

M.D./Ph.D. News

PENN STATE MILTON S. HERSHEY MEDICAL CENTER • PENN STATE COLLEGE OF MEDICINE

Alumni Spotlight

COMPUTING THE DATA WAVE...

BY KIRK SHELLEY MD, PHD '81, PROFESSOR OF ANESTHESIOLOGY,
YALE UNIVERSITY, NEW HAVEN, CT

"So, you know something about computers?" That question started quite an adventure for me. In 1976, as a first year medical student, it was a fairly reasonable question coming from one of the biochemistry professors. Like many of my generation, I was infatuated with these new 'thinking machines'. At that time, I use to hang out at the medical center computer center (Fig 1) which was running a PDP-11 with 256k core RAM (Fig 2). Trust me, in its day it was a monster requiring a full time staff and rooms filled with equipment.

That professor, Alexander McPherson, outlined a medical student project for me that, at its core, used Fourier analysis to examine electron micrographs of crystalline structures. Fourier analysis allows one to take a complex waveform and break it down into its fundamental components. At that time, computers were allowing for a renewed examination of the complexity of nature.

In my case, this opportunity created a situation where a simple medical research project quickly spiraled out of control. Towards the end of summer, spent working in McPherson's lab, he declared that with six months of additional effort a PhD was possible. When I entered medical school (mid 1970's), the idea of combining an MD with a PhD was fairly unheard of. While the extra degree was intriguing, the idea of working full time with a computer system on real world problems was intoxicating. Regarding the effort required to get a PhD, one clearly has to have a passion for research; otherwise I doubt it is worth the effort.

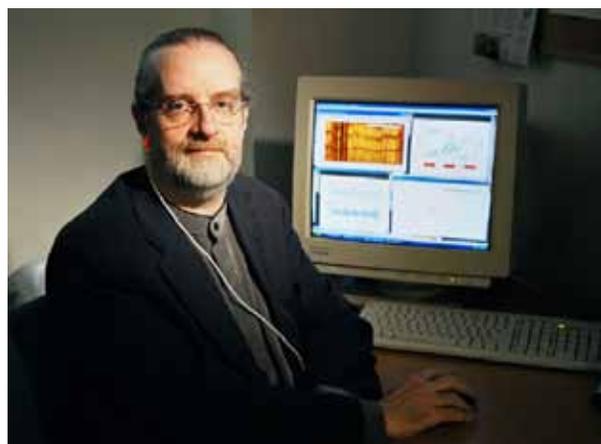
In the end, it took more than six months. My thesis required that I write a 10,000 line FORTRAN program and a number of complex interfaces to early computer devices (i.e. scanners, graphic terminators, color printers, etc.). The final thesis was 234 pages long. It was also one of the first Hershey Medical Center theses done inside a primitive word

processor. I used a program (RUNOFF) designed to do line editing of computer code. It should be noted that I was able to use my knowledge of FORTRAN to fulfill my foreign language requirement. Computers were considered that exotic at the time.

Suffice it to say, the project would not make a good high school science fair project today, with its 10,000 line computer program now reduced to less than a half a page of MatLab code. Computing capabilities have advanced that much. At the time, it was a bit of an overwhelming project and I was not sure I could succeed. It is now clear to me that one of the key jobs of the mentor is to generate problems at the edge of do-ability.

When it was over, I had clearly advanced my computer programming skills and learned digital signal processing, before it was even a defined field of study. Both skill sets have served me well, allowing me to design medical devices for patient monitoring (based mostly on photoplethysmographic technology). As important, if not more important, is that I learned the politics of academics. This included everything from the choice of members on my thesis committee, to working the red tape of the university when my mentor left for a chairmanship at another university. One quickly learns that research is never done in isolation, but always in the context of a complex real world.

Over time, I developed a computer related project with every member of my thesis committee. Some of these projects would go on to have a significant impact on their respective labs. The introduction of computers often allows the qualitative observation to be quantified for the first time. I believe these



Kirk Shelley, M.D.

side projects contributed as much to my being awarded a Ph.D. as my main thesis topic.

The training I received during the MD/PhD ultimately allowed me to straddle the line between Anesthesiology/Internal Medicine and Biomedical Engineering. In retrospect, Fourier analysis is one of the most powerful methods of analysis ever developed

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Space Flight

Dr. Henry J. Donahue is a Michael and Myrtle Baker Professor, Vice Chair for Research (Orthopaedics), and Director of the Division of Musculoskeletal Sciences in the Department of Orthopaedics and Rehabilitation here at the Penn State College of Medicine. Dr. Donahue began his training on the west coast, earning his Bachelor of Science from the San Diego State University and his PhD in Physiology from the University of California, Santa Barbara. He went on to complete a postdoctoral fellowship in Endocrinology at the Mayo Clinic in Rochester, Minnesota.

The focus of Dr. Donahue's current research involves the role of gap junctions in the bone cell response to physical signals as well as the effect of biomaterial surface characteristics on stem cell differentiation.

Dr. Donahue is principal investigator on two NIH R01 grants and others related to these topics. His laboratory utilizes numerous in vitro and in vivo models to study bone cell mechanotransduction. These include an in vitro fluid flow apparatus that allows for quantifiable fluid shear stress to be applied to cell cultures. In vivo, the laboratory utilizes a murine loading mechanism, a model of allograft transplantation to study fracture repair, and a hindlimb suspension model to study the effects of simulated microgravity. The lab was recently involved in an experiment aboard the space shuttle Atlantis designed to study the effects of spaceflight on bone cell differentiation.

Dr. Donahue has published numerous peer-reviewed articles over the course of his

career, including publications in top bone biology journals, including The Journal of Bone and Mineral Research, Bone, and The Journal of Orthopaedic Research. In addition to his research endeavors, Dr. Donahue has served as Director of the Graduate Program in Cellular and Molecular Biology (CMB) and as Member of the Board of Directors of the Orthopaedic Research Society. He also serves as President of the Derry Township Board of School Directors.

Dr. Donahue is currently training Shane Lloyd, an MD/PhD student in the CMB graduate program. Shane's research focuses on the role of the gap junction protein Connexin 43 in the bone loss associated with spaceflight or prolonged periods of immobilization.

