Volume 2, Issue 2

Spring 2009

A.B.S.T.R.A.C.T.

Annals of Biomedical **Student/Trainee** Research and Current Trends

Spotlight Post-doctoral Scientist: Sarah Kucenas, PhD

-Rebecca Thomason

"Don't NOT do an experiment just because it involves learning a new technique or model system. Science should never be limited by what you already know. It should only be limited by your imagination, which, as a scientist, should be *limitless*." This helpful advice has inspired Biological Sciences post-doctoral fellow Dr. Sarah Kucenas to excel as a scientist. It's the driving force that guides her aspirations.

Sarah has been at Vanderbilt for four and half years, working in the Appel Lab on developmental neuroscience using zebrafish as a model organism. Although Dr. Bruce Appel has moved his lab to Denver, Colorado, Sarah has stayed and is finishing her work up in the laboratory of Dr. Jonathan Gitlin, Chair of the Department of Pediatrics. Sarah and her husband, Adam, who is a member of the Air National Guard and a Metro Nashville police officer have a five-year-old boxer, Roxy, and just added a new member to the family, Dyna, a four-month-old Bullmastiff. When Sarah isn't in the lab, she enjoys spending time with her family and outdoor activities, specifically white water rafting.

Stats on Sarah
Born: St. Louis, MO
Undergrad: Valparaiso University, IN 2000
Grad School: Pharmacological & Physiological Science, St. Louis University 2005
VU post-doc: November 2005-present, Dr. Bruce Appel's Lab, Dept. of Biological Sciences
Fun Fact: Sarah was on the Division I swim team all four years in college.

Before coming to Vandy, Sarah was a graduate student in the lab of Dr. Mark Voigt at Saint Louis University. She investigated the developmental roles of P2X receptors, ATP ligand gated cation channels in the nervous system. By disrupting the function of the receptors and found that in the absence of normal P2X receptor function, cranial neural crest cells failed to migrate normally, the embryos developed craniofacial defects and cranial sensory neuron development was perturbed[1,2].

Upon completion of her graduate work, Sarah was drawn to the Appel lab and grew more interested in the developmental and genetic aspects of neurobiology. Sarah's current work involves the investigation of nervous system assembly and how it matures in the zebrafish embryo. Sarah has utilized transgenic and mutant zebrafish embryos to explore the development of the peripheral nervous system (PNS). Using *colourless*, a zebrafish line harboring a mutation in the *Sox10* gene and a combination of transgenic lines, she has been able to genetically manipulate the embryo and assess the effects on *(continued on p. 3)*

INSIDE THIS ISSUE

ABOUT A.B.S.T.R.A.C.T.

~Founded by Julie Field and Erica Bowton in 2007
~Written and edited by graduate students & post-docs
~Sponsored by the VUMC BRET office

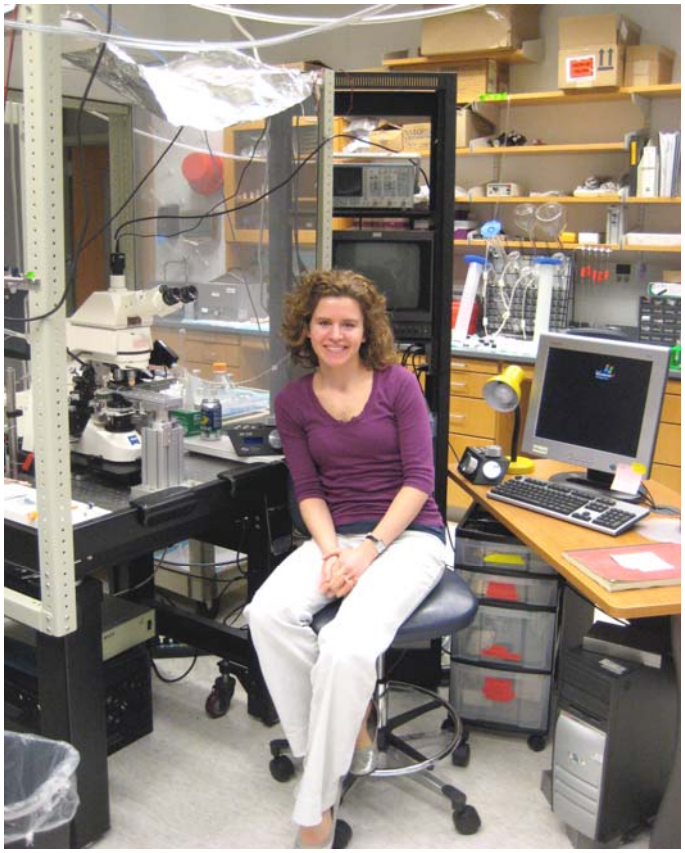
Also available online: http://bret.mc.vanderbilt.edu/bret/php_files/abstract.php

Spotlight Graduate Student Scientist: Molly Brown -Kt Moynihan

Molly Fricke Brown, a student in Dr. Gregory Mathews laboratory, researches neuropharmacology, specifically synaptic transmission, and she already has a first-author publication in the *Journal of Neurochemistry* titled "Glutamine uptake by System A transporter maintains neurotransmitter GABA synthesis and inhibitory synaptic transmission." She heads up the Pharmacology Graduate Student Association and is the Vice-President of Academic Affairs on the Graduate Student Council. Additionally, Molly is a teaching assistant in an undergraduate lab section in Biological Sciences. You could say that Molly has fully immersed herself in numerous aspects of graduate student life here at Vanderbilt!

