Dear VMD-PhD Alumni,

Greetings from Penn! This has been a busy spring for us. We have gone through another admissions season, worked hard on fund raising, and participated in the Annual Student Research Day. Our current students have focused on their curriculum and have generated an impressive list of publications this year (see below). Due to the generous support by alumni, the Vice Provost for Research (Steve Fluharty), the Mari Lowe Cancer Center, various NIH grants, private donors, the MD-PhD program, and the Office of the Dean, the Program was able to offer admission to three new students. This was a major accomplishment given our current difficult financial situation. All three candidates accepted the offer and will attend in the fall. The profiles of these new students will be provided in the Fall 2010 Newsletter.

While we have been successful this past admissions cycle, next year will require us to continue to find new sources of financial support. In particular, we need to identify matching funds for the $500,000 pledged by overseer Mindy Heyer. If you know of any sources for this endowment, or for any other aspect of the Program, please contact me.

We are particularly proud of our alumni and fondly recall our VMD-PhD 40th Anniversary Alumni Reunion Symposium held one year ago. Three new students will join the alumni ranks this spring and their information is presented here. Be sure to check out your alumni listing on our website. We hope this will enable our current students to learn more about those who completed the Program ahead of them, and will serve as a way for them to seek out advice on science, medicine, and career.

Wishing you the best in 2010,
Michael Atchison, Ph.D.
Director, VMD-PhD Program

Alumni are Online!
Check out:
www.vet.upenn.edu/Research/ResearchTrainingOpportunities/VMDPhDProgram/OurAlumni/
Find your profile, and send us feedback!
The 2010 Phi Zeta Student Research Day, March 25, 2010

Dr. Blackwell and Associate Dean for Research Phillip Scott

Keynote Speaker: Michael J. Blackwell, DVM, MPH, Assistant Surgeon General, USPHS (Ret.), and President and CEO of Blackwell Consulting, LLC.

Dr. Blackwell’s talk focused on 'One Health' and why veterinarians are critically needed in public practice (e.g. public health, research, regulatory medicine) and in clinical practice. Dr. Blackwell has enjoyed a productive and successful career, serving in diverse positions. He earned a doctor of veterinary medicine degree in 1975 from Tuskegee University and, in 1981, a masters of public health degree from Loma Linda University in California. He has served on many charitable trust boards and the national American Veterinary Medical Association One-Health Initiative Task Force. He earned the rank of Assistant Surgeon General (Rear Admiral) of the US Public Health Service Commissioned Corps after 20 years of active duty. From 2000 to 2008 Dr. Blackwell served as Dean of the College of Veterinary Medicine, University of Tennessee. From 1999 to 2000, he served as the Chief of Staff, Office of the Surgeon General. Prior to this Dr. Blackwell served for 20 years as an official of the Food and Drug Administration (FDA). During this interim with the FDA, he covered major mission areas in both human and veterinary medicine. Dr. Blackwell also had more than 15 years of experience as a private veterinary practitioner. This diverse background prepared Dr. Blackwell to assist with providing solutions to many of today's public health challenges. From 1994 to 1998 Dr. Blackwell served as the Chief Veterinarian of the United States Public Health Service (USPHS). In this role he was chief advisor to the Surgeon General of the United States. In fact, Dr. Blackwell, served as an advisor with all Surgeons General from C. Everett Koop to David Satcher.

This year's’ VMD-PhD student presentation winners were:

First Place VMD-PhD Award: Gregory Rak
Granule secretion through the actin network at the lytic NK cell synapse.
Greg is a 4th year VMD-PhD student in the laboratory of Jordan Orange. His thesis work focuses on the NK cell response and dendritic cell interactions.

Second Place VMD-PhD Award: M. Noelle Knight
Testing models of Sup35 prion structure.
Meghan is a first year VMD-PhD student in the BMB graduate group. Her prior work focused on molecular structural biochemistry of proteins in yeast.

