Enhancing animal production, profitability, and well-being by improving animal health.
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[www.vet.uga.edu/research/vmes/]
VMES Objectives

The Veterinary Medical Experiment Station (VMES) supports a wide range of research that impacts on many aspects of our lives; the food we eat and the clothes we wear, our physical, emotional, and economic health, and the quality of our environment. VMES research includes efforts to improve the productivity and health of poultry and livestock, to better the quality of life for companion animals, and to improve public health through disease surveillance. This year’s research is profiled in our 2003-2004 VMES annual report.

VMES funds help support short-term applied research that directly benefits the health of animals and livestock in Georgia and are used to develop extramurally funded research programs at the College of Veterinary Medicine. Projects supported by VMES funds are evaluated for scientific merit, importance to animal health, consideration for experimental animal welfare, and their roles in meeting the research objectives of the VMES.

Our objectives are as follows:

- To improve the health and productivity of domestic livestock, poultry, fish, and other income-producing animals and wildlife through research;

- To assist in preventing disease epidemics by providing laboratory resources and highly skilled scientific personnel;

- To assist in protecting human health through the control of animal diseases transmissible to man;

- To improve the health of companion animals, which serve to enrich the lives of humankind;

- To train new scientists in animal health research in order to provide continuity and growth in this vital area of veterinary medicine.

All programs and activities of the Veterinary Medical Experiment Station are conducted without regard to race, color, national origin, age, sex, or handicap.
In this, the 28th Annual Report of the Veterinary Medical Experiment Station (VMES), we present a summary of the research activities of the College of Veterinary Medicine. Our research is an integral component of the veterinary profession, explicitly stated in the Veterinarian’s Oath as an obligation to advance medical knowledge that benefits both veterinary and human medicine, which we consider “one medicine”.

Veterinary medicine is an indispensable component of our State’s public health system. Veterinary researchers protect animal and human health by preventing and controlling infectious diseases, and their work ensures the safety and security of our food supply. Although veterinary research has the potential for great impact in many biomedical fields, support for animal-related research is limited. Thus, the continued commitment at the State level to support research on animal health is a critically important investment. The food animal industries of the State of Georgia are valued at well over $3 billion and sales of livestock, poultry and their products account for more than half of Georgia’s annual farm income. Protection of these resources is paramount to our State’s economy. A summary of the College’s research funding is provided in the accompanying table on the next page. Over the past year approximately 3.3 research dollars were leveraged for each VMES dollar invested.

The cover of this year’s VMES Annual Report depicts images evoking the history and scientific elements of vaccinology, an applied discipline of immunology. Dr. Ralph Tripp, a Georgia Research Alliance Eminent Scholar in Animal Health Vaccine Research who recently joined the faculty of the College of Veterinary Medicine, is building a research team and program of excellence in this area. His accompanying article provides an overview of the field and its importance to human and veterinary biomedicine.

The 28th VMES Annual Report provides an overview of peer-reviewed, competitive VMES-funded projects conducted during fiscal year 2004 (July 1, 2003 – June 30, 2004). In past reports we grouped project abstracts together based on the animal species on which the research was focused. In the 2004 VMES Annual Report we have changed this format and placed research project descriptions into groupings based on research disciplines. These various sections include: bacteriology and parasitology, virology, immunology, diagnostics, and biomedical sciences. A section describing projects and activities associated with the VMES-supported Food Animal Health Management Program is also included. Each section is succinctly and cogently introduced by a veterinary researcher with a specific expertise in the discipline. Additional information on any of these projects can be requested by contacting the VMES office by phone, email or website, or directly from the investigators themselves. A list of publications is provided as well. These peer-reviewed papers represent a selection of VMES supported work and other scholarly research originating at the College of Veterinary Medicine.

Harry W. Dickerson
Animal Health Research Center

The Animal Health Research Center (AHRC) is a 72,945 square foot biosafety Level 3 (BSL3)/biosafety level 3 agriculture (BSL3Ag) facility. Upon completion it will provide the University and the State of Georgia with state-of-the-art biocontainment laboratories that will enhance our response capabilities against bioterrorism and other emergencies involving infectious microbial pathogens. The AHRC will boost our capability to create vaccines against infectious diseases such as tuberculosis and SARS, and enable us to become national leaders in research on pathogens that require biocontainment.

Containment will be ensured by a series of engineering designs including HEPA-filtered supply air and double-HEPA-filtered exhaust air; differential pressures within containment zones; shower-out facilities for each animal room; decontamination and sterilization procedures for equipment and solid/liquid waste streams; and high security monitoring.

Completion of the AHRC is critical for UGA to attract federal and other external funding for biocontainment research. Funding levels are expected to reach over $10 million per year by 2010, contributing significantly to Georgia’s economic development initiatives.

### VMES Research Funding

<table>
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<th>Funding Source</th>
<th>FY 2001</th>
<th>FY 2002</th>
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<th>FY 2004 (Budgeted)</th>
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Published by the Veterinary Medical Experiment Station, The University of Georgia.
Vaccinology

Vaccinology is the science or method of vaccine development. Over 200 years ago, English physician Edward Jenner observed that milkmaids who contracted a mild viral disease called cowpox were rarely victims of a similar but deadly disease called smallpox. This observation led Jenner to infect a healthy young boy with cowpox, and six weeks later challenge the boy with fluid from a smallpox pustule. The boy remained free of smallpox, and the era of vaccinology began. The foundation that Jenner laid began a course of vaccine development that would lead to the eradication of smallpox and polio, and vaccines for a spectrum of human pathogens that include influenza, bacterial pneumonia, whooping cough, rubella, rabies, meningitis, and hepatitis B.

The term “vaccine” is derived from the Latin word “vaccinus” which means “pertaining to cows” – a reflection on Jenner’s pioneering studies using cowpox vaccinia virus to prevent human smallpox (variola). Vaccines take advantage of using relatively harmless foreign agents to evoke protective immunity that resists infection and/or disease pathogenesis. There are many different types of vaccines including attenuated microbes, inactivated microbes, inactivated toxins, and purified proteins or polysaccharides derived from human pathogens. Some examples include attenuated measles, mumps, and rubella (MMR) vaccine routinely administered to infants, inactivated influenza vaccine, inactivated tetanus toxoid vaccine, and purified hepatitis B virus protein antigen vaccine. Vaccines provide acquired immunity to pathogens and are generally used to prevent disease rather than cure it. There are a variety of vaccine strategies that may be commonly used in the future including DNA vaccines, skin patch vaccines, and edible vaccines.

Despite the ability to vaccinate people and animals for protection against several important pathogens, the majority of people and food or companion animals worldwide are still plagued by known and emerging infectious diseases. Emerging or re-emerging infectious diseases continually threaten human health and impact global security by affecting food for an increasing world population, access to international trade and economic growth, and raise concerns for potential use as pathogens in bioterrorism. The majority of emerging infectious diseases are of zoonotic origin, i.e. transmissible between humans and animals causing infection in both species. For example, in the past 10 years the world has had to respond to SARS-associated coronavirus identified in some domestic and wildlife species, Nipah virus from bats via pigs, influenza viruses from birds, and the West Nile virus from birds via mosquitoes. In addition, naturally occurring zoonotic diseases such as anthrax and antimicrobial-resistant organisms have emerged in part as a result of the agricultural practices that include use of antimicrobials for disease prevention and growth promotion of several domesticated species. Finally, the U.S. and

Dr. Ralph A. Tripp

In collaboration with investigators at the UGA nanoSEC facility, we are investigating the advantages of using an electrochemical flow cell with a quartz crystal microbalance (QCM) to measure mass changes associated with virus binding to antibodies conjugated to gold surfaces. Recent preliminary data suggests we can detect near fentogram quantities of virus in solution.

We are investigating if increasing the nanoparticles surface area enhances quartz crystal microbalance (QCM) detection of virus particles in aqueous media. (rtripp@vet.uga.edu)

View of a Cu/Si two-layer nanostructure fabricated by multi-layer GLAD

www.vet.uga.edu/research/vmes/
other countries remain vulnerable to agroterrorism by agents such as foot and mouth disease.

There are a number of factors that affect emerging infectious disease including (1) introduction of infection into new host populations, e.g. bovine spongiform encephalitis; (2) establishment and further dissemination within new host population, e.g. ecological factors favoring vectors or reservoir hosts; (3) agricultural or economic development, e.g. dams (shistosomiasis) or deforestation (malaria); (4) human demographics and behavior, e.g. population growth, international travel, drug use; and (5) microbial adaptation, e.g. antibiotic resistance (tuberculosis). Unfortunately, the capacity to address emergence or re-emergence of infectious diseases is limited in part by (1) lack of efficacious vaccines or therapeutic treatment modalities; (2) limited support for and deterioration of surveillance of vector-borne and zoonotic diseases; (3) erosion in the number of scientists, public health investigators, and particularly veterinarians who are educated in relevant fields that include medical entomology, vector ecology, epidemiology, tropical medicine, and microbiology of zoonotic pathogens; (4) limited tools to address emergence of drug resistant pathogens and arthropod vectors; and (5) limited biosafety facilities, e.g. BSL3 and BSL4, that can contain the pathogens and animal models need for study.

To effectively prevent and control known and emerging infectious diseases, the scientific and health communities need to develop a discovery-to-control continuum. It is imperative that those in human, animal, agricultural and environmental sciences work together to address threats associated with infectious diseases. Basic research and a greater understanding of disease epidemiology can lead to improved diagnostics and vaccine strategies to control infectious diseases; however, veterinary medicine must bridge the gap between recognizing zoonotic diseases and preventing transmission among animal and human populations. To achieve these goals, the veterinary medical mission must be closely aligned with training students and professionals in relevant fields, and in advanced technologies to combat zoonotic and animal infectious diseases.

The development of effective vaccines represents one of the most promising approaches for providing cost-effective interventions against zoonotic and animal infectious diseases. Animal models have contributed to the considerable progress in our understanding of the mechanisms of immunity and disease pathogenesis associated with infectious agents by providing identification of vaccine candidate antigens, and in demonstrating proof-of-principle vaccine strategies. It is clear that vaccines can be an effective strategy to control infectious diseases, and clearer that veterinary medicine is at the interface between animal and human health.

