SIGNATURE PROGRAM: INFECTIOUS DISEASE S AND BIODEFENSE

Introduction and Significance

A collaborative and innovative research community in infectious diseases flourishes at Texas A&M University. In the College of Veterinary Medicine and Biomedical Sciences, current and past scholarly accomplishments, along with substantial ongoing funding opportunities, make continued support and expansion of a *Signature Program in Infectious Diseases and Biodefense* a priority of the College. A variety of interrelated research endeavors address a critical public and animal health imperative: *Protection of people and animals against current and future threats from infectious diseases.* At Texas A&M University we are in a unique position to tackle infectious disease threats to both humans and animals, with active research programs in the major areas of microbiology, parasitology, virology and immunology. This broad range of expertise brings together basic scientists, clinicians, epidemiologists, pathologists and cutting edge diagnostic capabilities to respond to both extant and future infectious disease threats to health and food safety. In addition to active research programs, infectious diseases researchers participate extensively in teaching and outreach, activities that are critical to achieving and maintaining biosecurity for humans and animals.

Infectious Diseases and Biodefense necessarily spans multiple disciplines including: 1) the basic and molecular biology of hosts and pathogens; 2) host-pathogen interactions; 3) the genetic basis of susceptibility or resistance to infectious agents; 4) the detection of environmental pathogens, infected hosts and contaminated food supplies; 5) development of vaccines, therapeutics and preventative programs. Research in these areas is being conducted in multiple departments of the College of Veterinary Medicine and Biomedical Sciences and much of the effort involves collaborations with faculty and researchers in the College of Agriculture and Life Sciences (COALS), Texas Agrilife, the Institute for Countermeasures against Agricultural Bioterrorism (ICAB), the Integrative Center for Homeland Security (ICHS), and the National Center for Foreign Animal and Zoonotic Disease Defense (FAZD). These combined efforts address critical current and future infectious disease threats arising from population growth and movement, industrialized livestock production, international movement of food and animals, global warming, and human conflict.

The State of Texas enjoys an actively growing population and serves as a hub of international trade and travel. Texas also has national preeminence in agriculture and food production. For these reasons, natural or introduced infectious agents that pose a threat to public health or agriculture would disproportionately affect our state's economy. Our ability to respond quickly and decisively to outbreaks of infectious disease is key to our sense of well-being, just as the ability to assure the protection of agriculture and the food supply is important in maintaining consumer confidence. The *Signature Program in Infectious Diseases and Biodefense* includes elements of infectious disease research that range from basic and mechanistic studies of microorganisms and disease, to field research, to vaccine development, to detection, diagnosis, and surveillance systems.

Rationale

A 2005 National Research Council report titled **"Critical Needs for Research in Veterinary Science"** identified *infectious disease and biodefense research* as a critical future need. Specific research areas delineated in the report include:

- Rapid, sensitive, and accurate assays for detecting foodborne pathogens
- Identification of previously unrecognized foodborne pathogens of animal origin
- Improved ability to detect and identify disease and pathogens in animal populations
- Improved understanding of interactions between pathogens and hosts so that effective preventive measures and countermeasures can be developed
- Rational development of cost-effective countermeasures, both vaccines and nonspecific therapeutic agents
- Development of capacity and implementation of broad programs in comparative medicine to understand, rapidly detect, and control zoonotic and nonzoonotic diseases in food-producing animals
- Monitoring and assessment of trans-species disease transmission, epidemiology, and the delineation of resistance, susceptibility, and virulence factors across animals and pathogenic organisms

This national report provides significant rationale for continued support of the *Infectious Diseases and Biodefense Signature Program* within the College of Veterinary Medicine and Biosciences. Areas of particular strength in infectious disease research can be defined and should be considered for future investment. These include: 1) development of vaccines, diagnostics, and therapeutics; 2) the host-pathogen interface; 3) intracellular microbial pathogens; 4) virulence mechanisms; and 5) the genetic basis of host resistance. Continued College and University support are instrumental to maintaining excellence in *Infectious Diseases and Biodefense*.

