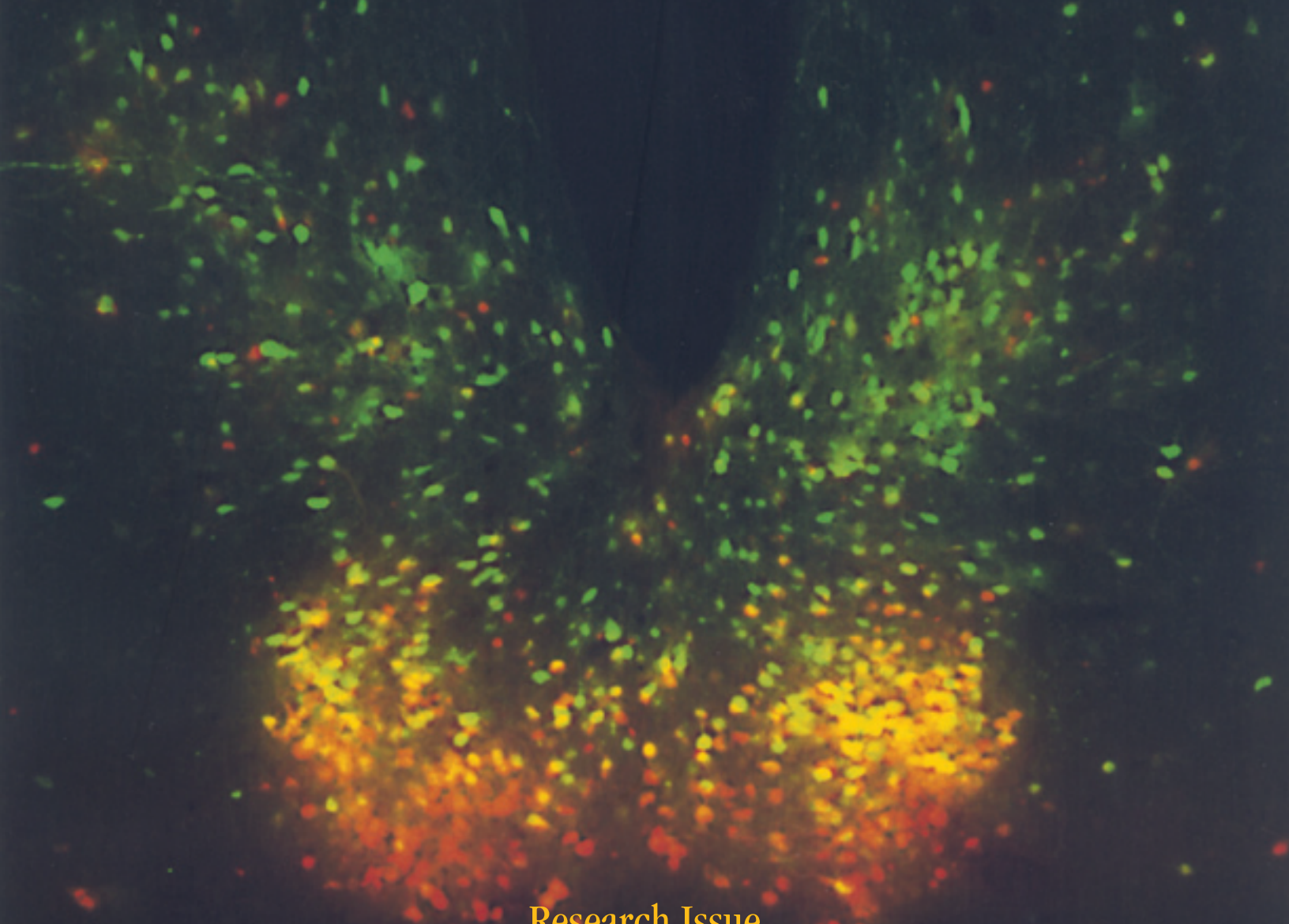
INSIGHT

Summer 2002

College of Veterinary Medicine and Biomedical Sciences



Research Issue

Colorado State University

Knowledge to Go Places

INSIGHT
Volume 29 Number 2
Summer 2002

COLLEGE OF VETERINARY MEDICINE AND BIOMEDICAL SCIENCES

On the cover:
It's not a butterfly but a hamster hypothalamic suprachiasmatic nucleus (SCN). The SCN sits at the base of the brain in the hypothalamus. Here, the SCN is stained with the pseudo-rabies virus expressing green fluorescent protein, and also with an antibody against viral protein that stains red, giving the SCN a red and green label. (See related story on Page 4).

