A.B.S.T.R.A.C.T.
Annals of Biomedical Student/Trainee Research and Current Trends

ABSTRACT’s ACCOLADES

Russell McConnell
Matt Tyska Lab (CDB)
AHA Fellowship

Leslie Meenderink
Steve Hanks Lab (CDB)
AHA Fellowship

Nidhi Jalan
Roger Colbran Lab
(MPB) AHA Fellowship

Guanglei Zhou
Jin Chen Lab
(Cancer) DOD Fellowship

Kristen Jernigan
Ethan Lee Lab (CDB)
AHA Fellowship

Andrew Benesh
Matt Tyska Lab (CDB)
AHA Fellowship

David Vaught
Jin Chen Lab
(Cancer) DOD Fellowship

Sabrina Doughty
Aurelio Galli Lab
(Neuroscience) NIH
NRSA Fellowship

Inside this issue:
Spotlight Scientist 2-3
Business News 4-5
Current News 6
Department Updates 7-11
Perspectives 11-12
Peer Review 12

About A.B.S.T.R.A.C.T.:
• Founded by Julie Field and Erica Bowton in 2007
• Sponsored by the BRET office
• Written and edited by graduate students and postdoc trainees

Also available online: http://bret.mc.vanderbilt.edu/bret/php_files/abstract.php

VUMC graduate students were nominated by their Department Coordinators.
Dr. Kristen Guglielmi of the Dermody laboratory in the Department of Microbiology & Immunology recently defended her dissertation on reovirus interaction with its cellular receptor, junctional adhesion molecule-A (JAM-A). Reovirus infects humans, but only causes minor disease in infants as most people develop antibodies against them early in life. This, along with its ability to induce apoptosis in certain tumor cells, makes reovirus a potential cancer therapy; phase I trials are underway for malignant glioma.

Guglielmi’s work, published in the Journal of Biological Chemistry last year, combined structural, biophysical, biochemical, and cellular techniques to formulate a model in which the reovirus attachment protein, σ1, disrupts JAM-A dimers to allow secure attachment of the virus to the potential host cell. Reoviral attachment comprises one step in the process of viral entry, following adherence via extracellular carbohydrates, and preceding internalization, which requires integrins. She and her collaborators identified specific residues of JAM-A in the dimer interface required to interact with σ1, revealed that σ1 binds JAM-A monomers, and showed that the three reoviral serotypes, which differ mostly in sequence for σ1, require different JAM-A residues for interaction. The latter suggests that differences in reovirus pathogenesis may be due in part to differences in affinity for JAM-A.

“[It’s] amazing how such small things can do so much good and so much harm.”

Guglielmi received a Dissertation Enhancement Grant to travel to Germany to work in Dr. Thilo Stehle’s lab on solving the crystal structure of the σ1-JAM-A complex. To complement these structural studies, Guglielmi rescued reoviruses with mutations that alter the capacity to bind JAM-A. This work has been provisionally accepted for publication in PLoS Pathogen (see figure) and represents an initial step toward engineering reoviruses that attach to receptors other than JAM-A, allowing treatment of cancers not targeted by wild-type reovirus.

Guglielmi credits her success with such a variety of methods to “determination and a little luck,” as well as to her “wonderful mentor, great lab team, and helpful and critical committee.” She believes her running habit (she has completed four half-marathons while at Vanderbilt) helped her manage the stress of graduate school, as it “clears the brain.”

Her love for research, discovered as an undergraduate at Auburn University, undoubtedly also contributed. She began as a pre-med student, but changed direction after her enjoyment of lab courses led her to join the lab of Dr. Zhaomin Yang, where she investigated the differential regulation of ‘adventurous,’ or individual, and social motility of Myxococcus xanthus, a saprotrophic bacterium found ubiquitously in soil. She stayed on for two years after graduating and published her work on a set of chemotaxis genes in the Journal of Bacteriology.

Guglielmi will continue to approach virology from a structural perspective in her postdoctoral work at NIH in the lab of Dr. John Patton where she will collaborate with Dr. Alasdair Steven studying the replication and assembly of rotavirus. Patton’s research aims to help create a successful vaccine for rotavirus, which contributes to a significant proportion of infant mortality in developing countries.

Guglielmi plans a career in research, either at a university or a research institute, because she loves “answering questions and thinking of new ones.” She intends to stay in the field of pathogenic microorganisms, as she finds it “amazing how such small things can do so much good and so much harm.”

You may recognize Dr. Kenneth Gagnon as the Interdisciplinary Graduate Program Methodology Course Director. What you may not know is that his love of science once led him to the oceans. After earning his undergraduate degree in Marine Biology from the University of British Columbia in Vancouver, he worked for 8 years as a field biologist with the Canadian Department of Fisheries and Oceans. He continued his education in Northeastern University’s East/West Marine Biology program, which provided unique opportunities to live and study in the Pacific Northwest, Caribbean, and Northeast Atlantic, then chose to return to the bench and pursue graduate studies in biomedical science.

As a graduate student at Wright State University, Gagnon studied members of the cation chloride cotransporter (CCC) family, membrane proteins that regulate cell volume under osmotic and other stress conditions. They also play a less well understood role in cell growth and proliferation. One particularly special CCC, the neuron-specific K⁺-Cl⁻ cotransporter KCC2, extrudes K⁺ and Cl⁻ under isotonic conditions, regulating internal chloride concentrations, thus controlling the direction of Cl⁻ movement through GABA receptors, which regulate excitability. As part of his studies on the functional relevance of CCCs in glial cells, Gagnon developed novel antibodies to KCC2 as well as the ubiquitous cell volume regulator KCC1.

