January 2011 Message

This new year, make a resolution to plan ahead and submit your NIH grant applications in advance of the deadline. With the error correction window going away as of January 25, 2011, submitting your application early is the best way to ensure success. PENN VET has a five day submission rule in getting your grant to your BA, before the official deadline. PIs should be aware that it is taking longer for Research Services to get applications submitted to NIH due to the number of grants being processed. For deadlines on or after January 25, 2011, all applications must be error free by the deadline. New resources at Grants.gov will help applicants in the event of an unforeseen issue. A new live chat feature allows applicants to chat directly with a Grants.gov staff member when they have questions or concerns about submitting their application. The chat feature can be found by clicking “Contact Us” in the upper right corner of the new Grants.gov Self-Service Web Portal.

What’s Newsworthy in Neuroscience

Science Now—up to the minute news from SCIENCE showcased the recent work of Tracy Bale, PhD, Associate Professor of Neuroscience, Department of Animal Biology. Her studies report that dieting makes the brain more sensitive to stress and the rewards of high-fat, high-calorie treats. These brain changes last long after the diet is over and prod otherwise healthy individuals to binge eat under pressure. The article by Diana E. Pankevich, Sarah L. Teegarden, Andrew D. Hedin, Catherine L. Jensen, and Tracy L. Bale is entitled “Caloric Restriction Experience Reprograms Stress and Orexigenic Pathways and Promotes Binge Eating” (J. Neurosci., Dec 2010; 30: 16399 - 16407).
Dr. Southwood completed a PhD at the Colorado State University (CSU) Equine Orthopaedic Research Center (1999-2002), studying the efficacy of gene therapy-mediated growth factor expression for treatment of infected long-bone fractures using a rabbit model. While pursuing her PhD, she was also a full-time after-hours large animal emergency clinician at CSU, and helped to develop their emergency medicine and critical care program. This experience prompted Dr. Southwood to subspecialize in emergency and critical care and she became Diplomate of the American College of Veterinary Emergency and Critical Care (ACVECC) in 2005.

Her current research is focused on equine gastrointestinal disease. Gastrointestinal disease causing acute abdominal pain (colic) is a leading cause of morbidity and mortality in the equine population. The annual national incidence of colic in the US horse population is 4.2 colic events/100 horses/year at an estimated annual cost of $115.3 million. The overall fatality rate is 11%.

In a recent prospective study of survival rates of horses admitted on an emergency basis to New Bolton Center over a 12 month period, horses admitted for small intestinal strangulating lesions had an overall mortality of 24-62% and for large colon strangulating lesions of 44%. Clinical and research studies are necessary to improve the survival of horses with these types of lesions. Dr. Southwood’s research is focused on assessment of current treatment and development of novel methods for managing horses with colic, particularly those with ischemia-reperfusion injury.

**Intestinal ischemia-reperfusion injury in horse: Is there anything we can do?**

Her research into the use of gene therapy to express growth factors to enhance bone healing conducted during her PhD prompted Dr. Southwood to investigate analogous methods to improve healing following intestinal ischemia-reperfusion injury. As little is known regarding growth factor expression in the gastrointestinal tract of equine patients, Dr. Southwood utilized an equine large colon volvulus (LCV) ischemia-reperfusion injury experimental model (Figure 1), to examine growth factor and growth factor receptor mRNA expression during ischemia and reperfusion. Vascular endothelial growth factor (VEGF) and VEGF-Receptor (-R) mRNA expression was greater in horses with a LCV compared to normal. VEGF, therefore, may be important in early intestinal healing and may also explain, in part, the increase in vascular permeability in horses with a LCV compared to normal. VEGF, therefore, may be important in early intestinal healing and may also explain, in part, the increase in vascular permeability in horses with a LCV. Insulin-like growth factor (IGF)-R mRNA expression increased in the control small intestine during ischemia and reperfusion. The latter finding was unexpected and warrants further investigation as IGF may be important for understanding postoperative complications in horses with small intestinal lesions, such as adhesion formation.