Dr. Zhen Fu

Dr. Zhen Fu’s lab is involved in development of rabies virus vaccines using reverse genetics technology. They are attenuating rabies viruses by producing mutations in viral genes. Their goal is to construct and select completely avirulent rabies virus which is still capable of stimulating a protective immune response in animals. Such mutant viruses will be safer and more efficacious than currently used vaccines and thus can be developed as live attenuated vaccines for both wild and domesticated animals. (zhenfu@vet.uga.edu)

Electron micrograph of a neuron infected with rabies viruses (Viruses are seen here inside and outside of the cell as shown by arrows)
It is estimated that >75% of emerging infectious diseases (EIDs) in humans are of zoonotic origin, i.e. transmissible from animals to humans sometimes causing infection in both species. These pathogens are bacterial, viral and prozoan in nature; some are vector borne, while others are aerosol, food or water-borne. EIDs impact public health, animal health, access to international trade and economic growth, the food chain for an increasing world population, and global security when used as pathogens in bio- and agro-terrorism (select agents). There is an acute need for comprehensive approaches to identify, prevent, and control all EIDs from all sources and select agents. To achieve these goals, it is imperative that those in human, animal, agricultural and environmental sciences work together to develop a discovery-to-control continuum. Toward this goal we propose to leverage the talent that presently exists in numerous disciplines in the College of Veterinary Medicine as well as recruit and train a new cadre of veterinarians and research scientists that will focus on the surveillance, research, control and prevention of BSL2-, BSL3- and BSL3(ag) - level infectious disease agents. New and planned research facilities including the new state-of-the-art BSL3+Ag Animal Health Research Center will complement the recruiting and training efforts.

The U.S. government and other organizations are acutely aware of the limitations associated with the response to EIDs and have recently made available considerable resources for addressing these agents in areas of biosensing, vaccine development, and prophylactic and/or therapeutic treatment intervention strategies. Thus, it is a critical time to develop a platform for adapting and developing laboratory capabilities to detect and study EIDs and select agents. For such an integrated agenda to be effective, the CVM must address both short- and long-term needs, involve basic and applied public health research, be multidisciplinary in nature, and utilize modern and robust molecular and quantitative tools and facilities.

Zebrafish: A model for the study of mycobacterial fish infections

Traditional animal models for studying mycobacterial infections include the guinea pig, rabbit and mouse. These models, however, are inappropriate for use with species that infect fish due to lower bacterial incubation temperatures, typically 22-28° C. Xenopus was recently developed as a model for examining late stage granuloma formation by the fish pathogen M. marinum. This frog model, however, is not amenable to

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Dr. Fred Quinn

A primary research area for Dr. Fred Quinn, Department Head of Infectious Diseases, is the newly discovered organism, Mycobacterium shottsii. Dr. Quinn came to the College of Veterinary Medicine from the Centers for Disease Control and Prevention (CDC) and provides a strong infectious disease research presence.

Striped bass represent an important commercial and recreational fish particularly for the U.S. east coast. Recently it was observed that 30-50% of striped bass in the Chesapeake Bay had observable skin ulcers. Subsequent studies identified a single new bacterial species, Mycobacterium shottsii, as the agent responsible for >70% of the cases. Very little is known about this pathogen except that it has an optimum growth temperature of 22° C and is one of a number of disease-causing Mycobacterium species that have been found to be very closely related to M. tuberculosis, the organism which caused tuberculosis in humans. These species infect fish, amphibians, reptiles and mammals and all affect the respiratory organs of the various animal hosts. This group presents some very interesting evolutionary questions that need to be addressed.

Additional anecdotal evidence suggests that M. shottsii may be infecting and producing ulcers in striped bass and other fish in coastal waters from Maryland to Georgia. Precisely why this pathogen has recently become so prevalent is not known. There are likely environmental factors at work that are enhancing the virulence of this pathogen and/or decreasing the resistance of the hosts. This pathogen also may be responsible for an increasing number of cases of “fish handlers granuloma” detected in the human population surrounding the Chesapeake Bay. For all of these reasons we are attempting to understand how this organism causes disease in the fish and how this infection can be stopped or prevented. This information could potentially prevent the development of more serious economic and public health issues on the Chesapeake Bay and elsewhere on the eastern U.S. coast.

(fquinn@vet.uga.edu)
forward genetic analysis or direct in vivo examination of the earliest events in the immune response leading to granuloma formation. A popular new model is Zebrafish (Danio rerio). This model has several advantages over the other animal models for the study of mycobacterial fish pathogens, including ease of care, short growth rate, readily available quantities, transparent embryos for convenient in vivo microscopic analyses, a sequenced and annotated genome, available DNA microarrays, a small but rapidly growing mutant library, and an adaptive and innate cellular immune response that appears to be similar to mammalian systems. Using Zebrafish, we identified and collected infected macrophages for further in vitro analysis (and perhaps eventual transformation into a cell line) and demonstrated that the Zebrafish immune system is capable of responding to infections by M. shottsii and M. marinum by forming mammalian-like granulomas. We will next use this model to identify bacterial and host genes differentially expressed at different stages of the infectious process and document each stage using real-time video microscopy. This model possesses the traits and we possess the tools to precisely define the infectious process used by the pathogenic mycobacteria. 

PI: Dr. Fred Quinn (fquinn@vet.uga.edu)

Identifying virulence mechanisms of Mycobacterium shottsii: An emerging disease of fish

Striped bass represent an important commercial and recreational fish particularly for the U.S. east coast. An epizootic of mycobacteriosis was recently reported in the Chesapeake Bay that was characterized by ulcerative lesions on 30-50% of the examined fish. Subsequent studies identified a single new species, Mycobacterium shottsii, as the agent responsible for greater than 70% of the cases. Very little information is known about this newly discovered pathogen except that it has an optimum growth temperature of 22°C and is a close relative of human pathogens M. tuberculosis and M. ulcerans and human/fish pathogen M. marinum. In this preliminary study, we determined that M. shottsii infects and replicates within fish macrophages using a mechanism similar to that observed for M. tuberculosis and M. marinum and not like the extracellular growth of M. ulcerans. Interestingly, M. shottsii kills macrophages using cytotoxic mechanisms as does M. ulcerans, and not by apoptosis as does M. marinum and M. tuberculosis. This dichotomy is unique and may indicate that M. shottsii is a “fork in the road” for these two groups of pathogenic mycobacteria. In collaboration with other laboratories, we are planning a future effort that will examine 12 additional new species of Mycobacterium that are 95 - 99% related genetically to M. shottsii, M. ulcerans and M. marinum (the ulcer group). These new species have been isolated from the skin lesions of fish, amphibians and reptiles and all possess similar growth requirements to the three named species. In addition to identifying a common toxin, and therefore a common vaccine, we want to examine the evolution of this fascinating group of mycobacteria. 

PI: Dr. Fred Quinn (fquinn@vet.uga.edu)

Microbial population dynamics and Salmonella colonization of the chicken’s gastrointestinal tract

Consumption of poultry and poultry products is a recognized risk factor for foodborne outbreaks of salmonellosis and campylobacteriosis. Since the implementation of Hazard Analysis and Critical Control Point (HACCP) Program in 1996, Salmonella contamination of broiler chicken carcasses in the US has been significantly reduced to 10%. However, some consumer groups call for additional measures to further reduce the level of Salmonella entering processing plants. Several on-farm intervention strategies have been proposed to reduce or eliminate Salmonella contamination of broiler chickens. One such intervention involves competitive exclusion of Salmonella by components of the animal’s resident microflora. Unfortunately, it is not well understood how the microflora affects Salmonella colonization of food animal species. We propose the development of green fluorescent protein (GFP)-tagged Salmonella for studying colonization, persistence, and interaction between this microbe and bacteria that normally inhabit the chicken’s gastrointestinal tract. Ribosomal RNA promoter whose expression is directly proportional to growth rate will be used to drive expression of the GFP in Salmonella. Therefore, the intensity of the fluorescent signal is related to the organism’s growth rate in vitro as well as in vivo. Combined with fluorescent in situ hybridization (FISH) using family and genera specific probes, we will be able to identify resident bacterial...
population that inhabit the gastrointestinal tract and their association with Salmonella that also occupy this niche. We can also determine the impact of gastrointestinal microbiota on Salmonella's colonization and persistence in poultry. This information will be useful in refinement of competitive exclusion products to reduce carriage of Salmonella by broiler chickens in Georgia.

Construction of rrn-promoter-GFP fusion for “tagging” Salmonella with a fluorescent marker. The above illustration shows the plasmid construct used to mark Salmonella by allelic replacement. The Salmonella rRNA (rrn) promoter was amplified by PCR and cloned into pGFPuv. In order to introduce this rrn-GFP promoter fusion construct into the Salmonella chromosome, we added the selectable marker, aph (kanamycin resistance) 3’ to GFP. The region flanking the phage P22 integration site in S. typhimurium was also amplified by PCR, cloned into the pGP704 suicide vector. Our rrn-GFP-aph cassette was finally introduced into the P22 phage integration site, creating plasmid, pAPO26. E. coli harboring pAPO26, will fluoresce under UV (C) light. During construction of pAPO26 vector, we have partially constructed several others for introducing other fluorescently-colored jellyfish proteins, with different antibiotic resistance markers, into Salmonella and E. coli. These tools will allow us to directly examine the effects of diet or antibiotics on bacterial populations and microbial interactions within the animal’s gastrointestinal tract that influence growth and survival of Salmonella within its animal host.

PI: Dr. John Maurer (jmaurer@vet.uga.edu)

Avian Mycoplasmosis (AV-060)

During the past year we have made significant progress in the development of Mycoplasma gallisepticum strain K5054 as a live vaccine for chickens and turkeys. Efficacy and safety studies have been completed in chickens and turkeys, and a safety trial in house finches was completed. UGA has sold the rights to the product to Intervet America, who are developing the vaccine, and it has been patented.

Significant progress has been made in fingerprinting of M. gallisepticum and M. synoviae strains. Amplified fragment length polymorphism (AFLP) analysis has been shown to be of value in identifying specific mycoplasma species, and it is highly discriminatory in identifying and differentiating among strains within a species. A significant database of AFLP patterns has already been established.

During the past year we have completed mycoplasma cultures from 227 accessions. There were a total of 2521 cultures, from which 1023 mycoplasmas were isolated; 250 were MG, and 106 were MS.