Third Place VMD-PhD Award: Catrina King
Constitutive Lin28B expression promotes tumorigenesis in the colon.
Catrina is a 5th year VMD-PhD student in the laboratory of Anil Rustgi. Her thesis work focuses on micro-RNAs and colon cancer.
The VMD-PhD poster winners were:

First Place: Abigail Shearin
*Whole genome association studies and fine mapping of loci for canine histiocytic cancer.*
Abby is an incoming VMD-PhD student who has spent the past two years working at NIH as a HHMI fellow in the lab of Elaine Ostrander.

Second Place: LaTasha Crawford
*Towards an understanding of the pathophysiology of anxiety: social stress alters the inhibitory input to serotonin neurons.*
LaTasha is a 6th year student in the laboratory of Sheryl Beck. Her work focuses on serotonin signaling and stress.

GRADUATING VMD-PHD STUDENTS

Xuan Pan
Mentor: Michael Atchison
Xuan Pan’s thesis project focuses on how transcription factor YY1 regulates B cell development. Her work focused on three inter-related projects. First, she worked on how elevated levels of YY1 promotes affects long-term hematopoietic stem cell development as well as apoptosis specifically in B cells. Xuan’s second project focused on how YY1 Polycomb Group (PcG) function influenced B cell development. For these studies, she performed bone marrow reconstitution studies in a YY1 conditional knock-out system using a YY1 mutant that removes the 25 amino acid REPO domain necessary for PcG function. These studies showed that YY1 PcG function is required for development past the pro-B cell stage. In Xuan’s third project she found that the YY1 REPO domain physically interacts with condensin and cohesin proteins and co-localizes with YY1 at various sites across the Ig kappa locus. These binding sites are believed to be involved in Ig locus contraction needed for rearrangement of distal V genes. She utilized both transgenic mouse and RNAi methods to study these mechanisms. Her work addresses key functions in B cell biology and development, and may also have clinical applications.

Xuan will complete her PhD work in June 2010. In mid-June she and her husband will move to Michigan where she will pursue a small animal clinical internship at Michigan State University. After completion of this program she plans to pursue clinical residency.

www.vet.upenn.edu/research/programs/vmstp
Mary’s thesis work focused on the effect of a hypoxic environment on macrophage function. Specifically, she was interested in effects on nitric oxide production, one of the key components of the respiratory burst. Oxygen is a known substrate for nitric oxide, but the amount of oxygen needed and speed at which changes in oxygen tension would alter nitric oxide production were unknown. She used a system developed by her mentor, Cindy Otto, to show that changes in physiologic oxygen tensions significantly alter nitric oxide production within 30 seconds. This research has direct relevance to how we think about macrophage function in wounds and tumors where oxygen is much lower than normal due to an aberrant vascular supply.

Post graduation, Mary has received a 3-year fellowship from the Racing Medication and Testing Consortium to study equine pharmacology at Penn's New Bolton Center with the guidance of Dr Larry Soma. They plan to use proteomics based techniques to enable the detection of horses treated with shock wave therapy prior to racing. Shock wave therapy has been shown to be as effective as denerving a horse in the first 24 to 36 hours after treatment, which means that horses running may over exert and seriously injure themselves. The racing jurisdictions consider it a priority to minimize catastrophic breakdowns at the track, and this research will help enable detection of horses that are at risk due to the illegal usage of shockwave therapy.

Jessica Bertout
Mentor: Celeste Simon
In July, Jessica, her husband Steve, daughter Isabelle, Golden retriever Tennessee, and cat Nikita are all moving to Seattle where her husband has accepted a human anesthesiologist position and she intends to pursue a post-doc in cancer biology after taking a little time with their soon-to-be-born new baby. Jessica is also considering pursuing an internship and residency in oncology to complement her research interests. Ultimately, she would like to become involved in clinically oriented academic research and teaching in oncology to hopefully make a difference both for our veterinary and human patients.