The Mathews lab studies how the metabolism of major inhibitory neurotransmitter GABA regulates inhibitory synaptic transmission in the rat brain. Molly's first project focused on the role of System A glutamine transport in regulating inhibitory post-synaptic currents in hippocampal pyramidal neurons. These neurons use GABA synthesis to maintain synaptic vesicle filling and require the precursor glutamate, possibly from glutamine. She found that inhibition of glutamine transporters reduced vesicular GABA content and that astrocytes constitutively supply glutamine to inhibitory neurons to maintain the filling of these vesicles. From these results, she concluded that glutamine transporters support inhibitory synaptic strength by maintaining GABA vesicle filling. These results are seen in immature rats, but not adults, suggesting an age-dependent change in the role of glutamine uptake on GABA regulation. Molly is currently investigating the developmental regulation of the System A transporter.

Molly hit the ground running when she arrived at Vanderbilt in Fall 2005. Pharmacology and Dr. Mathews' research had interested her from the start and she made great progress her first year in the lab by following up on preliminary data from a former post-doc, landing her first first-author paper early in 2007. Molly states that this process taught her a lot: "I had the great opportunity to set up my system and data organization early on in my graduate career," she says, and this has served her well since. "Early" is a word that applies to Molly in several ways; she also joined the Pharmacology Graduate Student Association soon after entering the department. "Students have a very strong voice in the Pharmacology training programs and the GSA is a big part of that," she says. She felt very fortunate to be a graduate student at Vanderbilt and knew she wanted to give back to this community, which led to her interest in the Graduate Student Council. Attending a meeting led to participating as an at-large member and eventual recruitment by the outgoing VP of Academic Affairs to take over that position. This officer organizes the annual Graduate Student Research Symposium, which occurred this past March. In Molly's words, "The research symposium was well attended and… I thoroughly enjoyed our keynote address by Dr. Susan Basalla—there was standing room only, indicating that we certainly have tapped a need regarding improving Vanderbilt's career services for graduate students." In addition to her own GSC duties, Molly has served on other GSC committees and co-organized the recent seminar on Gender Dynamics and Communication. She admits that juggling Pharmacology GSA, GSC, and TA responsibilities in addition to research in the lab have made her busier than expected, but adds that she has learned a great deal and developed new skills by taking advantage of these opportunities. These experiences have opened up career options beyond her initial goal of pharmaceutical research and she is now also considering teaching and education administration.



Stats on Molly
Born: Pendleton, IN
Undergrad: Purdue University, IN 2005
Grad school: 4th year graduate student, Pharmacology
VP Academic Affairs – Graduate Student Council
President – Pharmacology Graduate Student Association
Favorite lab escape: Baking!

Coming to Vanderbilt with a BS in pharmaceutical science, Molly was intent on working toward a career in the pharmaceutical industry. Undergraduate research in industrial and physical pharmacy had not been a great fit, but ultimately guided her in the direction of biomedical research. In fact, she credits the graduate student in that undergraduate research lab as the most influential scientist in her science career. Her advice to incoming graduate students would be "to remember that your thesis research does not have to define you as a person and monopolize your time and energy. I encourage students to continue to pursue hobbies, passions and personal interests—it will help you stay sane and not lose yourself in the midst of the emotional ride that can often define the graduate student experience." Given what she has accomplished as a graduate student both inside and outside of the lab, she will definitely make an impact in any field.

(Sarah Kucenas continued from front page)

PNS development. For decades, the field has believed that the central nervous system (CNS) and the PNS are separate entities that do not overlap. Using zebrafish genetics and confocal time-lapse imaging, Sarah has begun to uncover some crossover that occurs between the two nervous systems. She has identified a novel peripheral glial cell type—known as perineurial glia—that originate within the CNS but exit and migrate into the PNS. These findings have shed some light on how the CNS and PNS interact during development[3]. This data, representing her research focus at Vanderbilt, was published in *Nature Neuroscience*.

"I love science and I want the people who train in my lab to love science. This career is a tough road! If you don't love coming into work everyday, then it isn't worth it. So it is my goal to create an atmosphere that will be inspirational to all."

In addition to her research, Sarah has been actively involved in sharing her knowledge and expertise by teaching undergraduates in the lab and graduate students in a methodology course. As the post-doc representative for the Program in Developmental Biology (2006-2007), Sarah was involved in organizing speakers and events. Additionally, she has won multiple awards for poster and presentation categories at meetings, including grand prize for the post-doctoral category at the Southeast Regional Society for Developmental Biologists meeting in 2007. This award included a travel grant to attend the first Pan American Congress in Developmental Biology conference in Cancun, Mexico.

Now that her education and training phases are culminating, Sarah is preparing to take flight on her own. While she is excited about her future, which currently includes multiple job offers, she keeps herself grounded with goals for her own lab and her general philosophy: "I think a PI, regardless of rank, should run a lab that fosters collaboration and enthusiasm. I love science and I want the people who train in my lab to love science. This career is a tough road! If you don't love coming into work everyday, then it isn't worth it. So it is my goal to create an atmosphere that will be inspirational to all."