PI: Dr. S. H. Kleven (skleven@uga.edu)
Co-PIs: W. D. Hall and V. Leiting

Clinical Investigation of Poultry Diseases (AV-040)

The impact of this research provides timely answers and solutions to poultry health and management conditions impacting bird health. The poultry industry is the major agribusiness in Georgia and the research performed by the Poultry Disease Research Center (PDRC) clinicians and Master of Avian Medicine (MAM) students helped in preventing economic losses due to mortality and condemnations in processing plants. The PDRC clinicians and MAM students helped two integrated poultry companies with 4 problem broiler farms that were performing poorly and improved their performance; there were 4 research studies performed by the MAM students from this grant. The first study involved comparison of two different Enzyme-Linked Immunosorbent Assay (ELISA) tests for Salmonella enteritidis and S. typhimurium with environmental culture for salmonella. The second salmonella study looked at the effect of maternal antibody in broilers from vaccinated breeders to salmonella on protection from challenge by homologous serotypes. It was found that the broilers from vaccinated hens colonized from 10-30% less S. hadar, S. kentucy or S. heidelberg than chicks from non-vaccinated hens.
The third study involved the in ovo vaccination of an Infectious Laryngotracheitis (ILT)-Pox vector vaccine. It was found that the vaccine did not have any negative impact on hatchability or first week mortality. However, there was no protection afforded to the broilers by the vaccine when challenged with a virulent ILT. It was believed the reason for a lack of immune response to the vaccine was because the breeders had been vaccinated for fowl pox and the maternal antibodies to the pox virus inactivated the pox vector.

The final research study involved determining the effectiveness of the FTA filter paper as a method for field sample collection for Mycoplasma synoviae for Polymerase Chain Reaction (PCR) testing. Broiler breeders from an M. synoviae positive breeder flock were housed at PDRC. One half were treated with oxytetracycline and one half non-treated. It was determined that the oxytetracycline treatment resulted in a rapid inability to detect the M. synoviae organism by both standard PCR from culture fluid and also by tracheal swabs touched to the FTA filter cards. One week after treatment was discontinued, the hens became PCR positive again by both collection methods.

**PI:** Dr. Charles Hofacre (chofacre@uga.edu)

**Co-PIs:** Dr. Guillermo Zavala and Dr. Stephen Collett

Moxidectin Resistance in Gastrointestinal Nematodes of Goats

Production of goats for meat is an attractive alternative agricultural enterprise for farmers in the southern United States, particularly those with small land holdings. Over the past 10 years there has been tremendous growth in the size and scope of the United States goat industry, with most of this growth occurring in the southern-tier states where 70% of all meat goats are raised. Among the many challenges faced by goat producers, control of gastrointestinal nematode (GIN) parasites is the most difficult and important. The nematode species of primary concern is Haemonchus contortus (barber pole worm), a blood-sucking parasite that thrives in warm climates and causes severe anemia and death in infected animals. This historical problem of GIN parasitism has recently been magnified by the emerging problem of anthelmintic (dewormer) resistance, which is recognized globally as the single greatest threat to small ruminant production. Studies performed by this lab (Dr. Kaplan) in 2001 demonstrated an alarmingly high prevalence of multiple-drug resistance in GIN of goats in the southern US, and ivermectin (IVM) was the least effective of all dewormers tested. Moxidectin (MOX), a closely related drug was highly effective on all farms, but it is expected that IVM-resistant (IVM-R) worms rapidly will become resistant to MOX because these drugs share the same mechanisms of action and resistance. Unfortunately, currently available laboratory tests cannot detect MOX resistance, so the only way to test for resistance to this drug is by measuring the effect of treatment on animals. The purpose of this study was to measure the extent to which moxidectin resistance is developing on goat farms and to validate a laboratory test (DrenchRite® larval development assay, LDA) to detect MOX-resistant worms.

Fecal egg count reduction tests (FECRT) and DrenchRite LDA were performed on 9 goat farms in Georgia during the summer of 2003. Two farms served as controls; one of these farms had worms known to be IVM-sensitive, and the other had worms known to be IVM-R, but neither farm had ever used MOX (and were MOX-sensitive). All other farms (N=7) had IVM-R worms and a history of using MOX as the primary dewormer over the past 2-3 years. On each farm, goats were allocated randomly into 5 treatment groups: 4 groups received MOX at 4 different dose levels and 1 group was left untreated as a control. Fecal egg count reductions (FECR) were determined at each dose level and dose response in the DrenchRite LDA was calculated. RESULTS: At a dose that was 100% effective on the control farms (100 µg/kg), 7/7 farms with a history of MOX use, had resistant H. contortus and 6/7 had resistant T. colubriformis. At the recommended therapeutic dose (400 µg/kg), 3/7 farms had resistant H. contortus and 3/7 had resistant T. colubriformis. Results of DrenchRite LDA clearly correlated with the FECR results, but full statistical analysis is not yet completed.

Within a period of 2 years, multiple species of GIN have developed resistance to MOX on goat farms in Georgia. This is the first report of such resistance in the US. If MOX is to remain effective on goat farms that do not yet have resistance, it must be used sparingly, preferably in a selective treatment program based on the FAMACHA® method. The study also validated the DrenchRite LDA as a useful laboratory test for detecting MOX resistance in GIN of goats.

**PI:** Dr. Ray M. Kaplan (rkaplan@vet.uga.edu)

**Co-PIs:** L.H. Williamson, and T.H. Terrill
In the past 20 years, immunology has become a melting pot reflecting contributions of many scientific approaches. The original focus of immunology was to discover the mechanisms the body used to protect itself from infectious organisms. In recent years, immunology has developed into THE core health science. The impact of immunology is clearly seen as it provides models for the studies of the signals that control the differentiation and function of cells, defines the processes that remodel and repair the tissues of the body, stands at the forefront of gene therapy, provides the backbone of Vaccinology, stands as a pillar in the understanding of molecular pathogenesis, and provides the foundation of modern diagnostic tests and environmental monitoring tools.

Immunology is practiced as both a basic and applied science in the context of veterinary medicine. The health and wellbeing of animals from the womb to old age are impacted by the development and function of their immune systems. Within the context of veterinary medicine, we study immunology in a broad comparative fashion. For animals primarily used to produce food and fiber, we use our knowledge of immunology of each species to attempt to control the ecology of disease within the production setting. We attempt to produce efficient vaccines that protect herds against the spread of disease among animals, and strive to develop tools to protect individuals from infection. For companion animals, we attempt to provide vaccines that develop a zone of protection around their relationship with their human companions and other animals they encounter. We also attempt to use the specificity of the immune response to safeguard our food supply and trace potential contaminants in the environment.

Within our College, we have a Georgia Research Alliance eminent scholar in animal Vaccinology, Dr. Ralph Tripp. His laboratory and collaborators study the basic aspects of immunology and the vaccine process. They provide leadership for the application of technology to new and better vaccines. We also have scientists in the Food Animal Health and Management Program working on applied immunological problems facing the production of cattle and swine. Similar studies in poultry are being conducted at the Poultry Diagnostic and Research Center. Both groups are working on vaccines and the conditions in animals that enhance or inhibit their function to provide a stronger economic base for agriculture. We also have people working in applied immunology to help safeguard the health of the animals we chose to share our homes and lives with. This includes the immunological aspects of diseases of horses, dogs and cats. Others work on monitoring disease and management of the threat of diseases like rabies to humans in wildlife populations.
Identification of a novel granzyme from Tilapia.

The Economic Research Service of the USDA lists aquaculture production as the fastest growing segment in U. S. agriculture. While catfish production still accounts for the largest sector in the aquaculture industry of the United States, tilapia has surpassed trout to become second. Pressures to increase fish production have given rise to problems in sustainability and the greatest monetary loss in the industry is due to infections. Whereas immunological intervention in the form of vaccination could prevent many of these diseases, the development of effective vaccines necessitates a detailed knowledge of the immune system. Elucidation of the immune pathways necessary to maintain healthy stocks would undoubtedly assist the industry in raising their profitability and relative competitiveness. The economic impact that such knowledge would have in the aquaculture industry provides, in and of itself, very strong support for the study of teleost immunology. The long-range goal of the research in my laboratory is to understand the functional components of nonspecific cytotoxic cells (NCC) as sentinels of innate immunity in fish. Cytotoxic cells of the innate immune system (NCC) are the first barrier of defense against viral infections, tumor growth and protozoan parasites. One of the major pathways of target cell killing by NCC requires granule exocytosis with the release of apoptosis-inducing enzymes called granzymes. In this pathway of killing, the lack of requirement for death receptors on target cells suggests that it may have a predominant role in target cell lysis. We hypothesize that teleost granzymes are a major component in the killing of virus infected cells by CTL and NCC in tilapia. The following specific aims were proposed to test this hypothesis: First, the granzyme identified in tilapia NCC will be cloned and sequenced. Second, the recombinant tilapia granzyme will be expressed and its specific activity detected. The goal of this research is to gain more information about this important effector of innate and adaptive immunity in tilapia. The results obtained with the tilapia granzyme from non-specific cytotoxic cells has revealed the first evidence for a parallel evolution of cell-mediated cytotoxicity. The recombinant tilapia granzyme had a chymase-like activity, similar to granzyme H in humans. Comparison of tilapia granzyme with other fish granzymes suggests that fish cytotoxic cells do have granzyme A/K as well as granzyme B/H like molecules to induce target cell death. It can be hypothesized that, like their mammalian counterparts, exothermic animals also acquired multiple granzyme molecules by mutational changes to an ancestral protease with trypsin-like activity. The research outlined will shed light into the mechanisms of defense of aquatic animal species against foreign invaders.

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Evidence for a role of maternal vaccination with killed viral vaccines in the development of neonatal protective immunity against gastrointestinal and respiratory viruses

Based upon the literature, we feel that maternal vaccination with a killed vaccine can “prime” the development of neonatal protective immunity to gastrointestinal and respiratory viruses and therefore be used as a production management tool.

We will test this hypothesis by attempting to demonstrate the transfer of specific antibodies and cellular responses in calves against Rotavirus, Coronavirus, and Bovine Virus Diarrhea (BVD) virus due to maternal vaccination induced immunity. This immunity is found in maternal circulation and transferred in colostrum of vaccinated cows. Further, we want to demonstrate that the transfer of antibody and cellular recall activity to calves enhances calf response to subsequent vaccination with killed vaccines early (day 2-4 rota and corona and day 10 for BVDV) in life.