Gagnon and his current advisor Dr. Eric Delpire, Professor of Anesthesiology and Molecular Physiology & Biophysics, were already well-acquainted since Gagnon had completed his graduate work with Delpire’s postdoctoral mentor Dr. Peter Lauf, and had bumped into each other at conferences. Upon arriving at Vanderbilt, Gagnon learned an array of molecular biology techniques to study proteins that physically interact with CCCs, including SPAK (Sterile 20 proline alanine kinase). SPAK and its homolog OSR-1 (oxidative stress response kinase) function in cell differentiation, cell transformation, proliferation, and cytoskeleton rearrangement. A former postdoctoral fellow in the lab, Dr. Kerstin Piechotta, had found and confirmed the physical interaction of SPAK, PP1, and AATYK. These studies suggest that inhibition of the cotransporter requires the scaffolding of the inhibitory phosphatase PP1 in proximity to the activating kinase (SPAK). Although the role of PP1 as an inhibitor of NKCCs had been known for years, the identity of the kinase that activates NKCCs eluded researchers until Piechotta’s and Gagnon’s discoveries, and the Delpire laboratory continues to study this pathway.

Gagnon’s findings have opened a floodgate of research on the CCC regulatory pathway, especially due to its direct relevance to kidney disorders and a likely role in the nervous system, which he continues to explore. Gagnon and colleagues also design and build both straight and conditional knockout mice using homologous recombination with bacterial artificial chromosomes. The laboratory has created knockout mice for both SPAK and OSR1, as well as several of the CCCs, which they are currently characterizing.

Gagnon has been recognized by the American Physiological Society, receiving their Young Investigator Award in both 2005 and 2007. He has also been selected as Vanderbilt University Medical Center’s Postdoctoral Fellow of the Year in 2008. He has also been funded by an American Heart Association Postdoctoral Fellowship. He credits his success to hard work and the support of his mentor.

Gagnon will continue to apply his expertise in the cotransporter field, but plans to delve into cancer biology returning to the glioma model he studied as a graduate student. His future plans include running his own research laboratory to continue to make discoveries as well as mentor graduate students and postdocs. He also hopes to one day return to Canada...or at least somewhere there is snow at Christmas.

The U.S. Pharmaceutical Industry in Today’s Economy: Outlook Promising?

By Emily Cross

When considering one’s post-graduation career options, the effect of a slow economy on job opportunities raises concern. Among the options available, a scientific research career in the pharmaceutical industry has positive prospects. The US pharmaceutical industry invests a high proportion of revenue in research and development relative to global pharmaceutical research investment. In 2007 manufacturers spent $58.8 billion dollars, which was more than twice the entire NIH annual operating budget for the same year.

The staggering amount of money invested back into research reflects the importance of producing novel therapeutics for maintaining growth in this industry.

Pharmaceutical manufacturers need a strong research and development program to address several concerns. First, only one in five to ten thousand screened compounds makes it through FDA approval and reaches the market. Forwarding a new therapeutic costs an estimated $1.3 billion; attempting to advance a compound through the stages of drug development constitutes a great risk for pharmaceutical companies. An efficient and well-educated research staff minimizes this risk by reducing scientific error.

Secondly, competition increases as patents expire on brand name pharmaceuticals, allowing generic drugs to become available. The resulting pressure underscores the importance of research and development in production of novel or improved pharmaceuticals to maintain growth for manufacturing companies.

Despite the intrinsic demand for researchers in this lucrative industry, the dismal economic environment might still affect job prospects. Predictions by the Bureau of Labor Statistics, that demand for scientists to conduct this research will remain high until 2016, do not support such logic. The demand for pharmaceuticals will likely remain strong as the population continues to grow and age. In addition, the prevalence of chronic disease, often complicated by the obesity epidemic, adds to the stability of the industry. In general, drugs to treat life-threatening ailments, for example blood pressure medications, will probably remain a consumer priority even as prices of other essentials rise. Additionally, private and public health insurance typically cover these drugs, lessening consumers’ financial burden. This may partially protect the industry from user discontinuation as a money-saving measure. Generally, the rising health consciousness and lifestyle choices of the American people are expected to push the demand for novel pharmaceuticals.

Lastly, emerging markets in countries with rapidly expanding economies, such as China and India, will likely increase demand for American-made pharmaceuticals as global lifestyle standards improve.

So what does this mean for a job-hunting PhD graduate? While grant dollars may reflect the slow economy and become increasingly scarce, pharmaceutical research and development will probably continue to grow. A grant money crunch could push more new PhDs to seriously consider the industry side of research as a career. The biological, physical, and computational scientists who choose this path may feel confident that drug manufacturers will continue to offer job opportunities and lifestyle security in the near future. Additionally, this career choice will allow a researcher to remain in bench science and continue to help improve the American lifestyle standard through discovery.

Editor’s note: Since this article has been written, the economic downturn has significantly affected pharmaceutical companies. The economic slowdown has affected small companies’ abilities to raise capital. Larger companies have been laying off workers, from sales reps to chemists, in order to streamline business. For example, Wyeth is restructuring their Research & Development divisions and some of Pfizer’s R&D groups will disappear. Jobs are still posted at these pharmaceutical companies’ websites, but the constant news of layoffs at websites such as FierceBiotech’s are disheartening and it appears that previous predictions of the likelihood of procuring and maintaining a career in industry may not hold true. As industry tightens their belts simultaneously with stagnant NIH budgets, jobs remain, though competition for them has increased.