Insight is published three times per year by the College of Veterinary Medicine and Biomedical Sciences, Colorado State University, and produced by Publications and Printing.
Editor/Writer: Carol Borchert;
Photographers: Charlie Kerlee, Bill Cotton:
Production: Sandy Thode;
Production Coordinator Margaret Taunt.

Visit us on the Web at
www.cvmbs.colostate.edu

Welcome to *Insight*

Welcome to the Summer 2002 Research Edition of *Insight*. Once a year, we put the *Insight* spotlight on research because research plays such a vital role in the College's mission. Research creates new knowledge, provides teaching and learning opportunities for our faculty and students, and helps us tackle some of the most vexing problems in science today.

In this edition, we focus primarily on research in the biomedical sciences. While Colorado State is very well known for its research and teaching programs in veterinary medicine, our research centers in biomedical sciences are world-renowned as well. You'll read about exciting new developments in using genetic engineering to combat the human immunodeficiency virus, one of the most serious global public health problems today. You'll also read about research on taste cells, mapping of the brain, the disfiguring disease leishmaniasis, circadian rhythms, a new program to fund innovative research, and much more.

We welcome your questions and comments on *Insight*. If you'd like to get in touch with us, please send your correspondence to:

Insight Correspondence
Office of the Dean
W102 Anatomy/Zoology
College of Veterinary Medicine and Biomedical Sciences
Colorado State University
1601 Campus Delivery
Fort Collins, CO 80523-1601

You can e-mail *Insight* comments to Paul Maffey, director of development for the College at: rpmaffey@colostate.edu. We also invite you to visit us on our Web site at: www.cvmbs.colostate.edu. ■

Table of Contents

Message from the Dean

Dear Friends,

When we think of a university, we often picture students working diligently in laboratories, faculty lecturing in large halls, and joyous graduation ceremonies. But universities also are vibrant research communities working at the forefront of every facet of human endeavor. The College of Veterinary Medicine and Biomedical Sciences exemplifies the vital nature of research to the living entity that is the University.

In practical terms, the funds that sponsored research bring to the College are essential to the success of our mission. Nearly 50 percent of the College's budget is funded through research grants and contracts. With that money, the salaries of many faculty and staff are paid and supplemented, state-of-the-art equipment is made available, and capital improvement projects are possible. For our students, this expansive research network means learning from individuals who are at the top of their fields, having access to modern laboratories, gleaning work experience with highly technical equipment, and playing a critical role in the creation of new knowledge that will advance the fields of veterinary medicine and biomedical sciences. Our research work enables us to identify and resolve new and recurring disease problems while transmitting that information to students and end users in the greater community.

Veterinary medical research is, of course, something for which the College is very well known. But our research programs in the biomedical sciences are an equally important component of the College's mission to discover and disseminate knowledge. In fact, the College ranks first in the nation among veterinary schools in terms of funding from the National Institutes of Health.

That funding finds its way to a diversity of programs that are seeking to answer complex questions about the nervous system, deadly infectious diseases such as AIDS, the intimate interactions between human systems and toxins in their environment, and much more. Much of this research is basic science – understanding how and why things work. This type of reductionist science is the foundation upon which all applied science is built and it is essential to continued advances in science and medicine. Some is applied science, such as drug testing. And some science is so new, like proteomics and genomics, that its full potential is yet to be understood.

In practical terms, the funds that sponsored research bring to the College are essential to the success of our mission. Nearly 50 percent of the College's budget is funded through research grants and contracts.

Much of the funding for the research you will learn about in this edition of *Insight* comes from government organizations, notably the NIH. Other funding comes from non-profit organizations, such as the American Heart Association. The University also encourages excellence in research by funding select programs through its Centers of Research and Scholarly Excellence and through the new Academic Enrichment Program, which recently funded two proposals from the College.