1. Kucenas S, Li K, Cox JA, Egan TM, Voigt MM. Molecular characterization of the zebrafish P2X receptor subunit gene family. Neuroscience. 2003;(121)4:935-45.
2. Kucenas S, et al. Ectodermal P2X receptor function plays a pivotal role in craniofacial development of the zebrafish. 2009. (submitted).
3. Kucenas S, et al. CNS-derived glia ensheath peripheral nerves and mediate motor root development. Nature Neuroscience. 2008; 11(2):143-151.

Perspectives: *State of the IGP*

-Jeffrey Bylund

As the spring semester comes to a close, many of us are looking forward to the end of another school year and the beginning of summer. For the 2008-09 Interdisciplinary Graduate Program (IGP) students this may be especially so, as we look forward to the completion of our general curriculum and the start of "serious research" as we choose a Final Preceptor and settle in for the rest of our graduate career.

This is also a good time to reflect on the current state of the IGP. The IGP has changed in small ways through the years to become what it is today. Some of these changes include a reshuffling in the order of departmental presentations, the inclusion of flextime questions on exams, and an increase in the number of total students accepted into the program, with the 2008-09 class the largest to date.

Now, there is word that some major changes will be in store for IGP as the Biomedical Research, Education, and Training (BRET) office conducts a thorough review of the program, including a full audit by an external agency. As major tweaking of the IGP is considered, there seems to be consensus among the latest class about what kinds of changes would be welcomed.

A common sentiment expressed in the halls after class is that lectures tend to skip the introductory material that many of us were hoping to encounter. While the detailed, in-depth approach is certainly challenging and full of information, it is less effective when it comes to helping students gain an understanding of the subject in the context of biomedical research at large. The students in the IGP class come from varied backgrounds and are generally looking to be introduced to a new subject and become comfortable with it, not overwhelmed by it.

Another common sentiment seems to be that the end of the semester tends to run a bit long. By the time the second semester rolls around, some students are ready to join a department, and many would rather be reading papers based on their field of interest instead of the latest flextime paper. Allowing students to choose which IGP classes they'd like to take during the second semester via an *à la carte* system might be a welcome change.

There are also many things that everyone generally agrees on as being very effective. These include the variety of labs available for rotations, the exposure to many different disciplines and ways of doing science, and the overall congenial collaborative spirit that is encouraged in such an interdisciplinary environment.

Overall, the IGP seems to be in good shape. There is plenty of participation from many excellent departments and those who organize and manage the program are world class researchers who know what it takes to do good science in an ever more dynamic field. Hopefully the combined perspective of students and faculty can come together to help shape IGP 2.0 into an even more excellent program in the coming years.

National Institutes of Health's $timulus

-Hillary Hager

On January 28, 2009, all members of the Vanderbilt community received an ominous email from Chancellor Zeppos that spoke of campus-wide budget cuts, decreased discretionary spending, and freezes in hiring and salaries in response to the recent world-wide economic downturn. Graduate students and post-docs alike nervously laughed it off, hoping the economic strife would not hit home in their own department or lab. With decreased National Institutes of Health (NIH) funding levels in recent years, the future of scientific research has become a legitimate concern, even at a top university such as Vanderbilt[1]. Now with the stimulus package granting $10.4 billion to Research & Development (R&D), many are hopeful that research has once again become a priority to legislators[2]. But, what does the economic crisis really mean for graduate students and post-docs in the biomedical sciences, especially in light of the NIH stimulus package?

The two goals of the NIH stimulus money are to create and sustain scientific jobs and to pursue scientific opportunities. To accomplish these goals, funds have been allocated to several different areas: Scientific Instrumentation, Building Construction and Renovation, and even for the enhancement of Biomedical Core Facilities. However, the bulk of the stimulus ($8.2 billion) will go to "scientific research priorities" through competitive grant funding[3]. Among these opportunities are supplements and/or revisions to existing grants, new challenge grants, and funding of recently peer-reviewed R01s. Supplements are intended to either significantly expand the scope or increase the tempo of active research grants through hiring new personnel, investing in new technology, or forming collaborations[4]. Current students and post-docs are prime candidates for hire as the NIH has specifically recommended them as a means to accomplish new scientific objectives. Additionally, NIH supplements can be used to add slots to already active Institutional Training Grants, positions that are coveted by both pre- and post-doctoral trainees[4]. Overall, this influx of money has the potential to have a large impact on graduate student and post-doctoral support.