4. www.fiercebiotech.com/tags/layoffs
Discoveries in Research: Making it to the Marketplace with Technology Transfer

By Kr Moynihan

Can you imagine turning a power outage in the lab on a hot day into a startup company worth over 200 million dollars when it went public? On that fateful day 10 years ago in California, research labs opened their windows and Essam Enan, PhD, Professor of Biochemistry, noticed a startling difference among labs on his floor. While other rooms were abuzz with insects, his lab was remarkably free of them except for a few dead flies. Dr. Enan’s research focused on essential plant oils and he realized his was the only lab with these potentially insect-repellent substances. After extensive research, Dr. Enan uncovered the mechanism: particular chemicals in the oils block invertebrate-specific neurotransmitter receptors without affecting human receptors. Today, a newly formed company, TyraTech, is refining this technology to target many insect pests and even intestinal parasites. This amazing journey from bench science to successful product progressed through the Office of Technology Transfer and Enterprise Development (OTTED) at Vanderbilt University. Technology transfer describes “a formal transfer of rights to use and commercialize new discoveries and innovations resulting from scientific research to another party.” Technology transfer offices at universities around the country assist faculty in evaluating their innovations, pursuing patents and license agreements, and even spinning off startup companies to market these inventions exclusively.

University researchers have not always easily transferred intellectual property rights. Prior to 1980, all research products funded by government grants were the exclusive property of the federal government, which made the development by outside companies of unrefined discoveries highly restricted, lengthy, and expensive. Senators Birch Bayh and Bob Dole drafted a bill, enacted in 1980, to transfer ownership from the government to the university at which the technology was invented and allow the university to pursue technology protection and licensing options. This law also establishes the ownership stake of the individual inventor(s). The Association of University Technology Managers (AUTM) states that “before 1980, fewer than 250 patents were issued to U.S. universities each year and discoveries were seldom commercialized for the public’s benefit. In contrast, in 2002 ... 5,327 new license agreements were signed.” Some do not believe taxes should fund university research that leads to commercialization for the public’s benefit. In contrast, in 2002 there were 5,327 new license agreements signed.

Overall, universities profit only modestly from these efforts. The OTTED even covers expenses for the patent application process until payments are recouped by licensing. Vanderbilt is in the top 20% of AUTM universities in gross revenues from licensing as of FY 2007. Over 250 Vanderbilt faculty and staff in over 50 departments, divisions, and centers have used OTTED’s services to begin their technology transfer process, leading to remarkable outcomes. The field of technology transfer has grown tremendously in the last 30 years, with no sign of slowing down. As Rich Templeton, CEO of Texas Instruments, describes: “Universities have people who dream of what can be done or what may be possible. They also have a powerful capability to assemble multidisciplinary teams. In medical technology, they can get electrical engineers, computer scientists, biologists, chemists, and people from the med schools in the same room.” Vanderbilt faculty and staff in over 50 departments, divisions, and centers have used OTTED’s services to begin their technology transfer process, leading to remarkable outcomes. The field of technology transfer has grown tremendously in the last 30 years, with no sign of slowing down. As Rich Templeton, CEO of Texas Instruments, describes: “Universities have people who dream of what can be done or what may be possible. They also have a powerful capability to assemble multidisciplinary teams. In medical technology, they can get electrical engineers, computer scientists, biologists, chemists, and people from the med schools in the same room.”

The seventeen employees in the OTTED at Vanderbilt ensure just that and act as a conduit for the movement of discoveries from the laboratory to the open market for any Vanderbilt faculty or staff member. Physicists, chemists, physicists, engineers, neuroscientists, and administrators have invented a wide variety of potential therapies, research tools, and other products just in FY 2007. All of these successes began with evaluation of the new technology by the OTTED staff. From this point, the staff mapped out the necessary steps to bring the project to fruition via patent, copyright, etc. Sometimes the new technology requires further benchwork before patenting or licensing, and sometimes a partner company can be directly matched to license the discovery very quickly. And in some cases, as with Dr. Enan’s essential plant oils, a new company forms to develop and market the product. The OTTED provides an invaluable service to researchers by filing patent applications, attending to license agreements, and keeping abreast of the business situation, which allows the researcher to focus on their primary research.

Vanderbilt is in the top 20% of AUTM universities in gross revenues from licensing as of FY 2007. Over 250 Vanderbilt faculty and staff in over 50 departments, divisions, and centers have used OTTED’s services to begin their technology transfer process, leading to remarkable outcomes. The field of technology transfer has grown tremendously in the last 30 years, with no sign of slowing down. As Rich Templeton, CEO of Texas Instruments, describes: “Universities have people who dream of what can be done or what may be possible. They also have a powerful capability to assemble multidisciplinary teams. In medical technology, they can get electrical engineers, computer scientists, biologists, chemists, and people from the med schools in the same room.” These researchers will continue to generate new ideas and technology transfer can facilitate the path to the market-

(Tech Transfer references on page 10)
Vanderbilt University Medical Center has experienced spectacular growth over the last 8 years with a nearly 20% increase in NIH research funding. VUMC ranks first in funding growth this decade, ahead of such notable institutions as Duke University, UCSF, and the University of Washington. This trajectory has secured VUMC as a top 10 medical research institution in the nation in 2007 and a premier institution of the southeast region. Closely following this success, Vanderbilt has aggressively expanded research facilities to a total space of 578,000 sq ft. Since 2000, Vanderbilt has created an enviable cross-discipline environment by tapping a $100 million Academic Venture Capital Fund that has created the Institutes of Chemical Biology, Imaging Science, the Mass Spectrometry Research Center, an academic computing center (ACCRE), a nanotechnologies institute (VINSE), a cognitive neuroscience initiative (CICN), and aquatic facilities to house the Zebrafish Genetics Center. Many of these facilities have been housed in an ever vertically increasing skyline on campus, which can now be seen from Green Hills to downtown. Since 2004, the campus has seen the completion of the Monroe Carell Children’s Hospital and MRBIII, expansion of the Preston Research building and Light Hall (from 8 floors to 12), and construction of the Institute of Imaging Science and MRBIV above Langford Auditorium, which is currently the tallest structure on campus. The latest project so far announced is the Life Sciences Engineering and Clinical Research Building, which will replace the older portion of Medical Center North (MCN) facing Medical Center Drive.