Dr. Lance Perryman

None of this would be possible if the College of Veterinary Medicine and Biomedical Sciences did not have an extraordinary group of individuals on its faculty. Their passion, vision, intelligence, and dedication drive the College forward. Our students benefit from their commitment to research and the creation of new knowledge, while we as a nation reap the rewards every day of their combined efforts to improve the lot of humankind.

I hope you enjoy reading their stories and maybe even learn something new along the way. ■

With Best Regards,

Lance Perryman, D.V.M., Ph.D.
Dean

Studies of Circadian Rhythms Show Several Different Factors Affect Cycles

As a graduate student at the University of Wisconsin, Dr. Gary Pickard was happily studying the reproductive physiology of a variety of mammals when the arrival of a shipment of hamsters changed his life. Hamsters, it turns out, are seasonal breeders with reproductive hormonal secretions under the influence of a circadian rhythm generator. At that time, circadian rhythms were not widely understood beyond the common knowledge that most animals seemed to possess an internal clock. But nobody really understood how that clock was wound, and Dr. Pickard found himself intrigued by that question.

Dr. Gary Pickard

"Biological rhythms are a fundamental property of nature," said Dr. Pickard. "We are trying to develop a greater understanding of what the factors are that affect these rhythms and whether or not we can manipulate them. Such information could prove valuable in understanding abnormal phasing of the sleep/wake cycle, serious diseases such as seasonal affective disorder, and in developing better ways to treat jet lag."

Researchers have found that circadian oscillators that regulate circadian rhythms share three common properties: entrainment (synchronization to environmental cycles, mostly the light/dark cycle), free-running rhythmicity (rhythms persist under constant conditions), and temperature compensation (how length of cycle is affected by changes in the temperature). But there is a neural basis to circadian rhythms as well, and this is where Dr. Pickard focuses the work of his laboratory.

"What we are finding is that the hypothalamic suprachiasmatic nucleus (SCN) is an important component of the mammalian circadian system," said Dr. Pickard. "The SCN sits at the base of the brain in the hypothalamus and receives signals from the retina through what is known as the retinohypothalamic tract (RHT). Our research focuses on understanding this signaling system and tracking the cells that are responsible for transmitting and receiving signals important to the SCN and maintaining the circadian rhythm generating system synchronized to the environment."

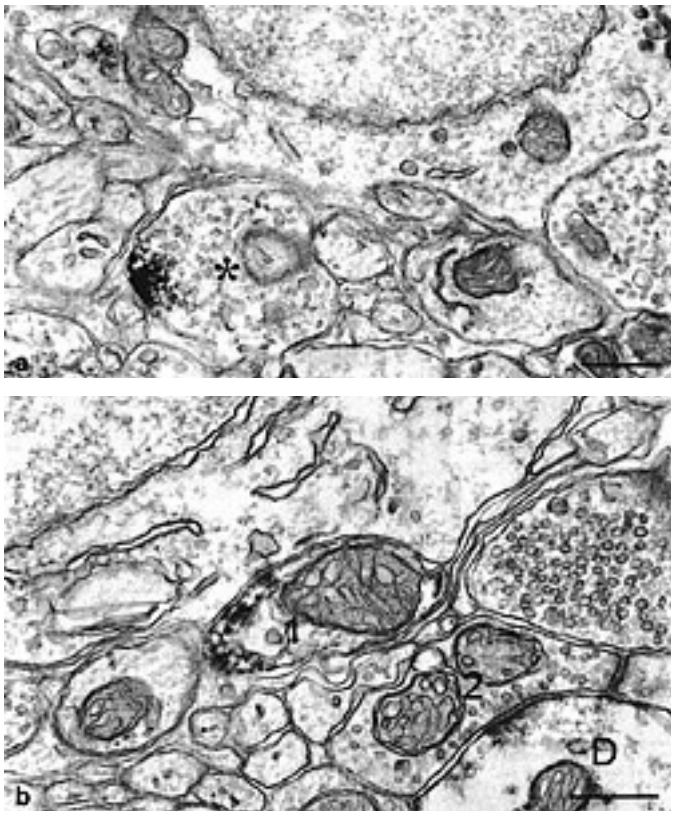
In Dr. Pickard's studies with mice as well as in human studies, when the test subjects are deprived of environmental information, researchers have found that animals continue to follow a distinct circadian rhythm. The main difference is that when subjects are in a temporal isolation unit, there is a "drift." Because humans have a 24.5- to 25-hour circadian cycle, in the absence of environmental cues to reset their clock each day, test subjects would simply revert to the natural cycle and start going to bed later and later until, by the end of the study, they were going to bed for the night at noon.

