"One Health: Integrating the Veterinarian Scientist into the Biomedical Research Enterprise"

Division of Comparative Medicine

Office of Research Infrastructure Programs

Division of Program Coordination, Planning, and Strategic Initiatives

Office of the Director, National Institutes of Health

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Meeting Summary

Overview

On April 7–8, 2015, the Office of Research Infrastructure Programs (ORIP) in the Division of Program Coordination, Planning, and Strategic Initiatives, sponsored a workshop on the NIH campus entitled, *One Health: Integrating the Veterinarian Scientist into the Biomedical Research Enterprise*. One Health is defined as the integrative effort of multiple disciplines working together to attain optimal health for people, animals and the environment. The purpose of the workshop was to identify how the concept of One Health can advance the NIH mission in regard to both basic and applied research, including training of the biomedical work force, concentrating on the veterinarian scientist. The morning sessions on day 1 involved case studies describing how multidisciplinary teams that included veterinarian scientists use both animal and human subjects to study various disease conditions, including HIV/AIDS and other viral infections, emerging infections, cancer, neurodegenerative diseases, and muscular dystrophies. Afternoon sessions included panel discussions and presentations addressing: (1) the role of veterinarian scientists in medical centers that receive Clinical and Translational Science Awards and in Cancer Centers; (2) updates on the role of the One Health concept across other federal agencies; and (3) One Health perspectives from Biopharma. On day 2, panel discussions addressed the challenges and best practices associated with training the next generation of veterinarian scientists, including integration into interdisciplinary biomedical research teams. Questions and comments were solicited from all workshop participants and audience members following case studies and panel discussions. Overall, there were 34 speakers and over 170 registered attendees, including NIH-supported extramural and intramural researchers, NIH program and review staff from 20 NIH Institutes/Centers/Offices, as well as representatives from the private sector and federal agencies including the Centers for Disease Control and Prevention, the U. S. Food and Drug Administration and the U. S. Department of Agriculture. Specific recommendations were suggested by workshop participants during the discussion sessions.

Tuesday, April 7, 2015

WELCOME AND INTRODUCTIONS

Franziska Grieder, D.V.M., Ph.D., Director, ORIP, NIH; Manuel Moro, D.V.M., Ph.D., ORIP, NIH

Drs. Grieder and Moro welcomed participants to the workshop and recognized the efforts of the organizing committee and speakers. The workshop's objective is to align the One Health concept —an integrative effort by multiple disciplines to attain optimal health for people, animals, and the environment—with the mission of the NIH in regard to basic and applied research and with respect to research programs and training of the biomedical workforce.

The One Health One Medicine concept originated in 2007 with the intent to forge bonds between the American Medical Association (AMA) and American Veterinary Medical Association (AVMA) leaderships. Later the two elements "One Health" and "One Medicine" were enhanced with "One World," representing the environment. People, animals, and the environment now are integrated into a single One Health One Medicine One World concept.

KEYNOTE PRESENTATION: ONE HEALTH CHALLENGES FOR THE 21ST CENTURY

Carolyn Henry, D.V.M., Associate Dean of Research and Graduate Studies, College of Veterinary Medicine, University of Missouri

Dr. Henry presented four challenges that face the One Health community: (1) refining the definition of One Health, (2) changing the culture of science and medicine as it relates to One Health, (3) communicating the One Health message effectively, and (4) better predicting and preparing for the future with regard to One Health issues.

The One Health concept covers a broad scope that would benefit from better definition and characterization. The AVMA's One Health Initiative Task Force Report, issued in July 2008, and defined One Health as "the collaborative effort of multiple disciplines— working locally, nationally, and globally— to attain optimal health for people, animals, and our environment." Improved integration of two major categories, zoonotic infections and comparative medicine/translational medicine, as well as wider recognition of the important role of veterinary medicine and research, would help to advance the overarching One Health initiative.

Changes in the culture of science and medicine with respect to the use of companion animal models also are needed. Their use can overcome concerns regarding the use of mouse models, such as an incompetent immune system, a non-natural course of disease, rapid disease progression, and biosampling limitations. Companion animals, like humans, spontaneously develop tumors and other diseases; for example, cancer is the leading cause of death in dogs. Other advantages to using companion animal models include a shared environment with humans, the lack of a standard of care for all diseases, and similarity in anatomical size and structure to humans. Likewise, the ability to assess long-term outcome, shorter lifespan, and controllable factors (e.g., lifestyle choices, diet, hormonal status, placebo effect) are reasons to employ companion animal models. The same imaging and radiation technologies used in human medicine are available in veterinary medicine, and significant recent advances in genetic and epigenetic associations in dogs have allowed certain breeds to serve as models for specific cancers in humans. In addition, companion animal clinical trials have fewer third-party payer and insurance issues, simplifying enrollment and procedural issues.

Several programs have recognized the need to shift from a "bench to bedside" approach to a "bench to cageside to bedside" approach: the Comparative Oncology Trials Consortium (COTC), a consortium of 20 teaching hospitals that was developed in 2006 under the National Cancer Institute (NCI) umbrella, and the Canine Comparative Oncology and Genomics Consortium (CCOGC), a targeted biospecimen repository established in 2007. A samarium compound developed at the University of Missouri's research reactor provides evidence of the efficacy of the translational model. After tests in dog models yielded promising results, further development by the Dow Chemical Company led to its current availability as Quadramet® for human use. Because of an approximately 22 percent drop in funding across states, investigators should consider seeking funding from animal foundations.

Communication about One Health should be amplified. Veterinarian scientists need to ensure that the One Health vision statement is accepted and adopted across disciplines. Discussions around One Health need to take place in an organized manner outside of closed meetings.

The veterinarian science community must be well prepared, collaborative, and proactive in addressing future challenges rather than being siloed and reactive. For example, teams need advance training on real-time global health concerns, as seen by animal exposure to the Ebola virus. Training the veterinarian scientist workforce, however, has been challenging because positive returns on investment are seen only in the pharmaceutical industry, the regulatory industry, and academia. Training opportunities should be

reexamined, and the University of Missouri's Global Innovation Fellowship Training program, which combines medicine, business, engineering, and journalism/communication, could serve as a model for cross-disciplinary programs.

Dr. Henry informed the participants of an Institute of Medicine (IOM) meeting being held June 8–9, 2015, in Washington, DC, about the role of clinical studies on companion animals with naturally occurring tumors in translational cancer research.

Discussion

A meeting participant inquired about additional examples of compounds that have been used in companion pets and transitioned to use in humans. Dr. Henry replied that three U.S. Food and Drug Administration (FDA)-approved drugs were a result of work at the University of Missouri's research reactor, a samarium compound for bone targeting and two compounds for imaging; a technology similar to a U.S. Department of Agriculture (USDA)-approved vaccine for use in dogs currently is being tested in humans. The veterinary oncology field is 20-years young, and the first therapeutic for treatment of cancer in dogs was approved only recently.

Dr. Deborah Kochevar, Tufts University, asked whether data exist demonstrating that time to market for a human drug decreases when research using companion animals is a component of the work, and wondered about this as a way to incentivize funding sources. Dr. Henry responded that insufficient time has passed to have acquired data regarding time to market, although drugs have been discarded more quickly based on toxicity results in companion animals.

An audience member commented on the limitations (e.g., cost prohibitive toxicity trials, difficulty in finding a facility) to obtaining FDA approval for therapies. Dr. Henry replied that working with a clinical trials office can significantly streamline clinical trials. In addition, a trial endpoint could be proof of target or concept, for example, rather than response or survival time.

Dr. Joe Kornegay, Texas A&M University, asked about the success of the multicenter approach in human versus veterinary medicine. Dr. Henry responded that motivating investigators at academic institutions to work across disciplines can be a challenge because of issues of tenure, authorship, and others, although the Specialized Programs of Research Excellence Grants in cancer research have seen success. She suggested implementing an administrative body and awarding funding only to collaborating researchers. Dr. Michael Lairmore, University of California, Davis, advocated for Clinical and Translational Science Awards (CTSAs) as a potential mechanism for cross-disciplinary research within a single institution.

A meeting participant asked about opportunities for international collaboration. Dr. Henry observed that although cultural differences between countries can affect the pace of change, international collaborations and interest in One Health have been increasing significantly. Consolidating One Health initiatives into a single website will be important.

An audience member inquired about the extent of characterization of dog models and the degree to which pathways in dogs are similar to those in humans. Dr. Henry said continued efforts to characterize dog models are needed. Well-characterized models, with shared databases, will be increasingly important as heritable diseases are discovered in dogs and their analogous targets are found in humans.

Dr. Cathleen Lutz, The Jackson Laboratory, commented on the marked improvement in mouse model research after the development of xenograft models and wondered about efforts to develop mouse xenograft models for canine tumors. Dr. Michael Lotze, University of Pittsburgh, stated that a major

problem with xenografts is the lack of an immune response, although this feature makes them perfect models for understanding tumor biology.

A meeting participant inquired about the extent of research on the genetic diversity of dogs. Dr. Henry described this as a major area of research, but noted a hurdle in evaluating differences between pure-bred and outbred dogs.

Ms. Sabina Hlavaty, NCI, NIH, asked about existing opportunities for medical students to learn about and participate in One Health-related activities. Dr. Henry suggested that One Health researchers publish in journals read by medical students.

COMPARATIVE MEDICINE TEAM APPROACHES

Moderators: *Jack Harding, Ph.D., ORIP, NIH; Manuel Moro, D.V.M., Ph.D., ORIP, NIH*

Comparative Medicine Team Approach: Human Immunodeficiency Virus (HIV)/Acquired Immune Deficiency Syndrome (AIDS)

James Hoxie, M.D., Ph.D., Professor of Medicine, University of Pennsylvania; Andrew Lackner, D.V.M., Ph.D., Director, Tulane National Primate Research Center (TNPRC)

Drs. Lackner and Hoxie presented on their collaborative efforts to study HIV/AIDS and recognized the critical support from the NIH's Division of AIDS in their research. The nonhuman primate model of AIDS has demonstrated that AIDS is caused by a virus and revealed that a vaccine for this disease is feasible. Among many other functions, the model serves as a testing ground for vaccine and microbicide concepts and products prior to human testing.