Continuing on the tradition of spurring cross-disciplinary research at Vanderbilt, the Life Science Engineering and Clinical Research Building will bring elements of both the University and Medical Center together. With the inclusion of engineering from both the medical center and university sides, Vanderbilt is ready to create a unique environment through which engineers can reside across the hall from many of the clinical research labs. The new building will also bridge between the new Institute of Imaging Science center's MRI facilities at Vanderbilt. As the name implies, the School of Engineering, especially the Chemical and Biomolecular Engineering and Biomedical Engineering departments, will occupy a significant proportion of the new structure. In addition, the clinical departments from the Medical Center will enjoy new and expanded laboratory space. Many of VUMC’s high-ranking specialties such as urology (13th), gynecology (10th), kidney (10th), endocrinology (19th), and respiratory disorders (20th) are slated to move to the new building (US News and World Report).

With Phase I set to commence in the spring of 2009, project manager Bobby Otten has his hands full. He is finding space to accommodate the clinical departments that will be displaced during demolition and construction. According to the current schedule, demolition will begin by late summer 2009 and phase I construction will start during the first quarter of 2010.

During Phase I construction, the D wing currently facing the Medical Center parking shuttle stop and adjacent C-courtyard will be replaced with a new 300,000 sq ft research space at a cost of approximately $150 million. This building will match the size and height of the new glass Vanderbilt Institute of Imaging Science (VUIIS) building on 21st Avenue. After Phase I, which is due to finish by late 2012, Phase II will fill in the remaining space between the Phase I structure and the VUIIS building, replacing the B and C wings to the depth of the S corridor, and will also replace the B-courtyard facing Medical Center Drive. Upon completion, the structure will span from 21st Avenue to the Round Wing turnaround of MCN. This structure as proposed will double the size of VUMC’s research space. At current revenue rates of $400 per square foot, the added space could potentially generate $240 million per year for Vanderbilt. Thus, the expected benefits from investment in new construction outweigh the costs of construction and uprooting of many laboratories. The changes in the national economy have not affected any of the new building plans for MRBV.

In 2007, Vanderbilt’s medical center ranked 10th in the nation in competitive NIH funding at $387 million. With the addition of the Life Sciences Engineering and Clinical Research Building by the start of the next decade, Vanderbilt appears poised to secure its future in the medical center elite.
Departmental Updates

Biochemistry: ASMS Conference  By Angela Boutte

Over 6,000 people attended the 56th annual American Society of Mass Spectrometry (ASMS) conference in Denver, Colorado in June. Unlike many conferences, ASMS offers a variety of hands-on training workshops, such as ion-trap technology, making the ASMS meeting not just a venue to exchange ideas, but also an opportunity for novices to learn about instrumentation. Short courses and tutorials focused on topics from basic principles of mass spectrometry instrumentation to practical aspects of project planning for small molecule screening or high throughput proteomics. ASMS also offered a well organized career center coupled to online databases.

Many researchers from the Vanderbilt Mass Spectrometry Research Center and collaborating laboratories attended. Vanderbilt dominated sessions on laser capture microdissection, tandem mass spectrometry, two-dimensional electrophoresis and imaging mass spectrometry.

Areas gaining popularity include microwave assisted protein cleavage, novel labeling chemistry, on-plate and on-line enzyme-substrate reactions, detection and confirmation of disease biomarkers, environmental analysis, and, the holy grail, label free proteomics. Many attendees are also working on improving the reliability and sensitivity of protein detection to minimize the need for antibody based verification. Many speakers also introduced novel approaches in bioinformatics, including database searching algorithms and statistical descriptions of quantitative data. Scientists from federal laboratories in the bio-defense and food safety fields and representatives from independent bioinformatics companies, introducing new and upgraded software (e.g., Peaks, Phenyx, Insilicos), seemed more visible compared to previous years.

Although smaller than conferences offered by other organizations, the diversity of topics and the excellent networking opportunities make the ASMS annual meeting worthwhile. The ASMS website offers message boards for multiple interest groups regarding techniques and analysis, allowing communication around the world.

Cell & Developmental Biology: Bootcamp  By Hillary Hager

Have you ever wondered why studies of early development employ frog and fish embryos? Or how to perform tissue transplantation studies in chicks? A new class in the CDB department addressed these questions and much more in Developmental Biology Bootcamp, which allowed incoming CDB students to gain hands-on experience with classic developmental model systems. Directed by Drs. David Bader and Jason Jessen, with guest lectures from several campus embryologists, Bootcamp packed the basics of developmental biology into 10 weeks. Students first learned fundamental concepts in development, including cleavage, gastrulation, and germ layer formation, before delving into the nuances of each model organism. Resident expert faculty taught seminal work, key techniques, and future applications of *Drosophila*, *Xenopus*, chick, zebrafish, *C. elegans*, and mouse. Throughout each module, the class discussed the advantages and disadvantages of each organism. Students used this information to complete an unusual project, to create the perfect model organism.