Cows will be selected and vaccinated using the following protocol:
* cows will be pregnant and within 45-60 days of calving as determined by palpation and divided into two groups, vaccinated and unvaccinated
* cows will be vaccinated twice prior to calving to follow accepted practice in the field with a vaccine containing Rotavirus, Coronavirus, Eschericia coli, Clostridium perfringens Type C, and killed BVD.

These cows will be bled prior to vaccination to get a pre-vaccination serum neutralization (SN), enzyme-linked immunosorbent assay (ELISA), and cell response titers. This data will be utilized in grouping as to treatment and control groups.

PI: Dr. Douglas Ensley (densley@vet.uga.edu)
Viruses are extremely small particles, about one-millionth of an inch in diameter, that can only be seen with high power microscopes (electron microscopes). They vary widely in shape and makeup but essentially are composed of an outer protein shell, sometimes encapsulated in a membrane, surrounding a nucleic acid center of either RNA or DNA. Viruses cannot survive by themselves; they need a ‘host cell’ (bacteria, plant, or animal) to reproduce. When viruses attach to and enter a host cell, they hijack the cell machinery and, using the information contained in the nucleic acid, the cell is forced to reproduce the virus. Eventually the cell dies but not before producing many new virus particles that go on to infect other cells or other organisms.

Viruses are an important concern in veterinary medicine because they are highly infectious and can cause many different diseases depending on the animal and type of host cell affected. Some viruses infect cells in the respiratory tract and cause diseases like the common cold or influenza. Other viruses infect cells in the gastrointestinal tract, causing diarrhea. Still other viruses infect cells in the liver causing hepatitis and so on. Some viruses have even been linked to cancer.

The economic impact of viral diseases in livestock and poultry is enormous, and Veterinarians are constantly looking for new and better prevention and control methods. Developing new and improved vaccines, therapeutics, and diagnostic tests are essential because viruses, by nature, readily adapt and change to cause disease in the host. In the College of Veterinary Medicine at the University of Georgia, scientists are conducting research on all aspects of economically important viral diseases in animals. At the Poultry Diagnostic and Research Center in the College of Veterinary Medicine, scientists focus on economically important diseases that affect commercial poultry. For the last 20 years, Georgia has led the nation in poultry production, and although there are many reasons for this success, one of the most critical is the successful diagnosis, prevention, and control of viral diseases.

Advancements in the Isolation, Characterization, and Control of Avian Viruses

Several avian viruses have been tested as vectors to deliver different genes to immunize chickens against several diseases. The avian adenovirus-associated viruses (AAAV) can be safely used for in-ovo inoculation, and is a widely used procedure in the US poultry industry. A plasmid-based system to generate recombinant AAAV coding for immunogenic proteins derived from
Newcastle disease, avian influenza and infectious bursal disease viruses, is being developed and tested for protection studies in-vivo. Several strains of infectious bronchitis virus (mV) have been adapted to grow in different systems in an attempt to decrease their pathogenicity for the respiratory tract. One Arkansas serotype strain has been tested in chickens and found that it does still replicates in the upper respiratory tract of chickens, but induces significantly less reaction than a commercial vaccine.  

PI: Dr. Pedro Villegas (pedrov@uga.edu)
Co-PI: John El-Attrache

Detection, Isolation, and Characterization of Avian Viruses (AV-280)

The mission of the diagnostic virology laboratory is to provide accurate and timely diagnostic virology services for the domestic and international poultry industry, improve detection and isolation methods for monitoring avian viruses and conduct applied research on current avian disease isolates from the field. This past year, several rapid diagnostic tests based on molecular technology were developed and implemented. Turkey Coronavirus (TCV) and Turkey Astrovirus (TAstV) are important turkey enteric pathogens that are responsible for devastating financial loss in the turkey industry. Diagnostic tests for TCV was limited to indirect FA (indirect fluorescent antibody) to detect seroconversion and virus isolation in turkey embryos. For TAstV identification, virus isolation followed by electron microscopy was the only test available. The above mentioned tests are time consuming and have limited detection ability. We developed an RT-PCR (Reverse Transcription – Polymerase Chain Reaction) test in a multiplex format, to detect both of these important turkey pathogens. The test is rapid, sensitive and specific and can be used to directly test intestines/feces from turkeys. Current Infectious Laryngotrachial Virus (ILTV) detection methods rely on the presence of diagnostic histopathologic lesions. In recent years, milder forms of ILTV have been identified where few diagnostic lesions are observed, if any. We developed a PCR generated digoxigenin-labeled DNA probe to the gC and ICP4 genes of ILTV. Using ISH (in-situ hybridization) testing, we are able to detect low virus loads in tissues infected with laboratory strains of ILTV. We are currently evaluating field tissues. Reoviruses play a role in numerous diseases of chickens and turkeys. They are a diverse group of viruses. The primers we use can amplify the S3 gene from both chicken and turkey isolates. We developed this test to look at genotypic differences between chicken and turkey reoviruses.

PI: Dr. Holly Sellers (hsellers@uga.edu)
Co-PI: E. Linneman

Dr. Susan Williams research focus is on tumor causing viruses in poultry, primarily avian leukosis virus and reticuloendotheliosis virus. These are both retroviruses that cause lymphosarcoma in older chickens often affecting production and feed conversion. She also collaborates with researchers at the Poultry Diagnostic and Research Center (PDRC) and the Poultry Science Department on the main campus on various projects that affect the poultry industry in Georgia and in the United States. Dr. Williams also provides diagnostic services in histopathology at PDRC and teaches avian histopathology and environmental toxicology to graduate students.

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Interactions between ALV subgroup J and IBDV in white leghorn chickens.

Avian leukemia virus (ALV) is a retrovirus of chickens that results in decreased production and can produce neoplasia, mainly B-cell lymphoma. Subgroup J ALV infection has been documented to cause myeloid leukemia in broiler chickens, a different disease than lymphoid leukemia typically produced by other subgroup ALV infections. Infectious bursal disease virus (IBDV) causes immunosuppression by destroying the bursa of Fabricius where B-lymphocytes reside, reducing humoral antibody response to any other disease. Previous research has shown that dual infections of ALV subgroup A and IBDV infection resulted in higher viral shedding and longer seroconversion times. However, there was decreased tumor formation. This research was conducted to determine if ALV-J would react in the same manner as ALV-A when a dual infection with IBDV was present.

Field reports of egg-laying chickens diagnosed with myeloid leukemia have been published; however, previously published experimental infection results indicate lymphoid leukemia can be the main tumor manifestation. Day-old experimental SPF white leghorn chickens were inoculated with either avian leukemia virus subgroup J (ALV-J), infectious bursal disease virus (IBDV), both ALV-J and IBDV, or uninoculated controls. At various time points, biological samples were collected including whole blood and cloacal swabs, to determine viremia, antibody status and ALV-J cloacal shedding. At 30 weeks of age birds were euthanized by CO2 and examined for gross evidence of neoplasia. Tissue samples were collected from birds with gross evidence of tumors for histopathological examination. Sample analysis is completed for 4 and 10 weeks of age and ongoing for 18 and 30 weeks of age. Histopathological analysis is ongoing.

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Co-PI: Dr. Holly S. Sellers

Infectious Bronchitis Virus: Characterization and Control

The long-range goal of this proposal is to control infectious bronchitis (IB) in commercial chickens. We propose to do this by monitoring IBV isolates circulating in the field and by developing and testing recombinant vaccines against infectious bronchitis virus (IBV).

It is important to monitor the genetic heterogeneity and mutation rates of IBV to prevent future outbreaks of the disease. In addition, sequence similarities with the newly emerged SARS-CoV make it extremely important to study host reservoir, evolutionary origin and mutation rates for coronaviruses. Submissions to the laboratory resulted in viruses having the same serotype as vaccines that have been previously characterized. We are continuing to monitor the genetic heterogeneity of the IBV isolates circulating in the field. We are also examining several isolates of turkey coronavirus (TCoV), which are very similar to IBV but cause enteric disease in turkeys. Sequence data of the spike glycoprotein shows a hypervariable region that suggests different serotypes of the virus may exist. We are currently examining several different isolates serologically.

Virus like particles (VLPs) lack genetic information and thus cannot replicate making them ideal vaccine candidates. We have demonstrated expression of the spike and envelope proteins in cell culture, but have not been able to visualize IBV VLPs by electron microscopy. Unfortunately more sensitive detection methods and ways to increase expression of spike and envelope in cell culture were not within the budget of the project.

Viral infectious clones allow the synthesis of tailor made viruses in the laboratory for use as vaccines. We cloned the entire Mass 41 genome into 5 overlapping segments, for development of an IBV infectious clone. We generated sequence data for each of the 5 cloned segments which represents the entire Mass 41 viral genome (approximately 28,000 bases). Appropriate restriction enzymes were identified and one unsuccessful attempt was made to piece the clones together. We are currently working to acquire financial resources to continue this project.

PI: Dr. Mark W. Jackwood (mjackwoo@vet.uga.edu)  
Co-PIs: Deborah Hilt, Scott Callison, and Tye Boynton
Food and Animal Health

A summary of Food Animal Health and Management Program (FAHMP) related research activities.

Since the FAHMP was initiated in 1999, a significant cluster of researchers has been established to attack problems facing livestock producers in Georgia. This group is made up of clinical veterinarians, outreach veterinarians, diagnosticians and laboratory researchers jointly seeking to define, validate and introduce new tools for enhancing the health and productivity of livestock. In this summary, the projects described have two common properties. First, they all involve an integrated approach based on collaboration among researchers with different talents, and second, they have application in the field as a central goal.

The research program has focused on tools for cattle production as the core of many of the projects. These include methods to reduce the impact of Johne’s disease, respiratory viral and mycoplasmal disease, ways to assess the efficacy of vaccines, and tools for monitoring the impact of management practices on the health of cattle.

We have three major thrusts in the area of Johne’s disease. These efforts are a collaboration among Drs. Hines, Hurley, Pence, Reber, Vandenplas, Okinaga and Donovan within the College of Veterinary Medicine. We are examining a new approach to vaccination against Mycobacterium avium ssp paratuberculosis (Map) based on the fundamental studies by Dr. Hines in developing a method to produce membrane and cytoplasmic antigens for a vaccine without the highly cross-reactive cell wall components. This is important because cattle that test positive for TB skin tests are an economic problem to producers. One objective of this research is to provide protection against Map without triggering the TB skin test response in cattle. Drs. Hines and Pence are collaborating with Drs. Hurley, Reber and Donovan to collect information that links protection against clinical disease with the immune response induced by the vaccine. This data will provide a basis for efficient and economical methods to assess larger numbers of animals in application trials if the vaccine achieves its goals. We are currently starting the second year of a two-year vaccine trial.