KIRK SHELLEY (Continued from page 1)



Fig 1. The actual sign from the Hershey Medical Center Computer Center from the mid 1970's. I saved it from when the center finally closed its doors.



Fig 2. Front panel from a PDP 11/70 with toggle switches to allow one to enter the 'bootstrap' code to allow the machine to boot.

since its true potential is unleashed by computers. As the saying goes "once one discovers the hammer everything becomes a nail". In my case, my life's work would come from doing a Fourier analysis on the pulse oximeter waveform. The training from my graduate school days immediately told me that that the waveform was rich in physiologic modulations. A quick literature search made it clear that a majority of these modulations were not described.

Finally as way of closing advice to people new to research, or even experienced ones, I have found that every significant discovery I have

made over the years has started as an artifact. I am the first to admit that a well-designed study that works exactly just as planned is very satisfying. The well designed study 'not working' is in reality the true path forward. So study your outliers, as uncomfortable as they may make you. The real lessons from nature come from them.

Kirk Shelley is boarded in Anesthesia and Internal Medicine. He is a Professor of Anesthesia at Yale University where he heads the Ambulatory Surgery Division. Dr. Shelley obtained MD and PhD degrees (biochemistry) from Penn State University in 1981. His

research focuses on developing tools for the noninvasive measurement of physiologic parameters. The photoplethysmograph (PPG) has been a particular study focus for twenty years. The goal has been to understand the physiology that underlies the PPG components, associated with respiratory and venous modulations, and then to utilize this understanding to develop new methods of patient monitoring. He has numerous awards for his work and is the current President of the Society for Technology in Anesthesia (STA).

Space Flight

Shane Lloyd is an MD/PhD student working in the laboratory of Dr. Henry Donahue in the Department of Orthopaedics and Rehabilitation at Penn State College of Medicine. This summer, Shane was part of a collaborative research effort to understand the mechanisms underlying bone loss that occurs in the weightless environment of spaceflight. Dr. Donahue and Shane were invited to be a part of this collaborative research project, headed by principal investigators at Harvard, The University of North Carolina, and The University of Colorado. Shane's role in this study was to examine the effects of spaceflight on the ability of bone marrow stem cells to differentiate into bone-forming cells called osteoblasts. Fifteen mice were launched aboard the Space Shuttle Atlantis on July 8th, 2011, with an additional fifteen kept on the ground as controls. "The data we gain from this experiment will help to advance our understanding of bone loss that occurs with aging or prolonged periods of immobilization", said Dr. Donahue.

Our bones are continually being remodeled, reflecting competing processes of bone formation by osteoblasts and bone breakdown by osteoclasts. In the weightless environment of space, astronauts lose bone about ten times faster than a post-menopausal woman would here on Earth. It is not yet fully understood how the development of bone cells from stem cell precursors is affected by spaceflight, or what role this plays in the characteristic suppression bone formation and enhancement of bone breakdown observed in microgravity. "If the formation of osteoblasts is inhibited during spaceflight" said Shane, "then it might be possible to identify genes or proteins involved in this process". The hope is to eventually develop therapeutic countermeasures that can be utilized to prevent bone loss in astronauts and bed rest patients.

Shane Lloyd worked for three weeks at NASA's Space Life Sciences Laboratory at the Kennedy Space Center in Florida to complete this study. He was able to view the launch of Atlantis – the final mission in the space shuttle program – up close, from a special viewing area for NASA employees and families. Upon return of the shuttle, Lloyd harvested bone marrow from both spaceflight and ground control mice and then worked to culture these cells back here at the Penn State College of Medicine. Under the direction of Dr. Donahue, Shane will examine the rate of stem cell differentiation into bone-forming osteoblasts based on RT-PCR and western blot analyses of type 1 collagen, osteopontin, and osteocalcin expression, as well as enzyme assays of alkaline phosphatase activity, all of which reflect osteoblastic differentiation. Shane will also determine the rate at which the cell cultures form mineralized tissue. Results will be compared between spaceflight and control groups in order to determine the effect of microgravity.

Dr. Donahue notes that, "As we have become better at treating ailments like cancer and heart disease, people are now living longer and longer, and problems from age-related bone loss [like fractures and vertebral collapse] are becoming more common and need to be addressed." "A better understanding of microgravity-induced bone loss will help us better understand age-related bone loss." The project, funded by the Michael and Myrtle Baker Orthopaedic Research Endowment, is part of Shane's graduate thesis research, funded by the National Institutes of Health and Department of Defense. Shane's work explores the underlying mechanisms responsible for bone loss associated with spaceflight or prolonged periods of bed rest. In particular, Shane is interested in elucidating the role of a gap junction protein called Connexin 43 in this process. Shane says that he would "ultimately like to provide support for the notion of Connexin 43 as a potential target for the prevention of spaceflight-induced bone loss".



Congratulations Graduating Students



Vance Albaugh

Residency: Vanderbilt University Medical Center, TN
Specialty: General Surgery
2005-2011
Ph.D.-August 2009
M.D.-May 2011



Joon (Andy) Lee

Residency: University of Chicago Medical Center, IL
Specialty: General Surgery
2003-2011
Ph.D.-July 2009
M.D.-May 2011



Bozo Todoric

Residency: Lehigh Valley Hospital, PA (Transitional); Duke Eye Center, NC
Specialty: Ophthalmology
2004-2011
Ph.D.-June 2009
M.D.-May 2011



Violetta Kivovich

Residency: New York Presbyterian Hospital-Weill Cornell Medical Center, NY
Specialty: Pediatrics/Infectious Disease
2003-2011
Ph.D.-August 2009
M.D.-May 2011



Kimberly Lumsden

Residency: York Hospital
Specialty: Family Medicine
2003-2011
Ph.D.-April 2009
M.D.-May 2011

Recent Thesis Defenses:

Melanie Dispenza

UNDERGRADUATE DEGREE: BA/BS/05
University of VA
GRADUATE PROGRAM: Physiology
ADVISOR: Diane Thiboutot, MD
THESIS DEFENSE DATE: April 18, 2011
THESIS TITLE: "Immunomodulatory Effects of Isotretinoin in Vivo"