Because humans have a 24.5- to 25-hour circadian cycle, in the absence of environmental cues to reset their clock each day, test subjects would simply revert to the natural cycle and start going to bed later and later until, by the end of the study, they were going to bed for the night at noon.

"The RHT entrains the SCN to the external day/night cycle so that there is a stable phase relationship between our internal clock and the environment," said Dr. Pickard. "This allows us to recognize local time, as well as predict events happening in the future. You can see how this would be very important to most animals. For example, if a nocturnal rodent foraging at night didn't have a biological clock to tell them when to go home – to, in essence, predict the onset of dawn – they would make easy prey for diurnal predators."

But the RHT is a nonvisual retinal pathway. An animal blinded by destroying visual centers in the brain still can entrain to the light/dark cycle. In February 2002, researchers at Johns Hopkins University discovered that the retinal

Above: Dr. Pickard and his team



Right: Electron micrographs illustrating receptors in nerve terminals in mouse SCN

ganglion cells that send information to the SCN are light-sensitive. Specialized ganglion cells (less than one percent of the total ganglion cell population of the retina) are the cells that give rise to the RHT. Dr. Pickard's team is studying the role of melanopsin, which is the light-sensitive protein, in these ganglion cells. Dr. Pickard has worked with colleagues at Princeton to develop techniques to tag and study these cells, using viruses and a jellyfish protein that fluoresces, lighting up ganglion cells like miniature Christmas trees. Along the way, Dr. Pickard has discovered communication pathways that show how the ganglion cells interact with each other and other neuronal cells in the retina. Dr. Pickard and his research team also are looking at the effect of the neurotransmitter serotonin on these cells.

"This is another major area of research for us," said Dr. Pickard. "We are developing a better understanding of how serotonin is involved in modulating the circadian rhythms. What we have found is that when serotonin is released, it inhibits the system. When it stops being released, the system is more sensitive to light. Serotonin seems to be involved in setting the gain of response of the system to light – setting the tone. Research shows that at times when we should be more sensitive to light – dawn and dusk – the release of serotonin is slowed. It helps us set our clocks."

"Biological rhythms are a fundamental property of nature. We are trying to develop a greater understanding of what the factors are that affect these rhythms and whether or not we can manipulate them."

Dr. Pickard is examining how serotonin interacts with cells in the RHT and the SCN and he is also looking at how drugs that cause the release of serotonin in the brain may create problems for circadian rhythms.

"For 30 years, no one really knew what serotonin did in the SCN, though its heaviest concentration in the brain is found in the SCN," said Dr. Pickard. "We are providing the first real definitive clues of at least one function of serotonin in the brain and developing a greater understanding of serotonin receptors. This is a very exciting time for us, as we are working on the cutting edge of retinal circuitry – we have great tools that are enabling us to see and understand things that we simply couldn't get at before."

Dr. Pickard's work is funded by Health and Human Services and its National Institutes of Health. ■

GIS Giving Researchers Better Handle on Environmental Risk Assessment

The interaction between humans and their environment is a complex one. When we farm, we use chemicals to prevent disease, kill pests, and increase yields. But these chemicals often end up in places they were never intended to be. When we manufacture, we dump waste products that often seep into underground aquifers, spreading contamination beyond the confines of factory property. When we build bombs, we leave behind nuclear waste that insidiously seeps from storage containers and runs with the rain water into drainages.

We actively are changing our environment in ways that sometimes we don't understand until it is too late – illness is caused, groundwater is contaminated, soil is ruined. For many years, this type of damage was done out of sheer ignorance. People didn't understand or acknowledge the very real risks of environmental contamination. Risk assessment tools were very one-dimensional and didn't reveal the full story.