In addition, we have two additional projects targeting control of Johne’s disease just beginning. One project, involving Drs. Vandenplas, Okinaga, Hines, and Hurley, will attempt to identify the form of specific genes related to resistance to Map infection. The project is based on observed cellular responses that occur in susceptible humans and have parallels in cattle. Cattle will be stimulated with Map, and then evaluated for their physiological response. The cattle should be sorted into two groups representing responders and non-responders. Then, specific genes controlling bacterial responses will be sequenced from cattle from each group. Differences in the gene sequences will allow us to make “probes” to identify animals that are genetically resistant to Johne’s disease and reduce or eliminate the impact of the disease on cattle production. Our second project, involving Drs. Hurley, Donovan, Reber and Pence, will examine the effects of maternal cellular immunity against Map transferred to newborn calves, and the impact of using fresh maternal or frozen colostrum on priming calves to be immune to Map during their most susceptible period, the first six months of life. Each of these projects is funded by the VMES, and each has just begun.

This research cluster is also addressing methods to improve the efficacy of vaccination. Currently, both the consumer and regulatory agencies are pushing for removal of antibiotics and chemical treatments as growth promoting agents. This means that the ecology of livestock and their microbial environment must be controlled by other means. A primary tool that enhances the environmental balance in favor of the food animal is vaccination. However, vaccination has many potential costs. First, an investment in the vaccine itself must be justified as part of the cost of production. Second, the duration of vaccine immunity is often limited relative to the production cycle, adding cost in the form of booster doses. Finally, there are costs associated with vaccine side effects, for example systemic inflammation that causes animals to go off feed or become susceptible to other environmental pathogens. Therefore, we are attempting to improve vaccination for livestock in three ways. First, we are working to find less expensive and more accurate methods to demonstrate vaccine efficacy. Second, we are working on tools to enhance and target the protection afforded by vaccines. Finally, we are trying to develop “vaccine com-
ponents that do not have production robbing side effects such as a large systemic inflammatory response.

The assessment of vaccine induced immunity and its role in protection are being addressed by Drs. Hurley, Woolums, Reber, Donovan, Okinaga and Ensley in our group in conjunction with the vaccine industry. We are currently evaluating an integrated set of immunological methods for the assessment of vaccines. We are trying to understand the value of each test and the relationship of the immune responses measured by set of tests in the process of immune protection. These studies were supported by the Georgia Research Alliance and Material, Limited to assess bovine viral diarrhea virus immunity. We found that the relationships between different methods to measure vaccine immunity were complex and that many assays that were assumed to measure the same immunological pathway did not fully agree. This research indicates that when vaccine efficacy is assessed, it is important to run more than one assay of immune function whenever possible.

We are also working on ways to improve the function of vaccines. A component of many vaccines is the adjuvant. Adjuvants are mixtures of components designed to enhance the immune responses and to direct what compartment of the body the immunity will target. Our goals are: 1) to enhance systemic immunity that circulates in the body, 2) to improve the protection of body surfaces where most pathogens enter the body, 3) to provide balanced antibody and cellular immune responses to give the broadest and longest lasting protection, and 4) to eliminate vaccine related side effects that add cost to production. We are working on several new adjuvants for food animals. These problems are being addressed by Drs. Hurley, Reber, Donovan, Moore, and Woolums from our group and Drs. Albersheim and Carlson from the Complex Carbohydrate Research Center on the UGA campus. Data acquired over the next year should yield the basis for better vaccines for food animals.

The members of our group are also working to provide a scientific basis for the application of new management practices to supplant the use of feed grade antibiotics in production. Currently, cattle are fed extra grain, that provides a concentrated energy source to promote growth in animals when they are eating a relatively small volume of feed. However, a combination of increased amounts of grain in the diet with physiological and social stress often leads to metabolic diseases, one of the most common being rumenal acidosis. Our group, lead by Drs. Donovan and Hurley, in conjunction with Dr. Ely from the Department of Animal and Dairy Science and Drs. Chase and Hippen of South Dakota State University, has addressed the impact of extracellular pH on inflammatory and immune function of bovine white blood cells under funding from VMES. These studies indicate that current practices of feeding a diet high in grains often induce acidosis that can reduce the effectiveness of the inflammatory and immune responses of cattle. This reduced immune cell efficiency, combined with the increased density and diversity of microbes in the internal environment of cattle, which are no longer fed antimicrobials, may well be a recipe for a variety of health problems. This group is using the data from these initial trials to develop tools for assessment of management models to prevent the effects of metabolic problems.

The final cluster of projects that we are addressing focuses on characterizing production problems facing Georgia producers. These include: 1) assessment of Mycoplasma as a problem of Georgia cattle going to Western feedlots, 2) characterization of an immune defect observed in a herd of Hereford cattle in Georgia, 3) assessment of the mechanisms of acute interstitial pneumonia, 4) effect of components of colostrum on the development of the capacity to mount an inflammatory response in the newborn 5) an assessment of patterns of antibiotic resistance, 6) characterization of antiviral proteins for use in semen extenders, 7) analysis of the potential benefit of intramammary therapy during the close up dry period on milk quality, and 8) the development of better facilities to be used for studies to assess improved methods to address cattle production problems.

Georgia cattle sent to Western feedlots have been anecdotally reported to have an increased rates of disease due to Mycoplasma bovis, as compared to cattle from other regions in the U.S. Mycoplasma bovis causes chronic pneumonia and joint infections, among other problems, in feedlot cattle. The true prevalence of Mycoplasma bovis infection in Georgia cattle has never been systematically evaluated. A group, headed by Drs. Woolums and Hurley of the Food Animal Health and Management Program and Dr. Sanchez of the Athens Diagnostic laboratory, is conducting a field survey of Mycoplasma bovis inbackgrounding and stocker herds in Georgia. Additionally, the impact of Mycoplasma bovis on bovine white blood
cell function will be assessed. Finally, management practices associated with the prevalence of Mycoplasma bovis will be characterized on operations sampled. This research will provide the first available description of the distribution of Mycoplasma bovis in Georgia backgrounded and stocker cattle. These studies have been supported by applied research funds from the FAHMP and the Terry Family Respiratory Disease Research Fund.

A herd of Hereford cattle in Georgia that would not maintain appropriate antibody levels following vaccination was identified in 2001. A group headed by Drs. Pence and Hurley has characterized an immunological defect in antibody production within this herd that helps explain the observation. This abnormality may be common to many Hereford cattle. The group is currently attempting to demonstrate a common physiological basis for this defect and to identify a genetic marker that could aid in identification and removal of animals carrying this trait. These studies have been funded by field investigation funds from FAHMP.

Dr. Woolums and collaborators from Colorado State University and West Texas A&M University have been studying the pathogenesis of acute interstitial pneumonia (AIP) in feedlot cattle under funding from the USDA. Acute interstitial pneumonia is a form of severe and usually fatal pneumonia that affects cattle in feedlots, but the cause is unknown. The research carried out to date by the group indicates that bacterial respiratory pathogens are present in some of the cattle with AIP. The data indicates that AIP may be caused by undetected bacterial infection in a subset of affected animals. However, it is likely that other factors cause the disease in cattle where no bacterial pathogens are identified.

Many components that are important in the management of inflammatory response and resistance to infection are found in high concentration in colostrum. A group, led by Drs. Barton, Donovan and Hurley, are investigating the role of lactoferrin, CD14 and antibody on the function of white blood cells from the blood of newborn calves and foals, prior to feeding colostrum. The findings have been quite unexpected in some ways. First, the function of many white blood cells is “damped” in newborns compared with adults. Second, it appears that interaction of these restricted white blood cells with antibody leads to their removal by apoptosis to make room for fully functional cells recruited from bone marrow. Finally, it appears that lactoferrin and CD14 may enhance the function of the cells already circulating in the neonate. The results of these studies should help us better define “quality colostrum”.

Dr. Reeves in conjunction with Dr. Paula Fedorka-Cary and Scott Ladely at USDA-ARS have examined the epidemiology of antimicrobial resistance on farms with different antimicrobial use strategies. One of the farms used no antimicrobials (NAU), one used limited antimicrobials (LU), and one used antimicrobials continuously (CU). At the time of sampling, the NAU farm had not used antimicrobials for 28 years. Resistance persisted on the NAU farm, particularly in Campylobacter and E. coli. Salmonella was not isolated from the NAU farm. This suggests that the removal of antimicrobics may have little impact on resistance persistence within given ecological environments. The two farms using antimicrobics demonstrated very different resistance characteristics, particularly in the Salmonella isolates. On the CU farm, Salmonella derby was the most common isolate. It was resistant to more than one antimicrobial. Ribotyping and PFGE suggested that this isolate was a clone. Further, this clone was the most common Salmonella isolate from the farm. These findings suggest that selective pressures exist on the farm that select for this particular clone’s survival i.e., give it preference for persistence within the farm. From the LU farm, untypable Salmonella was the most common isolate. Ribotyping and PFGE suggest that this isolate was a clone as well. In contrast to the CU farm isolate, the LU farm isolate was sensitive to all antimicrobials tested. This suggests that, while different clones were present on the LU and CU farms, there were selective pressures present on both farms which gave preference to farm specific clones. Campylobacter isolates across the farms did not demonstrate this clonal relationship suggesting that if resistant Campylobacter are to be eliminated from farms, very different strategies may be needed when compared to Salmonella. Many questions remain about the effects of antimicrobial use on resistance prevalence on farms. However, if reduction in resistance prevalence on farms is the ultimate goal, management that selects for non-resistant microbe clones needs to be defined.

Transmission of viral disease in semen is a problem associated with artificial insemination (AI) used in herd improvement. However, semen naturally contains proteins that can inhibit viral proliferation. A team lead by Drs.
Okinaga, Reeves and Hurley have been studying these proteins and characterizing their ability to suppress the binding and proliferation of viruses. They plan to clone effective proteins and to develop a process for their addition to semen extenders as an added measure of protection against undetectable levels of virus in the semen used in AI.