(BCB continued on page 8)

Biological Sciences: Cell Report  By Ashleigh Long

In the November 26th issue of *Cell*, Dr. Kendal Broadie’s lab, in collaboration with Dr. Craig Montell at Johns Hopkins, report a *Drosophila* model for mucolipidosis type IV (MLIV). MLIV, a debilitating autosomal recessive lysosomal storage disorder (LSD), begins early in childhood, causing severe motor deficits and mental retardation. The mechanisms of MLIV are poorly understood and there is no treatment. MLIV associates with a disruption in the gene for a member of the transient receptor potential (TRP) super family of cation channels. In the nervous system they function widely in sensory signaling and also impact neuronal survival; either constitutive activity or loss of function can induce neuronal cell death.

The paper reports a defect in autophagy, a lysosomal degradation process, that causes buildup of macromolecules, resulting in oxidative stress and severely impaired synaptic transmission. Also, the accumulation of late-apoptotic cells in TRPML mutant brains suggests diminished clearance of early apoptotic cells. Targeted expression of wild-type TRPML channel protein in neurons, glia, or hematopoietic cells rescues this phenotype.

Disruption of autophagy in neural tissues in the trpml mutant. Brains from 21 day wt (F) and trpml1 (G) flies expressing GFP-ATG8, (a protein required for autophagy) (H) Fold increase in GFP-ATG8 fluorescence in trpml1 brains normalized to wt. Mean ±SEM (n=3 brains; *p≤5x10^-4*).

The exciting finding that expression of wild-type TRPML protein in hematopoietic cells is sufficient to delay the onset of the mutant phenotype raises the possibility that bone marrow transplantation (BMT) in MLIV patients may delay disease progression, which will be tested in recently developed TRPML1 knockout mice. Approved drugs that stimulate autophagy may also suppress MLIV, especially in combination with BMT. Thus, the establishment of the *Drosophila* model for MLIV provides the conceptual framework for developing strategies to treat MLIV.

The class culminated in a mock trial challenging whether lineage tracing using Cre/R26R in the developing mouse truly reveals the lineage of the cell or only the cell’s genetic history. This technique allows irreversible marking of cells that express a specific gene, also marking their progeny. So, with a jury of senior graduate students, postdocs, and PIs, and Dr. Maureen Gannon as judge, students argued their sides, citing specific evidence from the literature, and called various model organisms, like C. elegans, and key developmental biologists from history, such as Jonathan Slack, the author of the development classic From Egg to Embryo, to testify in order to prove their case. Ultimately, the defense won, allowing continued usage of this lineage tracing technique in developmental biology labs at VUMC. Overall, the inaugural Developmental Biology ‘Bootcamp’ proved informative and stimulating for the aspiring developmental biologists.

**Chemical and Physical Biology**

*By Elisabeth Ariel Ring*

The Chemical and Physical Biology (CPB) Program welcomed 6 new students this year. Kelli Kazmier, Gordon Lemmon, Nathan Mutic, Izzi Nathaniel, Jennifer Pryweller, and I joined nine other students in this relatively new degree granting program. CPB originated as an admissions program in 2001, and students would spend one year rotating through research labs, then choose a department from which to obtain a PhD. In 2005, CPB established a degree-granting program. Many, though not all, of the students in the program come to Vanderbilt through either the CPB admissions program or via the Interdisciplinary Graduate Program. One of these exceptions is third year graduate student Matthew Deeley. “I came to the CPB program by way of a masters in medical physics here in the Medical School Department of Radiation Oncology…. I had studied pure physics in undergrad and didn’t feel a traditional Ph.D. in physics would suit my long term goals… Ultimately, I chose CPB because I believed it would provide the freedom necessary to tailor my courses and experience relevant to my individual goals.”

One of the strengths of the CPB program is that students in the program are able to choose from a wide variety of courses, and can work in research labs from over 12 departments. Students choose one of 4 tracks to specialize in—Chemical Biology, Molecular Biophysics, Structural Biology, or the newest addition, Imaging. The CPB program aims to provide students who may or may not have a background in the biological sciences with the ability “to recognize important biological problems and to have the quantitative tools to approach those problems,” according to Dr. Al Beth, Professor of Molecular Physiology & Biophysics. The program prepares students to tackle interdisciplinary problems at the interface of the chemical, physical, and biological sciences.

For Matthew Deeley, that means non-rigid image registration, a process of determining correspondence of features among images collected at different times or by different methods, and its application in automatic segmentation of human anatomy. “My effort is in further developing, implementing and validating these methods in a clinical setting. I work with a team of physicians, computer scientists and engineers, and medical physicists. At the most basic level our goals are to make certain radiotherapy cancer treatments more cost effective and widely available, and to extend the technology necessary for more advanced treatments.
Neuroscience Program: New VBI Director, Mark Wallace

Q: What drew you to neuroscience?
Dr. Mark Wallace: As a premed student I made the mistake of doing some research and worked with a phenomenal neuroscientist, Ed Gruberg, at Temple University. He had such a passion for science and the work was very interesting. I never looked back.

Q: Why multisensory integration?
MW: I have always had an interest in multisensory systems because we perceive the world multisensorily. In my post-doc I was fortunate to work with the father of multisensory integration at the neural level, Barry Stein.

Q: A lot of people, myself included, don’t have a clear definition of the VBI. What’s the VBI mission statement?
MW: It’s changing. The VBI was created 10 or 11 years ago to coalesce a disparate neuroscience community. Our faculty are very spread out among departments and across the campus, and the VBI brings them together. The primary mission is graduate education; the initial vision of the VBI went beyond that but the problem has been resources. I will try to reinvigorate development, strengthening the connection with the community to encourage donations so that the VBI can do more. I also want to make the VBI more transparent; I have an open door policy. We need students’ feedback.