Appreciation has grown over the past few years for the importance of location, timing, and order of events in AIDS and HIV pathogenesis. The scientific question that Drs. Hoxie and Lackner have addressed is whether rational perturbations in HIV/simian immunodeficiency virus (SIV) pathogenesis can reveal vulnerabilities in the host–virus relationship that can be exploited for vaccines or therapeutics. The ΔGY model uses a virus that renders the SIV highly susceptible to host control while retaining a wild-type level of replication. This leads to an immune response in the ΔGY-controlling animals that allows the animals not only to be healthy but also to become broadly protected from pathogenic challenge viruses. These ideas are fundamental to the key questions that HIV researchers are asking around the world.

Collaboration among the Centers for AIDS Research (CFARs) and National Primate Research Centers (NPRCs) has been further supported in HIV/AIDS studies. For example, collaboration between the CFAR at the University of Pennsylvania and the Tulane NPRC has been highly synergistic and bidirectional. The Tulane NPRC, which is also considered a core facility within the Penn CFAR, helps make the nonhuman primate model accessible to faculty and provides advice, mentoring, and encouragement to junior investigators. In addition the Tulane NPRC hosts investigators and students and provides infrastructure, regulatory oversight, and assistance. Because biomedical research is increasingly complex and requires collaboration among individuals with diverse skills, highly collaborative multidisciplinary networks such as CFARs and NPRCs are critical. CFARs and NPRCs are positioned to develop innovative approaches to complex problems, address research gaps, and translate research to relevant areas for humans; provide infrastructure in emerging technologies and animal models that can be leveraged to create new scientific opportunities for investigators; and provide unique multidisciplinary training opportunities for veterinarians and other biomedical scientists.

Discussion

Dr. Kornegay asked about how to enhance the training of veterinarians as principal investigators in research. Dr. Lackner emphasized that exposure to and involvement in multidisciplinary groups increases awareness among veterinarians about types of research and potential opportunities. He added that veterinarian researchers need to overcome any trepidation about working at medical institutions. Dr. Hoxie mentioned the advantage of the University of Pennsylvania's veterinary and medical schools being in close proximity.

Dr. Kochevar asked about corollary techniques to reach medical students to help them understand the value of One Health. Dr. Lackner stated that education regarding One Health must be integrated into the curriculum and needs to occur early in their training (i.e., during medical school).

Dr. Rodney Page, Colorado State University, asked about veterinarian representation on study sections. Dr. Lackner expressed the perspective that focus should be placed on engaging the most qualified individuals on study sections rather than on degrees.

Comparative Medicine Team Approach: Emerging Infections
Tony Goldberg, D.V.M., Ph.D, Professor, School of Veterinary Medicine, University of Wisconsin; David O'Connor, Ph.D., Associate Director, Wisconsin National Primate Research Center

Dr. Goldberg, a field biologist and primatologist, and Dr. O'Connor, an expert on deep sequencing technologies, detailed their collaboration regarding emerging infections. Their partnership began in 2009 with the study of RNA "virodiversity" (community diversity) in blood serum of wild communities of primates in Kibale National Park, Uganda. Together, the two researchers designed a pathogen virus discovery pipeline to understand the viruses existing in natural populations and their potential for transmission.

In one of their projects, the researchers stumbled upon the first natural reservoir of a virus that had been a mystery since 1964 but was a major cause of captive macaque morbidity and mortality: Simian hemorrhagic fever virus (SHFV). With next-generation sequencing techniques, the researchers used subtractive mapping to assemble genomes found in co-infected animals and compare them with previously assembled viral genomes. SHFV has since become a model for viral hemorrhagic fever comparative pathogenesis.

A second example is from a Bornean orangutan adopted by the Milwaukee Zoo that suddenly died from an unknown infectious agent. Drs. Goldberg and O'Connor adapted their virus discovery method and were able to subtract previously published orangutan DNA from the deceased orangutan's DNA; the resulting sequences suggested an organism resembling a tapeworm. The researchers designed barcoding primers to two clades of the tapeworm phylogenetic tree and determined that the mystery DNA sorted with a third and newly proposed tapeworm clade, *Versteria*. This was the first known fatal case of *Versteria* infection in a primate.

The One Health collaboration has opened opportunities for Dr. Goldberg as an ecologist and disease modeler to understand the diversity of pathogens that might affect humans in the future. A current project is focused on how people interact with primates at the edge of forests by trying to identify nodes in the human social network that are at particular risk of contacting primates. Knowing the structure of these types of networks will allow modeling of how a pathogen might travel through the human social network and eventually into the world. Dr. O'Connor spoke about the lack of work on the intersection of comparative medicine and linkages among human health, animal health, and the environment. By

focusing on primates and primate viruses, there is an opportunity to model cross-species transmission into macaque monkeys.

Dr. O'Connor called attention to challenges in NIH funding for One Health-friendly programs. He has been successful receiving funding from ORIP and the National Institute of Allergy and Infectious Diseases; however, reviewers of grants on which he and Dr. Goldberg have been co-principal investigators have had difficulty understanding that field research and laboratory animal research can be complementary.

Discussion

Dr. Henry asked whether students are trained to value the overlap between the types of research Drs. O'Connor and Goldberg conduct. Dr. O'Connor replied that although he and Dr. Goldberg train their graduate students jointly, students can sometimes find it difficult to report directly to multiple people. He also emphasized the importance of ensuring that when blending laboratory and field science, the personnel involved in each is a stakeholder in the shared projects. Dr. Lairmore commented that the students enrolled in an undergraduate course on global disease biology tend to be attracted to the ecology component of the class. Dr. Goldberg added that interest in One Health projects is strong in graduate and veterinary students. Although the One Health theme permeates the veterinary curriculum, and plant biology students are now entering the program, it remains difficult to infiltrate the medical school curriculum.

Dr. Susan VandeWoude, Colorado State University, wondered about solutions for the potential lack of interest in funding One Health projects from the NIH. Dr. Goldberg replied that funding from the Wisconsin Institute for Infectious Disease catalyzed his and Dr. O'Connor's work. They have pursued funding through the Department of Defense, Defense Advanced Research Projects Agency, National Science Foundation (NSF), and for related work, through the U.S. Fish and Wildlife Service and the U.S. Geological Survey.

Dr. Philippe Baneux, Cornell University, raised the issue of improving communication with the public and politicians. Dr. Goldberg suggested that the One Health community compile remarkable success stories that highlight how global public health has moved forward as a result of One Health efforts. Dr. Hoxie recommended emphasizing the work of Drs. Goldberg and O'Connor as one such success story. He added that communicating the value of One Health is difficult because medical students tend to focus on current problems rather than potential problems. Dr. Goldberg agreed and stated that he and Dr. O'Connor have argued that the lessons learned from AIDS should be applied to so-called pre-emergent pathogens.

Dr. Kochevar inquired about the amount of discussion taking place across funding bodies, noting that the U.S. Agency for International Development has included the phrase "One Health" on a grant application. Dr. Goldberg mentioned that many activities revolve around capacity-building or virus discovery, such as at The EcoHealth Alliance, whereas his and Dr. O'Connor's work is about developing the next phase of research.

In response to a query about the link between virus discovery and cancer, Dr. O'Connor indicated that the association is weak.

Comparative Medicine Team Approach: Cancer

The NCI Comparative Brain Tumor Consortium: One Health in Action
Mark Gilbert, M.D., Chief, Neuro-Oncology Branch, NCI, NIH; Amy LeBlanc, D.V.M., Director, Comparative Oncology Program, NCI, NIH

Drs. LeBlanc and Gilbert provided an overview of brain tumors in companion animals as a relevant animal model of human disease. The current drug development path has an unacceptably high rate of attrition with an unsustainable cost structure. A comparative and integrated approach to cancer drug development would offer opportunities to ask questions about, for example, dosage and combination therapies. Veterinarian clinician-scientists are valuable in comparative oncology because they provide specialized training, care, and research expertise.

Canine and human melanoma exhibit key differences in activating mutations, but demonstrate similar malignant potential in biologic behavior *in vivo*. Therefore, more work needs to be done to understand the commonality between and transitional relevance of dogs to humans. The NCI Comparative Oncology Program (COP) provides protocol and scientific input on study design and assists with data management, drug and trial package management, coordination of protocols, and other functions that are difficult for study sponsors to maintain in-house; however, it does not handle any financial or regulatory matters.

The potential value of canine clinical trials is shown through a double-blind control placebo trial led in humans for newly diagnosed glioblastoma, which revealed no significant improvement in survival and only slight improvement in progression-free survival. The researchers concluded that the tested treatment did not yield a benefit. Although an adequate preclinical model for angiogenesis does not exist, parallel or companion studies in a canine model could have helped predict the outcome of the trial before enrolling nearly 1,000 patients in a 4-year study. To demonstrate that canine brain tumors have translational relevance, however, researchers will need to identify similarities in histology, genomic landscape/molecular drivers, incidence, sensitivity to conventional and novel therapies, and clinical outcomes. They then can leverage dogs' physical size, intact immunity, and many other advantages.

The brain tumor community is considering forming a collaborative brain tumor consortium similar to the Collaborative Ependymoma Research Network (CERN). CERN focuses on five interacting projects: a Clinical Trials Network, a tissue repository of pathology and molecular markers, preclinical drug development, tumor biology and stem-cell-based models of ependymoma subgroups, and patient outcomes. The success of CERN is in its project-based approach, which provides a framework for critically examining the gaps in veterinary brain tumor knowledge.

Discussion

Dr. Kornegay asked about the ability to conduct preclinical trials in dogs given the relative infrequency of incidence in dogs. Dr. LeBlanc stated that the infrequency of incidence is a reason to lobby for greater multicenter efforts; however, more work is needed first to understand the basic biology and genomic landscape of these diseases.

Dr. Michael Salgaller, The Conafay Group, asked about the inclusion of pediatric oncologists in a glioblastoma network. Dr. Gilbert responded that pediatric neuro-oncology is a critical part of the neuro-oncology branch. CERN is a great model of a unique collaboration between pediatric and adult neuro-oncologists.