However, all of this money must be obligated by the NIH by fall of 2010 and is required to be used for research projects within the next two years. So, where will this leave scientists come fall of 2012? There is some speculation that the research community will be right back where it started, albeit with more personnel to support and several unfinished research projects that took longer than the allotted two years. Problems could be particularly acute for new students and post-docs that were hired with funds from the NIH economic stimulus. However, there is evidence that this 'running off the cliff' phenomenon will not happen. After two static years of NIH funding, the FY2009 omnibus bill was signed into law on March 11th giving the NIH budget a boost of 3.2%, which equates to approximately $1 billion[5]. According to a study conducted by Families USA, this increase has the ability to support over 4,450 new research jobs across the country.[6] Even though BRDPI (Biomedical Research and Development Price Index, calculated each year by the Bureau of Economic Analysis to estimate the cost of medical research) predicts this budget increase only keeps even with inflation, it is still a start.[7] Furthermore, total federal money appropriated to R&D increased by nearly $7 billion.[5]

For Vanderbilt faculty, students, and post-docs, an increase in total federal funding is quite encouraging. Since 2001, external funding at Vanderbilt has more than doubled, and the university now ranks 20th in federal awards for R&D in Science and Engineering. Overall, awards at Vanderbilt are up 5% from last year, even in light of the recent economy.[8] If the past six years are any indicator of things to come, Vanderbilt should fare quite well with the $10.4 billion the NIH is now distributing. However, to whom much is given, much is expected. In order to sustain this increased funding, the government must know and understand the accomplishments and discoveries made in the laboratory. Thus, once the money is allocated, it is up to the scientists (especially budding scientists) to not only obtain compelling results, but also to share their findings with congressmen appropriating the money.

Despite the current stormy economic climate, Vanderbilt continues to grow and thrive in the area of scientific research. With the recent influx of stimulus funding to the NIH, coupled with an increase in the overall federal R&D budget, the future could remain bright for Vanderbilt trainees.

1. NIH FY 2009 President's Budget. February 4, 2008.
2. From the Director: NIH's Role in the ARRA (www.nih.gov/about/director)
3. NIH's Role in the American Recovery and Reinvestment Act (ARRA). (www.nih.gov/about/director)
4.NIH Notice of the Availability of Recovery Act Funds. (grants.nih.gov/grants/guide/)
5. AAAS Analysis Finds 2009 Omnibus Budget Includes Significant Increases for US R&D Agencies. March 27, 2009. (www.aaas.org)
6. In Your Own Backyard: How NIH Funding Helps your State's Economy. Families USA's Global Health Initiative, June 2008.
7. ACD Hears US Stimulus Package Could Spur NIH Finances. NIH Record, January 9, 2009
8. From Famine to Feast: The Impact of an Influx of Federal Research Funding. Vanderbilt Federal Forum, March 16, 2009.

Departmental Updates

Biochemistry's New Graduates -Megan Wadington

The Department of Biochemistry wishes to congratulate its recent graduates. Twelve students were awarded PhDs this year. Their dissertation research covered a variety of topics ranging from the analysis of lipid distribution by MALDI imaging mass spectrometry to the mechanisms of genome maintenance during replication.

These most recent graduates are **Omari Bandele** (Osheroff Lab, "Bioflavanoids as Poisons of Human Type II Topoisomerases"); **Kristin Burnam** (Caprioli Lab, "Detecting Spatial and Temporal Distributions of Lipids and Proteins during Embryo Implantation by MALDI Imaging Mass Spectrometry"); **Joseph Deweese** (Osheroff Lab, "The DNA Cleavage Reaction of Human Type II Topoisomerases"); **Charles Knutson** (Marnett Lab, "Oxidative Metabolism of Exocyclic DNA Adducts"); **Courtney Lovejoy** (Cortez Lab, "Replication Dependent Mechanisms of Genome Maintenance"); **Charles Mobley** (Sanders Lab, "Biophysical Studies of Human Neurological Membrane Proteins: Peripheral Myelin Protein 22 and Amyloid Precursor Protein"); **Daniel Mordes** (Cortez Lab, "Activation of the DNA Damage Response Kinase ATR"); **Brian Weiner** (Chazin Lab, "Biochemical and Structural Analysis of the p58C and p68N Domains of DNA Polymerase Alpha/Primase"); **Cornelia Crooke** (Carpenter Lab, "Regulation of Fibronectin Assembly by PLC-γ1"); **Sarah Knutson** (Hiebert Lab, "*In Vivo* Characterization of the Role of Histone Deacetylase 3 in Metabolic and Transcriptional Regulation"); **Tiffany Farmer** (Hiebert Lab, "Characterization of the Transcriptional Co-repressor, Myeloid Translocation Gene Related-1, in Cell Lineage Decisions of the Gut and Hematopoietic Systems").

These recent graduates have pursued career paths as varied as their research interests. Dr. Charlie Knutson is currently a post-doctoral associate at the Massachusetts Institute of Technology in the lab of Dr. Steven R. Tannenbaum. His research focuses on the chemistry and biology of tissue damage associated with diseases of chronic inflammation, including Crohn's disease and ulcerative colitis. Dr. Joseph Deweese will start his postgraduate career at Lipscomb University's College of Pharmacy as an Assistant Professor in the Department of Pharmaceutical Sciences. Dr. Daniel Mordes has returned to medical school at Vanderbilt University after defending his thesis in September. He plans to pursue a research-oriented residency after medical school.

