CVM LANDMARK PROGRAM IN NEUROSCIENCE

Introduction and Significance

Neuroscience, which is the study of the nervous system and behavior, is the most rapidly developing field of intellectual inquiry today. The Society for Neuroscience, which is one of over 200 organizations devoted to study of the nervous system, is the world's largest society of scientists and physicians (38,000 + members) devoted to advancing understanding of the nervous system. The National Institutes of Health (NIH) devotes a large proportion of its intramural and extramural funding to study of the nervous system. This is particularly evident in the National Institute of Mental Health, National Institute on Drug Abuse, National Institute of Neurological Disorders & Stroke, National Eye Institute and National Institute on Aging. Other institutes also have emphasis on the role of the nervous system in disease processes, including the National Institute on Alcohol Abuse & Alcoholism and National Institute of Child Health & Human Development. The USDA has an important focus on investigation of behavior of domestic farm animals with emphasis on the quality of life for livestock.

The nervous system, including the brain, spinal cord and the peripheral nervous system, is by far the most complex of all biological systems and, therefore, represents the greatest challenge to biological scientific inquiry. Everything we learn about the nervous system brings us closer to preventing and/or curing a multitude of diseases and disorders such as Parkinson's disease, Alzheimer's disease, multiple sclerosis and mental illness. The cost of caring for the over 5 million Americans suffering from Alzheimer's disease alone exceeds $100 billion annually. Neuroscience research also will help to eliminate or diminish the devastating effects of alcoholism, drug abuse and traumatic brain and spinal cord injuries. Translational medicine, which has at its core the goal to use basic research to provide fundamental discoveries that can be used to develop novel and improved therapies, is currently the center of focus for the NIH. Through its research roadmap, the NIH intends to accelerate fundamental discovery and translation of knowledge from the "bench to the bedside".

Texas A&M University has a rapidly growing neuroscience research and teaching program, which was officially recognized as the TAMU Interdisciplinary Faculty of Neuroscience (IFN) in 2001. The IFN is currently developing a PhD training program in neuroscience and the Texas Higher Education Coordinating Board site visit for this program was held on October 13, 2008. It is anticipated that the PhD degree program in neuroscience will begin in the fall of 2009, which will be a combined program between TAMU and TAMUS-HSC. CVM neuroscientists play an integral role in neuroscience research, graduate teaching and the TAMU undergraduate minor in neuroscience.

One of the unique opportunities made available to neuroscience through veterinary medicine is our ability to diagnose and treat neurological disorders in domestic and companion animals. Natural disease in animals often mimics human disease more closely than animal models, in which disease is induced through genetic or experimental manipulations. For example, rodent glial tumor xenografts do not exhibit the necrosis and vascularity that human glial tumors can have, but naturally occurring glial tumors in dogs often do. In addition, veterinary patients have diverse genetic backgrounds, which is an advantage when trying to understand disease genetics or response to treatment. Also, the size of veterinary patients allows for drug pharmacokinetics to be performed and adverse effects to be monitored, which is

sometimes challenging in mice and even rats. Thus, "natural models" can greatly enhance understanding of disease, which results in the development of better care for both human and veterinary patients. **Only two of the top 25 universities ranked by NIH dollar amount have a college of veterinary medicine, therefore Texas A&M University is uniquely positioned to take advantage of the study of spontaneous animal disease.**

Rationale

The goal of Vision 2020 is to elevate Texas A&M University into the ranks of the top ten U.S. public research universities by the year 2020. This will not be achieved without enhancing the existing research programs on this campus, including neuroscience. Neuroscience programs are all well established and highly visible at the current top ten research universities in the United States. The IFN and especially the CVM neuroscientists form a cohesive working group of basic scientists and clinicians. This strong base forms an excellent starting point to build a nationally recognized research and training program in neuroscience. The CVM neuroscientists are in an excellent position to enhance the teaching program at TAMU through close interactions between clinical and basic science faculty.

Interdisciplinary Impact

Neuroscience by its very nature is a highly interdisciplinary area of research. This is abundantly demonstrated by the number of on-going collaborative research relationships in which CVM neuroscientists are involved. CVM neuroscientists are collaborating with faculty across the TAMU system, including faculty in the TAMUS-HSC College of Medicine (departments of Neuroscience and Experimental Therapeutics, Molecular and Cellular Medicine and Systems Biology and Translational Medicine), the College of Engineering (departments of Computer Science, Biomedical Engineering, Electrical Engineering, Mechanical Engineering), the College of Agriculture and Life Sciences (departments of Biochemistry and Biophysics and Animal Science), the College of Liberal Arts (Psychology department) and the College of Science (departments of Biology and Chemistry). Many collaborations also extend beyond the University and Health Science Center to outside institutions, including the University of Maryland, Cornell University, UCSF Medical School and M.D. Anderson.