Carolina Pinzon-Guzman

UNDERGRADUATE DEGREE: BS/03 Texas A&M, TX
GRADUATE PROGRAM: Neuroscience
ADVISOR: Colin Barnstable, PhD
THESIS DEFENSE DATE: May 12, 2011
THESIS TITLE: "Protein kinase C (PKC) β 1 and γ isoforms are essential for rod photoreceptor differentiation"

James Bauer

UNDERGRADUATE DEGREE: BS/03 University of Wisconsin, Madison
GRADUATE PROGRAM: Bioengineering
ADVISOR: Christopher Siedlecki, PhD
THESIS DEFENSE DATE: May 24, 2011
THESIS TITLE: "Influence of surface composition and wettability upon contact activation of blood plasma"

Kathryn Erickson

UNDERGRADUATE DEGREE: BA/BS/03
University of Southern California
GRADUATE PROGRAM: Cell & Molecular Biology
ADVISOR: Philip Lazarus, PhD
THESIS DEFENSE DATE: June 9, 2011
THESIS TITLE: "Metabolism of Second-Generation Antipsychotics by Uridine Diphosphate-Glucuronosyltransferases"

Emilie Muelly

UNDERGRADUATE DEGREE: BA/BS/06
University of Pittsburgh
GRADUATE PROGRAM: Neuroscience
ADVISOR: Scott Bunce, PhD
THESIS DEFENSE DATE: June 14, 2011
THESIS TITLE: "Neuropsychiatric and Neurochemical Squelae of Maple Syrup Urine Disease"



Annual MD/PhD Retreat

The annual MD/PhD retreat was once again held in State College at the Penn State Conference Center on the weekend of March 26th. This year, the retreat's main talks focused on career options and career development. Two invited speakers, John Bogdan (NIH/NIAID) and Faoud Ishmael (Penn State MD/PhD program alumnus and current faculty member), spoke in depth about their respective career paths in government and academia. Additionally, a panel featuring Michael Verderame, Diane Thiboutot, Kenneth Keiler, and John Bogdan discussed alternate career pathways for physician scientists. The talks were not limited to professors and invited guests, however. Senior students Violetta Kivovich and Bozho Todorich both gave clinical case presentations, and many students in their graduate years participated in the Data Blitz, which were 5-minute talks about their research topics. Students also presented posters, and this year Theresa Carr and Emilie Muelly were honored for having the best abstracts of 2011.

On the last day of the retreat, breakout sessions divided current students in half by seniority. Older students discussed the transition from graduate school back to clinic, while less senior students gave each other advice about Step 1 and the transition into their labs. Elections for PSSA were also conducted, and the results were as follows: Dan Lapp was elected president and Darrin Bann and Francis LeBlanc were elected co-vice presidents. Many students also volunteered to help with various committee duties such as recruiting, retreat planning, newsletter composition, and social activities.

Luckily, the retreat was not all business. Students and faculty enjoyed mingling during the big group meals, getting to know one another outside of a normal school setting. There were also optional activities after hours, and many students ventured out to experience State College nightlife together.

New Physician-Scientist Welcome Reception

On October 19, 2010, the MD/PhD department held a dinnertime reception for the new physician scientists on campus. Students and faculty were able to familiarize themselves with one another at the University Conference Center in an informal atmosphere. Various faculty members also elected to speak briefly about their research interests, giving a quick summary of the projects in their labs.

Director's Letter, Fall 2011

This year marks several important transitions in leadership as the MD/PhD program moves forward. First, Diane Thiboutot, MD, has stepped down from her role as Co-Director of the MD/PhD program (but will remain on the steering committee) to assume her new role as Director of the CTSI Research Education and Training Program. Thanks again Diane for a job well-done, and best of luck in your new role in the CTSI. We welcome Dr. Leslie Parent, MD, as the new Co-Director of the MD/PhD program. Leslie brings a great deal of experience and energy to the program, having already served on the steering committee and as the residency advisor for MD/PhD students. Leslie received a BS degree from Dartmouth and her MD from Duke where she also completed a residency in Internal Medicine in the Clinical Investigator Pathway working in the lab of Warner Greene, MD, PhD. Leslie then did a clinical fellowship here at PSU and was a postdoctoral fellow in John Wills' lab. Leslie has spent her professional career at the College of Medicine where she is now Professor of Medicine and Chief of the Division of Infectious Diseases and Epidemiology. Leslie's research, which has been funded continuously by the NIH since 1993, focuses on understanding the molecular mechanisms of retrovirus assembly and retrovirus-cell interactions.

During the past year, we have added several new members to our steering committee. These include Jennifer Baccon, MD/PhD, John Wills, PhD, and our Vice Dean for Research, Dan Notterman, MD. Melissa Rolls, PhD, and Ken Keiler, PhD from the University Park campus have also joined the steering committee and have been hard at work screening applications and hosting students when they visit the UP campus. This year, Bill Su (G1) and Theresa Carr (G3) are the student representatives on the committee, and provide valuable insight about the program from the student perspective. Special thanks to Dr. Steve Rannels, Professor of Physiology, who recently stepped down from the committee, for his many years of service and valuable contributions to the MD/PhD program.

Over the past year, we have added several new training faculty to the MD/PhD program. These include Andra Hajnal, MD, PhD, José Stoute, MD, Chris Yengo, PhD, Faoud Ishmael, MD, PhD, and Jiyue Zhu, PhD. We would like to welcome these new members of the training faculty, and look forward to your participation in the program.

Finally, we have reconstituted our board of Internal Advisors. Our new advisory committee consists of Michael Verderame, PhD (Chair), Wafik El-Deiry, MD, PhD., Ross Hardison, PhD (University Park), Thomas Loughran, MD, Barbara Miller, MD, Dan Notterman, MD, Scott Selleck, MD, PhD (University Park), and Judy Todd, PhD (University Park). The Internal Advisors are advisory to the Co-Directors, and make recommendations regarding improvements

that can be made to the program. We also look forward to working with the two new chairs that were recently recruited to the College of Medicine. James Broach, PhD is joining us as Chair of Biochemistry and Molecular Biology, and Aron Lukacher, MD, PhD is coming from Emory University (where he was Co-Director of the MD/PhD program) to be Chair of Microbiology and Immunology. Welcome Drs Broach and Lukacher.