Q: Does a stronger connection with the community mean more events like Brainstorm?
MW: I’m creating an outreach committee which will give us a presence within the community all year. We can go to schools and teach kids, have public lectures in conjunction with the Science Center to promote information about mental illnesses, such as Alzheimer’s and Parkinson’s. We’d like to partner with some of the clinical departments to bring in a very high profile speaker, for example Oliver Sacks, to talk to a large audience, say one thousand people.

Q: So there’s a chance we’d get Oliver Sacks? Really?!
MW: Unfortunately his speaking fee is too high, even for Vanderbilt (!!). Sorry, I can’t say whom we are considering.

Q: What timeline do you see for establishing a stronger community presence?
MW: Almost immediately. Discussions are already happening at certain schools in Nashville.

Q: Is there any thought towards making a true neuroscience department?
MW: It’s been an active discussion since my arrival. We’re still 3-5 years away. We’re working on a refined structure. We need a strong identity.

Q: What’s changed since Dr. Sanders-Bush handed over the directorship?
MW: Elaine has done a phenomenal job. We’re now moving into middle age. Decisions may now be made quickly; it’s time to expand. Committees (now including the training faculty) will tackle administrative issues. Soon we’ll have the first VBI faculty meeting ever. It’s an evolutionary process, always changing. People will know who we are, what we do, how they can interact and benefit.

Molecular Physiology & Biophysics: New chair, Roger Cone

Dr. Roger D. Cone recently moved from Oregon Health and Science University in Portland to become the new chair of MPB. He accepted the position because of the quality of science conducted here, the collegial atmosphere, and the "opportunity to chair a department as great as this." Though he acknowledges the difficulty of replacing the number one physiology department in the US, Cone hopes to diversify its research areas by hiring faculty working with a variety of model systems, as well as increasing the proportion of faculty working in neurobiology (especially energy homeostasis) and biophysics.

Dr. Cone himself has recently begun working with zebrafish, which will allow identification of additional genes involved in the control of metabolism and feeding behavior. More generally, his lab studies the central melanocortin system, which integrates long-term signals of fat levels (e.g., leptin and insulin), mostly through the hypothalamus, with acute hunger and satiety signals (e.g., stomach and intestinal distension and peptides released by the gut upon food ingestion, such as cholecystokinin [CCK]), mostly through the brainstem.

Other specific research goals include characterizing the central melanocortin system’s sensation of and response to acute hunger and satiety signals, which include PYY3-36 and ghrelin in addition to CCK; and investigating the effects of altered melanocortin signaling on insulin resistance, hypercholesterolemia, fatty liver, and inflammation, especially through the melanocortin receptor MC3-R. These studies will lead to better understanding of the mechanisms of development of obesity and related syndromes, and may reveal potential therapeutically targets.

He came to work on energy homeostasis somewhat serendipitously, after changing research areas during his postdoctoral work from gene transfer to GPCRs upon realizing that their high degree of conservation would allow rapid identification of many of their sequences. His lab cloned the receptor for thyroid-stimulating hormone (TSH-R), quickly followed by the five melanocortin receptors, MC1-R through MC5-R. They soon showed that the agouti mouse obesity syndrome, a popular model in obesity research identified ~100 years earlier, likely resulted from agouti’s antagonism of MC1- and MC4-R.

Dr. Cone believes he has accomplished so much (138 publications, including 6 in Science and 5 in Nature; and 8 awards for research, including the Oppenheimer Award from the US Endocrine

(MPB Chair continued on page 6)
Microbiology & Immunology: B Cell Memory
By Patrick Collins and Megan Clancy

The healthcare community often assumes that the elderly have a poor quality of immunity, and that their immune systems would not recognize pathogens encountered earlier in life. Conventional wisdom also says that, unless a vaccine's effectiveness is known to be long lasting, a vaccine can provide protection for ten years on average. Dr. James Crowe's laboratory recently made a discovery that calls these views into question.

Crowe wondered whether antigen-specific B cells can persist throughout a lifetime, or if they last only a few years. His team decided to study elderly people who were children during the influenza pandemic of 1918. They chose 32 subjects who remembered having a family member ill with the 1918 flu, as they were likely to have been exposed to the virus. The results, surprisingly, demonstrated that all the subjects retained 1918 flu-targeting B cells. To confirm that the response was to the 1918 flu, the team then tested subjects younger than 70 years old who would not have been exposed to the 1918 flu. As they did not have 1918 flu antibodies, the team determined that the long-lasting protection was specific to that virus.

The antibodies that Crowe's team found had a high affinity for the 1918 flu. These antibodies, among the highest quality published so far, possessed three times the mutations one would find in normal memory cells, which suggests that a large number of mutations will give rise to high quality antibodies.

Since the 1918 flu hasn't resurfaced, there is the question of how the elderly study participants' antibodies became so highly mutated without being repeatedly exposed to the 1918 flu. Crowe speculates B cell memory may function similarly to cognitive memory: the memories that are created in childhood are the strongest because they are the ones that are revisited repeatedly over time. Similarly, the B cells formed early in life may be strongest because they are stimulated repeatedly over the years. The nature of the stimuli are open to debate—they may be other flu viruses, something environmental, or an unknown cause within the body.

Current research the Crowe lab includes the exploration of how HIV specific antibodies change during the course of an HIV infection; producing antibodies from mummified humans, such as that of Peruvian mummies and the Ice Man; and computer modeling of high-affinity antibodies.