An additional strength at TAMU is collaboration with the Texas Institute of Genomic Medicine (TIGM), which maintains the world's largest C57BL/6N gene trap library, a knockout mouse embryonic stem (ES) cell resource that contains over 350,000 cell lines representing more than 10,000 unique genes. The NIH has obtained rights to a subset of these lines, allowing TIGM to make them available for distribution to the academic research community on a subsidized basis.

CVM faculty also participate in the Texas Brain and Spine Institute, which is a center of excellence in clinical and academic neurosciences. The Institute is a multidisciplinary collaboration between clinicians, scientists, and supporting institutions with the purpose of furthering superior clinical and academic missions.

Assessment /Expectations

The interdisciplinary nature of neuroscience provides a natural synergism to research conducted across this campus and with the Health Science Center. The strong collaborations that exist through the Interdisciplinary Faculty of Neuroscience are expected to be maintained and strengthened in the future. To enhance the stature of the interdisciplinary neuroscience program in the college and the university and to continue to be competitive for individual NIH, NSF and private foundation grants, program project grants and training grants, additional senior level faculty are needed. We propose to add a senior level neuroscientist who is using animal models to study basic mechanisms of neurological disease that would complement current strengths in the College of Veterinary Medicine. Ideally, this neuroscientist would be a senior level researcher who is using nonrodent animal models in their research program, such as dogs, pigs, goats or sheep. Using animals in preclinical trials for human diseases and combining expertise and experience of veterinarians and basic scientists is an extremely fruitful and highly underutilized avenue of scientific endeavor. As an example, one CVM neuroscientist currently uses the sheep to study the basic mechanisms by which prenatal alcohol exposure damages the developing brain. The focus of this research is on basic mechanisms of the action of alcohol, developing prevention and identifying better ways to identify affected individuals. Fetal Alcohol Syndrome (FAS) is the leading cause of mental retardation in the western world and has a $6 billion annual cost in the US. FAS is estimated to occur at a rate of 1 per 1000 live births, and when the more minimal effects are included, the rate jumps to 1 per 100 live births.

In general assessment will include funding received from federal (e.g., from NIH, NSF, DOD, USDA) and private foundations. Total publications and the ranking of the journals also will be included. In addition, teaching responsibilities as well as how many graduates students (MS, PhD, DVM-PhD), undergraduate students and postdoctoral fellows trained will be included in the assessment.

Indices of Excellence in the CVM Neuroscience Program

The College of Veterinary Medicine and Biomedical Sciences at Texas A&M University is one of the top veterinary programs in the United States. The Texas Veterinary Medical Center's clinical neurology program is rapidly growing and sees over 750 neurology cases/year. The clinical neurology program also has an established track record with respect to translational medicine projects. CVM neurology clinicians have initiated the first NIH-funded clinical veterinary trial through the CAPTR program, which focuses on spinal cord injury treatments. Both clinicians and basic scientists in the CVM are working on a multi-institutional (involving UT-Houston Medical School and M.D. Anderson) glioma collaboration, which will study naturally occurring disease in dogs. Pet owners are increasingly more willing to invest in treatments for medical and surgical neurological diseases. Moreover, there are many neurodegenerative disorders in dogs, cats and other domestic animal species that serve as animal models for similar human neurological disorders. Study of spontaneous disease in animals provides invaluable information that can be used to develop new therapeutic strategies for both animals and humans. Therefore, neuroscience is extremely important to both humans and animals, and neuroscience research is an ever-increasing component of Texas A&M University's research, teaching and engagement missions.

The CVM faculty currently has 19 faculty members who are clinical and/or basic research neuroscientists. CVM neuroscientists are conducting cutting edge integrative research into mechanisms by which environmental factors interact with the genetic background to induce pathology and dysfunction in neurological diseases. Research areas range from whole animal behavior to the cellular and molecular level. The unique combination of strong research, teaching, presence of clinical neurology in the teaching hospital and the multiple core research laboratories, allow this group to be uniquely placed to advance our knowledge base in mechanisms of neurological disease. Diseases under investigation include: Alzheimer's disease, ataxia telengiectasia, autism, epilepsy, hereditary rat neuronal system degeneration, meningoencephalomyelitis, multiple sclerosis, macular degeneration, neurofibromatosis, neuromuscular diseases, Parkinson's disease, Fetal Alcohol Syndrome, tumors of the nervous system and spinal cord injury. Individual faculty within the group study a number of different cell types within the nervous system, including: oligodendrocytes, astrocytes, neurons and endothelial cells that form the blood-brain barrier. Environmental factors that are currently being studied include: toxicants, viruses and psychological stress. The impact of environmental toxins on neural development and the onset of puberty and toxicants under current investigation include: lead, mercury, cadmium, manganese and organophosphorous compounds. Infectious diseases of the nervous system induced by retroviruses and picornaviruses are under investigation. The effect of psychological stress on the development of multiple sclerosis is also a topic of investigation. A growing emphasis in CVM neuroscience research is translational neuroscience involving both clinical and basic neuroscientists.