Jessica’s thesis focused on the role of Hypoxia Inducible Factors (HIF1alpha and HIF2alpha) in tumorigenesis and tumor responses to radiation therapy. Hypoxia Inducible Factors (HIFs) are alpha-beta heterodimeric transcription factors that regulate important cellular processes, allowing both normal and cancerous cells to adapt to low oxygen conditions. Two central HIFalpha subunits, HIF1alpha and HIF2alpha, are highly expressed in many tumors and are correlated with poor patient prognosis. Jessica sought to further characterize their roles in cancer therapy responses and in tumorigenesis. While HIF1alpha promotes p53-dependent cell death in tumor cells, HIF2alpha has been suggested to regulate a subset of antioxidant enzymes, leading us to hypothesize that HIF2alpha may protect cells against Reactive Oxygen Species (ROS)-dependent damaging agents such as radiation. She demonstrated that HIF2alpha inhibits the p53 pathway both in vitro and in Renal Clear Cell Carcinoma (ccRCC) patient samples, by limiting the amount of DNA damage incurred by the cell. HIF2alpha’s protective effect stems from its ability to maintain cellular redox balance, in the absence of which intracellular ROS increase and cells become much more sensitive to damage. Moreover, a novel p53 mutant mouse model suggested a role for HIF1alpha-mediated Notch stabilization in tumorigenesis. Indeed, HIF1alpha heterozygosity led to a significant reduction in the incidence of thymic lymphomas strongly associated with impaired Notch pathway activity. Both studies elucidated mechanisms whereby the HIFalpha subunits impact directly on tumor biology and provided evidence in support of the development of specific HIF inhibitors for use in cancer therapy.
Student Publications


**LaTasha K Crawford**, Caryne P Craigie, and Sheryl G Beck. Increased intrinsic excitability of lateral wing serotonin neurons of the dorsal raphe: a mechanism for selective activation in stress circuits Journal of Neurophysiology.  Mar 17, 2010 (Pubmed ID 20237311)


www.vet.upenn.edu/research/programs/vmstp


Student Honors/Awards and Recognitions:


NIH Consensus Development Conference Statement: Lactose Intolerance and Health.

LaTasha Crawford
Abstract selected for oral presentation, Basic Research "Hot Topics” Session, American College of Neuropsychopharmacology 48th Annual Meeting, 2009
Women In Neuroscience Graduate Student Travel Award, Society for Neuroscience 2009
Speaker Award (3rd Place), Phi Zeta Veterinary Student Research Day, March 2009
Pre-doctoral National Research Service Award (NRSA), NIMH, NIH 2007-present

www.vet.upenn.edu/research/programs/vmstp
Advising News

As the VMD-PhD Program has grown considerably over the past nine years, new efforts at student advising have been implemented. The VMD-PhD Advisory Committee consisting of Michael Atchison, Bruce Freedman, Kurt Hankenson, and Sue Volk now share all advising responsibilities. In addition, the committee has implemented some new efforts. Specifically, new programs for preparing students for the transition into clinical rotations have been developed, and discussion sessions on applying for clinical internships have been held. These activities have been spearheaded by Susan Volk. We hope that these new advising initiatives will augment the mechanisms already in place, and will serve our current students needs.

Fundraising

Heyer Endowment for the VMD/PhD Program

Through the generous gift of Mindy and Andy Heyer, a one million dollar endowment for the VMD/PhD Program has been launched. We are very excited about this new endowment because it will enable us to continue to expand the VMD/PhD Program at Penn, and to initiate innovative research and educational experiences for our students. This is a matching endowment, which requires us to raise an additional $500,000 from other sources. If you know of matching sources, please let us know.

Mindy Heyer, College ’70, Wharton ’80, currently serves as the Chair of the Board of Overseers for Penn Vet. Andy Heyer, Wharton ’79, is a member of the University Board of Trustees.

To contribute to this endowment, please contact:

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