Milk quality is one of the top economic concerns of the dairy industry. Maintaining low somatic cell counts is particularly difficult in the Southeast where frequent rainfall and heat stress contribute to higher pathogen exposures and lower immunity. Dr. Cole is working with a team led by Dr. Graves in Animal and Dairy Science to evaluate the effectiveness of prepartum intramammary therapy to prevent intramammary infection and reduce somatic cell counts. This work is a field project sponsored by Fort Dodge Animal Health.

To address the current and future needs of Georgia producers, the CVM must be equipped and prepared to do well-designed and productive applied research studies. Under the leadership of Drs. Ensley, Reeves and Hurley the VMES is optimizing the infrastructure of the Rose Creek Farm to maximize our flexibility to conduct applied research and testing. The addition of a more flexible fence line backbone and modifications to improve utilization of the buildings on the site have improved the ability of researchers in the FAHMP group to conduct important food animal trials at the site.

Establishment of a research herd for assessment of vaccine and management programs in Georgia.

Proper facilities and systems for the evaluation of new vaccine and management tools for use by Georgia producers is of paramount importance to providing a transition from chemical/antibiotic based production of cattle to newer methods that are more acceptable to consumers of meat and milk. We have set in motion a program to modernize and better equip the Rose Creek Farm in Watkinsville, GA to allow us to conduct controlled trials that support these ends. The facilities improvements include the construction of a working facility under roof, which will allow the collection of samples in the event of inclement weather. The fence housing research animals was upgraded to reduce the risk of injury to researchers and animals. These upgrades will allow for better animal flow and provide a consistent research environment for future projects.

Further, we have also place new practices in place to improve our movement toward GCP/GLP practices on the farm. They include:

- Improved record keeping
- Consistent preventive health practices
- Beef Quality Assurance

Without proper research facilities the producers of Georgia are at a significant disadvantage to those of other states. Our long-term goal is to develop a facility and program that will allow us to work with the feed, pharmaceutical, biologicals and probiotic industries to establish best practices for the producers in Georgia with respect to sustainable biological control of disease and predictable input costs of production without the use of antibiotics or chemical undesirable to the consumer.

The goals of our current program include: 1) providing environmental control for animals studies, 2) establishing a set of SOP guidelines for animal studies, sampling and treatment at the facility, and 3) assuring full biosecurity relative to the studies conducted on the farm.

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Co-PIs: David J. Hurley, Douglas C. Donovan, Adrian J. Reber, Amelia R. Woolums

www.vet.uga.edu/research/vmes/
Diagnostics

The College of Veterinary Medicine offers diagnostic services to veterinarians and animal owners throughout Georgia, through the Athens Veterinary Diagnostic Laboratory, the Tifton Diagnostic and Investigational Laboratory and the Poultry Diagnostic and Research Center. Complete diagnostic capabilities including necropsy examination, histopathology, toxicology, isolation and identification of bacteria, viruses and fungi, serology, and parasite identification are available to aid in disease diagnosis. These laboratories also are utilized by Georgia to provide surveillance support for control programs on specific diseases such as bovine spongiform encephalopathy (BSE), pseudorabies, West Nile virus infection, equine infectious anemia (EIA), Newcastle disease, and Avian Influenza. All segments of the livestock industry utilize the laboratories to help improve the health and safety of their animals.

Investigation of Natural Disease Outbreaks - AV-030

The Diagnostic Services/Teaching Laboratory of the Poultry Diagnostic and Research Center received 5851 clinical case accesses during this reporting period. The major activity of this project is to provide clinical diagnostic support for the commercial poultry industry of Georgia. This is accomplished through the application of field investigation acquisition of flock and farm histories, application of analytical, microbiological, histopathological testing using classical and molecular methods. Activity is summarized in a typical case approach and a numerical summary of lab activity. An example of clinical investigations includes investigation of vaccine reactions causing increased condemnations at processing using serology, histopathology and molecular detection of disease agents. Another scenario might include investigation of early chick mortality which might include bacteriological and mycological cultures. And another might include investigation of condemnations at processing using serology, histopathology and molecular detection of disease agents. Another scenario might include investigation of early chick mortality which might include bacteriological and mycological cultures. And another might include investigation of condemnations at processing using serology, histopathology and molecular detection of disease agents.

Dr. Susan Sanchez

Dr. Sanchez serves as the director of the microbiology section for the Athens Veterinary Diagnostic Laboratory. In this role she is actively engaged in supporting the State’s veterinary practitioners and livestock and poultry producers. Alongside traditional bacteriology techniques, her laboratory has implemented the widespread use of molecular tools for diagnosing bacterial infections. Additionally, Dr. Sanchez has a productive research program which significantly complements her diagnostic activities. She involves undergraduate, professional and graduate students as collaborators in these activities. Dr. Sanchez’s role as student mentor has been recognized with the Center for Undergraduate Research Opportunities Award for Excellence in Undergraduate Research Mentoring. Her research focuses on the resistance of bacteria to antibiotics and how this resistance is selected for by the use of antibiotics. Her research also looks at how this resistance to antibiotics spreads between bacteria, how the bacteria move in the environment and how these bacteria are shared by animals and humans. This research is currently funded by a grant from NIH. Another area of work that her laboratory is known for is the investigation of veterinary hospital-acquired infections and their control. Dr. Sanchez is also currently involved in studying the role of Staphylococcus aureus super-antigens in animal disease. This work has led to the description of toxic shock syndrome in horses caused by S. aureus. (ssanchez@vet.uga.edu)

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serotyping, Avian adenovirus, and Avian pneumovirus (through a cooperating lab) PCRs have been added to those for Avian leukosis virus-J, Infectious laryngotracheitis virus, and infectious bursal disease viruses have been placed on-line and provide useful and very timely diagnostic information. Research continues and new PCR tests will be applied to diagnostics as applications are developed. Time continues to be spent helping poultry companies implement and maintain HACCP plans, standards and compliance. These plans help poultry companies maintain compliance with government standards for control of food-borne microbes hazardous to consumers of processed poultry. More time will be spent in the future and more research effort continues to be made in the area of food safety. The Diagnostic Services/Teaching Laboratory has implemented direct email and fax of lab reports without the need for hard copy. We are investigating the use of the world-wide web for delivering lab data especially to clinical veterinarians that spend a lot of time on the road. Laboratory activity is represented by 5,851 accessions, 34,445 bacterial procedures, 170 antimicrobial susceptibilities, 75,408 ELISA tests, 31,099 IBV-HI tests, 1,343 diagnostic PCR tests, and 2,606 necropsies.

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PI: Dr. Stephan G. Thayer (sthayer@uga.edu)

Dr. Stephen Thayer

Dr. Steven Thayer is Senior Public Service Associate in charge of the Diagnostic Services and Teaching Laboratory which provides diagnostic support to the commercial poultry industry of Georgia as well as to clients of the United States, Canada, Central and South America, South Africa, Europe and Asia. The lab maintains complete identification and susceptibility testing for bacteria and fungi. We perform serological tests for the presence of antibodies to disease agents which are detected in the form of antibodies which can be produced in advance of overt disease. Histopathological services which offer the ability to see the effects of disease in tissues are important in the diagnosis of disease in commercial poultry. The diagnostic virology lab offers numerous conventional virus isolation capabilities in addition to molecular techniques which can detect the presence of viruses by polymerase chain reaction (PCR). This is an amplification procedure that makes many copies of DNA or RNA which can then be visualized. Most PCR’s can be performed in a matter of hours instead of days required by isolation methods. There is a newer PCR called the real-time PCR which eliminates one of the steps in a standard PCR permitting results in less than 1 hour. Molecular techniques are revolutionizing diagnostics often yielding highly specific results in far less time than conventional methods. PCR techniques are also applied to Mycoplasma, fungi and bacteria allowing the investigator to identify organisms, toxins, and even genetic sequences within that are responsible for the minute to major difference between pathogenic organisms. (sthayer@uga.edu)
Biomedical Sciences

Biomedical research represents an important area of health care in which veterinarians are uniquely positioned to make significant contributions to improving the well-being of both human beings and animals. By studying naturally-occurring animal models of human diseases, biomedical researchers (including veterinarians) have gained insights that have been valuable for understanding the corresponding human conditions. Animal models have been used to investigate cancerous, degenerative, and infectious processes and this work has provided valuable information regarding the pathogenesis and treatment of human diseases. For example, the most common treatment for men with prostate cancer, androgen-deprivation therapy, was instituted in the 1940's by Charles Huggins, MD, after observing the marked decrease in size of the canine prostate gland that occurred following castration of adult male dogs.

In addition to naturally-occurring animal models, the past decade has seen an explosion in the number and usefulness of genetically-modified rodents. By using molecular techniques, these animals allow us to evaluate the effects of single-gene deletion or overexpression and greatly enhance our understanding of the complex molecular signaling pathways that are deranged in diseases ranging from cancer to abnormal bone formation.

As veterinarians, we are the ultimate animal biologists. Our understanding of the normal anatomy, physiology, and biochemistry of a variety of species allows us to maximize the benefits of investigations concerning these model systems, whether naturally-occurring or as a result of genetic manipulation. These studies may hasten the development of translational research eventually leading to improved treatments for both humans and animals. Recently, the National Cancer Institute has announced an exciting initiative aimed at including naturally-occurring cancers in pet animals into studies of cancer biology and drug development. The goal of this initiative will be to use the data from clinical trials of pet animals with cancer to accelerate the development of therapeutic agents for human cancer patients. Based on collaborations such as this one, the partnership between veterinarians, physicians, and basic scientists involved in biomedical research has a bright future!

Dr. Bruce LeRoy

Despite the advances made in early detection and treatment, prostate cancer remains a significant cause of cancer-related death and illness. Prostate cancer is the most common non-skin cancer in men. The American Cancer Society projects over 230,000 new cases in 2004, with almost 30,000 men dying of prostate cancer in 2004. To learn more about this important disease, researchers have used the dog as a model system for studying diseases of the prostate gland for many years. Dogs are an excellent animal model for studying the prostate because dogs closely share our environment, and the anatomy and embryology of the dog prostate are very similar to those of the human gland. A significant advantage of the dog model over rodent prostate cancer models is that the rodent prostate is composed of several finger-like lobes and is very different from the canine and human glands.