We've recruited another outstanding group of students from a variety of excellent undergraduate programs across the country. We're looking forward to getting to know them better as they emerge from the rigors of Anatomy and begin CMBMP. We salute our 2011 graduates and look forward to keeping in touch with them as continue on the pathway to careers as physician scientists.

Opportunities for graduate training on the University Park campus continue to grow. The proposal for the joint MD/PhD program in Engineering Sciences and Mechanics (ESM) has been submitted and is under review by Penn State's graduate council. We are excited by the opportunity to partner with other outstanding departments at UP in following the lead by ESM in developing exciting new curricula.

This year we have continued with our efforts to recruit the best students to Penn State. Bob represented our program at the second NIH graduate and professional school fair held in Bethesda, MD in July and will be attending the 11th Annual Biomedical Research Conference for Minority Students (ABRCMS) being held this year in St. Louis. In addition, Bob has visited Goucher College, Bard College, and Penn State Shreyer Honors College to promote our MD/PhD program. Several Schreyer students attended last year's retreat at the PennStater Hotel, and we are hoping that more will join us at our upcoming retreat to be held March 17th and 18th at the Nittany Lion Inn in State College. We were pleased make connections with these students and look forward to receiving an increased number of applications!

Once again, we would like to congratulate everyone involved with Penn State's successful application for a Clinical and Translational Sciences Award (CTSA) from the NIH. This funding for our Clinical and Translational Sciences Institute will greatly benefit the University and provide new opportunities for our MD/PhD, MD and graduate students to collaborate in a team-based approach to clinical and translational research.

Entering the lab

Steve Steinway

PI: BART ROUNTREE, PH.D., REKA ALBERT, PH.D.

I have joined the laboratories of Bart Rountree (Dept of Pediatrics & Pharmacology- Hershey) and Reka Albert (Dept of Physics & Biology- University Park) in order to pursue an interdisciplinary research project spanning the fields of systems biology and liver cancer metastasis. Liver cancer is the third most common cancer worldwide, and metastasis is responsible for 90% of deaths from solid tumors. Epithelial-to-mesenchymal transition (EMT) is a process utilized by liver cancer cells to leave the primary tumor site and establish distant metastases. I am using principles of network theory to identify the key regulators of this complex process in liver cancer. This research will predict critical mediators of EMT, which will be confirmed using siRNA and chemical inhibitor screens in liver cancer cell lines, followed by in vivo mouse studies. The overall goal of these studies is to rationally target critical mediators of liver cancer metastasis in order to prevent liver cancer progression in patients with chronic liver disease.

Zainul Hasanali

PI: DR. ELLIOT EPNER

My current research focuses on T-PLL, a rare aggressive leukemia, that has a median survival of about 2 years with conventional chemotherapy. Dr. Elliot Epner has been treating patients with this disease for the past 10 years with a new therapeutic regimen using already FDA approved drugs for other diseases. This therapy focuses on epigenetically modifying the cancer genome (i.e. changing DNA methylation, modifying histone acetylation, etc.) to reactivate cell cycle controls and create susceptibility to other drugs. We are using this new treatment regimen as a model to study the specific cell processes and pathways that are responsible for causing cancer cell death and durable remissions. I am conducting this research under a joint mentorship by Drs. Elliot Epner and Tom Loughran to get a handle on this disease with the idea that understanding the pathways involved in initiation and maintenance will lead to better utilization of current therapeutics and the development of new more effective ones.

Francis LeBlanc

PI: DR. LOUGHRAN

LGL leukemia is a rare proliferative disorder with two classifications - CD3+/T-LGL and CD3-/NK-LGL. These patients typically present with various cytopenias leading to complications such as anemia and chronic infection associated with neutropenia. In addition, there is an unusual association with a variety of autoimmune diseases. My project focuses on the NK-LGL subtype and will investigate the sphingolipid rheostat and its role in leukemia pathogenesis; specifically sphingosine-1-phosphate signaling through S1PR5 and its role as a survival pathway. This will hopefully uncover possible therapeutic targets as NK-LGL is currently an incurable disease, with death occurring in the acute form within a few months of diagnosis.

Xiaowei Su

PI: JAMES CONNOR, PH.D.

My research in Dr. James Connor's lab in the Department of Neurosurgery will focus primarily on amyotrophic lateral sclerosis (ALS, also known as Lou Gehrig's disease), a debilitating neurodegenerative disorder affecting both upper and lower motor neurons. Research from our lab and others has shown that approximately 30% of ALS patients with the sporadic form of ALS carry a mutation in the HFE gene, which is associated with iron overload in hemochromatosis. Furthermore, ongoing studies suggest a role for mitochondrial dysfunction in the pathogenesis of ALS. Changes in mitochondrial morphology, localization, calcium buffering capacity, and regulation of oxidative phosphorylation as well as apoptosis occur in mouse models of the disease. Building upon these findings, my research will investigate the role of mitochondrial dysfunction in various model systems relevant to ALS. I will study human cell lines carrying mutant HFE vectors, as well as mice with HFE, superoxide dismutase (SOD, implicated in familial ALS) or both HFE and SOD gene mutations. Finally, I will build upon current lab collaborations with the Penn State Hershey ALS Clinic to analyze mitochondrial dysfunction in patients.

Jeffrey Nguyen

PI: DAVID LIU, PH.D.

Dr. Liu's lab focuses on delineating the signaling mechanisms that regulate cell death and survival in neurons and cancer cells. One main focus of his lab is the transcription factor, ATF5. ATF5 is upregulated in several different types of cancer and appears to have a pro-survival function; interference with its function leads to the selective destruction of cancer cells, while sparing normal cells, even those that express ATF5. I am interested in elucidating how ATF5 exerts its pro-survival function using a combination of cellular, molecular, genetic, and biochemical techniques with the hopes that it will result in novel strategies and targets for the treatment and prevention of cancer.