Publications by these 19 people for the past five years number over 225. These publications are highly collaborative among the current CVM neuroscience faculty and between the CVM neuroscience faculty and other non-neuroscience faculty members across the TAMU campus such as the interdisciplinary toxicology, genetics, and reproductive biology programs, as well as Colleges of Science and Engineering. For example, over 40 different publications in the past five years have been co-authored by two or more of the 18 CVM neuroscience faculty. Many of these joint publications include both clinical and basic science CVM faculty. In the past five years grant dollars for the CVM neuroscience faculty totals $11.8 million in funding from federal funding agencies including NIH, USDA and NSF or from private foundations such as the National Multiple Sclerosis Foundation. An additional $6.9 million has been acquired for science education. Funding also has been made available through the TAMU NIEHS Center for Environmental and Rural health (CERH) for neuroscience-related research that is carried out mainly in the area of neurotoxicology. The funded proposals demonstrate the highly integrative and collaborative nature of the neuroscience research being conducted at the College of Veterinary Medicine. 40% of the funded grants involve collaborations with faculty in other TAMU Colleges or other universities.

There is significant interdependence between clinical and basic scientists with respect to teaching in the college. We have developed an excellent system of combining clinical and basic science expertise in our first year veterinary professional program with an introduction to neurology course. In addition, several undergraduate and graduate courses in neuroscience topics are taught, including six new courses and a clinical neurology elective that were developed in the past year. It is anticipated that the teaching hospital will start training neurology residents in 2009.

APPENDIX

Abbott, Louise C.	developmental neurotoxicology and the role of heavy metals in autism and neurodegenerative disease.
Bratton, Gerald	toxic metal effects on the neuroendocine system and behavior; trace metals analysis.
Cudd, Timothy	how prenatal alcohol exposure causes neurodevelopmental defects, how defects might be prevented or mitigated and identifying better screening tools in order to identify affected children earlier as early intervention has the best opportunity for mitigating damage.
Dees, W. Les	investigation of endogenous and exogenous substances that control or alter female pubertal development.
Dziezyc, Joan	ophthalmology; ophthalmic surgery; ocular ultrasonography, ocular inflammation.
Hicks, Daniel	biomechanics of the spine, specifically, the effect of implant stabilization in the cervical spine and lumbosacral joint in dogs; canine cervical spondelomyelopathy (wobblers); lumbsosacral disease; and surgical neuro-oncology.
Hong, Don	genetic basis of retinal degeneration; molecular and cellular basis of pathogenesis caused by mutations in retinal degenerative disease genes; new gene therapy through the genetic and cellular understanding of retinal biology and disease pathogenesis.
Kerwin, Sharon	advancing diagnosis and treatment of spontaneously occurring neurologic diseases in the dog and cat, including discospondylitis, intervertebral disk disease and meningomyelitis; advances in surgical stabilization of the spine.
Klemm, William	ganglioside structure and function, action potential interval analysis, alcohol, narcotics, animal hypnosis, vomeronasal function, brainstem arousal, hippocampal theta rhythm, and veterinary neurology; current interests include educational neuroscience and memory.
Ko, Gladys	cellular mechanisms underlying the circadian regulation of retina physiology and function; risk factors leading to photoreceptor degeneration.
Levine, Jonathan	spinal cord injury; epidemiology of neurologic diseases; intra-cranial neoplasia; translational research.

Li, Jianrong	axon-glia interactions, oligodendrocyte development, white matter injury, and CNS myelination, demyelination and myelin repair.
Milichamp, Nick	ophthalmology; inherited retinal diseases; ocular inflammation; equine cataract surgery; ophthalmic telemedicine.
Pine, Michelle	effect of in utero and peripubertal exposure to type II pyrethroid pesticides on timing of female puberty using the Sprague Dawley rat as a model; effects of in utero exposure to these pesticides on neurodevelopment.
Porter, Brian	comparative neuropathology; diseases of special interest include necrotizing meningoencephalitis of pug dogs and GM2-gangliosidosis of Jacob sheep; the study of S100 protein inhibitors for the treatment of Alzheimer disease.
Stoica, George	mechanism(s) of retroviral-induced neurodegeneration; pathogenesis of brain and bone metastases of mammary gland tumors; application of flow cytometry in the study of tumors; lectin and immunohistochemistry; chemical carcinogenesis; animal models for retrovirus-induced neoplasia.
Tiffany-Castigioni, Evelyn	glial cell biology; cellular neurotoxicity of environmental contaminants.
Welsh, C. Jane	investigation of the underlying mechanisms by which viruses cause autoimmune disease in the central nervous system using Theiler's murine encephalomyelitis virus-induced demyelination (TVID) as a model for multiple sclerosis (MS); evaluating therapies for MS and the role of the blood-brain barrier.
Zimmer, Danna	mammalian calcium signal transduction pathways, their role in the pathobiology of neurological disorders/cancers, and the discovery/development of therapeutic agents that target these pathways; development and characterization of genetically modified mouse models for human/veterinary diseases.