-synthetic generation, isomeric resolution, and characterization of Fapy-dG within oligodeoxynucleotides: differential anomeric impacts on DNA duplex properties. *Nucl. Acids Res.* 39, 5776. [PMID: 21415012]

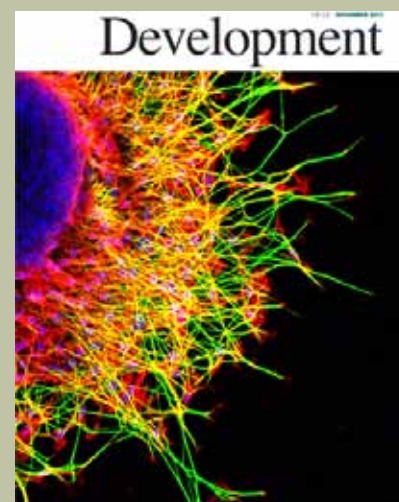
A. GROLLMAN, K. DICKMAN. B. Jelakovi, et al. (2011) Aristolactam-DNA adducts are a biomarker of environmental exposure to aristolochic acid. *Kidney Int.* [PMID: 22071594]

New and Notable

Dr. David Talmage, Dr. Lorna Role (Neurobiology & Behavior), and their colleagues at Harvard Medical School show in a recent issue of *Development* that the type III isoform of neuregulin 1 regulates axon pathfinding.

Their findings “reveal a molecular mechanism whereby type III Nrg1 signaling can regulate the responsiveness of neurons to a guidance cue, and show that type III Nrg1 is required for normal sensory neuron survival and axon pathfinding in both central and peripheral targets.”

Their work was featured on the cover:



Hancock, M.L., Nowakowski, D.W., Role, L.W., Talmage, D.A. and Flanagan, J.G. (2011) Type III Nrg1 regulates guidance of sensory projections in the developing spinal cord and periphery. *Development*, 138, 4887-4898. [PMID: 22028026]

Researcher Spotlight: The Vinh Ho

by Burak Derkunt



In his thesis research, Dr. The Vinh Ho played a key role in establishing the first *in vitro* ICL repair assay for elucidating the mechanism of replication-coupled DNA interstrand crosslink (ICL) repair.

After obtaining his PhD, Vinh moved to Switzerland to take on a new challenge with Tecan Group Ltd., global provider of advanced automation and detection solutions for life sciences laboratories.

On the PhD: “I’m happy how [my graduate work] turned out. It was frustrating to work on ICL repair in the beginning because of the lack of knowledge in the field. However, I was fortunate to work on multiple approaches, and had a great experience working through my PhD.”

Advice to current students: “Even in these economically challenging times there are opportunities for all of you.”

“The focus of graduate school is to educate people, open their minds for possibilities in order to solve problems wherever they are.”

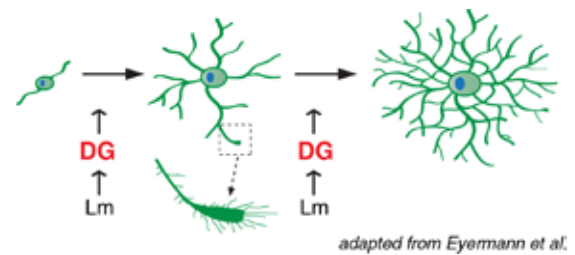
Recent Research: Neural Cell Differentiation and Passing Over DNA Crosslinks

by Wahida Ali

In the *Journal of Neurochemistry*, Christopher Eyermann from the Colognato lab reports that the receptor protein dystroglycan, through its interaction with the adhesion protein laminin, plays important regulatory roles in promoting the differentiation of brain oligodendroglia.

Building on reports that laminin enhances the surface area of differentiating oligodendrocytes, Chris observed increased process formation and outgrowth, filipodia formation, and complexity of process branching in newly formed oligodendrocytes (see figure below). He then showed that these changes are significantly reduced when dystroglycan function is muted by siRNA or blocking antibodies.

“These results suggest that dystroglycan-laminin interactions influence oligodendroglial process dynamics and therefore may regulate the myelination capacity of individual oligodendroglia,” says Chris.