Dr. Ronald Sokol, University of Colorado Denver, asked whether a website similar to www.clinicaltrials.gov exists for animal trials other than www.vetcancertrials.org. Dr. LeBlanc stated that

a task force currently is determining how a multicenter clinical trial clearinghouse website could be developed.

Comparative Medicine Team Approach: Neurodegenerative Disease

Developing Therapies for Central Nervous Dysfunction in Niemann-Pick Type C Disease (NPC)
Forbes Porter, M.D., Ph.D., Clinical Director, Eunice Kenney Shriver National Institute of Child Health and Human Development (NICHD), NIH; Charles Vite, D.V.M., Ph.D., Associate Professor, School of Veterinary Medicine, University of Pennsylvania

Drs. Vite and Porter presented on the role of veterinary medicine in treating the central nervous system disease NPC, a lysosomal storage disease with progressive disease onset. Small molecule therapy of NPC began when an investigator discovered a compound, hydroxypropyl beta cyclodextrin (HPßCD) in mice that seemed to remove cholesterol from cells. Dr. Vite's study in cats at the National Referral Center (NRC) for Animal Model Human Genetic Disease showed that HPßCD given presymptomatically prevents the onset of brain disease until more than 1 year of age; however, it resulted in dose-related hearing loss. The cat model also informed about drug toxicity and serves as an example of preclinical animal models being used for investigational new drug (IND) enabling.

A Phase 1 HPßCD clinical trial for treatment of NPC in humans focused on safety and biochemical efficacy with a cohort dose-escalation design (e.g., safety, pharmacokinetics, pharmacodynamics, pathological efficacy). Two-thirds of patients showed a positive biochemical response, and there has been minimal impact on quality of life to date. Drug-naïve patients have confirmed target engagement; however, the trial did hit significant ototoxicity, with variable recovery. The pharmacodynamic response is not as robust in patients as in preclinical animal models. Researchers are working hard on clinical outcome measures and planning a multicenter/multinational clinical efficacy trial under a cooperative research agreement.

Discussion

Dr. Kathryn Wagner, The Johns Hopkins University, inquired about the levels of ototoxicity that resulted from different drug regimens in the preclinical drug space. Dr. Vite replied that the effects depended on the location of drug administration. A safety study is now being conducted in dogs, cats, and mice.

Dr. Sokol asked about the effect of treatment on the liver and any anticipated long-term effects of repeated lumbar punctures. Dr. Porter acknowledged that pediatric patients can have severe liver disease, especially in the neonatal period, but that the liver disease tends to resolve and become subclinical and the neurological disease becomes prominent. He expects that when resolution of the neurological disease is achieved, investigators will return to focusing on the liver. Lumbar punctures frighten patients and parents, but are easier to perform in children than even a blood draw. The next step in product development will be to use a drug-device combination.

Dr. Carol Robertson-Plouch, Eli Lilly, posed a question about whether the mechanism behind ototoxicity in cats could be further evaluated in an attempt to decrease its frequency or severity. Dr. Vite stated that HPßCD appears to have a direct biophysical effect on the outer hair cells that result in their structural damage. Next steps include a Phase 2 trial that will attempt to avoid getting the drug into hair cells, seeking the development of a less toxic compound, and determining whether the VIII nerve was spared to potentially allow the use of lithium cochlear implants.

Comparative Medicine Team Approach: Viral Infections

One Health Approach to Viral Infections and Biomedical Research Training
Genoveffa Francini, M.D., Head, Animal Models and Retroviral Vaccines Section, Vaccine Branch, NCI, NIH; Michael Lairmore, D.V.M., Ph.D., Dean, School of Veterinary Medicine, University of California, Davis (UC Davis)

Drs. Lairmore and Francini presented on viral infections in the contexts of their joint research and on recent recommendations regarding the One Health theme. Scientists currently are trying to understand which genes are responsible for the lifelong persistence of human T-lymphotrophic virus type 1 (HTLV-1) in monocytes and their relationship to viral persistence *in vivo*. Rabbit and macaque models were used to verify the concepts. The results of work obtained in humans mirrored those obtained in nonhuman primates, but not those in rabbits, underscoring the importance of identifying the right systems for use in biomedical research. The rabbit allowed researchers to study pathogenesis and perform kinetic studies following infection; however, the rabbit model was not adequate for studying virus infectivity.

The National Research Council in 2012 recommended that the veterinary workforce increase its commitment to research, its development of future faculty, and its work across disciplinary and professional boundaries. Global food security is one of the most pressing challenges of the 21st century, and veterinarians trained at this intersection will be important. Also in 2012, the NIH Physician-Scientist Workforce Working Group concluded that training and career paths of physician-scientists are different than those of the non-clinician Ph.D. workforce. Veterinarian scientists uniquely contribute to biomedical research through specialized training in animal biology and medicine to the modeling of human physiology and disease and to animal disease models and preclinical studies; however, they comprise approximately 3 percent of the total workforce and few dual D.V.M./Ph.D. programs are funded. Other challenges include poor recruitment into research, as 80 percent of veterinary students have a clinical focus; inadequate training and mentorship, including a lack of mentors; student debt, and insufficient funding for training; and poor retention, including funding mechanisms for loan repayment programs, training grants, and NIH centers focused on research training. Veterinarian scientists compete for funding at equivalent rates to physician-scientists and are needed because the majority of diseases that occur in humans also occur spontaneously in animals. Approximately 70 percent of human pathogens are zoonotic.

Several programs at UC Davis could serve as models for other medical schools. Through the One Health Clinic program at UC Davis, medical and veterinary students conduct joint rounds that take care of both people (primarily migrant workers) and animals with unmet health needs. The UC Entrepreneurship Academy allows training with venture capitalists. Faculty, graduate students, and postdoctoral researchers working on research with a potential commercialization application are brought together to analyze, enhance, and communicate the potential of the project; explore commercialization opportunities and strategies; develop a presentation pitch for the project; and develop a network of mentors and industry connections.

Discussion

Dr. Bernadette Dunham, FDA, reflected on the critical need to communicate the value of One Health to both veterinary and medical students. Dr. Lairmore agreed and stated that leaders must continue to discuss communication and awareness as well as focus on bringing students together around case studies to illustrate connectedness across One Health disciplines. Dr. Nicolas Kenyon, UC Davis Medical Center, advocated for improving training and interaction at the medical resident and fellow levels, because each year only one to two D.V.M. students join the M.D./Ph.D. students in training at the UC Davis Clinical

and Translational Science Center. Dr. Lairmore concurred, but added that covering the patient load is problematic given time constraints on medical residents and fellows.

Dr. Grieder wondered about how best to package One Health success stories for effective and impactful communication. Dr. Kochevar suggested forming consortia around defined goals to make the One Health discussions less diffuse. Veterinary schools with CTSA programs are hoping to acquire resources that will allow the veterinary schools to collaborate more effectively. Dr. Maeva May, NCI, NIH, asked whether a similar conversation around One Health is occurring within medical programs. Dr. Lairmore stated that conversation needs to be occurring within the leadership of CTSA programs. Dr. Kochevar shared with meeting participants that the Zoobiquity Conference will be taking place on April 25, 2015, in Boston, MA. She added that students from Boston's four medical schools and one veterinary school have been invited to this conference in hopes that they will begin incorporating the One Health concept early in their careers.

Comparative Medicine Team Approach: Muscular Dystrophies
Joe Kornegay, D.V.M., Ph.D., Professor, College of Veterinary Medicine, Texas A&M University; Kathryn Wagner, M.D., Ph.D., Director, Center for Genetic Muscle Disorders, Kennedy Krieger Institute, The Johns Hopkins University

Drs. Kornegay and Wagner discussed their translational work on golden retriever muscular dystrophy (GRMD), a naturally occurring spontaneous model of human Duchenne muscular dystrophy (DMD), to inform about the potential role of inhibition of myostatin (a widely conserved negative regulator of muscle growth) in treating DMD. Results from studies in mice have shown that the effects of myostatin are different *in utero* and postnatally. Limitations of the available mouse model include a mild phenotype compared to humans, a uniform effect on muscles, their relatively short lifespans, and their different telomerase activity than larger animals.

Whippet dogs are a breed naturally heterozygous for a myostatin gene mutation; whereas homozygous whippet dogs (so-called bully whippets) have gross muscle hypertrophy. Cross-breeding of the two mutations produced myostatin-heterozygous GRMD carrier dogs termed GRippet dogs. Postural abnormalities seen in GRippet dogs did not become apparent until around 3 months of age. Although muscle imbalance is not a feature of myostatin inhibition in the mouse model, findings in a larger animal model may translate to human patients.

Limitations in the use of large animal models for DMD include small group size, a lack of coordination in identifying key questions and required resources, a lack of incentive, a lack of veterinarians motivated to conduct comparative veterinary research, and the expense of maintaining colonies of large animal models such as GRMD. All of these limitations, however, can be overcome through initiatives such as the Muscular Dystrophy Coordinating Committee's Action Plan to guide funding for muscular dystrophy research, funding mechanisms that target submissions from interdisciplinary teams, funding mechanisms that require trainees to spend time in different laboratories, and governmental infrastructure and support for canine colonies like those in Japan and France.

Dr. Kornegay pointed out that missing from the frequently referenced One Health umbrella diagram is genetic disease, an idea that could lead to One Genome.

Discussion

Dr. Henry inquired about disadvantages of receiving research funding through scientific philanthropy. Dr. Wagner stated that differences in expectations can be a challenge because patient advocacy groups hope to see improvements in medical conditions in the near term, whereas research operates over the long

term. Dr. Kornegay added that a focus on associating each patient with a specific foundation has reduced foundations' budgets for scientific research, particularly translational work.

Dr. Lairmore directed a question to Dr. Kornegay about whether the One Health approach adopted at Texas A&M University has impacted his work positively. Dr. Kornegay replied that the university's approach has resulted in a highly collaborative atmosphere, especially among students. He also mentioned that the Texas A&M Institute for Preclinical Studies, which he directs, makes use of spontaneous animal models but focuses much of its work on Good Laboratory Practices, experimental models, and medical devices.