Dogs develop many prostatic diseases in common with men, including prostatitis, benign prostatic hyperplasia (BPH), and prostatic cancer. In fact, dogs are the only large mammals other than men to develop spontaneously-occurring prostate cancer with any regularity. An important similarity is that advanced or highly aggressive prostate cancer in both men and dogs commonly targets the bones of the pelvis and spine, resulting in painful, debilitating bone metastases. The prostate cancer cells induce large amounts of new bone formation at these metastases, the reasons for which are not clear. Our laboratory is using the dog model to investigate the role of molecules such as parathyroid hormone-related protein and endothelins in the pathogenesis of prostate cancer metastases-stimulated new bone formation. Investigations using the canine model of prostate cancer may help guide the development of new treatments to prevent or reduce the occurrence of this devastating complication.

(bleroy@vet.uga.edu)
Functional and Histochemical/Immunohistochemical Analyses of Bovine Laminar Arteries

Lameness is a debilitating condition in cattle and has a great economic impact on the dairy and beef industries. Laminitis, the major cause of bovine lameness, is a multi-factorial disease involving dysfunction of the laminar microcirculation. A major barrier to understanding the mechanisms underlying bovine laminitis is the lack of functional studies on the laminar microcirculation. Acidosis is a major precipitating factor of bovine laminitis and is associated with increased blood concentrations of L-lactate.

The hypotheses driving this VMES project are that (1) high levels of L-lactate generate reactive oxygen species via the activation of lactate dehydrogenase and NADH oxidase, and (2) dietary pyruvate or administration of selective NADH oxidase inhibitors may be effective strategies to prevent and/or ameliorate bovine laminitis. The objective of this project is to provide preliminary data to support the above hypotheses.

Aim 1: The studies under Aim 1 examined the roles of the above enzymes in mediating L-lactate-induced changes in vascular function in bovine laminar arteries. The key findings were that lactate had pronounced pH-dependent and pH-independent effects on function/activity of G protein-coupled receptors (and their intracellular signaling cascades) that mediate vasoconstriction in endothelium-intact small laminar arteries including, α1-adrenoceptors and 5-HT2 receptors. Moreover, lactate had pronounced pH-dependent and pH-independent effects on the activity of voltage-gated Ca2+-channels. Taken together, the results support the concept that lactate dehydrogenase and NADH oxidase may play a vital role in altering the vasoactivity of small bovine laminar arteries.

Aim 2: Little is known about the distribution of key enzymes such as NADH oxidase and nitric oxide (NO) synthase and markers of oxidative stress such as nitrotyrosine, in bovine microvessels. The studies under Aim 2 obtained morphological, histochemical/immunohistochemical information on the presence and distribution of these proteins in bovine laminar arteries and veins. Our studies determined the basic architecture of the laminar microcirculation and neural networks and have demonstrated the relative distributions of NADH oxidase, NO synthase, NADPH diaphorase and tumor necrosis factor-α (TNFa) in vascular and neuronal tissue. For example, NADH oxidase was present in certain nerves as well as smooth muscle and endothelium of arteries and veins, whereas NO synthase was present in the vascular endothelium but not muscle of arteries and veins. Little immunostaining for nitrotyrosine or tumor necrosis factor-α was present in arteries, veins or nerves. Which is consistent with there being little inflammation and oxidative stress in these tissues from “normal” cows.

We recently submitted a proposal to the USDA, which was entitled (Functional, Histochemical and Immunohistochemical Analyses of Bovine Laminar Arteries, $257,730). This proposal set forward our hypotheses that high levels of L-lactate in bovines generate reactive oxygen species via the activation of lactate dehydrogenase and NADH oxidase, and (2) dietary pyruvate or selective NADH oxidase inhibitors may prevent and/or ameliorate bovine laminitis. The project was well received, however, preliminary studies on the effects of lactate on bovine laminar artery function were suggested to solidify these compelling and novel ideas. We believe that the studies funded by the VMES project have provided us with all of the background necessary to obtain funding from the USDA.

PI: Dr. Stephen J. Lewis (slewis@vet.uga.edu)
Co-PIs: Jonathan E. Graves, Ph.D., Wendy E. Harrison, B.vet.Med., Ph.D.

The role of acidosis in the pathogenesis of infectious and vascular diseases of cattle.

Acidic pH has an effect on both humoral and cellular immunity. The objective of this experiment was to determine the effects of extracellular pH on phagocytosis, and on the production of nitric oxide (NO) and reactive oxygen species (ROS) by bovine leukocytes. Sixty milliliters of blood was obtained by jugular venipuncture from cows at least 250 days in milk with an average body condition score of 3.2 for use in ROS (n = 10), phagocytosis (n = 12), and NO (n = 4) assays. One medium used in these studies was composed of Phosphate Buffer saline, with the addition of 0.5% Bovine Serum Albumin and 5 mM Glucose (PBG). PBG was aliquoted, and individual samples adjusted to pH 6.0, 6.4, 6.8, 7.2, 7.6, 8.0 with HCl or NaOH. PBG medium containing 3x106 total leukocytes per ml was used for measurement of ROS and
phagocytosis. ROS was assessed in quadruplicate (100ml of cells in 96 well plates) after stimulation with 10-6, 10-7, 10-8, and 10-9 M phorbol myristate acetate (PMA) for 1 hr by measuring the conversion of dihydrorhodamine 123 to its fluorescent form by comparison with PBG controls. Phagocytosis was assessed by incubation of 200ml of cells with commercial bodipy labeled S. aureus or E. coli particles for 1 hr. The number of bacteria associated with the leukocytes was evaluated by flow cytometry. Minimal Essential Medium with addition of 10% Fetal Bovine Serum, 2 mM L-Glutamine, 2 mM sodium pyruvate and 50 µg/ml of Gentamycin sulfate (MEMG) was aliquoted and individual samples adjusted to pH 6.0, 6.4, 6.8, 7.2, 7.6, 8.0 with HCl or NaOH for use in the experiments. One hundred microliters of MEMG, after adjustment to the desired pH, was added to quadruplicate wells with 6 x 105 mononuclear cells. To induce nitric oxide, 10 µl of 100 µg/ml, 10 µg/ml, 1 µg/ml, or 0.1 µg/ml E. coli 055 LPS was added to each well. Supernatants were removed after sixty hours of incubation and nitric oxide production was evaluated using the Greiss reaction. Data were analyzed by mixed procedures of SAS 8.2 (2002). It was determined that pH (P < 0.01) greatly effected the production of ROS, and acidic pH decreased (P = 0.031) the production of ROS relative to alkaline conditions. When phagocytosis of multiple E. coli or S. aureus particles showed a tendency toward increased phagocytosis under acidic medium pH relative to basic pH conditions. Alkaline conditions appeared to favor nitric oxide production over acidic conditions (P < 0.05). Acidosis appears to hinder the functions of innate immunity, which could result in a delayed response to bacterial infections. In other studies, lymphocyte recall response to antigen and circulating virus neutralizing antibody titers were diminished in acidotic animals.

Prostate cancer is a common cause of cancer-related death in western populations. Dogs are a commonly used model for studying prostatic diseases and are a good model for studying prostate cancer. This is because, among other factors, they share a similar environment with humans and are the only large mammals that develop spontaneous prostatic carcinoma with any regularity. Also similar to humans, dogs with late-stage prostate cancer commonly develop bone metastases, especially in the lumbar vertebrae and pelvis. The bone metastases of prostate cancer are unique in that they induce marked new bone formation, so-called ‘osteoblastic’ metastases. The factors responsible for the new bone formation of prostate cancer metastases are not known. We have shown that normal dog prostate can stimulate new bone formation in mouse calvaria. We will now investigate the effects on bone morphology by normal dog prostate tissue implanted into the tibias of rats. Microscopic characterization of the effects of the prostate tissue on trabecular bone formation will provide useful information regarding the mechanisms of epithelial cell-stimulated bone formation and lysis. Additionally, to identify the importance of specific factors in prostate-stimulated bone formation and/or destruction, in vivo models of bone formation (osteoblast cultures and calvarial explant tissue cultures) will be established. We will then measure the effects that antagonism of three candidate molecules (parathyroid hormone-related protein [PTHrP], platelet-derived growth factor [PDGF], and endothelin-1) has on prostate-stimulated osteoblast activation (as determined by alkaline phosphatase activity and histology).

PI: Dr. David J. Hurely (dhurley@vet.uga.edu)
Co-PIs: Douglas Donovan, Robert Parks, Tats Okinaga, Chandler Collar, Jon Graves, Wendy Harrison and Adrian Reber. Collaborators – Christopher Chase and Arnold Hipp (South Dakota State University)
Baldwin, Charles. Diagnostic services relative to the control, diagnosis, treatment prevention, and eradication of livestock diseases 2004. Tifton Diagnostic Lab. Ga. Dept. of Agriculture. $1,962,928

Barton, Michelle. Culture of a species of Helicobacter from equine gastric mucosa. Merial Limited. $0

Brown, Corrie. Veterinary curriculum and the future: Public health, food security and agroterror. FIPSE - U.S. Dept. Education. $78,360

Brown, Corrie. Emergency management of agricultural bio-terrorism training curriculum. GA Tech Research Institute. $58,880

Brown, Corrie. Molecular pathogenesis of vesicular stomatitis virus in cattle. USDA-ARS. $10,000

Brown, Corrie. Pathogenesis of Nipah virus in guinea pigs. NIH-National Institutes of Health. $92,448

Brown, Corrie. Preparing veterinarians to deal with global issues in animal health, trade and food security. FIPSE - U.S. Dept. Education. $58,530


Brown, Thomas. Septicemia/toxemia disposition of broilers: Increasing accuracy within current regulations. U.S. Poultry and Egg Assoc. $32,346


Budsberg, Steven. In vivo protocol for testing effects of teopenazin on whole blood, gastric mucosal and osteoarthritic synovial fluid prostaglandin and leukotriene … Schering-Plough Animal Health. $95,033

Carmichael, Paige. Training in clinical ophthalmology and pathology. Graduate Assistantship support for Dr. Shannon Boveland. Tuskegee Univ. $26,425

Carmichael, Paige. Mucopolysaccharidosis IID senogenic CNS stem cell therapy. Sanfilippo Children's Research Foundation. $56,923

Coifield, Julie. Neuromuscular targets of botulinum toxin. NIH-National Institutes of Health. $342,756

Coifield, Julie. Identification of botulinum toxin membrane targets. NIH/NIAID. $291,804

Cole, Dana. Using climate variability and weather to model human outbreaks of Salmonella and Campylobacter and their environmental prevalence in Georgia watershed. NOAA - Sea Grant. $126,424