To further explore the potential for gene therapy in the treatment of gastrointestinal injury, Dr. Southwood has completed pilot studies in both an equine and rat model in collaboration with Drs. Julie Johnston and Peter Bell at the Gene Therapy Program at the University of Pennsylvania Medical School.

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WHAT IS A CDA?

A CDA is a Confidential Disclosure Agreement—a document which protects against the unauthorized disclosure of confidential information before it has been made generally available to others in the public domain. CDAs can protect a one way disclosure of information from a discloser to a recipient, or it can protect a two or more way disclosure between multiple parties. Typically, a CDA will establish a defined subject area around which potentially confidential information may be disclosed (e.g., a specific patent application, a proposed work plan for an SRA, or unpublished data and research results) and a time frame within which the confidential information that is shared must be maintained in confidence by the recipient. Most CDAs also provide certain exceptions to the requirement to maintain disclosed confidential information in strict secrecy, including exceptions due to subsequent public disclosure, independent development or receipt of the same information, and legal requirements. There are numerous agencies at Penn that can implement and assist in the placement and review of CDAs, including the Center for Technology Transfer, the Office of Research Services and the Office of General Counsel. This review is done on behalf of Penn for purposes of determining whether the obligations create any conflicts with any established Penn policies, and advice is often provided to the faculty member regarding how to address any such conflicts. Because a private consulting agreement or CDA imposes legal obligations on the faculty member, it may also be desirable for a faculty member to have such an agreement reviewed by his or her own counsel if they are so inclined. If any questions arise, please feel free to contact CTT at 215-898-9591 or ORS at 215-898-7293. http://www.ctt.upenn.edu/

PROFESSIONAL DEVELOPMENT WORKSHOPS

“Basic Wet Laboratory Techniques for Genomics Research for UPenn Postdocs and Graduate Students”

The Penn Genome Frontiers Institute (PGFI) is a university-wide institute dedicated to the advancement of the multidisciplinary genome research being conducted at PENN. As part of its mission, PGFI has a strong commitment to genomics education at all levels. PGFI offers a free development workshop for Penn postdocs and graduate students for February 2011. This workshop is aimed at Penn postdocs and graduate students who are interested in molecular biology and genomics, but who do not have the opportunity to learn or use basic wet laboratory techniques as part of their primary research. This 6-day workshop will teach methodologies for isolating genomic DNA from mammalian cells, PCR, restriction enzyme digests, plasmid purification and automated DNA sequencing. The workshop will be taught at a basic level, with no previous laboratory experience required or expected.

When: Friday, February 4 through Friday, February 11, 2011 (participants attend for all days)

Times: Feb. 4, 1:30-2:30 PM, and Feb. 7-11, 12 PM – 4 PM daily

Location: PGFI Educational Facility, 328 Lynch Laboratories, 433 University Ave.

To apply: Interested postdocs and graduate students should go to the PGFI Educational Facility page at: http://www.genomics.upenn.edu/education/educational-facility-upcoming_workshops to apply.

Later workshops: Apr. 1-8, 2011

COST: FREE
The studies showed that the marker gene for enhanced green fluorescent protein (eGFP) was present at 72 hours in the intestine, liver, lung, and kidney but not in the control intestine of horses following injection of recombinant adeno-associated virus (AAV2/5-eGFP), demonstrating efficient gene transfer to the equine intestine via an arterial route. Subsequently they have compared various serotypes of AAV2 carrying the firefly luciferase and eGFP marker genes following delivery via the cranial mesenteric artery in a rat model and have demonstrated protein expression at 3 days (Figure 2).

Future studies will be directed toward achieving early protein expression (i.e. <24 hours) in normal intestine of laboratory animals and horses and then evaluating the delivery of growth factor genes in an intestinal ischemia-reperfusion model.

Most recently, Dr. Southwood has begun pilot studies with Drs. Ralph Meyer and Mirella Meyer-Ficca in the Department of Animal Biology investigating the potential benefits of PARP-I inhibitors during ischemia-reperfusion injury and endotoxemia. The initial in vitro work is being performed by Dr. Hart and Ms. Hope Douglas (2nd year veterinary student) and the results of the initial in vitro studies have been promising.