"ONE HEALTH" AND CENTERS, AGENCIES, AND INDUSTRY

Moderator: *Manuel Moro, D.V.M., Ph.D., ORIP, NIH*

CTSAs and Veterinarians

Deborah Kochevar, D.V.M., Ph.D., Dean, Cummings School of Veterinary Medicine, Tufts University; Cheryl London, D.V.M., Ph.D., Professor, College of Veterinary Medicine, The Ohio State University (OSU); Ronald Sokol, M.D., Director, Colorado Clinical and Translational Sciences Institute, University of Colorado School of Medicine and University of Colorado Denver, University of Colorado; Susan VandeWoude, D.V.M., Associate Dean for Research, College of Veterinary Medicine, Colorado State University

The panel discussed potential opportunities for the more than 60 CTSAs to interact with veterinarians and others interested in One Health. Dr. Kochevar explained that CTSA support is intended to accelerate the translation of laboratory discoveries into treatments for patients, support the entire spectrum of translational research from scientific discovery to improved patient care, train a new generation of clinical and translational researchers, and engage communities in clinical research efforts. The CTSA One Health Alliance (COHA) is comprised of 10 veterinary schools that are partnered with medical and other colleagues through a CTSA. COHA, which is comprised of four subcommittees, leverages the expertise of physicians, research scientists, veterinarians, and other professionals to find solutions for medical problems and address the well-being of humans, animals, and the environment through collaborative investigation and shared resources. Its next steps are to: (1) launch a pilot grant program with the Association of American Veterinary Medical Colleges (AAVMC) to encourage coordination across COHA institutions and enhance competitiveness of COHA investigators for funding; (2) respond in a coordinated, strategic way to opportunities to translate biomedical discoveries into clinical applications; and (3) consider mechanisms for broadening the scope of COHA to include other veterinary schools.

Dr. London explained that the COHA Clinical Studies Subcommittee is charged with characterizing the breadth of veterinary clinical trial resources and expertise across member institutions and establishing recommendations for uniform operating procedures to facilitate multi-institutional trials. A survey is being conducted to get feedback from institutions to determine how veterinary schools that are integrated with a CTSA are running the clinical trials, and how the data are captured, analyzed, and integrated with the One Health initiative. A current priority is to develop a coordinated effort for instituting clinical trials across these institutions.

Dr. VandeWoude stated that the COHA Tissue and DNA Banking Subcommittee is charged with developing a plan that outlines infrastructure, data management systems, and personnel needs required to establish a national veterinary biospecimen repository or repository registry and create a resource that provides archival access to well-characterized and broadly phenotyped biological samples from veterinary patients. The directors of the University of Florida biorepository have agreed to provide their

biorepository expertise to the veterinary community. An additional goal of this collaboration is to determine the animal samples that are most valuable to collect.

The main goal of the Clinician-Scientist Education Subcommittee is to expand opportunities for clinical and translational research training for veterinarians. White papers and proposals have been developed that include looking at direct funding lines for D.V.M./Ph.D. students through the CTSA, the potential for a transitional 2-year postdoctoral residency fellowship in translational research for veterinarians, and an early career faculty "boot camp" for success in translational research.

Dr. Kochevar stated that the Communication and Collaboration Subcommittee is developing priorities and an implementation plan to increase awareness of the capabilities of veterinary schools and COHA to support collaborative, translational research. They also strive to foster research collaborations and encourage transdisciplinary grant-seeking. This includes an innovation video series featuring stories from COHA institutions and collaborators, One Health tracks at national medical meetings, One Health regional research symposia, and One Health columns in medical journals. The Subcommittee will seek initiatives that enhance inter-professional collaborations among academic institutions and industry, educates patients and clients, and enhances clinical trials recruitment.

The CTSA Program seeks to improve in six areas: (1) cohort identification and feasibility assessment prior to site choices, especially because electronic health records are now being implemented in all hospitals; (2) efforts to improve recruitment in clinical trials; (3) rapidity of Institutional Review Board (IRB) approval and agreement across multisite studies; (4) budgeting and contracting, which has seen success with 60 CTSAs having agreed upon a template; (5) Good Clinical Practice (GCP) training, given that most institutions do not have a GCP requirement for investigators; and (6) standardizing the review of local pilot studies.

Discussion

A meeting participant inquired about whether the Clinical Studies Subcommittee survey is being conducted as a feasibility study. Dr. London replied that the goal of the survey is to understand how clinical trials are conducted across CTSAs (e.g., structure of clinical trial unit, software used) and to try to develop a platform that is equitable across institutions and could be implemented rather quickly.
Dr. Sokol elaborated on the newly implemented Research Electronic Data Capture (REDCAP) software database system developed at Vanderbilt University. REDCAP is based on Microsoft Excel spreadsheets but is open-source, Web-based, backed up on servers, and HIPAA-compliant, unlike Excel and Access.
Dr. London added that REDCAP allows for the development of a library of case report forms that can be shared by the entire user group.

Dr. Henry asked whether the Clinician-Scientist Education Subcommittee separates veterinarian and physician training. Dr. Kochevar stated that focus is placed on veterinary trainees because more resources typically are available to medical house officers and fellows. She added that veterinarian house officers at Tufts spend a week on medical rotations at Tufts Medical Center, a highly successful albeit unstructured program. Dr. Henry expressed that the opposite training would be more effective. She cited a translational medicine oncology fellowship begun last year at the University of Missouri through which a medical school fellow spends 1 month performing clinical trials in animals, attends the Veterinary Cancer Society meeting, and ultimately becomes a veterinary ambassador to the medical school.

Dr. Robertson-Plouch asked whether Institutional Animal Care and Use Committees (IACUCs) exist at all institutions and whether their clinical trial review committees handle naturally occurring disease differently. Dr. London replied that approvals needed at various institutions range from a strict IACUC requirement to a less formalized approval structure.

Dr. Page inquired about the potential for future support from the National Center for Advancing Translational Sciences (NCATS). Dr. Sokol stated that accelerating more safely and cost-effectively the process of bringing discoveries into patient care is a major goal of NCATS. NCATS is gradually reducing all CTSA budgets, with some of the extra funds being allocated to the Collaborative Innovation Award. Whether NCATS is interested in clinical studies in natural animal models is unknown, because NCATS amended the direction of its program to focus on multisite clinical trials in humans.

Cancer Centers

Amy LeBlanc, D.V.M., Director, Comparative Oncology Program, NCI, NIH; Mark Gilbert, M.D., Chief, Neuro-Oncology Branch, NCI, NIH; Rodney Page, D.V.M., Director, Flint Animal Cancer Center, Colorado State University

The panel members reviewed the collective activities of the more than 60 NIH-designated Cancer Centers as they relate to companion animal research. Dr. LeBlanc explained that the COTC is a network of 20 Cancer Center sites united by a Memorandum of Understanding signed every 4 years on how clinical protocols are developed, executed, and managed between the study site, the COP, and the study sponsor. A well-staffed clinical trial office is critical to adequately supporting clinical trial efforts. Study sponsors have included the NCI, pharmaceutical companies, and the Morris Animal Foundation. The COTC is funded to support clinical trials for the benefit of human health, although in many instances it can be equally important for animal health.

The CCOGC biorepository is a canine tumor archive with samples from the most common cancers as well as from cancers that might be of interest to the pharmaceutical industry. The biorepository, located in Frederick, MD, has been populated with high-quality specimens from dogs with treatment-naïve cancer of specific histologies chosen due to their relevance to human cancer. All tissues are collected in a specific manner according to strict standard operating procedures. Tumor tissues, normal tissue, blood, urine, plasma, and serum are available and awaiting use by researchers.

Dr. Gilbert transitioned to a discussion of the potential for the collection of canine primary brain tumor tissue for research. Because the biology and pathogenesis of human brain tumors is well understood, developing a program in canine brain tumor research would be fairly straightforward. The only barrier is tissue collection. The potential exists for large-scale clinical trials with molecular stratification that ask questions about enrichment and targeting particular tumor subtypes. A consortium of human and veterinary pathologists could work together to reproduce much of the work that has been performed in human brain tumors. Researchers would be able to ask questions about whether canine brain disease recapitulates that seen in adult or pediatric human cancers, and ask hypothesis-based questions in parallel.

Dr. Page called attention to the IOM workshop to be held June 8–9, 2015, at the National Academy of Sciences in Washington, DC. The workshop will strive to identify the gaps in comparative medicine from the perspective of regulatory and policy issues as well as research (e.g., a canine cancer genome atlas, canine-specific reagents). Additional topics include how to increase the pace and effectiveness of clinical trials and how to provide oversight of and guidance for clinical trials. The resources built by the CTSA program for human research should be considered for canine research.

Discussion

Dr. VandeWoude asked why oncology has seen greater advancements than other disciplines, suggesting perhaps sociological or opportunistic reasons. Dr. LeBlanc speculated that the intersection of many factors, including significant press, is likely to have led to oncology's success. A meeting participant added that efforts began earlier in the field of oncology than in other disciplines and that in many ways

CTSAs were designed with oncology in mind. The participant added that global populations are likely most significantly impacted not by cancer but by infectious diseases.

Dr. Lairmore asked about how best to compile a comprehensive database of existing clinical trials in companion animals. Dr. Henry responded that a list of the relevant eight websites she could identify is found in an article she published in the *European Journal of Medicine*.

Dr. Kochevar wondered whether patients who have enrolled a pet in a clinical trial are more likely to enroll in a clinical trial themselves. Dr. Gilbert juxtaposed the public's desire for rapid development of cancer treatments with the low participation rate (5%) of cancer patients in clinical trials.