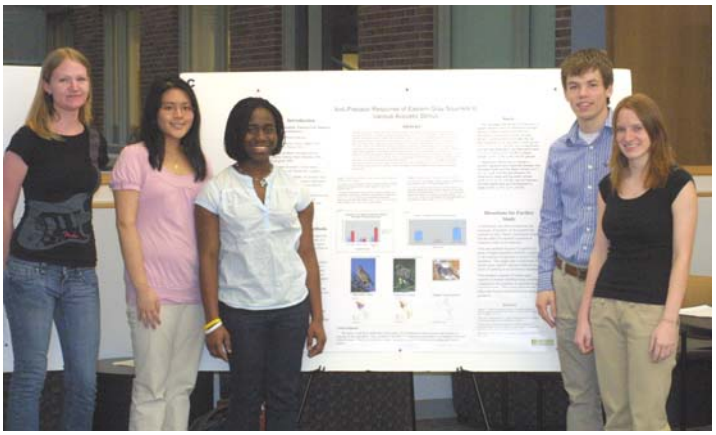
In Memoriam

Anne Karpay was awarded a posthumous PhD for her studies in the "Application of Solution NMR Spectroscopy to Multi-Span Integral Membrane Proteins, Including G Protein-coupled Receptors." Anne passed away January 5, 2008 after a four-year struggle with breast cancer. In the words of her advisor Dr. Chuck Sanders, "Anne had an absolute passion for science that was matched only by her passion for friendship and life in general." For everyone in the Department of Biochemistry, Anne was a more than a student; she was a very good friend. Anne is deeply missed.

Biological Sciences: Teaching Opportunities -Karen Gamble

Have you ever wondered how you can gain independent teaching experience during your training at Vanderbilt University? Some graduate students and post-doctoral fellows highly value teaching opportunities because it is only through interaction with students that one can determine if a teaching career is something to pursue. Others would like to develop a teaching portfolio. Whatever the case, teaching allows for the development of mentoring skills that are important for nearly every scientific career path. The Department of Biological Sciences is unique in that it is one of the few departments at Vanderbilt that offers a structured program through which graduate students and post-docs can lead and develop their own research component in a semester-long laboratory course through a newly instituted alternative laboratory module for Introduction to Biological Sciences (BSCI 111). Steve Baskauf, the Laboratory Coordinator for the introductory course, developed this module in the fall of 2007 in an effort to provide undergraduate students with an opportunity to engage in longer-term research projects designed to foster critical thinking skills. Undergraduates have a choice of taking the standard lab component of the second semester of the course (BSCI 111B) or the new lab component (BSCI 111C), which features a mentor-led project and two credit hours.

Graduate students from departments or programs outside of Biological Sciences—including Pharmacology, Pediatric Cardiology, and Neurology—have recently taken advantage of the unique experience that this newly developed course offers. According to Baskauf, BSCI 111C is an alternative to the traditional "cookbook" laboratory course and allows undergraduates to obtain real research experience as an introduction to biomedical research.



Undergraduate students present work from their mentored research.

Interested in mentoring/teaching? Contact Steve.Baskauf @vanderbilt.edu

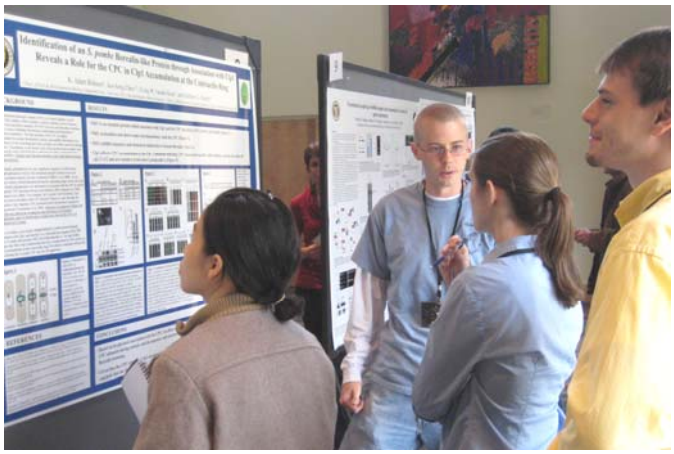
At the beginning of the semester, students are encouraged to choose a project and mentor. With a 4:1 student:mentor ratio for sub-projects, students work very closely with their mentors and collaborative teammates and present a poster and a paper at the end of the semester. Students have been very responsive to this newly structured laboratory alternative, and enrollment has tripled from the first year to its current, second year. Clearly, there will continue to be a need for enthusiastic and experienced graduate students and post-docs to serve as mentors for this lab course. In return, mentors will receive experience in developing training projects and mentoring skills that are valuable in nearly every research career.

Cell & Developmental Biology: Retreat -Emily Cross

The Cell and Developmental Biology department hosted their 7th annual departmental retreat on April 16. This year, a major venue change was made; prior retreats were held in the conference center of Cheekwood Botanical Gardens, but budget considerations led to setting up at Vanderbilt's Student Life Center. With the help of the CDB Graduate Student Association led by president Becca Thomason and vice-president Billy Carver, the department was able to take advantage of Vanderbilt's Student Life Center as the new venue. There were prize giveaways throughout the day, including gift cards to iTunes, Panera, and Amazon.com, with a grand prize of a Nikon digital camera.