Clinical observational studies help provide the link between the laboratory and the patient

Clinical observational studies are used to (1) determine accurate survival and complications rates to provide to owners as well as to assess the impact of various factors on these outcome variables and (2) identify areas where research is necessary to improve outcome. A simple lack of knowledge with regards to outcome can lead to euthanasia of patients without an attempt to treat, thereby contributing to a lower survival rate. Notably, clinical observational studies provide an effective means to answer many questions that horse owners and veterinarians have about colic surgery and may help reverse such trends. For example, it is commonly perceived that older horses do not do as well as younger horses after colic surgery. Dr. Southwood and colleagues have recently completed a large retrospective study evaluating survival and complication rates in geriatric horses with gastrointestinal disease determining that: (1) the survival of geriatric horses with a strangulating lesion or requiring jejuno-jejunostomy was equivalent to that of mature horses; (2) geriatric horses presenting with colic were more likely than mature horses to be euthanized without surgery (i.e. lower survival with medical treatment) or during surgery; (3) geriatric horses undergoing surgery for a large colon simple obstruction had a lower survival than mature horses; and (4) postoperative complication rates between geriatric and mature horses were similar and no difference was observed in the mortality between geriatric and mature horses developing postoperative complications.
investigating the effect of ARC Medical Devices Inc. recently completed a study with Dr. Southwood and colleagues have following abdominal surgery.

Intra-abdominal adhesions are an important long-term criterion of success. Postoperative morbidity following abdominal surgery. The goals of this clinical research are to obtain an objective assessment of survival and performance in these patients and to identify areas where we can improve our case management to optimize outcome.

What about postoperative complications and long-term survival? While the focus is often on short-term survival of horses undergoing colic surgery, recovery without complication and long-term survival is an essential criterion of success. Postoperative intra-abdominal adhesions are an important long-term cause of morbidity and mortality in horses following abdominal surgery. Dr. Southwood and colleagues have recently completed a study with ARC Medical Devices Inc. investigating the effect of intraperitoneal fucoidan solution (PERIDAN™ Concentrate Adhesion Reduction Device) on clinical findings, infection, and tissue healing in an adult horse jejunojejunostomy model. The results of the study were favorable and the device is being used in our hospital as well as other hospitals to prevent adhesion formation particularly following small intestinal surgery. Long-term follow-up studies of the impact of this device on survival are pending. In addition, Dr. Southwood and her colleagues are also looking at the relationship between fever, infection, and antimicrobial drug use following colic surgery (Dr. Kendra Miller, Surgery Intern) and have recently obtained funding from the Raymond Firestone Research Foundation to investigate the use of serum amyloid A for early detection of infection (Dr. Melissa Mackinnon, Surgery Resident). The ultimate goal of these studies is to lower postoperative morbidity following colic surgery.

Dr. Southwood carries out her research at New Bolton Center, the large animal campus of the School, located at Kennett Square, Pennsylvania. Her office is in the George D. Widener Hospital for Large Animals.

References

RECENT AWARDS

Carolina Lopez
NIH 5 R01 AI083284
A novel virus-derived adjuvant
9/1/10-6/30/13 $735,809

Carolina Lopez
NIH 5 R21 AI083481
Lung and bone marrow crosstalk during a respiratory infection
9/1/10-6/30/11 $120,150

Carolina Lopez
NIH 7 R03 AI080917-03 ARRA
Initial study of the dendritic cell response to SeV DI particles
9/1/10-5/31/11 $46,384

Phillip Scott
NIH U01 AI088650
Myeloid-lineage cells and immunopathology in Leishmania braziliensis
12/1/10-11/30/15 $2,711,530

Julie Engiles
Novartis Fellowship
Veterinary Pathology Residency
7-1-2010-6/30/2013 $141,666