Updates on the "One Health" Landscape Across Federal Agencies
Joseph Annelli, D.V.M., Animal and Plant Health Inspection Service (APHIS), USDA; Cyril Gerard Gay, D.V.M., Ph.D., Agricultural Research Service (ARS), USDA; Linda Pimentel, V.M.D., Centers for Disease Control and Prevention (CDC)

Dr. Gay presented on the recent activities of the USDA ARS. The Food and Agriculture Organization (FAO), the World Organization for Animal Health (OIE), and the World Health Organization (WHO) defined in April 2010 the mission of their collaborative effort: a world capable of preventing, detecting, containing, eliminating, and responding to animal and public health risks attributable to zoonoses and animal diseases with an impact on food security through multisectoral cooperation and strong partnerships. Livestock, which contribute up to 40 percent of the global value of agricultural output, support the livelihoods and food security of almost 1 billion people. Veterinary scientists are needed in food animal medicine to help solve one of the great challenges of the 21st century: feeding the projected world population of 9 billion. There is also a need for research to support the FAO and OIE call for the progressive control of transboundary diseases, funds to establish international research collaborations, new vaccines designed for control and eradication, and access to large animal research facilities. More veterinary scientists are needed in government, as only 1.8 percent of USDA veterinarians work in research.

Four of the ARS' 14 animal health research locations house biodefense research programs that focus on measures taken against disease outbreaks caused by pathogens, whether natural, unintentional, or intentional, and a National Bio and Agro-Defense Facility is currently being built in Manhattan, KS. Current zoonotic threats include avian influenza, Rift Valley fever, the Nipah and Hendra viruses, Japanese encephalitis, Venezuelan equine encephalitis, eastern equine encephalitis, and *Coxiella burnetii*. Because a large majority of new and emerging diseases are zoonotic, integrated research programs that include veterinary scientists are needed, as are animal models of human diseases. Recommendations regarding veterinary scientists include: (1) support postgraduate training programs to increase the number of veterinarians with D.V.M./Ph.D. degrees; (2) provide resources for recruiting, training, and retaining veterinary scientists in animal health research; (3) increase animal health research programs that support global food security and disease control initiatives; and (4) increase the participation of veterinary scientists in One Health initiatives.

Dr. Annelli provided an overview of One Health-related work within the USDA APHIS. The One Health Joint Working Group at the USDA works on zoonotic disease engagement, pre-harvest food safety, antimicrobial resistance, animal and pandemic influenza preparedness, and global health security. The USDA APHIS Veterinary Services, which safeguards the health of animals, people, and the environment, is developing a One Health Engagement Field Guide for how to conduct joint epidemiological investigations on zoonotic diseases. APHIS Veterinary Services also assesses root causes of foodborne-related illnesses, estimates on-farm prevalence, identifies risk factors associated with shedding of potential foodborne pathogens on U.S. livestock and poultry operations, and describes on-

farm antimicrobial usage and resistance. APHIS' antimicrobial resistance goals are to: (1) slow emergence of and prevent the spread of resistant infections; (2) strengthen national One Health surveillance efforts to combat resistance; (3) advance development and use of rapid and innovative diagnostic tests for identification and characterization of resistant bacteria; (4) accelerate basic and applied research and development for new antibiotics, other therapeutics, and vaccines; and (5) improve international collaboration and capacities for antibiotic research and development.

APHIS provides leadership in the North American Plan for Animal and Pandemic Influenza, strengthening trilateral preparedness and response capabilities to influenza, regardless of source, among Canada, Mexico, and the United States. APHIS also works both domestically and internationally to protect the United States from global health threats posed by infectious diseases. Outbreaks of H7N9 avian influenza, novel coronavirus (MERS) of camel origin, and Ebola have exposed gaps in the global system for managing emerging infectious disease threats and demonstrate the need for enhanced U.S. leadership to strengthen global threat detection, preparedness, and response capacity. Coordination and collaboration across all levels of the human, livestock, and wildlife health sectors are essential to meet the Global Health Security Agenda (GHSA) vision for "a world safe and secure from global health threats posed by infectious diseases." Making the goals and objectives of GHSA understandable and operational required the development of 11 action packages with input from multiple countries at three international meetings.

Dr. Pimentel presented an overview of the CDC's domestic and global One Health activities, training programs available for veterinarians, and research related to One Health. The CDC's programs are grouped by diseases, with the majority of One Health activities housed in the National Center for Emerging and Zoonotic Infectious Diseases. The CDC works with local and national governments as well as animal, environmental, and human health partners, including the WHO, OIE, and FAO. Human–animal interface officers are stationed across the globe at Global Disease Detection sites, which strengthens the CDC's global capacity to rapidly detect and respond to zoonotic diseases. A guidance document was published in November 2014 by the AVMA Ebola Companion Animal Response Plan Working Group regarding pets that have been exposed to human patients with Ebola. The CDC has also published guidelines for concerned animal owners, which is available online. Veterinarian scientists at the CDC focus work on influenza, poxvirus and rabies, HIV, and viral special pathogens (e.g., Ebola, Marburg, Rift Valley fever).

The goal of a 2-year, agency-wide review of the CDC's animal research programs was to ensure that animal research at the CDC was obtaining the greatest possible public health impact, meeting the highest scientific and ethical standards, and making optimal use of available resources. Recommendations of the review were to prioritize program areas, consider a reduction of animals where feasible, and conduct ongoing institutional monitoring of the program's response to the review. The review highlighted the translatability of animal models to human health to foster One Health in CDC laboratory science via the design of animal models for disease prevention, transmission, and treatment.

The CDC has multiple training opportunities in epidemiology, including its Epidemic Intelligence Service (EIS) program, which is a 2-year post-graduate training program of service and on-the-job learning for health professionals, and the CDC Epidemiology Elective Program, which is open to third and fourth year veterinary and medical students.

Discussion

Dr. May commented that veterinarians are highly qualified for many CDC positions listed on the USAJOBS website but that they are advertised for medical officers only. Dr. Annelli stated that he was

willing to share the text of multidisciplinary job descriptions written by the USDA. Dr. Pimentel added that many veterinarians enter the CDC through the EIS program.

A meeting participant wondered whether a Ph.D. is necessary to conduct research at ARS given that many paths to research are possible. Dr. Gay emphasized the importance of basic research at ARS and reiterated the need for the ARS to fill the significant gap in the number of veterinarian Ph.D. scientists who are able to conduct high-quality research in areas of virology and immunology. He added that only 40 of 2,200 Ph.D. scientists at ARS are veterinarians.

"One Health" Perspectives From BioPharma
Cathleen Lutz, Ph.D., Senior Research Scientist, The Jackson Laboratory; Carol Robertson-Plouch, D.V.M., Eli Lilly and Company

Dr. Robertson-Plouch presented on Eli Lilly's approach to drug development. Its timely value medicines (TVMs) refer to a patient-centric, data-driven quality approach consisting of five key steps: (1) a better understanding of disease, (2) appropriate tailoring of medicines, (3) the right therapeutic agents, (4) robust Phase 2 data, and (5) differentiation in Phase 3. Clinical trials, however, have been consuming an increasing portion of research and development funds, and poor efficacy has been the cause of half of Phase II drug failures and two-thirds of Phase 3 failures. Therefore, Eli Lilly has placed a stronger emphasis on better predicting drug efficacy.

Translational and comparative research with naturally occurring, parallel disease states in animals can increase the probability of human efficacy success, provide cost and time savings, increase the value of the early drug candidate package, inform the overall safety dataset, and provide a potential alternate or parallel development strategy for veterinary medicine. Animals and humans share exposure to environmental influences, and they often have the same active targets. Moreover, their genetic causes may be homologous, and treatment regimes in animals are often extrapolated from humans. Pet owners are motivated, the animals are usually cared for well, and the clinical interface is similar to that of pediatric medicine. Translational comparative medicine is beneficial because it can demonstrate drug activity in actual diseased animals. Examples of the success of the animal-to-human drug development paradigm include the anti-parasitic drug ivermectin for use in animals that became Mectizan® and later Stromectol® for use in humans, samarium 153 radioisotope treatment for bone cancer in dogs was redeveloped into Quadramet® for humans, Palladia® kinase inhibitor for canine mastocytoma was developed in concert with Sutent® for renal cell carcinoma in humans, and Optimune® for canine dry eye became Restasis® for human dry eye.

Dr. Lutz presented a perspective from The Jackson Laboratory, a nonprofit organization and research institute with a mission to provide resources to the biomedical community to advance the research and find cures for diseases. The Jackson Laboratory's Rare and Orphan Disease Center has established disease-specific mouse repository cores that function to import and standardize the genetic background of existing mouse models, provide genetic and phenotypic quality assurance, promote reproducibility and accessibility, phenotype and cross-compare in longitudinal studies, establish phenotypically relevant outcome measures for use in preclinical testing platforms, perform dosing studies, and assist in generating future models.

Despite the challenges of working with mice, disruptive technologies in the field such as whole genome sequencing and genome editing via CRISPR/Cas9 are incredibly powerful compared to traditional gene targeting. With the adoption of CRISPR/Cas9 technology, investigators will no longer be able to sequester mouse models. The technology allows for precision modeling for specific human mutations, and models can be made with different genetic backgrounds. Potential concerns include the influx of mouse models, oligogenic licensing, and reproducibility issues. The mouse modeling community needs to

come together and recognize how such technologies will affect business models. One possible solution is to outsource the creation of mouse models to a third party, which would remove aspects of oligogenic licensing, make mouse models available as soon as they are made, and allow researchers to characterize and study the mouse models rather than creating them, which will promote accessibility, competition, and drive forward progress.

Discussion

Dr. Gaylen Edwards, University of Georgia, expressed concern about reproducibility as a major issue in animal research, noting that animal rights organizations have been lobbying to cut funding to science. Dr. Lutz replied that not sequestering mouse models or establishing prohibitive licenses will benefit the patient community. Also important is to simultaneously perform second site validation. Dr. Edwards added that studies criticized for reproducibility are low-powered and lead to clinical trials that fail in efficacy. Dr. Lutz emphasized the need to work with contract research organizations to ensure that studies are well-powered, blinded, and randomized.