Lauren Weiler

PI: CHRISTOPHER C. NORBURY, PH.D.

I am currently using an animal model of smallpox infection to study the early stages of the spread and control of viral infection.

POST-MATCH QUESTIONNAIRE

Vance Albaugh

WHERE DID YOU MATCH?

Vanderbilt University Medical Center
(Nashville, Tennessee) in General Surgery

WHAT FACTORS LED YOU TO CHOOSE THE SPECIALTY YOU DID?

Surgery was by far the rotation that I enjoyed the most out of my third year clinical clerkships. There were several factors that made a career in surgery attractive. Unlike many specialties, surgical patients improve much more rapidly than patients with chronic medical conditions for which there are limited treatment options. Being able to see patients improve quickly following operative management and to be able to make a quick and significant difference in a patient's health was very powerful. I also spoke with several of the faculty surgeons who had experience with basic and translational research either as faculty or residents. These surgeons explained the value of research in surgery and the rich opportunities for research that a surgical career affords. Additionally I enjoyed the day-to-day activities of the surgical team and seemed to 'connect' with the surgical residents and the surgery-attending physicians much more than I did on other rotations. I completed my surgery rotation at the end of my third year, and at that time it was a no-brainer to decide to apply to general surgery for residency.

WHAT FACTORS LED YOU TO CHOOSE THE PROGRAMS YOU RANKED HIGHLY?

With the help of the Surgery faculty, I formed a list of the top general surgery programs and ended up interviewing at 14 academic programs. All of the programs had strong research facilities and Surgery departments with long-standing traditions of excellence in patient care and research – basic, translational and clinical. Furthermore, it was clear from the mission statements of these programs that they aimed to train individuals who would pursue academic careers in research, teaching and patient care. The clinical training and experience at my top 10 programs was for the most part very similar, since all the top programs do most of the same things very well. The characteristics that helped me differentiate and rank my top programs were things like (1) the number of surgeon-scientists who had basic research labs at the institution, (2) the amount of NIH RO1 funding in the surgery department as well as the institutional NIH support, (3) how many residents continued basic research careers following graduation from residency, (4) where the chief residents matched for fellowship training, (5) the research interests of the surgeon-scientists at the institution, (6) the types of opportunities that I would have access to during my post-doctoral research training, and (7) how many of the surgery faculty were MD/PhD surgeons.



IF YOU COULD GO THROUGH THE PROGRAM AGAIN, WHAT WOULD YOU DO DIFFERENTLY? WAS THERE ANYTHING YOU DID THAT WAS MORE IMPORTANT THAN YOU HAD EXPECTED?

I matched to my number one program and thus I wouldn't necessarily say that I would change anything during my time in the MD/PhD Program. There were several things, though, that I did as a student that I didn't realize would help me out during the residency application and interviewing process. The biggest one of these things was getting involved in research projects outside of my dissertation work. Luckily for me I ended up working with a surgeon-scientist at Penn State who was RO1 funded and had a productive basic science laboratory. Before I even considered surgery as a career, I had already presented at two surgical research conferences and at the American College of Surgeons Annual meeting. That collaboration led to two second-author publications and a lot to talk about during my interviews for residency. The mentorship that I received from this Penn State surgeon-scientist is something that I was asked about at every one of my interviews. Being able to say I had some type of plan or roadmap for how I was going to incorporate surgery into my future practice was a huge benefit for me. The other things that helped me out were things like being involved on committees (e.g. Institutional Review Board) and being active in student leadership positions in my medical student class and for the Student Assembly at the medical center. To be a surgeon you have to be comfortable being the leader of a team. I think that having a track record of positions of responsibility as a student helps validate your qualifications for a residency spot in surgery.

HOW DID HAVING A PH.D. AFFECT YOUR EXPERIENCE OF THE MATCH?

I don't think that 'having' a Ph.D. affected my experience in the match. However, I think that having a significant research experience, including several papers, numerous national and international presentations, and having a surgeon-scientist mentor helped out immensely. Like many areas of life, making a lot of professional connections and networking at every opportunity you have can go a long way.

It's important to realize that 'having' a Ph.D. could potentially hurt your chances at some programs – think about it! For example, if you spend several years in the laboratory and you only have one first-author paper it might look like you slacked off for a few years (unless, of course, that one paper is in Nature Medicine, Journal of Clinical Investigation, etc). You need to be productive - The key to success as an MD/PhD student is use the 7-8 years that you're in the program to get as involved as you can and work on building your CV as much as possible. Don't waste your precious time on insignificant experiences or playing around in the lab. Merely having three extra letters behind your name isn't necessarily a good thing.

POST-MATCH QUESTIONNAIRE

Bozo Todoric

WHERE DID YOU MATCH?

Duke University Eye Center

WHAT FACTORS LED YOU TO CHOOSE THE SPECIALTY YOU DID?

I can say that I struggled to decide for a very long time as to which specialty to choose. In the end it was a decision based on factors that I liked about a variety of different specialties that I experienced in medical school. First, I always really enjoyed “diagnosing by seeing”.

Ophthalmologists rely heavily on the biomicroscopic exam at the slit lamp, and the ability to see the eye pathology and then watch your intervention (whether medication, drops or surgery) fix it and improve vision was fascinating. Secondly, it was a perfect combination of medicine and surgery in mainly outpatient setting. Even for heavier surgical cases, most patients were able to go home the same day after local anesthesia. Finally, there were numerous opportunities to apply my training as a basic neuroscientist and to be involved in academic ophthalmology.



WHAT FACTORS LED YOU TO CHOOSE THE PROGRAMS YOU RANKED HIGHLY?

I was mainly looking for the best clinical and surgical training. Duke has a great track record of training top notch ophthalmologists, and prepare them well to practice ophthalmology independently, which made the program very appealing. Secondly, I wanted to be in a strong academic environment where folks were encouraged to ask the “why”, not just “how” questions. Finally, I wanted to go to a place that has had a track record of training physicians scientists, and has supported their development through research and subspecialty training.