The focus of the CDB retreat is to provide a relaxed atmosphere in which primary and joint faculty, graduate students, post-doctoral fellows and research staff are able to update fellow labs on their current research pursuits and initiate discussions about their work. This year, many students and post-doctoral fellows presented posters and twelve students were chosen to present 15-minute talks. The department also honors one graduate student and one post-doctoral fellow for their achievements during the year. This year, the awards were given to Rachel Roberts-Galbraith, a graduate student in Dr. Kathy Gould's laboratory and Dr. Elizabeth Tran, a post-doctoral fellow with Dr. Susan Wente.

In addition, following tradition, a speaker was invited from an outside institution to present the keynote address. This year, CDB invited Jeffrey Gordon, M.D, from the Center for Genome Sciences at Washington University School of Medicine in St. Louis. In his talk titled "The human microbiome project: exploring the microbial side of ourselves," Gordon expounded on the topic of human and microbial synergy, specifically in the digestive system. His lab focuses the characteristics and factors that influence the stability of the human microbiome. He hypothesizes that the microbiome is affected by human lifestyle choices and thereby affects human health. Some of the questions he has addressed include: How do we acquire our microbiota? And, do humans have a replicable gut microbiome, or are microbial landscapes specific to each individual? The CDB department thoroughly enjoyed learning about this unique perspective on human wellness, as well as spending a day sharing science and socializing together!



Chemical & Physical Biology -Megan Wadington

The Vanderbilt Institute for Chemical Biology (VICB) is entering its 7th year as the primary organization devoted to the application of chemistry to the solution of important biomedical problems. The VICB is a trans-institutional center with 70 members from 18 departments. A primary focus of the institute is to provide research and training in the area of chemical biology. A collection of core facilities provides access to techniques and equipment at the frontier of biomedical research. Recently, the Chemical Synthesis Core (CSC) hired a new director. Dr. Alex Waterson joins the CSC from the medicinal chemistry department at GlaxoSmithKline. When asked about services the CSC can provide, Waterson stated, "The Chemical Synthesis Core is equipped with a variety of advanced equipment, including automated purification systems and an experienced full-time professional staff. We are available to take on a wide variety of projects that range from the gram synthesis of tool compounds to the resynthesis of hits to follow up high throughput screen results. The core is even able to take on full scale medicinal chemistry hit optimization campaigns." Often the core's services are more affordable than outside vendors.

Another VICB core facility is the Vanderbilt Monoclonal Antibody Core (VMAC), a shared resource dedicated to the generation, purification, and characterization of monoclonal antibodies. Dr. Robert Carnahan, Director of VMAC, states, "The core's central mission is to make state of the art hybridoma/monoclonal antibody technology cost effective and readily available to Vanderbilt investigators." Efforts to upgrade and redevelop the facility have "led to significant improvements in the success and throughput of monoclonal development projects, enhancements in the quality and efficiency of antibody purifications, and the introduction of numerous new services including antigen preparation and polyclonal affinity purification."

The VICB's other core services include the Small Molecule NMR Core and the High-throughput Screening Facility. Researchers interested in utilizing VICB core facilities are encouraged to visit www.vanderbilt.edu/vicb/ for more information.

Human Genetics: Genes & Drugs -Jevon Plunkett

Dr. Marylyn Ritchie's lab, in collaboration with other members of the International Warfarin Pharmacogenetics Consortium, reported on a pharmacogenetic algorithm for warfarin dosing in the February 19 issue of the *New England Journal of Medicine*. Globally, warfarin is the most popular prescribed blood thinner. Determining the appropriate dose of warfarin is challenging because the optimum dose varies widely among patients and taking an inappropriate dose can be fatal.

Pharmacogenetics, the study of genetic differences in drug response among individuals, may facilitate appropriate warfarin dosing and minimize negative outcomes. Using 4043 patients of a 5700 international patient cohort, Ritchie and colleagues developed a pharmacogenetic algorithm to predict optimal dose of warfarin, combining clinical factors, demographics and variation in the cytochrome P450,family 2, subfamily C, polypeptide 9 (*CYP2C9*), and vitamin K epoxide reductase complex, subunit 1 (*VKORC1*) genes, known to contribute to warfarin dosing variability. The authors then compared the effectiveness of this pharmacogenetic algorithm to an algorithm based on clinical data only and to a fixed-dose model, in a validation cohort of the remaining 1009 patients. The pharmacogenetic algorithm accurately identified the optimal warfarin dose for more patients in the low dose and high dose categories than the clinical algorithm and fixed-dose model; however, the three models performed equally well for patients in the average dose category.

Overall, dose estimates determined by the pharmacogenetic algorithm were closer to the actual dose than were estimates from the clinical algorithm for 60% of patients and were closer to the actual dose than estimates from the fixed-dose model for 69% of the patients. As a result, the pharmacogenetic dosing algorithm presented by Ritchie and colleagues lays the foundation for a prospective clinical trial to determine the effectiveness of warfarin dose estimations incorporating genetic information.