Today, a new assessment tool, GIS (geographic information system), is breaking new ground by helping environmental scientists better understand and assess damage that has already been done to the environment, and better protect against poor decisions made upon incomplete data. Dr. John Nuckols is at the forefront of this new technology and is actively involved in developing and testing GIS assessment tools that can provide a multidimensional picture of risks in agricultural chemicals, pollution from chemical factories, the varied risk of the by-products of water chlorination, and much more.

"Historically, risk was assessed by distance – for example, how close is the house to the factory," said Dr. Nuckols, who is a special appointment faculty member with the Department of Environmental and Radiological Health Sciences. "This one-dimensional approach made everyone look the same and resulted in a misclassification of exposure. With GIS, we are able to develop a multidimensional database and analyze risk assessments spatially. It really is a new arena for health scientists."

> "With a geographic information system (GIS), we are able to develop a multidimensional database and analyze risk assessments spatially. It really is a new arena for health scientists."

Dr. John Nuckols

> "We are really at a crossroads, and Colorado State is out in front by already housing a GIS environmental health research program."

Dr. Nuckols, who has been working with GIS technology for 10 years, said the technology helps identify the population that is really exposed and at risk by using more than one parameter to model risk. For example, the layers of data fed into the system to assess pesticide risk could include aquifer maps, crop types, timing of chemical release, types of chemicals used, drift in the environment, geologic and geographic details, well locations, and much more. Using these layers of data, GIS can provide a three-dimensional "map" that more accurately assesses risk.

"We are forging very new territory, so we are still in the process of proving the validity of our studies," said Dr. Nuckols. "Right now we are doing a prospective study where we go in and map crops, collect dust and environmental samples, and conduct health assessments on local residents. We hope to show the value of GIS through studies like these that reflect the importance of this technology in predicting and possibly even preventing the ill effects of environmental contamination."

Dr. Nuckols actively is involved in several areas of environmental contaminant research. His primary focus is using GIS to assess the risk of agricultural chemicals (pesticides, fertilizers, etc.) in the environment with a specific focus on risk to children, particularly the risk of

continued on page 8

Laboratory Looking to Understand Tantalizing World of Taste

When one looks simply at our sense of taste, it seems to be rather straightforward. Some things taste good (chocolate chip cookies), and some things taste bad (cod liver oil). Taste is something we take for granted in our everyday lives, yet the complexity of the simple act of tasting is providing fodder for researchers around the world who are trying to understand how this complicated process works.

Dr. Sue Kinnamon

Explaining taste on an anatomical level is pretty easy. On our tongue and soft palate, we have taste buds filled with specialized cells that act as receptors to different taste qualities. Human taste buds detect sweet, salty, sour, bitter, and umami (that rich beefy, brothy taste found, for example, in foods with MSG). Cells within our taste buds send signals to the central nervous system so the brain can decide what to do (poisons are usually bitter, leading to a strong signal to gag or spit out). But exactly what is happening on a cellular and molecular level is still mostly a mystery to scientists involved in this field. Dr. Sue Kinnamon and her colleagues at the Rocky Mountain Taste and Smell Center are only just beginning to understand the inner workings of mammalian taste.

"What we are working to understand is how different qualities of taste are detected by cells found in the taste buds," said Dr. Kinnamon. "Thanks to advances in molecular biology research technology and the mapping of the mouse and human genome, we now have the tools we need to ask and answer difficult questions regarding what kinds of cells we find in taste buds and how those cells work."

It turns out there is a fairly big collection of cells in each taste bud. Dr. Kinnamon and her research team are particularly interested in the mechanisms these cells use to communicate with the nervous system. Cells known as Type III cells synapse with nerve fibers that hook up to the central nervous system, while the communication model for Type II cells remains unknown. One possibility is that the cells communicate by releasing a gaseous messenger, such as nitrous oxide, which in turn stimulates the Type III cells to communicate with the nervous system. Alternatively, the Type II cells may communicate with nerve fibers or Type III cells by "gap junctions," which are electrical rather than chemical synapses. Dr. Kinnamon's original research work used mud puppies as a model for human taste, but she since has moved on to a mouse model that more closely relates to human taste.