Hannah Galantino Homer
Texas A & M (prime USDA funding)
Whole genome functional analysis in horses to dissect important diseases
1/15/2010-1/14/2013 $60,950

Gary Smith
Texas A & M (prime Dept of Homeland Security funding)
Effect of model transmission kernels and farm density & distribution upon recommendations concerning alternative culling strategies for farm animal diseases like Foot & Mouth & Avian Influenza
9/1/2010-6/30/2011 $103,920

Dean Richardson
US Equestrian Federation
In vivo gene transfer for treatment of laminitis
7/15/2010-6/30/2011 $25,000

Lawrence Soma/Mary Robinson
Racing Medication and Testing Consortium
Detection of extracorporeal shock wave therapy in the race horse using biomarkers
9/1/2010-8/31/2013 $225,000

Lawrence Soma/Mary Robinson
Racing Medication and Testing Consortium
Detection and pharmacokinetics of AICAR in horses 9/1/2010-8/31/2011 $74,000

Charles Vite
Washington University
07/01/10 - 06/30/11 Novel Therapies for Globoid Cell Leukodystrophy $51,443

Nicola Mason
Translational Genomics Research Institute
09/01/10 - 08/31/11 Canine Hereditary Cancer Consortium: From Bark to Bedside $63,868

Cynthia Otto
American Kennel Club
09/15/10 - 09/14/11 Establishment of a DNA and Health Registry for Search Dogs $73,050

Deborah Silverstein
Abbott Laboratories
10/18/10 - 10/17/11 The Effects of Fluid Administration on Microcirculatory Perfusion during General Anesthesia in Dogs $38,789

William Beltran
University of CA, Berkeley
10/20/2010-9/30/2015 NDC for the Optical Control of Biological Function $1,197,600

Gustavo Aguirre
Case Western Reserve University
11/01/10 - 10/31/15 Pharmacological Treatment of Retinal Diseases $500,000

Mark Oyama
AKC-Canine Health Foundation
12/01/10 - 05/31/11 Platelet, myocardial, & valvular serotonin concentrations in healthy dogs & dogs with heart disease & valvular serotonin concentrations in healthy dogs & dogs with heart disease $12,000

Barbara Zangerl
American Kennel Club
12/01/10-11/30/11 Pharmacological Treatment of Retinal Diseases $59,991

Marky Zangerl
Foundation Fighting Blindness
12/01/10 - 05/31/11 Pharmacological Treatment of Retinal Diseases $59,991

Meryl Littman
AKC-Canine Health Foundation
01/01/11 - 12/31/11 Genome-wide Association Study of PLE/PLN (Protein-losing Enteropathy/Nephropathy) in Soft-coated Wheaten Terriers $46,296

Paula Henthorn
AKC-Canine Health Foundation
02/01/11 - 07/31/11 DNA Sequence Examination of a Gene Region Associated with Mastiff Cystine Stone Formation $12,000

Recent Publications


The new BD LSRFortessa is the latest high-end research grade cell analyzer from BD Biosciences. The cutting-edge instrumentation has been installed in the Hill Pavilion, 3rd floor, in the flow cytometry core. To support research needs, the new Fortessa offers the latest innovations in laser technology to researchers. “For all of our scientists at Penn Vet, this provides a powerful tool that is relevant to diagnostics, regenerative medicine as well as cancer and infectious disease research and puts us on an even footing with the wider biomedical community at Penn”, said Chris Hunter, Chair of the Department of Pathobiology.

The unit is equipped with four lasers (blue, red, green and violet) and allows for the detection of 14 individual fluorophores simultaneously. The Fortessa both complements and expands on the existing capability of the three-laser, eight-color BD FACSCanto in Hill Pavilion. The BD LSRFortessa™ cell analyzer offers the ultimate choice for flow cytometry, providing power, performance, and consistency. The ‘Fortessa’ has the flexibility to support the expanding needs of multicolor flow cytometry assays.