IF YOU COULD GO THROUGH THE PROGRAM AGAIN, WHAT WOULD YOU DO DIFFERENTLY? WAS THERE ANYTHING YOU DID THAT WAS MORE IMPORTANT THAN YOU HAD EXPECTED?

I think our MD/PhD program is as good as any other in providing training opportunities for students. I think the importance of doing well at each phase of training (in particular clinical clerkships) should be emphasized heavily and this will likely allow people to be most competitive in applying for their chosen specialty.

HOW DID HAVING A PHD AFFECT YOUR EXPERIENCE OF THE MATCH?

No matter what specialty, people like physician scientists! Having a PhD and being able to communicate a genuine interest in advancing the field forward through research has helped a tremendous amount!

Recent Award Recipients

Vance Albaugh

D. Eugene Rannels Award

2011 Endocrinology & Metabolism Section Research Recognition Award from the American Physiological Society

Howard E. Morgan Travel Award to attend the Experimental Biology meeting in Washington, D.C.

Department of Surgery Award

Kimberly Lumsden

Ted & Millie Kantner Family Practice Award

Steven Steinway

PSU Institute for Cyberscience Summer Student Award

Bozo Todoric

Marian Kies Award, American Society for Neurochemistry

Sylvia & Gilbert Nurick Medical Achievement Award

Department of Ophthalmology Achievement Award

John Kreider Award

Linda Flickinger Award in Neuroscience

Moskowitz Family Endowment Award

Yanli Wang

Madeline K. Dietz Memorial Scholarship

Judith S. Bond Award

Jay Jin

Judith S. Bond Award

James Bauer

Villforth Scholarship in Bioengineering

Melanie Dispenza

Dean's Travel Award

Recent Grant/Funding Awards

Theresa Carr

NIH/F30 Ruth L. Kirschstein National Research Service Award for Individual Predoctoral MD/PhD and Other Dual Doctoral Degree Fellows

Allison Cleary

Department of Defense Predoctoral Traineeship

Darrin Bann

NIH/NCI/F30 individual grant

Steven Steinway

NIH F30 individual grant

New Students

Paul Hsu

EDUCATION: B.S. in Biophysics; Minor in Accounting (UCLA)

HOMETOWN: Diamond Bar, CA

AWARDS/HONORS: Peer Learning Facilitator

RESEARCH BACKGROUND: UCLA Neurobiology; Presentations at UCLA Science Poster Day; Society for Annual Neuroscience meetings 2009 & 2010

RESEARCH INTERESTS: Neuroscience, neural networks, regeneration, and neuroengineering

MEDICAL INTERESTS: Anesthesiology, Neurology

WHY PENN STATE HERSCHEY? Strong, well developed graduate program with the possibility of doing my dissertation in neuroengineering and/or neural regeneration

ANY SURPRISES SINCE STARTING THE PROGRAM?

There are several of medical students who share similar interests or backgrounds in research. I expected more, but realistically, that probably wasn't going to happen. Other faculty are doing really cool things outside of neuroscience that I would love to pursue if I had all the time in the world. Courses definitely require a lot of work, but the material is not difficult. Weather is getting cold real quickly.

HOBBIES: Photography, Web Design

Trevor Jackson

EDUCATION: BA in Psychology (U of PA)

HOMETOWN: Philadelphia, PA

AWARDS/HONORS: none

RESEARCH BACKGROUND: U of PA Pharmacology dept.; Publication in Neurochemistry International

RESEARCH INTERESTS: From a research standpoint, I am interested in studying metabolic processes, especially the mechanisms of anabolism, catabolism and the various molecules which may affect these processes.

MEDICAL INTERESTS: At this point, my medical interests are primarily surgical specialties. Of these, I am most interested in surgical oncology, orthopedic surgery, and possibly neurosurgery.

WHY PENN STATE HERSCHEY? I chose Penn State because I like the atmosphere here as well as the faculty.

ANY SURPRISES SINCE STARTING THE PROGRAM?

I haven't really had any surprises since starting classes in August. The only one I can think of, is that I have taken much more of an interest in surgery than I would have predicted for myself before starting school.

HOBBIES: My hobbies include weightlifting, running, fly-fishing, playing guitar, and hiking. Luckily for me there are many great areas to fish and hike in the immediate area, and even more if I make the two hour drive to State College.

Amy Lu

EDUCATION: BA in Biology; Minor in Economics (Columbia U)

HOMETOWN: Penticton, British Columbia, Canada

AWARDS/HONORS: Dean's list; Samuel Rudin Scholarship

RESEARCH BACKGROUND: Multiple Sclerosis research at the MS Research Center of NY;

Presentation at Columbia U Summer Undergraduate Research Symposium; International Society for Stem Cell Research Conference; Presentation at American Society for Virology Conference; Yale Microscopy Workshop & Symposium; Stem Cell research at Columbia U; clinical research at Academic Assoc., NY; Molecular Plant Virology Research at Pacific Agriculture Agri-food Research Center; International Multiple Sclerosis Mgmt. Practice symposium, NY, NY; Biomedical Engineering Society, 2nd Annual Mtg, Austin, TX; Publications: stem Cells & Dvt. and Virus Research

RESEARCH INTERESTS: Stem cell research / regenerative medicine

MEDICAL INTERESTS: Neurology or Oncology, but pretty open to other specialties too.

WHY PENN STATE HERSCHEY? I liked the smaller collaborative atmosphere of the PSU program.

ANY SURPRISES SINCE STARTING THE PROGRAM?

Anatomy lab gives more reason for laughter than I ever imagined it to.

HOBBIES: Cooking and watching TV when I should be studying.

Saumya Maru

EDUCATION: BA in Biology; Minor in Psychology, South Asia Studies (U of PA)

HOMETOWN: King of Prussia, PA

AWARDS/HONORS: Joseph Leidy Award for Research Achievement at U of PA Biology dept.; University Scholar, U of PA

RESEARCH BACKGROUND: Symposium for Undergraduate Research in Biology, U of PA; Undergraduate Research Symposium, U of PA CURF; Children's Hospital of Philadelphia Clinical Trial: Phase I Therapy for Wiskott-Aldrich Syndrome; Publications: J of Immunology, J of Clinical Investigation; Undergraduate Thesis Research at CHOP

RESEARCH INTERESTS: Immunology, but I would love to get involved with some interdisciplinary work here in Hershey.