"We also are interested in the second messengers that interact with ion channels to depolarize the taste cells," Dr. Kinnamon said. "These second messengers are formed by the interaction of taste receptors with intracellular signaling proteins known as G proteins. It turns out that a subset of Type II cells expresses a particular G protein called gustducin which is known to mediate the intercellular signal cascade for sweet and bitter tastes. We are using behavioral studies with genetically modified mice that lack the gustducin protein to determine if gustducin plays a role in other tastes."

It's tough, of course, to ask a mouse what it likes, so Dr. Kinnamon and her associates use the two-bottle method to determine preference. A mouse is given two bottles from which to drink, one containing a taste substance and the other containing water. If the taste is preferred, the mouse will drink primarily from the taste bottle, but if the taste is aversive, the mouse will drink from the water bottle. If mice don't have the necessary receptors to pick up the sweetness of artificial sweeteners like aspartame, they will show no preference. Likewise, if they lack other components of the signal cascade, such as a particular G protein, they will show no preference. Dr. Kinnamon's research group now knows that gustducin is involved in

continued on page 8

Cells within our taste buds send signals to the central nervous system so the brain can decide what to do. But exactly what is happening on a cellular and molecular level is still mostly a mystery to scientists involved in this field.

GIS Giving Researchers Better Handle on Environmental Risk Assessment

continued from page 6

cancer. Most of his work in this area has been sponsored by the National Cancer Institute, with four grants/contracts for the agricultural initiative.

Another area of study is investigating chlorination by-products in treated water, where the degree of threat to human health still is not clear. Through several projects funded by the Environmental Protection Agency, Centers for Disease Control (CDC), and the American Water Works Association Research Foundation, Dr. Nuckols is involved in the exposure assessment for epidemiology studies concerning possible risks of these by-products – risks that may include birth defects, cancer, reproductive problems, and other health concerns.

"Using GIS and computer simulation modeling, we can more accurately track the dispersion and concentration of these by-products through the water treatment and delivery system and, through epidemiological studies, more accurately determine if there is a correlation between the by-products of chlorination and human health risks," said Dr. Nuckols. "The key is that these tools can really re-define how we understand risk by creating a more valid picture of the environment in which the risk exists. Decisions that impact human health will be made with a greater appreciation of the risks involved."

The GIS program within the Department of Environmental and Radiological Health Sciences is one of a half-dozen such programs across the nation. Dr. Nuckols expects the demand for environmental health professionals schooled in GIS to increase rapidly as the tool is more widely accepted within the field. The key is having the technology, faculty, and students to support this innovative field.

"We are really at a crossroads," said Dr. Nuckols, "and Colorado State is out in front by already housing a GIS environmental health research program. The next step will be to fully integrate GIS into the environmental health sciences curriculum, while we continue to expand our research program. It's a really exciting time to be in this field, and we are looking forward to fully deploying GIS as the newest technology that will improve human and environmental health." ■

Laboratory Looking to Understand Tantalizing World of Taste

continued from page 7

the processing of the umami taste quality, as mice without gustducin showed no preference in the two-bottle test while control mice with gustducin preferred the umami taste.

Dr. Kinnamon's laboratory also is using genetically modified mice in which the taste cells that express gustducin are fluorescent and can be targeted for electrical recording. By recording directly from the fluorescent taste cells, researchers can select taste cells that are likely to respond to sweet, bitter, and/or umami taste qualities. By recording directly from the gustducin-expressing taste cells, Dr. Kinnamon hopes to learn what second messengers and ion channels are involved in the signaling of these taste qualities.

Understanding the mechanisms of taste is important as basic science but it's equally important in clinical applications. People with a compromised sense of taste often don't want to eat and can become malnourished.

Dr. Kinnamon's original research work used mud puppies as a model for human taste, but she since has moved on to a mouse model that more closely relates to human taste.

A compromised sense of taste can be the result of medical treatment for conditions such as cancer or because of other problems. Better understanding of how taste works can help researchers develop more effective treatments for a diminished sense of taste. Fooling taste cells is another important area of food and drug development. For example, for diabetics and others who must limit their sugar intake, artificial sweeteners are lifesavers, making foods more palatable while not being metabolized by the body. Masking tastes – making a child's medicine more palatable, for example – is another component of research affected by an understanding of the basic mechanisms of taste.