Pathology: Highlighting Trenis Palmer's NRSA
By Jessica Moore

Trenis Palmer was recently awarded NRSA funding by the National Cancer Institute on the role of CD151-interacting adhesion molecules in regulating migration and metastasis. CD151 belongs to the tetraspanin family, which generally act as scaffolding proteins; their interactions with other proteins determine their functions. Palmer's mentor, Dr. Andries Zijlstra, discovered in his postdoctoral work that a monoclonal antibody against CD151 inhibited intravasation and metastasis of tumor cells in the chick embryo and nude mice, suggesting that the antibody promotes immobility. Further, the antibody recruits CD151 to the cell surface, which implies that its residence on the surface prevents metastasis. However, CD151 knockout cells do metastasize, and anti-CD151 cannot inhibit their intravasation, so other interacting proteins likely participate more directly in cell anchoring. Palmer is testing the importance of specific CD151-interacting adhesion molecules, some recently identified by the Zijlstra lab in a proteomics study, as well as others previously known, in CD151-mediated immobility. To do this, he alters expression of each adhesion molecule separately in tumor cells and determines whether anti-CD151 further diminishes mobility in a combination of in vitro and in vivo migration and invasion assays. He then further investigates promising leads by measuring metastasis in chick embryos, using real-time PCR for human-specific Alu sequences. Future live cell imaging investigations will complement these experiments. Palmer also plans to study the role of vesicular trafficking in delivery of CD151 and its partners to the plasma membrane, as mass spectrometry also identified several proteins involved in this process. This research may identify possible targets for cancer therapies that would promote tumor cell immobility and thereby prevent metastasis.

The news of his funding, which arrived in September, pleasantly surprised Palmer, as he found the reviewers' comments discouraging although his score was quite good. He believes the success of his application stems in part from the letters from his committee members, which he included on the advice of Dr. Chalkley. Including photos of the core facilities available and evidence of the capabilities of his model system, which his mentor developed recently, also improved the promise of his proposal. Palmer advises other NRSA applicants to begin the administrative process and request recommendations early; “don’t procrastinate like I did.” He speaks enthusiastically about the project, clearly enjoys the work, and says he has a great lab, all of which favor his future accomplishments.
A t the unlikely interface between energy-efficient lighting technology and neuronal membrane biology sits the laboratory of Dr. Sandra J. Rosenthal, Professor of Chemistry and Associate Professor of Pharmacology. Her lab studies semiconductor nanocrystals, also called quantum dots, which exhibit a variety of fluorescent properties suitable for both LED light generation and monitoring biological systems. They exhibit the same crystal structure as their parent bulk material, typically cadmium selenide, cadmium sulfide or zinc sulfide, but their nanometer-diameter size allows departures from the properties of the bulk material.

Fluorescence of quantum dots is “size-tunable;” smaller dots emit visible light at the blue end of the spectrum and larger dots emit red light. Rosenthal’s group developed cadmium selenide nanocrystals that emit light across the visible spectrum, producing white light. This technology may result in an energy-efficient alternative to the traditional light bulb.

Rosenthal does not confine her efforts only to interesting optics. Her team has used quantum dots to engineer a variety of probes for biological systems. Quantum dots offer a superior alternative to organic fluorescent dyes: they exhibit greater brightness and stability, enabling real-time monitoring of protein trafficking, as well as narrower emission spectra, allowing simultaneous labeling of multiple proteins. This application, however, required adapting the nanocrystals to the aqueous environment of biological assays. After another group reported that coating in amphiphilic polyacrylamide (AMP) yielded a quantum dot protected from hydrolysis, enzymatic degradation, and pH changes inherent in cell-based assays, Rosenthal’s team pioneered the conjugation of polyethylene glycol (PEG) derivatives to AMP to reduce non-specific binding to cell membranes. Using this PEGylation approach, Dr. Rosenthal and her colleagues have developed high affinity ligands for 5HT2 serotonin receptors, nicotinic receptors, dopamine and serotonin transporters. Most recently, Rosenthal’s group, in collaboration with researchers at the University of Illinois, used quantum dots conjugated to a PEG derivative of muscimol, a GABAA and GABAC receptor agonist, to specifically label GABAC receptors in Xenopus oocytes.

With demonstrated potential in applications from high throughput drug screening to in vivo imaging of cancer cells to energy-efficient luminescence, quantum dot technology offers a dynamic and valuable tool for multiple areas of science. Dr. Rosenthal and her colleagues use quantum dots to illuminate key players in neuronal signaling, but the implications of her work reach far beyond the synapse.


Perspectives  Clearing the Air: Is the VUMC Smoking Ban Beneficial to All?  By Carl Weitlauf

The campus-wide smoking ban enacted by Vanderbilt University Medical Center on September 1st marks the latest step in a two decade-long effort to protect hospital patients, visitors, and employees from second-hand smoke. Although it inarguably benefits patients’ and employees’ health, many still perceive flaws in the Medical Center’s plan.

Prior to the ban, policy required that those who chose to smoke did so in designated smoking zones in lightly-trafficked areas. Hired patrolers directed smokers to these designated spots. In addition, signs depicting sickly children in the more heavily-trafficked areas reminded students, staff, and visitors that patients recover more quickly when they’re not struggling to breathe. This system seemed to satisfy both those who prefer not to be exposed to smoke as well as those who exercise their right to light up—as long as people restricted their smoking to the designated zones.

The question therefore arises: Does the campus-wide smoking ban exist to protect people from second-hand smoke, or is it a mandatory enforcement of good health practices by making it more difficult to smoke?

If a visitor or employee absolutely needs to smoke, they may do so along the outskirts of VUMC. According to a statement from Vanderbilt’s Plant Services, areas that line 21st Avenue and Blakemore Avenue will be emphasized. However, several other areas remain beyond the jurisdiction of the smoking ban. Unfortunately, many of those areas are also used as outdoor break areas for employees of the VA, Light Hall, and other medical research buildings. Another question arises: Will the reduced exposure for some result in increased exposure for others? All one has to do is take a stroll along 21st Avenue down to Hillsboro Village or grab a bench outside of MRBII to answer that one.