Neuroscience: Changing of the Guard -C. M. Ciarleglio

In 2008, the directorship of the Vanderbilt Brain Institute (VBI) was handed over to Dr. Mark Wallace (*see A.B.S.T.R.A.C.T.* ***2:1*** *p. 9*). Dr. Wallace, Associate Professor of Hearing and Speech Sciences and Psychology, succeeded Dr. Elaine Sanders-Bush, who served as the Institute's director since its inception. These were, of course, enormous shoes to fill, but Dr. Wallace took up the reins at full steam. While working quietly in the background to reorganize the VBI and the ever-expanding Neuroscience Graduate Program, his first major executive responsibility was to appoint a new director of graduate studies (DGS). In November of 2008, Dr. Wallace announced that Dr. Douglas G. McMahon—then concluding his term as DGS for the Department of Biological Sciences—would take over as DGS for the Neuroscience Graduate Program in January 2009. In his formal announcement of the appointment, Dr. Wallace said of Dr. McMahon that he "has an exemplary record of success in the research, teaching and mentoring arenas, making him ideally suited for his new role in neuroscience graduate education and training." Dr. McMahon completed his graduate training under Dr. Gene Block, currently Chancellor of UCLA, at the University of Virginia and post-doctoral research under Dr. John Dowling at Harvard. As Professor of Biological Sciences and Pharmacology at Vanderbilt, McMahon studies mechanisms of neural plasticity in three linked subsystems of the central nervous system: the visual, circadian and serotonergic systems that together mediate sense of sight, drive daily rhythms and influence mood.

Dr. Doug McMahon, the new Neuroscience Program DGS (from vkc.org)

The appointments of Dr. Wallace and Dr. McMahon to leadership positions within the Vanderbilt Brain Institute constitute a move from complete focus on graduate education—the primary goal of the young VBI—to a more mature delegation of focus on the Institute's development and community missions. This changing of the guard represents a critical transition as the Institute moves towards the formation of a proper Department of Neuroscience. Dr. McMahon, in particular, brings a perspective that spans not only scientific disciplines, but also crosses borders between the College of Arts and Sciences (his primary appointment) and the School of Medicine (his secondary appointment) within the University. This emphasis on interdisciplinary and intracollegiate collaboration is a hallmark of the VBI. While one can expect to see many changes to the Program in the coming years, both Dr. Wallace and Dr. McMahon hope to build on the achievements of Dr. Elaine Sanders-Bush and Dr. Randy Blakely, whose efforts have made the now middle-age program so successful.

Microbiolgy & Immunology -Patrick Collins

The immune system is a powerful organ, capable of easily killing most organisms that invade the host. However, this capability comes with a problem: If the immune system is misdirected, it can destroy the body's own organs. For example, autoimmune diabetes occurs when the host immune system inappropriately targets its own pancreatic beta cells. This process is accompanied by B cells, the cell type which produces antibodies, with specificity for beta cell targets. How the immune system prevents the formation of B cells specific for insulin, a key auto-antigen in autoimmune diabetes, is the research focus of Dr. James Thomas' laboratory.

How does the immunue system prevent the formation of B cells specific for insulin?

It is estimated that up to 75% of developing B cells recognize host tissue. These cells must be killed, made useless (anergy), or forced to change their target. It has classically been thought that anti-insulin B cells escape this tolerance process because insulin is too small to be efficiently recognized. However, Rachel Henry, from the Thomas lab, shows that developing B cells do indeed recognize insulin. Her work further shows that anergy, but not cell death, is a primary mechanism of protection against autoimmunity from insulin-specific immature B cells. In subsequent work, Henry shows that the insulin-recognizing developing B cells can proceed to change the target of their antibody by rearranging the DNA encoding for their antibody.

Early events in immune tolerance appear to be different in individuals and mice who develop type one diabetes and those who do not. Future work in the Thomas lab will focus on how insulin tolerance differs between autoimmune susceptible individuals and healthy individuals. Work will also focus on identifying other key auto-antigens in autoimmune diabetes, and determining the mechanism by which the functionally anergic B cells, which Henry's work describes, can still promote autoimmune diabetes.

Pathology: "Superhealer" stem cells -Robin Marjoram

Currently, a highly pursued area of medical research is the study of stem cells, cells that possess self-regenerative capabilities and have important potential therapeutic applications. Maria Alfaro, a graduate student in Dr. Pampee Young's lab , recently published a paper in *the Proceedings of the National Academy of Science* [Vol. 105(47), pp.18366-71] on the use and modulation of mesenchymal stem cells (MSCs) in myocardial repair.

In this paper, the authors addressed the function of stem cells in tissue regeneration and wound healing. They show that the expression of the gene *secreted frizzled-related protein 2* (sFRP2) directly regulates MSC proliferation, engraftment, and formation of wound granulation tissue. The sFRP2 gene encodes a protein that functions as a secreted inhibitor of the canonical Wnt signaling pathway. Identification of sFRP2 as a stem cell engraftment enhancer was accomplished by comparing gene profiles and functional activities of MSCs from wild-type mice with those from MRL/MpG mice, a strain known as a "superhealer" due to the fact that these mice have increased ability to repair injured tissue. These MSC comparisons showed that MRL/MpG mice had greater MSC proliferation and engraftment as well as increased expression of sFRP2. Treatment of MSCs with recombinant sFRP2 greatly increased their proliferation. Further support for the role of sFRP2 in promoting the regenerative capabilities of MSCs came from the over-expression of sFRP2 in MSCs (sFRP2-MSCs), which increased MSC proliferation and engraftment. More importantly, injection of sFRP2-MSCs or MRL-MSCs into post-infarcted mouse hearts caused enhanced repair and greater regain of myocardial function. Knock-down of sFRP2 by shRNA in MRL-MSCs showed a loss of these enhanced regenerative activities.