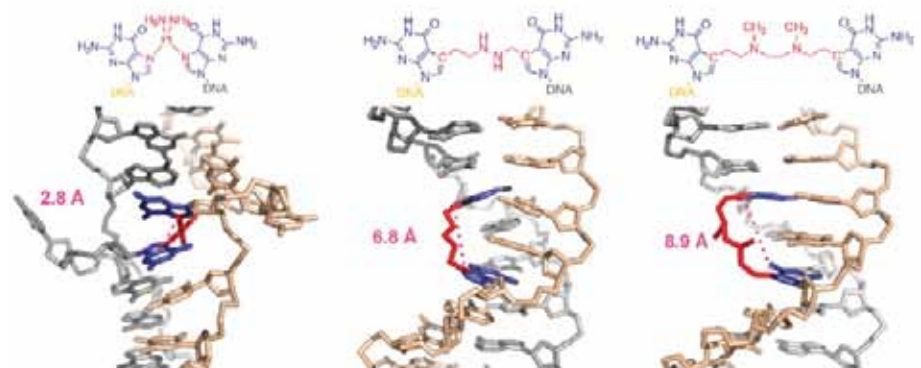


Eyermann C., Czaplinski K., Colognato H. Dystroglycan promotes filopodial formation and process branching in differentiating oligodendroglia. *J Neurochem.*, in press [PMID: 22117643]

In a pair of papers published in *Cell* and *Nucleic Acids Research*, The Vinh Ho and Angelo Guainazzi from the Schärer lab and collaborators from Harvard Medical School used defined DNA crosslink substrates to elucidate the mechanisms of the eukaryotic DNA replication machinery.

In their work in *Cell*, they compared the effect of site-specific blocks affecting one or two strands of DNA on replicative helicase translocation. Based on this and other supporting data, they concluded that the eukaryotic replisome complex translocates along ssDNA—not dsDNA—in S phase. Their results have implications for fundamental models of replisome architecture, assembly, and interactions with DNA damage lesions.

In the *Nucleic Acids Research* paper, Vinh systematically investigated how structural variation in interstrand crosslinks (ICLs) affects the ability of DNA



repair polymerases to bypass the lesions. Using a series of ICLs synthesized by Angelo that induce various degrees of DNA helix distortion, Vinh found that the amount of dsDNA surrounding the crosslink and the length of the interstrand linker greatly influenced bypass efficiency.

The Schärer lab's findings provide insight into the fundamental biochemistry of translesion synthesis polymerases, with implications for unraveling the multiple pathways involved in ICL repair and how they are dysregulated in diseases such as Fanconi Anemia.

Fu Y.V., Yardimci H., Long D.T., **Ho T.V.**, **Guainazzi A.**, Bermudez V.P., Hurwitz J., van Oijen A., **Schärer O.D.**, Walter J.C. (2011) Selective bypass of a lagging strand roadblock by the eukaryotic replicative DNA helicase. *Cell*. 146, 931-41. [PMID: 21925316]

Ho T.V., **Guainazzi A.**, **Derkunt S.B.**, Enoiu M., **Schärer O.D.** (2011) Structure-dependent bypass of DNA interstrand crosslinks by translesion synthesis polymerases. *Nucleic Acids Res.* 39, 7455-64. [PMID: 21666254]

Fond Farewell for a Mentor, Colleague, and Friend

by Cindy Leiton

In September 2011, the department gathered to bid farewell to Dr. Howard Crawford, a department faculty member since 2003. During his tenure at Stony Brook, Dr. Crawford advised several students in the MCP program, most of whom are now post-doctoral fellows in distinguished laboratories and institutions and are continuing to pursue interesting and exciting research, no doubt thanks to Dr. Crawford's conscientious advising and mentorship.

Dr. Crawford contributed to the department and the university in diverse ways, including his involvement in the Medical Scientist Training Program and the Cancer Center. We thank Dr. Crawford for being an admirable colleague, friend, mentor, and teacher and wish him all the best in his new position as associate professor at Mayo Clinic Florida.



All the best, Howard!