Patients with limited mobility who habitually smoke will probably feel the impact most. Are these patients expected to leave the hospital grounds and venture across the street for a cigarette, or simply go “cold turkey” while receiving treatment? Although measures like nicotine patches may relieve the physical withdrawal symptoms, the individual will undoubtedly endure the emotional stress of smoking withdrawal during their recovery.

The smoking ban for employees unquestionably benefits employees by heightening awareness of, and increasing motivation to utilize, the smoking cessation services and support Vanderbilt offers. (For more information on these programs, visit www.vanderbilt.edu/HRSwellness/smoking_cessation.htm). Of course, at this rate, one wonders how long we have before these programs become mandatory in Vanderbilt’s quest to be healthy and smoke-free.

MPB Chair continued from page 3

Society) partly by the luck of finding “tractable, biologically important problems” to study. He believes this matters most in scientific success, as he instructs young scientists to choose “an important problem that you find motivating.” Cone seems to find science inherently motivating, as he most appreciates that he “can learn something completely new about nature every day.” He also acknowledges the importance of his “fabulous students and fellows” in completing and helping to direct the work. His previous trainees include many tenure-track faculty, as well as industry scientists and a biotech entrepreneur.
For an incoming graduate student in the biomedical sciences, selecting a thesis advisor shapes the rest of his or her nascent career. For many, this selection seems ominous, as one’s tenure at Vanderbilt will not be brief and work hours will be abundant. But fear not! With a wary eye, open lines of communication, and clearly outlined priorities, you can make the best of your time here.

Communication aids greatly in selecting a satisfactory mentor. Unfortunately, many scientists find social interaction challenging and may display infrequent eye contact, incapacity to comprehend non-literal meaning (metaphor, irony), and an inability to stray from “scientist-talk.” Some of the best scientists excel by breaking this mold, through communication with peers and lab members. Remarkably, others rarely leave their offices, their hermitage limited only by mini-fridge capacity and restroom proximity. You must also consider your desired degree of independence. Whether you produce only under the intense, coffee-infused breath of a managerial tyrant, or you prefer complete freedom, you will find a PI to fit your style. A PI’s experience level correlates with interaction with the lab, such that rookies tend to spend more time with students, while elder statesmen often leave training to experienced students or post-docs. However, experience brings reputation; established mentors can often offer stable funding and an easier path to publication. Current lab members will inform you best on the PI’s style, both through direct questions and observation of mood and workload.

Picking an advisor and lab ultimately entails sealing your dissertation research fate on a narrowly focused topic. However, a series of courses and departmental requirements begin your career. Each program will attempt to woo you, but remain critical, even as a witty PI pours you a fourth glass of wine at a recruiting event. A wonderful lab may belong to a requirement-heavy department. Unfortunately, it is not all about the science, as the departmental environment will deeply influence your stress level and graduate career length. Finally, ensure that you understand an advisor’s expectations. Some PIs expect to see their students at 8:00 AM, on weekends, and at every relevant seminar. For most, graduate school retains a bit of the freedom and independence of the undergraduate heaven we all remember fondly. The dark side of this autonomy represents the unavoidable maxim: time away from lab only adds to your graduate tenure.

Do not despair! With an apt advisor selection and an optimistic attitude, you can enliven the lab with awkward dancing and impromptu roller chair-based Olympic competitions.

- Meet with your PI regularly during your rotation.
- Though rotation projects are often handed out, try to help shape yours. (This entails some preparation – read some papers.)
- Speak at length with grad students/post-docs in the lab (Though they are certainly biased (or jaded) they could be your most important source.)

---

**Perspectives Choosing an Advisor**

By Caleb Doll

---

**‘Peer Review’: Advice for Research Trainees**

Dear reviewers, I have fallen in love with a labmate. She helps me troubleshoot my experiments, jokes with me about the rest of our lab, and even looks cute in her lab coat! I’ve tried ignoring my feelings and keeping it professional, but we are together all day every day and my feelings keep growing. Should I let her know how I feel? -Unexpected chemistry

Reviewer 1: When you socialize with your labmates often (and probably don’t get out much because you’re a graduate student), lab relationships are inevitable. I know several married couples who met as labmates. If she’s available and seems interested, go for it!

Reviewer 2: Lab romances are a horrible idea. They start out fine, but when you get sick of each other (because you are together nonstop), guess what? You’re stuck for the next several years!! Everyone else in the lab has to choose between you and it’s a huge mess! Trust me and forget about it!

Reviewer 3: You may have found the love of your life, or you may find yourself in a complicated situation—this will either be the best or worst decision of your life. Good luck!

Dear reviewers, Someone is stealing my food from the lab fridge. I have raised the issue in lab meeting several times, but my Lean Cuisines just disappear and everyone says it isn’t them! How do I make this stop? -Thief Grief

Reviewer 1: Laxatives.

Reviewer 2: As a biomedical engineer, I would rig a camera inside the fridge to snap a photo every time the door opened.

Reviewer 3: You’re not a failure, you’re a grad student! Take a day off, then try again. Check if you have overlooked something—did a reagent go bad? Turn to your labmates, your PI, and/or your committee for help. And talk to someone to relieve the stress.

Reviewer 2: Not all experiments work. Multitask as much as you can. If you’re doing 3 things at once, you have a better shot at something working. Ask if there is another way you can answer your question, so you can try multiple approaches. Consider a new direction.

Reviewer 3: Not all experiments work. You’re not a failure, you’re a scientist!! That’s why they call it research.