Overall, the authors have revealed sFRP2 as a key molecule in modulating the efficacy of potential MSC-based therapies for wound and myocardial repair. Exploiting this mechanism could improve stem cell therapies.

See amazing "superhealer" pictures:

www.bu.edu/sjmag/scimag2008/Story pages/DARPA Mouse.html

'Peer Review': Advice for Research Trainees

Hosted by Rachel Roberts-Galbraith

Dear Reviewers: My advisor is an incredibly serious person who requires weekly meetings with us. However, every time I step into his office, I am terribly distracted by a large, framed, ridiculous portrait of my advisor, dressed as a Jedi knight. I spend so much time and energy focusing on not laughing that I can barely talk about my research progress. Office visits are required. Help! - *Meeting Misery in MRBIII*

Reviewer 1: Does your advisor leave his door open when he is out for a short period of time (during a seminar, for example)? If so, go in and stare at the picture. Repeat as necessary until you are completely desensitized and it is no longer funny.

Reviewer 2: When you walk into your advisor's office for your next meeting, confidently turn the photo face down. Explain calmly to your advisor that while you respect his right to decorate his personal space as he sees fit, you are distracted by the photo during your meetings. Then, when you are finished, put the photo back in its place. If you're doing this for the sake of scientific communication, your advisor can't argue with you! May the Force be with you!

Reviewer 3: For your advisor's next birthday (or next major grant renewal) give him a collage of lab member photos, framed. The gift can be from the whole lab but the card should read: "To replace that crazy Jedi photo that scares away all the rotation students."

Dear Reviewers: I just finished the IGP and joined a lab that I thought was the right fit. Now my advisor is encouraging me to choose a project and get started, but I feel totally lost. When I arrive in the morning I just don't know what to do. My advisor thinks I am totally independent, but I am overwhelmed. Have I chosen the wrong lab? *-Post-rotation Blues*

Reviewer 1: It sounds like you are having trouble making the adjustment from rotation student to graduate student. While in your rotation you probably had someone telling you what to do every day, but now you don't. This is just another stage in your scientific development. Re-read some recent papers from your lab and see what interests you the most. Get a calendar to plan your experiments a week at a time. And don't be scared to get your feet wet.

Reviewer 2: Your advisor can't help you if you don't ask. You're only in the wrong lab if your advisor refuses to help you at all. I recommend scheduling a meeting with your advisor to discuss your project options. Come prepared, but be honest about your feelings.

Reviewer 3: You're a deer in the headlights, and you're stuck in the middle of the road. Get un-stuck by talking to the graduate students and post-docs in your lab to see what they are working on and what projects are available. You can even ask them for advice on what scientific questions they find interesting to guide your first few experiments.

If you have questions for the reviewers, email us at peerreviewers@gmail.com and we'll try to help!

Dear Reviewers: I am a post-doctoral fellow trying to finish up a paper so that I can go on the job market. This paper has been in the works for nearly a year, but we still have not submitted it. Sometimes my mentor takes weeks to return a draft. Other times, she will repeatedly change her mind about data to include/exclude. I don't know how much longer I can wait. *-Impatient to Publish*

Reviewer 1: Hopefully your advisor is well-intentioned and just wants your paper to be published in the best journal possible. You should discuss with her your frustration about publishing sooner rather than later and see if you can reach a compromise.

Reviewer 2: Get a "final draft" together and tell your mentor that you would like to submit in 2 weeks. As a post-doc, you are really supposed to be (at least partly) a master of your own fate. If you are happy with your paper, your advisor should be willing to hear you out.

Reviewer 3: Perhaps you should send your draft to other professors you trust (e.g., your previous doctoral advisor, others in your department). This might give you a better idea whether you or your advisor is right about your paper's readiness for submission.

EDITORS
NELLIE BYUN
KT MOYNIHAN

FACULTY ADVISORS
AARON BOWMAN
DAN POLLEY

COLUMNISTS
JEFFREY BYLUND
C.M.CIARLEGLIO
PATRICK COLLINS
EMILY CROSS
KAREN GAMBLE
HILLARY HAGER
ROBIN MARJORAM
JEVON PLUNKETT
RACHEL ROBERTS-GALBRAITH
REBECCA THOMASON
MEGAN WADINGTON

Congratulations 2009 graduates!

LANDING AN ACADEMIC FACULTY POSITION: Wednesday, May 20, 2009
1:00-2:30, 512 Light Hall
Sponsored by the BRET Office of Career Development

PREPARING RESEARCH TEAM LEADERS: Tuesday, June 2, 2009
12:45-4:45 p.m., Light Hall
Sponsored by the BRET Office of Career Development, BRET Office of Postdoctoral Affairs, Vanderbilt Postdoctoral Association
Open to postdoctoral fellows and research track faculty. Advance application and registration is required
medschool.mc.vanderbilt.edu/scientific-leadership-workshop/

More workshops & seminars at
bret.mc.vanderbilt.edu/career_development/