A meeting participant, recognizing that Eli Lilly is in the minority among pharmaceutical companies with respect to expressing interest in companion animal research, asked about the perceived risks of placing human-destined drugs in companion animals in clinical trials. Dr. Robertson-Plouch, noting that companion animal research at Eli Lilly began about 1 year ago, responded that perceived risks include the perception that diseases are not similar enough. There also is concern about an adverse event occurring in animals that does not occur in humans. Perceived risks can be mitigated once they are incorporated into the construct of drug development, either prior to testing in humans or, to address dosing schema, dose reductions, or split dosing, in parallel with humans.

SUMMARY

Deborah Kochevar, D.V.M., Ph.D., Tufts University; Susan VandeWoude, D.V.M., Colorado State University

The *Physician-Scientist Workforce Working Group Report*, which was prepared per a charge by Dr. Francis Collins, NIH Director, and issued in June 2014, included veterinarians in its definition of physician-scientist. This would suggest that veterinarians will be qualified to submit applications for any initiatives or program announcements that result from the report. Recommendations of the *Report* included encouraging the inclusion of veterinary scientists in applications using animals, expanding programs for training veterinarians concurrent with research and veterinary school, and recruiting more female scientists.

Dr. VandeWoude expressed that the One Health umbrella's large number of encompassed disciplines might be a disadvantage when trying to disseminate One Health ideas and applying for funding opportunities. She proposed separating the comparative approach to translational medicine from the intersection of human, animal, and environmental health, a much larger issue that requires transdisciplinary solutions among engineers, sociologists, and other disciplines. Dr. Kochevar reflected on the need to train a generation of students and house officers who will consider themselves as members of a health professional team.

Dr. VandeWoude added that animals such as sheep and goats also can be used in comparative medicine, for example, to study rare diseases (e.g., NPC, muscular dystrophy). Diseases that are of less "relevance" in companion animals, such as obesity, dementia, and diabetes, have not been recruited into clinical trials but do occur in human populations in large numbers and could be an avenue for future research.

PANEL DISCUSSIONS

Training Director Roundtable: Best Practices for Training Involving "One Health"
Peter Ernst, D.V.M., Ph.D., Head, Division of Comparative Pathology and Medicine, University of California, San Diego; James Fox, D.V.M., Director, Division of Comparative Medicine, Massachusetts Institute of Technology; Michael Kent, Ph.D., Professor, Oregon State University; Peter Preusch, Ph.D., Chief, Biophysics Branch, National Institute of General Medical Sciences (NIGMS), NIH; Mark Simpson, D.V.M., Ph.D., Head, Comparative Molecular Unit, NCI, NIH

Dr. Fox reflected on the importance of the T32 predoctoral training program. ORIP funding has been a critical element in increasing the number of veterinarian scientists, and the T32 predoctoral training program in particular has allowed veterinary students to participate in NIH-sponsored research programs. Training programs need to be integrated into an institution's research infrastructure because they foster the importance of individual research by fellows and help fellows to enter into collaborative arrangements. Structured research seminars and journal clubs help increase interaction between students.

Dr. Ernst stated that the veterinarian scientist pipeline suffers because people do not understand the path of veterinarian graduates and proposed that outreach expand to middle schools, high schools, undergraduates, and pre-veterinarians. One Health lectures also need to be given to M.D. and Pharm.D. students. Because of the approximately 9 years of post-D.V.M. training necessary, loan repayment programs are a critical asset.

Dr. Preusch presented on the participation of D.V.M./Ph.D. students in the Medical Scientist Training Program (MSTP). MSTP is the largest training program run by the NIH, with 45 grants supporting 60 institutions and more than 900 trainees each year. Although at least eight programs are associated with a veterinary school, only one—University of Pennsylvania—has a significant veterinary component. Dr. Preusch noted that several institutions that currently do not support MSTP programs but have co-located medical and veterinary schools have a reasonable chance of being awarded a MSTP grant. Important considerations should go to the integration of the curriculum, clinical training, and medical or veterinary training; the commitment of students to the program and research career (e.g., duration of training, separation from entering cohort, advising); and financial support, given that the MSTP award covers only 25 percent of the cost, with other mechanisms covering the remaining 75 percent.

Dr. Simpson shared the NIH intramural perspective on veterinarian scientist training. He described the NIH Comparative Biomedical Scientist Training Program, a combined residency/Ph.D. program that involves four NIH Institutes and five veterinary schools and is now in its 13th year. After completing the veterinary degree, students spend 2 years at a university completing required coursework before relocating to Bethesda, MD, to be placed within a laboratory at the NIH where they undertake research training. Students ultimately receive their Ph.D. degree from their university.

The Medical Research Scholars Program (MRSP) immerses students in the middle of their veterinary training in research at the NIH for 1 year. Veterinary students compete successfully with medical and dental students for MRSP positions. Greater awareness and support from veterinary schools is needed, however, to encourage participation in the program due to the significant sociological hurdle students face in stepping away from the veterinary curriculum. The MRSP experience helps trainees envision themselves as future principal investigators and has led to high success rates in the launching of independent careers.

Dr. Kent discussed the aquatic training model at Oregon State University's Comparative Health Sciences Graduate Program. The program, which has three slots and has been running for approximately 5 years, focuses on zebrafish research. Its directors have found greater success in recruiting students interested in research and teaching them about fish rather than recruiting students interested in clinical work and pulling them toward research. The program plans to target students with laboratory animal backgrounds.

Discussion

Dr. Michael Atchison, University of Pennsylvania, remarked that T32 applications from veterinarians stand out in study sections and encouraged participants to take a One Health approach in their application materials. Dr. Lairmore commented that because the Veterinary Scientist Training Program at UC Davis can afford only two slots, the graduate school component must be covered by other funds or grants. If additional NIH funds were made available, they could assist in leveraging resources from other schools to help fund additional students. Dr. Ernst added that upwards of $250,000 is budgeted for each D.V.M./Ph.D. student. Dr. VandeWoude suggested establishing a supplement award to an existing MSTP award, and many participants agreed with this suggestion.

Dr. Kochevar inquired about the existence of metrics regarding long-term outcomes for D.V.M./Ph.D. trainees. Dr. Sherry Mills, Director, Office of Extramural Programs, NIH, and co-chair of the *Physician-Scientist Workforce Working Group Report*, recalled that making recommendations for the Report was difficult because of the lack of data on the veterinary science community; especially given the decentralized nature of veterinary training programs and that not all programs are funded by the NIH. Dr. Ted Mashima, Association of American of Veterinary Medical Colleges (AAVMC), remarked that a gap exists between the data collected while students are in veterinary school and the data collected externally about the veterinary community. The AAVMC will be committed to filling this gap. Dr. Mills acknowledged that the medical community also lacks sufficient data on physician-scientist outcomes.

Trainee Roundtable: Perspectives on the "One Health" Concept
Tracie Baker, D.V.M., Ph.D., University of Wisconsin; Pierre Comizzoli, D.V.M., Ph.D., Smithsonian Institution; Cheryl London, D.V.M., Ph.D., Professor, College of Veterinary Medicine, The Ohio State University; Julita Ramirez, D.V.M., Ph.D., University of Washington; Robert Rebhun, D.V.M., Ph.D., University of California, Davis; Katie Sheats, D.V.M., Ph.D., North Carolina State University

Dr. London presented on current paradigms for advanced training and associated challenges. More than 80 percent of students who enter veterinary training are tracked to general practice, and although students occasionally are exposed to alternative careers during training, it is often intermittent and not sustained. Advanced training appears daunting to students given the $100,000 to $300,000 debt load that most carry following completion of the veterinary degree. Current challenges include limited support for advanced training, the intense didactic veterinary curriculum, the restriction of many fellowships to M.D. applicants, and the limited awareness of awards to support advanced training (e.g., T32, K01, K08 awards). Changes to the paradigm might include integrating alternative career paths into early didactic education, offering internship opportunities in industry and at the NIH during training, early intervention with respect to career counseling, mentorship programs involving experts within and outside a student's institution, and sustained contact with prospective trainees throughout their entire veterinary training program.

Dr. Ramirez completed a D.V.M./Ph.D. program because she had difficulty choosing between a biochemistry Ph.D. and a D.V.M. degree. Loan repayment programs are critical for veterinarian researchers, however, because the debt load is paralyzing for most students, many of whom enter graduate programs with significant undergraduate debt. To increase awareness in veterinary science careers,

children should be engaged in problem-based learning approaches, and high school level education and cross-disciplinary training programs should teach the capabilities of each discipline. The University of Washington's strong emphasis on research and achieving a first-author publication is a major advantage of its program. Its clinical research residents appreciated being required to engage in a basic research project as trainees.

Dr. Sheats discussed the excellent interdisciplinary training that was part of the culture at her institution. Internal funding programs and the opportunity to write two pilot grants helped foster her success, coupled with exceptional access to other institutions through well-established collaborations with nearby institutions. Participation in the Merial-NIH Veterinary Scholars Program during her second year of veterinary school also was valuable.

Dr. Baker completed her Ph.D. through the Molecular and Environmental Toxicology Center at the University of Wisconsin, a program that was not associated with the veterinary school but that had strong crossover of disciplines and interaction between trainees and mentors in different areas. The One Health concept has not been formally incorporated into the curriculum at the University of Wisconsin, but the University is poised to do so due to having medical, veterinary, pharmacy, and nursing schools as well as public and global health programs.

Upon relocating to the U.S. after completing veterinary and Ph.D. training in France, Dr. Comizzoli found that veterinarians in the United States were allowed more freedom than those in Europe. Working on One Health issues at the Smithsonian Institution was highly satisfying, and to remain in research he applied for a K01 grant. An ongoing concern is that medical students are surprised to discover that animal pathologies are similar to human pathologies. More championing of One Health's focus on animal welfare, physiology, fertility preservation, and other topics shared by humans and animals is needed.

Dr. Rebhun reflected on the importance of recognizing the differences and challenges between M.D./Ph.D. and D.V.M./Ph.D. programs. The duration of training is a major concern for veterinary students, who realize when they separate from their peers for Ph.D. training how many years of training are needed before they are able to begin careers and stably establish families.

Dr. London added that an important component of training programs is to review papers and write grants. K awards have been a common path to success for veterinarian scientists and need to be made more visible to students by mentors.