MEDICAL INTERESTS: I've always been interested in Cardiology and Immunology. I'd also consider doing Medicine and going into a sub-specialty like Endocrinology.

WHY PENN STATE HERSCHEY? The program here at Hershey is great and affords a lot of opportunities to students, Hershey is a fantastic little town, I love roller coasters, and I'm only two hours away from my family in Philadelphia. I'm a big family person, so the proximity was a large factor in deciding to come here. So was Fahrenheit.

ANY SURPRISES SINCE STARTING THE PROGRAM?

The only thing I've been exposed to so far is Anatomy, so I guess what surprised me the most is how aware everyone else in the hospital is of the smell of formaldehyde, and how oblivious I am.

HOBBIES: I love playing sports, tennis in particular, but I'll try anything. I also love to travel and explore new things, although I'm not sure how much of that I'll be getting to do these next eight years...

Olivier Noel

EDUCATION: BA in Biochemistry (CUNY Queens)

HOMETOWN: Port au prince, Haiti

AWARDS/HONORS: Biology Honors Society; Dean's list; Phi Theta Kappa; CUNY International Student Essay Competition award recipient; Region 15 Excellence in Sports & Academics award; T. Eileen Cummings Scholarship; Excellence in Tutoring award; NIH Marc U-Star Fellowship award; AHA Summer Research fellowship; Tau Epsilon Phi; Trudy Rothman Chemistry award

RESEARCH BACKGROUND: Conferences attended: NAMME, SNMA, Mid-Atlantic Regional Society for Dvt. Biology; Presentations/Posters: Sigma XI Annual Research Day, Early Career Research Symposium, 2010 Mid-Atlantic SDB Mtg., Society of Dvt. Biology; ABRCMS oral presentation 2010

RESEARCH INTERESTS: Cancer and signaling pathways - Cancer Suppression - Drug Discovery

Medical Interests: Surgical Oncology - Radiation Oncology

WHY PENN STATE HERSCHEY? Faculty is very supportive and doing interesting research in my fields of interest.

ANY SURPRISES SINCE STARTING THE PROGRAM?

How fun intramural sports actually are in Hershey!

HOBBIES: Soccer

Akua Sarfo

EDUCATION: BS in Biology, Urban Studies; Minor in Chemistry (U of Pittsburgh)

HOMETOWN: York, PA

AWARDS/HONORS: Phi Sigma Pi, Alpha Epsilon Delta; Helen Faison Scholarship; HH Medical Institute fellowship; Dean's list

RESEARCH BACKGROUND: Undergraduate Research Symposium, U of Psbgh; Undergraduate research investigator Dept. of Biological Sciences, U of Psbgh; Poster presentation at U of Psbgh Summer Undergraduate Research Symposium

RESEARCH INTERESTS: My background prior to joining the program was in developmental biology, specifically in investigating the planar cell polarity pathway using Drosophila as a model to try and understand cell patterning and arrangement during development. My first rotation, however, was in a microbiology/immunology lab, which I really enjoyed, so I'd say that my research interests are currently still pretty broad.

MEDICAL INTERESTS: Currently, I'm interested in pursuing a career in either infectious disease or obstetrics and gynecology.

WHY PENN STATE HERSCHEY? I chose Penn State Hershey because I feel like the program leadership is supportive of the students and developing our future careers as physician-scientists, and I like the fact that we have the freedom to do research either in Hershey or at main campus. Being less than an hour away from where I grew up also did not hurt my decision.

ANY SURPRISES SINCE STARTING THE PROGRAM? To be honest, I don't think I've had the time to even be surprised since anatomy's kept me so busy!

HOBBIES: My current hobbies include trying to catch up on my reading list and spending time with my family and friends.

Recent Student Publications

Lumsden KR, Nelson AM, **Dispenza MC**, Gilliland KL, Cong Z, Zaenglein AL, Thiboutot DM (2011) Isotretinoin increases skin surface levels of neutrophil gelatinase-associated lipocalin in patients treated for severe acne *Br J of Derm* 165(2): 302-10 PMID: 21466536

Kharas MG, Okabe R, Ganis JJ, Gozo M, **Khandan T**, Paktinat M, Gilliland DG, Gritsman K (2010) Constitutively active AKT depletes hematopoietic stem cells and induces leukemia in mice *Blood* 115(7):1406-15 PMID: PMC2826762

Peng B, Ling J, **Lee AJ**, Wang Z, Chang Z, Jin W, Kang Y, Zhang R, Shim D, Wang H, Fleming JB, Zheng H, Sun SC, Chiao PJ (2010) Defective feedback regulation of NF-kappaB underlies Sjogren's syndrome in mice with mutated kappaB enhancers of the I kappa B alpha promoter *Proc Natl Acad Sci USA* 107(34):15193-8 PMID: PMC2930541

Lloyd SA, Donahue HJ. (2010) Gap Junctions and Biophysical Regulation of Bone Cells. *Clin Rev in Bone and Miner Metab* 8(4):189-200

Jones NP, Siegle GJ, **Muelly ER**, Haggerty A, Ghinassi F (2010) Poor performance on cognitive tasks in depression: Doing too much or not enough? *Cognitive, Affective & Behavioral Neuroscience* 10(1):129-40 PMID: PMC2841800

Girgenti MJ, Collier E, Sathyanesan M, **Su XW**, Newton SS (2010) Characterization of electroconvulsive seizure-induced TIMP-1 and MMP-9 in hippocampal vasculature *International J of Neuropsychopharmacology* 14(4):535-44 PMID: 20678305

Yee S, Qiu F, **Su XW**, Rider A, Kunselman AR, Guan Y, Undar A (2010) Evaluation of HL-20 Roller Pump and Rotaflow Centrifugal Pump on Perfusion Quality and Gaseous Microemboli Delivery *Artif Organs* 34(11):937-43 PMID: 20946282