High School Students in Department Labs Garner Top Honors

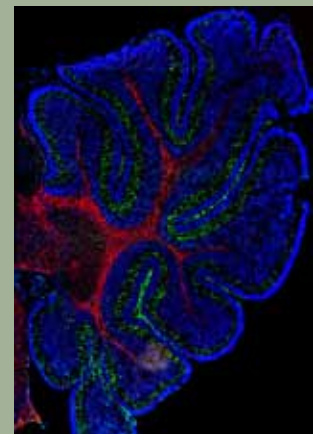
In January 2012 two high school students mentored by Dr. David Talmage and Dr. Lorna Role (Neurobiology & Behavior) were announced as finalists in the prestigious 2012 Intel Science Talent Search:

Savina Kim, Commack High School
"Cognitive Deficits in Neuropsychiatric Disorders".

Neil Mehta, Jericho High School
"Co-Restoration of Type III Nrg1 Back Signaling through Depolarization: Implications for Schizophrenia."

"I would like to express my admiration for their amazing dedication and work ethic," says Dr. Talmage. "They have been inspiring to watch over the last year. These are two independent young scientists: they formulated and executed their projects on their own."

Stony Brook University mentored a record 8 of the 40 competition finalists this year.



Laminin-expressing cells (green) and nascent white matter (red) in the developing cerebellum (F.McClenahan, Colognato Lab)

MCP Graduate Student Awards & Presentations

FELLOWSHIPS

Eileen Carpenter

Predocorial Fellowship
NIH Ruth L. Kirschstein NRSA
Fellowship for MD/PhD (F30)

Cindy Leiton

Predocorial Fellowship
Neuroscience Scholars Program
Society for Neuroscience

Ashleigh Pulkoski-Gross

2011 Chemical Biology Training
Program (SBU)

Luisa Torres

2011-2012 Fellow, 3MT
Integrative Graduation Education &
Research Training Program (SBU)

MEETING PRESENTATIONS

Wahida Ali

"Altered PA localization leads to
abnormal actin dynamics in innate
immune cells from mice lacking
phospholipase D isoforms." (2011)
**16th Phagocyte Gordon Research
Conference**. Davidson, NC. (Poster)

Jim McCann

"Organization of PDZ Domains
in Full-Length PSD-95". (2011)
**Biophysical Society 55th Annual
Meeting**. Baltimore, MD. (Poster)

Onika Murray

"Phosphosulindac inhibits
pancreatic cancer growth" **14th
International Symposium on
Molecular Medicine**. Rhodes,
Greece. (Talk. Session Co-chair)

Messenger Molecule Tells Microglia Which Way to Go

GRADUATE STUDENT PROFILE

by Luisa Torres



The newly minted Dr. Yao celebrates his well-deserved title at his thesis defense party.

Yao Yao obtained both his undergraduate and masters degrees in pharmacology at Sichuan University in China. He then moved to the U.S in 2007 and joined the lab of Dr. Stella Tsirka. Yao's work focuses on the role of monocyte chemotactic protein-1 (MCP-1) in microglia recruitment during brain injury, and the effect of MCP-1 cleavage on blood-brain barrier integrity.

Yao's interest in microglia originates from his master's research, which focused in part on lycopene and its effects on cerebral ischemia. While at SBU, Yao received a number of awards from Sigma Xi for research support and travel. In addition, in 2009 he won a BioLegend Young Investigator Travel Award to attend the Gordon Research Conference on Chemotactic Cytokines in Lucca, Italy.

As a student in the Tsirka lab, Yao has published on diverse aspects of MCP-1, including its chemotactic potency, its role in blood-brain barrier integrity, the molecular regulation of these activities. His latest publication details the influence of chemotactic signaling on microglia recruitment in intracerebral hemorrhage.

Yao defended his dissertation in April 2011 and is now a postdoctoral fellow at Rockefeller University. In the words of his labmates, who wrote for him the traditional Tsirka-lab good-bye song: "So, you're all done and you've got yourself four papers / Because no one could do it better / You're a doctor, so when's it gonna sink in? / Manhattan just won't know what hit them!"