Discussion

Dr. Kenyon commented that veterinary students, unlike medical students, rarely take 1 year away from their studies to engage in research. Dr. London replied that students prefer not to interrupt the rush of didactic training in their first 3 years. Dr. Mashima stated that the NIH in response to this concern is developing a mechanism that would allow students to complete such training during the year following completion of the D.V.M. degree. He urged the participants to provide their input on such initiatives when requested to do so by the NIH.

Ms. Hlavaty inquired about the training opportunities available in clinical veterinary research as opposed to basic biomedical research. Dr. London acknowledged that a formalized training program for clinical veterinary research is lacking and has noticed gaps in clinicians' ability to formalize clinical research and understand how to formulate a hypothesis, statistically power a study, and have meaningful and realistic objectives. Dr. Ernst advocated for core and basic research as a path into clinical research. These scientists understand the biology and have developed their own set of skills in clinical research based on their own questions. Dr. Rebhun added that many residency programs do have an associated Master's

degree. Conducting basic research during residency is time-consuming and therefore difficult. There are programs, however, for junior faculty who do not have a basic research background to be trained in clinical research.

DISCUSSION

Peter Ernst, D.V.M., Ph.D., University of California, San Diego; James Fox, D.V.M., Massachusetts Institute of Technology

Dr. Dunham voiced a concern about the future of careers for veterinarian graduates and suggested ensuring that there is a need to fill prior to encouraging veterinarians to continue down this path. Dr. Ernst highlighted that although the NIH has drawn the ire of many investigators, states have made large cuts to faculty positions. He is confident that careers for people who are bright, well-trained, and will apply themselves will exist, although these careers might look different in 10 or 20 years. Dr. Lairmore echoed Dr. Ernst's remarks, noting that recent appointments at UC Davis are marked by people who have had research training and a K award. When measuring research productivity, veterinarians must understand that they will not be hired as researchers without prior research experience. In addition, when veterinarians leave their clinic positions to conduct research, funds are needed to hire staff veterinarians to help offset their absence in the clinic.

Dr. Goldberg proposed that programs targeting Ph.D. graduates to enroll in a veterinary school could be an efficient way to finance the One Health workforce. Dr. Fox agreed, adding that several fellows at the Massachusetts Institute of Technology who have taken this path have returned to the research track with a veterinary emphasis.

Dr. Scott Mischler, Pfizer, commented that at least three research positions have opened within comparative medicine at Pfizer that are intended for D.V.M./Ph.D. researchers without the requirement of Board Certification. Because Pfizer struggled to find candidates to apply, Dr. Mischler wondered about effective methods for disseminating job postings.

Dr. Ernst shared an anecdotal observation that many biomedical engineers have considered enrolling in veterinary school. He encouraged the participants to give more attention to this talented group.

Dr. VandeWoude posed a question about the necessity of a Ph.D. degree for veterinarians interested in conducting biomedical research and that it is not as time-consuming but just as effective. Dr. Ernst stated that a Ph.D. is not necessary if a candidate has sufficient research experience. Dr. Fox added that an M.D. is acceptable and competitive in terms of being awarded research dollars. Dr. Redhun has told trainees that high productivity during their fellowship is likely equivalent to a Ph.D. degree, especially with two or three high-impact papers. Dr. Kochevar added that a cultural shift at the level of veterinary school hiring is needed. Dr. Kelly Metcalf Pate, The Johns Hopkins University School of Medicine, reminded the participants that many programs default to a Ph.D. because certain components of training are inherent in fellowships (e.g., grantsmanship, publication writing, study design). Dr. Henry encouraged residency training programs to consider having residents at least earn a Master's degree and to consider accepting residents who have been in private practice, as they often bring valuable experience and personal wisdom. Dr. Lairmore noted the value in veterinary students seeing excitement and passion in their laboratory science mentors. He added that in the University of California system, residency programs are separated from graduate programs, prohibiting residents from receiving a Master's degree, although they are all engaged in research projects to some extent. Dr. Vilma Yuzbasiyan-Gurkan, Associate Dean for Research, College of Veterinary Medicine, Michigan State University (MSU), said that institutions should reflect on the recruiting taking place and the message they are sending to prospective students. MSU has made it a rule to talk about research because earlier discussion and planning leads to superior returns.

Dr. Baneux said that veterinary clinical studies are extremely important but recognized that compensation is very poor. Dr. Ernst remarked that tuition costs to investigators once students reach candidacy are high; however, administrators must not succumb to the temptation of uneven pay and must separate student enthusiasm and passion from fairness.

Dr. Barbara Fuller, Elanco, stated that only having a D.V.M. has limited her career and ability to advance. A meeting participant shared that after receiving a D.V.M. degree and becoming CEO of a small medical device startup company that performed clinical research in humans and animals, she felt that she needed additional letters behind her name so that the medical community would feel more at ease. She has noticed a marked change since completing the M.P.H. degree. Dr. Robertson-Plouch agreed that D.V.M. scientists are underappreciated in the medical community and must devise a way to demonstrate that they have value-added expertise. Dr. Ernst acknowledged that the culture has to change.

Dr. London remarked that veterinarians doing translational research in the clinical realm face the challenge of lack of acceptance by the extramural NIH regarding alternative models. A number of colleagues are doing cutting-edge research on models that are not mouse or zebrafish, but they are disregarded by study sections because the study sections lack expertise about those models. Dr. Fox agreed, adding that increasing engagement in study sections by veterinarians is one of the recommendations presented in the *Physician-Scientist Workforce Working Group Report*. Dr. Yuzbasiyan-Gurkan called upon the meeting participants to volunteer as reviewers for study sections or to suggest colleagues as reviewers.

Dr. Vite stated that large animal veterinarians with a Ph.D. find it difficult to obtain funding and to survive when their institution requires funding support. Dr. Lairmore suggested pursuing international work in global security through APHIS and ARS, and added that further discussion about the demand for veterinarians to enter this workforce is needed. Dr. Ernst suggested incorporating a link to humans to find greater success in obtaining funding through the NIH. Dr. VandeWoude added that this issue is amplified because the USDA's research funding is relatively small. Dr. Dunham highlighted the value of travel externships that highlight alternative career paths upon graduation.

Dr. Mashima commented that with regard to ethnicity and race, the research community needs to better reflect the demographic of the society it serves, noting that veterinarians are the least diverse profession according to the Bureau of Labor. The NSF and other research training programs specifically seek to address this issue. Dr. Fox added that some NIH Institutes offer minority supplements. Dr. Lairmore stated that tremendous support is offered by NSF ADVANCE: Increasing the Participation and Advancement of Women in Academic Science and Engineering Careers.

Dr. Sheats recommended, based on her experience that students be offered training opportunities on communication across disciplines (e.g., how to collaborate, establish outcomes, work on mutual expectations, resolve conflicts).

Dr. Grieder advocated for stimulating students' interest in veterinary medicine early. ORIP's Science Education Partnership Awards (SEPA) allow investigators to set up engaging science programs for elementary, middle, or high school students. At least two such programs are linked to veterinary schools.

FUTURE AND NEW DIRECTIONS FOR "ONE HEALTH" EFFORTS

Deborah Kochevar, D.V.M., Ph.D., Tufts University; Michael Lairmore, D.V.M., Ph.D., University of California, Davis

Dr. Lairmore summarized common themes discussed during the meeting and recommendations for ORIP. Prominent ideas included the One Health umbrella diagram, canine models and their translation to human health, the role and value of clinical trials in patient-owned animals in predicting and advancing the therapeutic pipeline, and reproducibility of animal models and natural animal models. Additional themes included the need to expand opportunities and partnerships, case studies of transdisciplinary teams that include veterinarians as primary investigators, existing resources (e.g., Cancer Centers, Primate Centers, CTSAs), resource development (e.g., biorepositories, REDCAP), the need for trained veterinarians in areas of focus within Federal agencies, success stories (e.g., the NCI COP), and communications and culture (e.g., the importance of a broader One Health audience). The biopharmaceutical industry also was discussed, specifically the recognition of industry's research and development needs in academic and research centers, barriers to academia, and the unique value of mouse models and resources.

Training was a major theme during the meeting. Highlighted were the values of the T and K programs; the value of and concerns about the MSTP program (e.g., duration of training, cohort influences, student debt); and the importance of mentorship, joint advising, and cross-training within One Health. Also discussed were the need for comparative training in alternative models, training data, and an increased focus on research in veterinary schools. An area of significant concern was the student debt load.

Recommendations for ORIP include MSTP program slot expansion for veterinarians or, if possible, the establishment of parallel veterinary programs; unique aspects of T and F programs regarding veterinary science; and collaborations across Federal agencies in areas of need. Veterinarian input in study sections and program development is needed, as is reviewer training in One Health themes as well as the inclusion of One Health language in training grants.

Dr. Kochevar discussed avenues for expanding and developing the veterinarian scientist workforce. National student mentoring networks are needed that address the role of veterinarians in research, both through longitudinal veterinary scientist training "tracks" that are accessible and well communicated and through robust government support, including an industry-funded 5-year program that serves as a clearinghouse about current information for the many paths into veterinary research. All government programs should be open to veterinarian researchers, including those that incentivize students to enter research. Dr. Kochevar hopes that by 2020 the average debt will be down by 15 percent, the number of D.V.M./Ph.D trainees will have increased by 50 percent, accrediting bodies will have included a standard that addresses interprofessional education, and one-half of the NIH Institutes will have incorporated a One Health element into their requests for applications.

Another recommendation is a national clinical studies platform for the study of naturally occurring animal disease. Industry should play a key role by making clinically based research programs a top priority. Characterizing naturally occurring animal models and determining which are most validated and best established will be important. Broadening the research agenda to include the impact of human-animal interactions on human health as a potential component of NIH-funded research is critical.

Discussion

Dr. Grieder informed participants that ORIP is in the process of developing its first 5-year strategic plan that should be published in early 2016. A request for input was sent to all grantees, and Dr. Grieder

invited the meeting participants to send their comments via email to Stephanie Murphy, V.M.D., Ph.D., DACLAM, Director, Division of Comparative Medicine, ORIP, NIH.