Qiu F, Guan Y, **Su X**, Kunselman A, Undar A (2010) Evaluation of Neonatal Membrane Oxygenators with Respect to Gaseous Microemboli Capture and Transmembrane Pressure Gradients *Artif Organs* 34(11):923-29 PMID: 21092035

Su XW, Undar A (2011) Brain Protection During Pediatric CPB *Chin J ECC* Vol 9 No 1

Su XW, Guan Y, Barnes M, Clark JB, Myers JL, Undar A (2011) Improved cerebral oxygen saturation and blood flow pulsatility with pulsatile perfusion during pediatric cardiopulmonary bypass *Ped Res* 70(2): 181-5

Dluzen D, Li G, **Tacelosky D**, Moreau M, Liu DX (2011) Bcl-2 is a downstream target of ATF5 that mediates ATF5' pro-survival function in a cell type-dependent manner *JBC* 286(9):7705-13 PMID: PMC3045024

Todorich B, Scott IU, Flynn HW, Johnson MW (2010) Evolving Strategies in the Management of Submacular Hemorrhage associated with CNV in the Anti-VEGF Era *Retina* [Epub ahead of print] PMID: 21562448

Todorich B, Flynn HW, Scott IU, Rodrigo J, McCabe CM (2010) Management of Submacular Hemorrhage. Introductory overview for ophthalmology residents and vitreoretinal fellows http://eyewiki.aaopt.org/Management_of_Submacular_Hemorrhage

Allen DL, **Cleary AS**, Hanson AM, Lindsay SF, Reed JM. (2010) CCAAT/enhancer binding protein-delta expression is increased in fast skeletal muscle by food deprivation and regulates myostatin transcription in vitro *Am J Physiol Regul Integr Comp Physiol* 299(6):R1592-601 PMID: 20844262 PMID: PMC3007187

Lloyd SA, Simske SJ, Bogren LK, Olesiak SE, Bateman TA, Ferguson VF (2011) Effects of Combined Insulin-Like Growth Factor 1 and Macrophage Colony-Stimulating Factor on the Skeletal Properties of Mice. *In Vivo* 25(3): 297-305 PMID: 21576402

Wiley JS, **Lloyd SA**, Nelson GA, Bateman TA (2011) Ionizing Radiation and Bone Loss: Space Exploration and Clinical Therapy Applications. *Clin Rev in Bone and Miner Metab* (accepted)

Weston CL, Glantz MJ, Connor JR (2011) Detection of cancer cells in the cerebrospinal fluid: current methods and future directions *Fluids Barriers CNS* 3:8(1):14 PMID: 3059292

Lumsden KR, Nelson AM, **Dispenza MC**, Gilliland KL, Cong Z, Zaenglein AL, Thiboutot DM (2011) "Isotretinoin increases skin surface levels of neutrophil gelatinase-associated lipocalin in patients treated for severe acne" *Br J of Derm* 165(2): 302-10 PMID: 21466536 PMID: 3142306

Woll MP, De Cotiis DA, Bewley MC, **Tacelosky DM**, Levenson R, Flanagan JM. "Interaction between the D2 Dopamine Receptor and Neuronal Calcium Sensor-1 analyzed by fluorescence anisotropy" *Biochemistry* [Epub ahead of print]

Research Highlights

NAME: Diana Tacelosky

TITLE/AFFILIATION: MD/PhD Candidate, Dept of Pharmacology, Penn State College of Medicine

MENTORS: Robert Levenson, PhD and Patricia Sue Grigson, PhD

On my lab cart—the one that makes its daily trip to the animal facility—there is a Tupperware box loaded with heroin. The heroin passes through a 20 mL syringe into a line of plastic tubing before emptying into the venous blood supply of a male Sprague-Dawley rat. The rat may lick and poke its nose to get his fix, but the pattern of his behavior over time tells me that there may be more to addiction than drug exposure.

What accounts for this craving—the seeking

and working for a drug of abuse? Why don't I see the same patterns of addiction in all my rats, but only a small percentage? How does a casual drug user transition to a state of substance dependence?

For the past three years, I've probed cell lines and brain homogenates to characterize novel protein interactions at the key receptor that mediates the rewarding properties of opioid drugs. I have used everything from co-immunoprecipitation assays to cutting-edge animal models to further elucidate the molecular mechanisms of opioid tolerance and addiction. My studies are a key component of opioid addiction research in the Translational Research Center on the Neurobiology of Drug Abuse and Addiction. In our lab, several novel protein targets,

including GPR177, the mammalian ortholog of Wntless in *Drosophila*, and VAPA, a synaptic scaffolding protein that mediates intracellular transport were identified using a split-ubiquitin screen. I have utilized highly selective antibodies to confirm the protein interactions, and I have probed for protein expression changes in brain samples from my behavioral studies.

Recently, I had the opportunity to meet with leading scientists at the Cold Spring Harbor Laboratory Cellular Biology of Addiction course. By presenting my findings and learning the latest ideas for how the brain adapts at the molecular and cellular level to drugs of abuse, I have been able to further my thesis research.

Penn State M.D./Ph.D. Program

Penn State College of Medicine M.D./Ph.D. Program provides an opportunity for students interested in careers in academic medicine and research to obtain the necessary training in clinical and basic sciences. This eight-year, dual-degree program provides students with knowledge of the breadth of clinical science plus the ability to design experiments and conduct biomedical research with modern technology.

Applications to the Penn State College M.D./Ph.D. Program can be submitted through the AMCAS application service by choosing the Combined Medical Degree/Ph.D. program.

For students in the MD/PhD Program, tuition and stipend are provided for all years in the program.

For more information, visit www.pennstatemdphdprogram.com or contact Barb Koch at 717-531-1188, bkoch2@hmc.psu.edu.

THE GRADUATE PROGRAM CHOICES FOR THE PH.D. PART OF THE DUAL DEGREE ARE:

- Anatomy
- Biochemistry and Molecular Biology
- Bioengineering
- Cell and Molecular Biology
- Genetics
- Immunobiology
- Microbiology and Immunology
- Molecular Medicine
- Neuroscience
- Pharmacology
- Physiology
- Integrative Biosciences (including Chemical Biology and Molecular Toxicology)

U.Ed. MED 12-5146 MDC

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