Cole, Dana. Estimating the risk of human exposure and resultant spread of highly pathogenic avian influenza. SECEBT - Southeastern Center for Emerging Biological Threats. $24,952

Corn, Joseph. Mycobacterium avium subspecies paratuberculosis in free-ranging birds and mammals on livestock premises. USDA-APHIS. $119,665

Corn, Joseph. Exotic tick surveillance in the southeastern United States and Puerto Rico. USDA-APHIS. $200,000

Corn, Joseph. Distribution of pseudorabies virus and Brucella suis in feral swine. USDA-APHIS. $50,000

Dickerson, Harry. A research training experience for veterinary medical students. Merck Company Foundation. $20,000

Dickerson, Harry. Surveillance of Newcastle Disease virus in Georgia. Matched with GA Poultry Imp. Assoc. Funds. For PCR machine at GA Poultry Lab. Georgia Research Alliance. $13,950

Ferguson, Duncan. Recombinant feline thyrotropin (fTSH): Immuosassay validation and thyroid radiosensitizing agent. Morris Animal Foundation. $43,975

Ferguson, Duncan. Development of a biologically based model for chemical mixture induced perturbations of the pituitary. Centers for Disease Control. $33,148

Ferguson, Duncan. Recombinant thyrotropin (TSH): Standard for the next generation of canine TSH immunoassays with improved sensitivity. AKC-American Kennel Club Foundation. $47,785

Fischer, John. USDA-APHIS Wildlife Services Disease Training. USDA-APHIS. $125,000

Fischer, John. Cooperative Agreement for development and evaluation of data relative to disease relationships that may simultaneously involve wildlife, domestic livestock, & poultry. USDA-APHIS. $350,000

Fischer, John. Investigation of and assistance with wildlife disease problems in the SE region of the U.S. U.S. Dept. of Interior. $231,500

Fu, Zhen. Human antibodies for postexposure prophylaxis of rabies. Molecular Targeting Tech., Inc. $231,104

Fu, Zhen. Developing avirulent rabies virus vaccines. NIH-National Institutes of Health. $88,320

Fu, Zhen. Developing avirulent rabies virus vaccines. NIH-National Institutes of Health. $253,400

Glisson, John. Surveillance for West Nile Virus Encephalitis (WNVE) and other arboviral pathogens. GA Dept. of Human Resources. $32,000
<table>
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<tr>
<th>Researcher</th>
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<td>Glisson, John</td>
<td>UGA Foundation SA/Wildlife Treatment Fund, UGA Foundation. $1,985</td>
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<td>Hernandez-Divers, Stephen</td>
<td>Single-dose intravenous and oral pharmacokinetics of meloxicam in green iguanas (Iguana iguana), Boehringer Ingleheim. $5,845</td>
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<td>Hines, Murray E</td>
<td>Efficacy of spheroplast whole cell vaccine for the prevention of Johne's disease. USDA-APHIS. $99,102</td>
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<td>Hoenig, Margarethe</td>
<td>Effect of diet on fat and glucose metabolism in lean and obese cats. Nestle Purina. $198,275</td>
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<td>Pharmacokinetics and Effect of compound X in cats. Adenosine Therapeutics. $9,989</td>
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<td>Hofacre, Charles</td>
<td>Research support. USDA. $19,258</td>
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<td>Howerth, Elizabeth</td>
<td>Development of assays to detect IL-6 in white-tailed deer infected with epizootic hemorrhagic disease virus. Morris Animal Foundation. $11,826</td>
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<td>Alterations in leukocyte function during the onset of acute equine laminitis. American Quarter Horse Association. $42,885</td>
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<td>Turkey poult enteritis vaccine development. U.S. Poultry and Egg Assoc. $54,050</td>
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<td>Kaplan, Ray</td>
<td>Maintenance of gastrointestinal nematodes for in vitro drug efficacy testing. Divergence, Inc. $21,728</td>
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<td>Combination therapy to overcome anthelmintic resistance in cyathostomes of horses. Pfizer Inc. $37,500</td>
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<td>Karls, Russell</td>
<td>Regulation of Mycobacterium tuberculosis sigma factor C and identification of Sig-C transcribed genes. American Lung Association. $17,500</td>
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<td>Development and validation of a rapid diagnostic test for Mycoplasmosis infectious bronchitis and Infectious Laryngotracheitis. USDA-ARS. $34,000</td>
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<td>Ischemia-reperfusion injury in equine laminar arteries. Grayson-Jockey Club Research Foundation. $27,000</td>
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<td>Vesicular stores of S-nitrosothiols in vascular endothelial cells. American Heart Assoc. - National Center. $214,500</td>
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<td>Little, Susan</td>
<td>Infection dynamics of Ehrlichia chaffeensis. NIH-National Institutes of Health. $101,098</td>
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<td>UGA Foundation - GA Cancer Research for Pets Fund. UGA Foundation. $11,878</td>
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<td>McCall, John</td>
<td>Furnish Brugia malayi adult worms and/or Brugia malayi infective larvae. NIH-National Institutes of Health. $130,365</td>
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<td>Diagnostic services relative to the control, diagnosis, treatment prevention, and eradication of livestock diseases 2004. Athens Diagnostic Laboratory. GA Dept. of Agriculture. $1,226,750</td>
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<td>Improving the educational impact of 3-D animations of signal transduction mechanisms with basic scientific modules (equine). USDA - Higher Ed. Challenge Grants. $99,996</td>
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<td>Moore, James</td>
<td>Evaluation of phospholipid emulsion in horses (equine) administered endotoxin. Septicure, LLC. $71,335</td>
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<td>Moore, Julie</td>
<td>Microarray analysis of gene expression changes in placental trophoblast cells exposed to malarial parasites. UGA - Faculty Research Grants. $4,500</td>
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<td>T-cell memory and protection against placental malaria. NIH-National Institutes of Health. $340,856</td>
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<td>Inhibition of endotoxin with adenosine receptor agonists. Grayson-Jockey Club Research Foundation. $36,670</td>
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<td>Neurotoxins from marine algae and cyanobacteria. Oregon State University. $129,936</td>
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<td>Characterization of the A2A adenosine receptors as modulators of endotoxin-induced cytokine synthesis in horses. Adenosine Therapeutics. $24,997</td>
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<td>Affinity labels for opioid receptors. University of Kansas. $67,588</td>
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<td>Cellular activation induced by multivalent ligands. NIH-National Institutes of Health. $71,981</td>
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<td>Application of molecular biology and serology to understand the pathogenesis of Ovine Pulmonary adenocarcinoma. Istituto Zooprofilatico Sperimentale A&amp;M.</td>
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<td>Palmarini, Massimo</td>
<td>Distinguished Cancer Clinicians and Scientists Program. Georgia Cancer Coalition.</td>
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<td>Pence, Melvin</td>
<td>Georgia John's Disease demonstration herd project 2003. USDA-APHIS.</td>
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<td>Peroni, John</td>
<td>Regional variation in endothelial control of equine pulmonary microvasculature. USDA-CSREES.</td>
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<td>Peroni, John</td>
<td>Role of oxidant stress in microvascular dysfunction in equine laminitis. Morris Animal Foundation.</td>
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<td>Prasse, Keith</td>
<td>Section 1433, Animal Health and Disease Research Funds. USDA-CSREES.</td>
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<td>Quinn, Fred</td>
<td>Mycobacterium shotgun: An emerging pathogen of fish and humans. Southeastern Center for Emerging Biologic Threats.</td>
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<td>Radinsky, Mary</td>
<td>Evaluation of pharyngeal function in dogs with laryngeal paralysis prior to and after unilateral arytenoid lateralization. American Kennel Club.</td>
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<td>Reeves, David</td>
<td>Manage the Rogers State Prison Dairy Farm. GA Dept. of Corrections.</td>
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<td>Ritchie, Branson</td>
<td>Experimental induction of persistent KHV infection. Associated Koi Clubs.</td>
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<td>Ritchie, Branson</td>
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<td>Preliminary evaluation of a novel adjuvant for the oral immunization of Koi using inactivated virus. JPD America LLC.</td>
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<td>Robertson, Thomas</td>
<td>Novel insights into Ca++ homeostasis in equine laminar arteries. USDA-NRL.</td>
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<td>Atypical regulation of vascular tone by protein kinase C. NIH-National Institutes of Health.</td>
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<td>Sanchez, Susan</td>
<td>Ceftiofur use in cattle: a public health concern? NIH-National Institutes of Health.</td>
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<td>Sandenson, Sherry</td>
<td>Comparison of two dietary approaches to managing canine chronic renal failure. Iams Company.</td>
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<td>Stallknecht, David</td>
<td>West Nile Virus surveillance in wild birds. GA Dept. Natural Resources.</td>
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<td>Peridomestic avian species as amplifying hosts and sentinels of WN and SLE viruses in Georgia. Centers for Disease Control.</td>
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<td>Stallknecht, David</td>
<td>Replication of west nile virus in avian macrophages: A predictor of species susceptibility? Morris Animal Foundation.</td>
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<td>Varela, Andrea</td>
<td>Infection dynamics of Ehrlichia chaffeensis. NIH-National Institutes of Health.</td>
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<td>Wagner, John J.</td>
<td>Cocaine-induced metaplasticity in the hippocampus. NIDA-National Inst. Drug Abuse.</td>
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<td>Wilson, Heather</td>
<td>Etiology, pathology, and control of an enterocolitis epornitic in a large commercial hamster population. Petsmart Charities Foundation.</td>
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<td>Pharmacokinetics and bioavailability of Meloxicam in ring-necked parakeets. Boehringer Ingleheim.</td>
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<td>Chemical castration of domestic pigeons via endoscopic in trastesticular injection of zinc gluconate neutralized by arginine. UGA - Faculty Research Grants.</td>
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<td>Zavalla, Guillermo</td>
<td>In vitro and in vivo characteristics of avian leukemia virus (ALV) contaminating poultry vaccines and development of a molecular-based assay for detection of ALV. U.S. Poultry and Egg Assoc.</td>
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Administrators & Advisors

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He, Q., Kim, J-Y., and R.P. Sharma. Silymarin protects against liver damage in BALB/c mice exposed to fumonisn b1 despite increasing accumulation of free sphingoid bases, Toxicol. Sci., 80:335-342, 2004.


Selected Publications


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