Maintenance of current activities and enhancement of future growth and excellence in the *Infectious Diseases and Biodefense* Signature Program require not only a cadre of dedicated faculty, but significant shared infrastructure. The overall need for biocontainment laboratories for Veterinary Research was also addressed in the 2005 National Research Council's report "Critical Needs for Research in Veterinary Science". Design, development, and testing of innovative vaccines and diagnostics require safe and effective facilities. The costs of building and maintaining appropriate infrastructure are significant, but are well-justified when considering the dual major threats of natural infection and bioterrorism. Several agents currently under investigation at TAMU have been recognized by the Centers for Disease Control (CDC) and the United States Department of Agriculture (USDA) as potential threats to national security, increasing the demand for research and resources to enhance detection, to improve protective immunity and to develop new drugs to prevent or cure infection. The ability to sustain excellence and for CVM faculty to grow new national and international collaborations requires the appropriate infrastructure. *We currently have a critical need for additional BSL3 laboratories and BSL3Ag facilities for large animals, poultry and fish.* The lack of such facilities is having a

negative impact on the ability of CVM faculty to grow their research and to remain competitive for new funding. Ongoing investment to maintain and update *BSL2 and BSL2Ag* facilities is also of great importance. The protection of health and agriculture from the threat of infectious agents is an imperative that is clearly recognized by funding agencies. Federal funding for research in *Infectious Diseases and Biodefense* is available through the U.S. Department of Homeland Security, U.S. Department of Agriculture, U.S. Department of Defense, National Institutes of Health and the National Science Foundation. Therefore continued support by the CVM and the University will leverage significant future research funding.

The *Signature Program in Infectious Diseases and Biodefense* is also central to the mission of the College of Veterinary Medicine (curing and preventing animal disease), the Agrilife 'Scientific Roadmap' (improve agricultural production and efficiency through advances in animal and plant breeding and health, use risk analysis to minimize the impacts of foodborne hazards and biosecurity threat agents, prevent transmission of human disease agents through insect/pest vector control) and Texas A&M University (discovery, development, communication, and application of knowledge).

Interdisciplinary Impact

Interdisciplinary activities are key to the *Infectious Diseases and Biodefense* initiative as illustrated by the following examples: (1) **Development of novel vaccines and therapeutics** and/or **production of genetically resistant animals** require collaboration between microbiologists, geneticists, cell biologists, immunologists, pathologists and clinicians. Understanding the infectious disease process increasingly focuses on the host, host response, and host genetics. (2) **Design and implementation of disease surveillance and pathogen detection systems** are facilitated by the combined expertise of microbiologists, biomedical engineers, epidemiologists, public health experts, and wild-life biologists among others. (3) Population dynamics and food distribution systems must be understood in order to **model the economic impact of naturally occurring or introduced human, animal, or plant pathogens**.

Infectious diseases researchers at the College of Veterinary Medicine and Biosciences are actively engaged in cross-college collaborations as indicated by their membership in the university-wide intercollegiate faculties of Genetics, Virology, and Toxicology. Within the Texas A&M System, significant collaborative efforts involve Agrilife Research and the Health Science Center. An example of one such notable collaboration is the NRSA Institutional Training Grant (T32) titled 'Mechanistic Studies at the Host Pathogen Interface'. This training grant (submitted for renewal September 2008) includes nine faculty affiliated with CVM/TAMU and ten faculty from the College of Medicine and the Institute of Biosciences and Technology. At the national level, several *Signature Program in Infectious Diseases and Biodefense* affiliated faculty are affiliated with the National Center for Foreign Animal and Zoonotic Diseases Defense. FADZ develops products to protect U.S. public health and the national economy from the introduction of high-consequence foreign animal and zoonotic diseases – with an emphasis on prevention, surveillance, intervention and recovery. The Center leverages the resources of six major universities, five national laboratories, two state agencies, two fellow DHS Centers of Excellence and an expanding number of Minority Serving and tribal institutions.

Indices of Excellence

Productivity and success of over 30 CVM faculty with interests in *Infectious Diseases and Biodefense* can be measured through publications and research support. Faculty members have published over 220 peer-reviewed research articles from 2003 through 2008. The areas of strength of the group (molecular biology of hosts and pathogens, host-pathogen interactions and immunity, the genetic basis of susceptibility, pathogen detection and vaccine development) as well as diverse expertise in viruses, bacteria and parasites, is demonstrated by the breadth of high quality journals in which the faculty publish. These include, among others: Emerging Infectious Diseases, Journal of the American Medical Association, Cellular Microbiology, Molecular Microbiology, Journal of Virology, Virology, International Journal for Parasitology, Parasitology, Vaccine, Immunogenetics, Infection and Immunity, Neuroimmunology, Journal of Neuroimmunology, Journal of Biochemistry and the Journal of Molecular Biology.