The flow cytometry core housing our units is managed under the School of Medicine Flow Cytometry and Cell Sorting Resource Laboratory (FCCSRL). Please visit: www.med.upenn.edu/bmcr for information on rates, all locations and training. Training is required before using the facility. To further inquire about the services offered, contact the Technical Director, Hank Pletcher at 215.898.3528.

From a PI’s point of view... Roselyn Eisenberg, PhD.

I have seen this from both sides - as an applicant (supplicant) and as a reviewer (I served as a Standing Member on two Study Sections and many ad boc). So this distills some of what I learned. When preparing an NIH proposal in the new format think about the following:

- First - Go to the NIH website - they now have sample grants with commentary on what is good about the presentation (not the science, but how it is packaged). http://funding.niaid.nih.gov/researchfunding/grant/pages/appsamples.aspx

- Next - Remember - they are really tightening up on getting all of your ducks in order including letters of collaboration, biosketches, animals, human subjects, and all compliance information. Don’t get knocked out for administrative reasons.

- Money: It is really all about the money. You are asking the taxpayers to shell out money to let you do this work. The reviewers will not only criticize the science but will and should ask themselves – “Is this worth over a million dollars in direct costs and another 60% of that in indirects?”

- Remember: you only have two chances to get the brass ring. Pay-lines are very low, e.g. NIAID is currently at 8% for established investigators and around 12% for new investigators.

Student Awards

American Kennel Club Canine Health Foundation (CHF) has named Jonathan Wood of the University of Pennsylvania School of Veterinary Medicine as a recipient of a Robert L. Kelly Memorial Scholarship. Wood’s research projects with Penn Vet faculty have included studies of cardiac deficiencies with Paula Henthorn and work in hereditary disorders in companion animals with Urs Giger. Jonathan Wood received a $2,500 scholarship to help pay tuition expenses. The scholarship is intended to encourage research and young investigators as they pursue dual degrees in veterinary medicine and research.
• Critical: Low numbers of grants make it—this means you must consider if your grant is strong enough to rise above the pack of good grants that will sadly not be funded. What it means is you should try to make the grant as perfect as possible on round 1. So shoot for perfect. If need be, wait a cycle.

• Question: How do you perfect your grant? The secret is good clear writing. Turn those tough 12 page limits into an opportunity to clarify—leave out distractions and say what you mean in one sentence instead of 3 or 4.

• Remember: The Vet School has a valuable resource—Grant Editor, Leslie King. She can help with putting your best foot forward. But she can only do so much if she is given the grant at the last minute. She needs to see your Specific Aims page very early in the process. Don’t simply rely on Leslie; ask one or more colleagues to read it—again, do it early!

• Specifically: The aims page sets the stage—you have to catch their attention right away. Don’t be modest—you are selling this to a skeptical audience. So rewrite this page many times as you write the grant. Re-arrange the aims if need be. The significance section is probably the most critical part. So take a hard look at this at the final stage of writing. The same applies with innovation.

• Make sure it is hypothesis driven. Start with an overall goal or an overall hypothesis that you will test—and make sure that they see this multiple times—in the Abstract, Specific Aims, Significance and even in the Aims themselves. Be creative in how you say the same thing—so it does not seem repetitious.

• Make sure you work on the budget and budget justification early. Too many times, grants are cut because of poor justification, especially for personnel—even with modular budgets.

• Use diagrams instead of lots of words. A good rule of thumb is that every page should have some sort of picture—a diagram, a piece of preliminary data, a model.

• Get to know the Program Officer. He/she is your advocate though they cannot speak at the meeting. They can provide feedback on what was said but not necessarily written. Make sure to remind them to attend the review so you can get feedback.

• Look over the roster of the Study Section you want your grant to go to—that is independent of the Institute. Sometimes, you will have a choice—and will know who some of the likely reviewers might be. Third, send a cover letter suggesting not only Institute, but Study Section as well. They encourage this. Take advantage of it. It is optional but important.

• Good Luck! Stay in the game, even if you don’t make it in two rounds. Take the best parts preferred by the reviewers and change the direction to a genuinely new grant with a new perspective.