Dr. Lackner asserted that communicating to biomedical researchers how veterinarians' breadth of knowledge can be of value to their research is necessary to make significant progress. The NIH then can determine how to support such efforts. Dr. Kochevar asked whether NIH Institute or Center directors have discussed how veterinarian scientists can help advance the NIH mission. Dr. Simpson responded that the suggestion to include more veterinarians on study sections was made in 2004 and embraced by the NIH Director, but was never followed up by the veterinary profession. He encouraged veterinarians to assume greater responsibility for progress within their profession. He also suggested that participation on study sections will help D.V.M. researchers become recognized as experts and aid in the success of their applications for research grants. Dr. VandeWoude commented that AAVMC has focused on efforts to have veterinarians listed on study section rosters but that finding individuals with the necessary time and expertise has been difficult. Dr. Mashima clarified that the AAVMC does not ask for preferential treatment but simply advocates on behalf of the veterinary profession. Some in the veterinary community see it as a disadvantage to list their veterinary degree on their form, but he urged meeting participants to respond positively to requests to participate in study sections. Dr. VandeWoude and Dr. Hoxie pointed out that having 1 to 2 veterinarians on study sections may do little to advance the research efforts of veterinarian scientists and that the directive to change how grants are triaged needs to come from Institute directors. Dr. Lairmore urged participants to listen to Institute directors and their priorities. Dr. Dunham suggested including Institute directors in the discussion.

Dr. Page suggested engaging in discussions with the National Institute of Environmental Health Sciences, whose researchers might benefit from conducting research in animals that they cannot conduct in humans.

Dr. Gary Sherman, Institute of Food and Agriculture (NIFA), USDA, emphasized the many programs that exist within NIFA and USDA, particularly two successful programs that might serve as launching points for further development within the veterinary science initiative: Ecology and Evolution of Infectious Diseases, and Dual Purpose with Dual Benefit: Research in Biomedicine and Agriculture Using Agriculturally Important Domestic Animal Species. Dr. Sherman added that the loan repayment program he oversees at USDA provides an incentive for private practicing veterinarians to work in underserved areas.

Dr. Robertson-Plouch suggested that the NCI COP be used as template for other disciplines to emulate. The entire veterinary oncology community influenced the development of the COP.

Workshop Participants' Suggested Next Steps

Based on speaker presentations and attendee discussions at the One Health Workshop, the following next steps were suggested for ORIP relative to veterinarian scientists.

<u>Biomedical Research Training</u>

- Expansion of the Medical Scientist Training Program (MSTP) to include more training slots for veterinary students pursuing dual doctoral degrees.
- Development of comparative training mechanisms in alternative models.
- Development of unique T and F training program mechanisms designed for veterinary students and veterinarians.
- Promotion of joint training programs and opportunities involving both medical and veterinary students to enhance role of veterinarian scientist in interdisciplinary team science.

- Expansion of the Loan Repayment Program to include public practice veterinarians in One Health areas.
- Promotion of training opportunities related to global health for veterinary students and veterinarians.
- Promotion of collaborations across Federal agencies in areas of need.

Pipeline

- Development and promotion of national student mentoring networks to address the role of veterinarians in research.
- Promotion of examples of longitudinal veterinarian scientist training "tracks" that are accessible.

Strategic Planning

- Leverage Physician-Scientist Workforce Working Group Report and its recommendations.
- Development and support of naturally occurring animal disease models for biomedical research applications.
- Expansion of research agenda to include impact of human-animal interactions on human health.

APPENDIX 1: ORGANIZING COMMITTEE

Dr. Peter Ernst, University of California, San Diego

Dr. James Fox, Massachusetts Institute of Technology

Dr. John Harding, ORIP, NIH

Dr. Michael Kent, Oregon State University

Dr. Deborah Kochevar, Tufts University

Dr. Andrew Lackner, Tulane National Primate Research Center

Dr. Manuel Moro, ORIP, NIH

Dr. Stephanie Murphy, ORIP, NIH

Dr. Ronald Sokol, University of Colorado

Dr. Susan VandeWoude, Colorado State University

APPENDIX 2: WORKSHOP AGENDA

Agenda

Lister Hill Auditorium, Building 38A, National Institutes of Health

Day 1 – Tuesday, April 7, 2015

7:30 a.m. – 8:00 a.m. **Registration**

8:00 a.m. – 8:15 a.m. **Welcome and Introductions**
Franziska Grieder, D.V.M., Ph.D., Office of Research Infrastructure Programs (ORIP), National Institutes of Health (NIH)
Jack Harding, Ph.D., ORIP, NIH
Manuel Moro, D.V.M., Ph.D., ORIP, NIH

8:15 a.m. – 9:15 a.m. **Keynote Presentation: "One Health" Challenges for the 21st Century**
Carolyn Henry, D.V.M., University of Missouri **(Introduced by Stephanie Murphy, V.M.D., Ph.D., ORIP, NIH)**

Moderator: Jack Harding

9:15 a.m. – 10:00 a.m. **Comparative Medicine Team Approach: HIV/AIDS**
James Hoxie, M.D., Ph.D., The University of Pennsylvania
Andrew Lackner, D.V.M., Ph.D., Tulane National Primate Research Center

10:00 a.m. – 10:15 a.m. **Break**

10:15 a.m. – 11:00 a.m. **Comparative Medicine Team Approach: Emerging Infections**
Tony Goldberg, D.V.M., Ph.D., University of Wisconsin
David O'Connor, Ph.D., Wisconsin National Primate Research Center

11:00 a.m. – 11:45 a.m. **Comparative Medicine Team Approach: Cancer**
Mark Gilbert, M.D., National Cancer Institute (NCI), NIH
Amy LeBlanc, D.V.M., NCI, NIH

11:45 a.m. – 12:30 p.m. **Comparative Medicine Team Approach: Neurodegenerative Diseases**
Forbes Porter, M.D., Ph.D., *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), NIH
Charles Vite, D.V.M., Ph.D., The University of Pennsylvania

12:30 p.m. – 1:30 p.m. **Lunch Break**

Attendees will be responsible for meals/light refreshments on their own and at their own expense. The government and/or government contractors are not involved in facilitating the provision of food and/or light refreshments.

Moderator: Manuel Moro

1:30 p.m. – 2:15 p.m. **Comparative Medicine Team Approach: Viral Infections**

Genoveffa Franchini, M.D., Vaccine Branch, NCI, NIH
Michael Lairmore, D.V.M., Ph.D., University of California, Davis

2:15 p.m. – 3:00 p.m. **Comparative Medicine Team Approach: Muscular Dystrophies**

Joe Kornegay, D.V.M., Ph.D., Texas A&M University
Kathryn Wagner, M.D., Ph.D., The Johns Hopkins University

3:00 p.m. – 6:00 p.m. **"One Health" and Centers, Agencies, and Industry**

3:00 p.m. – 3:30 p.m. **CTSAs and Veterinarians**

Deborah Kochevar, D.V.M., Ph.D., Tufts University
Cheryl London, D.V.M., Ph.D., The Ohio State University
Ronald Sokol, M.D., University of Colorado
Susan VandeWoude, D.V.M., Colorado State University

3:30 p.m. – 4:00 p.m. **Cancer Centers**

Rodney Page, D.V.M., Colorado State University
Amy LeBlanc, D.V.M., NCI, NIH
Mark Gilbert, M.D., NCI, NIH

4:00 p.m. – 4:15 p.m. **Break**

4:15 p.m. – 5:15 p.m. **Updates on the "One Health" Landscape Across Federal Agencies**

Joseph Annelli, D.V.M., Animal and Plant Health Inspection Service, U.S. Department of Agriculture (USDA)
Cyril Gerard Gay, D.V.M., Ph.D., Agricultural Research Service, USDA
Linda Pimentel, V.M.D., Centers for Disease Control and Prevention

5:15 p.m. – 6:00 p.m. **"One Health" Perspectives From BioPharma**

Carol Robertson-Plouch, D.V.M., Eli Lilly and Company
Cathleen Lutz, Ph.D., The Jackson Laboratory

6:00 p.m. – 6:45 p.m. **Summary and Discussion**

Deborah Kochevar, D.V.M., Ph.D., Tufts University
Susan VandeWoude, D.V.M., Colorado State University

Day 2 – Wednesday, April 8, 2015

7:30 a.m. – 8:30 a.m. **Registration**

8:30 a.m. – 8:40 a.m. **Welcome**

8:40 a.m. – 9:40 a.m. **Training Director Roundtable: Best Practices for Training Involving "One Health"**

Peter Ernst, D.V.M., Ph.D., University of California, San Diego
James Fox, D.V.M., Massachusetts Institute of Technology (MIT)
Michael Kent, Ph.D., Oregon State University
Peter Preusch, Ph.D., National Institute of General Medical Sciences, NIH
Mark Simpson, D.V.M., Ph.D., NCI, NIH

9:40 a.m. – 10:40 a.m. **Trainee Roundtable: Perspectives on the "One Health" Concept**

Tracie Baker, D.V.M., Ph.D., University of Wisconsin
Pierre Comizzoli, D.V.M., Ph.D., Smithsonian Institution
Cheryl London, D.V.M., Ph.D., The Ohio State University
Julita Ramirez, D.V.M., Ph.D., University of Washington
Robert Rebhun, D.V.M., Ph.D., University of California, Davis
Katie Sheats, D.V.M., Ph.D., North Carolina State University

10:40 a.m. – 11:00 a.m. **Break**

11:00 a.m. – 11:45 a.m. **Summary and Discussion**

Peter Ernst, D.V.M., Ph.D., M.S., University of California, San Diego
James Fox, D.V.M., MIT

11:45 a.m. – 12:30 p.m. **Future and New Directions for "One Health" Efforts**

Deborah Kochevar, D.V.M., Ph.D., Tufts University
Michael Lairmore, D.V.M., Ph.D., University of California, Davis

12:30 p.m. **Acknowledgements and Adjournment**

Stephanie Murphy, V.M.D., Ph.D., ORIP, NIH