Grant support from 2003 through 2008 totals over $28 million. National funding agencies include: USDA APHIS, NIH (National Institute of Allergy and Infectious Diseases, National Cancer Institute, National Institute of Aging, National Institute of Neurological Disorders and Stroke), DHS, and DOD.

Assessment/Expectations

The impact of College and Univeristy support of the Signature Program in Infectious Diseases and Biodefense will be monitored by quantitative metrics of productivity including: 1) extramural funding levels, 2)scholarly publication records, 3)successful graduate training programs, 4) international collaborations and 5) the production and/or implementation of technologies and programs to benefit our constituents. External review and recognition will be used where appropriate to evaluate progress.

APPENDIX

Participants

Adams, L.G. Host-pathogen interaction in immunity and disease; intracellular pathogens; host:pathogen genomics.

Ball, J.M. Viral pathogenesis and mechanisms of disease.

Berghman, L. Immuno-neuro-endocrine network in the chicken model; development of immunobiotechnological tools.

Budke, C.M. Parasitology; ecology of infectious diseases.

Caldwell, D. Gastrointestinal immunity and disease resistance in poultry; immunopotentiation of disease resistance in poultry.

Cohen, N.D. Infectious diseases of equines.

Craig, T.M. Epidemiology and control of internal parasites of grazing animals.

Criscitiello, M. Mechanisms of adaptive immunity.

Cyr, T. Medical and veterinary entomology.

Davis, D.S. Infectious and parasitic diseases of wildlife; brucellosis, tuberculosis, anthrax, hemaprotozoon, trematodes, and nematodes.

deFigueiredo, P. Molecular mechanisms mediating plant and animal diseases.

Edwards, J. Diagnostic pathology, infectious diseases of domestic livestock.

Ficht, A.R. Microencapsulation and vaccine delivery vehicles; innate immunity and host gene expression in response to paratuberculosis infection.

Ficht, T. Mechanisms of invasion and survival of intracellular bacteria within host cells; development and application of biosignatures.

Holman, P. Interactions between *Babesia spp.* and their hosts; potential vaccine or drug targets for *babesiosis*; development of DNA-based diagnostic tests for hemoprotozoan parasitic infections.

Lawhon, S.D. Interactions between the intestinal pathogens and mammalian hosts.

Leibowitz, J.L. Replication and pathogenesis of Coronaviruses.

Libal, M. Epidemiology of infectious disease; antimicrobic sensitivity testing; antimicrobic resistance.

Lupiani, B. Development of immunoassays for detection and rapid subtyping of Avian Influenza viruses; molecular mechanisms of pathogenesis of avian influenza viruses.

Norby, B. Ecology and transmission dynamics of food safety and infectious disease organisms and antimicrobial resistance; surveillance, control and eradication of zoonoses and infectious disease in animals.

Musser, J. Dairy production medicine, mastitis prevention and control, and quality milk production; vaccine development.

Mwangi, W. Improvement of vaccine efficacy in livestock and humans; optimizing in vivo antigen presentation by dendritic cells; evaluation of strategies for induction and maintenance of memory cellular immune responses in outbred species.

Payne, S.L. Molecular aspects of retroviral replication, pathogenesis, and evolution.

Reddy, S.M. Molecular basis of pathogenesis of poultry viruses.

Russell, K.E. Platelet pathophysiology and the interaction of platelets with infectious agents.

Scanlan, C. Competitive exclusion cultures for the control of salmonellae in poultry; investigation of anti-salmonellae mechanisms with emphasis on short-chain fatty acids.

Snowden, K.F. Parasites of public health importance; development of animal models for the study of parasitologic diseases and treatments, and development of molecular and immunologic methods for parasitologic diagnosis.

Stoica, G. Mechanisms of retroviral-induced neurodegeneration.

Tizard, I. Comparative avian and mammalian immunology; evolution of the immune system; avian diseases.

Wagner, G. Molecular basis of virulence of protozoal parasites; identification of antigens for serodiagnosis and immunization; host-parasite interrelationships.

Welsh, C.J.R. Viral causes of autoimmune diseases; Theiler's virus-induced demyelination as a model of multiple sclerosis.

Welsh, T. Regulation of genes that control metabolic, reproductive and immune functions; stress-related hormones impacting virally-induced neuropathogenesis in a mouse model of multiple sclerosis.

Zhu, G. Molecular biology, biochemistry and pathogenesis of parasitic protests; molecular interactions between parasites and host cells; discovery of molecular targets for the drug development.