Yao Y., Tsirka S.E. The C terminus of mouse monocyte chemoattractant protein 1 (MCP1) mediates MCP1 dimerization while blocking its chemotactic potency. *J. Biol. Chem.* 2010 285, 31509-16. [PMID: 20682771]

Yao Y., Tsirka S.E. Truncation of monocyte chemoattractant protein 1 by plasmin promotes blood-brain barrier disruption. *J. Cell Sci.* 2011 124,1486-95. [PMID: 21486949]

Yao Y., Tsirka S.E. Mouse MCP1 C-terminus inhibits human MCP1-induced chemotaxis and BBB compromise. *J. Neurochem.* 2011 118, 215-223. [PMID: 21615737]

Yao Y., Tsirka S.E. The CCL2-CCR2 system affects the progression and clearance of intracerebral hemorrhage. *Glia.* 2012 60, 908-18. [PMID: 22419223]

Annual Pharmacological Sciences Symposium

by Cindy Leiton

The department gathered for its annual symposium on September 14, 2011, at the Old Field Club adjacent to beautiful Stony Brook Harbor.

This year's program included talks from a wide variety of graduate program faculty, including Dr. Maricedes Acosta-Martinez, a recent addition to our program faculty and the newest member of the Department of Physiology and Biophysics.

Faculty talks were complemented by research "snapshots" presented by third-year graduate students. Each snapshot was a one-slide, five-minute presentation providing a synopsis of a definitive experiment that proved exciting and revealing. Presenters had the task of keeping the message clear and concise—and competitive. This year's "Best Snapshot" award went to Elena Hambardjjeva, a fourth-year student in the Garcia-Diaz lab,



At Old Field Club (l-r): **Eileen Carpenter**, Julie Cavallo, Jason Hall, Tiffany Tsui, **Jim McCann**, **Elena Hambardjjeva**, Dr. Maricedes Acosta-Martinez, Viki Fischer, Ashley Pulkoski-Gross, George Georghiou, Lynda Perdomo-Ayala, Janice Kito, Dr. Jessica Seeliger, Viki Fischer, Luisa Torres.

Also awarded were the annual van der Kloot Awards for Excellence in Research and Teaching. Jim McCann, a fifth-year student in the Mark Bowen lab, was awarded for his structural studies on tandem PDZ domains, which appeared in *Structure* in 2011 [PMID: 21645852]. The award for excellence in teaching was given to Elena Hambardjjeva for her successful and highly esteemed teaching assistance in the undergraduate pharmacology laboratory class.

Finally, all Ph.D. candidates presented posters and competed for the fourth and final prize, which was won by Eileen Carpenter, a third-year MD/PhD student in the Richard Lin lab, for her work on the role of PI3 kinase in pancreatic cancer.

We congratulate all of the winners and wish them continued success in their research and teaching!

Why I Came to Stony Brook for A Ph.D. in MCP

Many diverse factors go into choosing a graduate school. In this recurring feature, current graduate students weigh in on why they chose Stony Brook MCP.

CINDY LEITON
Colognato Lab



I was recruited to the MCP program through the Alliance for Graduate Education and the Professoriate (AGEP), an NSF-funded program at SBU that supports minority students in the sciences.

As an undergraduate, my summer placement in Holly Colognato's lab provided me with my first bench experience and was crucial to my decision to apply to graduate school.

I loved the ambiance and positive energy of the students in the MCP program, and I quickly became aware of the department's strong reputation.

I knew that Stony Brook was going to be a great place to develop as a scientist.

Department of Pharmacological Sciences – Summer 2012

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Stony Brook University/SUNY is an affirmative action,
equal opportunity educator and employer.

A Warm Welcome to Graduate Program Coordinator Odalis Hernández!



The department is pleased to introduce our new Graduate Program Coordinator, Odalis Hernández. Odalis joined in January 2012 from the Music Department, where she handled the progress of around 250 students. In her new position, she administrates the MCP graduate program as well as the graduate program in Neurobiology and admissions for Biophysics and Physiology. As GPC, Odalis wants to help students succeed by personalizing their experience. “I want students to know they can count on me if they need help.” She says that she couldn’t be happier with her experience interacting with everyone in the department.

“The sense of community that has been built in this department is commendable, and I think it’s a major part of what makes MCP an attractive graduate program.”

When she’s not shepherding students, Odalis can be found delving into the arts scene as a freelance director, producer and stage manager—including for the opera here at Stony Brook University. Whether she is behind the scenes at a performance or here in the main office, we are all glad to have her on our team.



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