"In our laboratory, we are teasing apart the intricate workings of taste, a complex system that has evolved as we have evolved and is mainly driven by nutrition," said Dr. Kinnamon. "We are learning something about the different animal systems, how taste cells communicate with the central nervous system, and what the roles are of different cells and proteins. We have much to learn, but we are beginning to understand some of the underpinnings of taste. With continued advances in tools, technology, and knowledge, we look forward to enhancing and expanding our work and developing a greater understanding of the sense of taste." ■

When It Comes to Males and Females, Hormones Make All the Difference

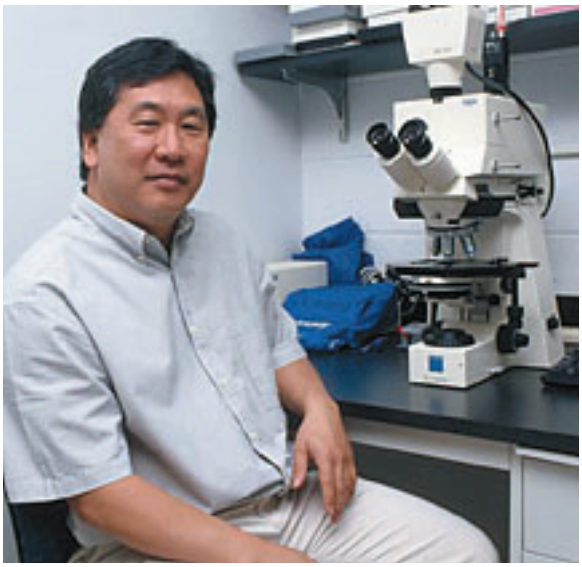
When Dr. Bob Handa thinks about the rats in his laboratory, it's hard not to make comparisons to humans. Young male rats exhibit play behavior that is amazingly like boy behavior on the school playground – they wrestle, jump, and show rough-and-tumble play. The females, however, are more circumspect. They hit and then run, trying to get the males to chase them. Sound familiar?

Distinctions between male and female behavior in any species can be obvious or can be subtle, but much of where it comes from has to do with the "maleness" or "femaleness" of the brain and the hormones, primarily estrogen and testosterone, that affect behavior and function. For Dr. Handa, a professor in the Department of Biomedical Sciences, understanding the effects of hormones on the brain, and how those hormones work by binding to receptors, really are where things start to get interesting and are the focuses of work at his laboratory.

"What many people don't realize is that our brains are inherently female," said Dr. Handa. "Surprisingly, it's the release of testosterone that then is converted to estrogen, most commonly thought of as a female hormone, that changes the female brain to a male brain in utero. As we can see, the effects of certain hormones on the brain are profound, and we just now are beginning to understand the role those hormones play in the development and functioning of the brain. What we do know is that the brain is very complicated, and the differences between the male and female brain are just amazing."

Dr. Handa came to Colorado State University in 1998 from Loyola University, Chicago Medical Center, where he honed his skills as a neuro-endocrinologist. He now conducts a number of studies looking at sex differences in the brain and how estrogen and testosterone turn on different sets of genes.

"One of the things we are looking at here is how estrogen and testosterone in adult animals set up differences in hormonal and behavioral responses to stress," said Dr. Handa. "We have found that those responses are different. In the male brain, testosterone turns down the hormonal response to stress, while in the female brain estrogen turns up the response. But we have found that behavioral responses to stress in females are milder, while a behavioral response to stress is greater for males."



Dr. Bob Handa

"What many people don't realize is that our brains are inherently female. Surprisingly, it's the release of testosterone that then is converted to estrogen, most commonly thought of as a female hormone, that changes the female brain to a male brain in utero."

The hormonal response in females turns out to be a double-edged sword. While estrogen is protective of neurons, it also can be destructive. Hormones such as estrogen that increase the production of glucocorticoids are beneficial in the short-term, but if glucocorticoids are chronically elevated, the individual can end up with health problems.

"We see a much higher incidence of affective disorders in females and are more closely examining the role estrogen plays in the development of these disorders," said Dr. Handa. "The development of these disorders – such as bulimia, bi-polar and uni-polar depression, and anxiety disorders – may be partially tied to estrogen levels in susceptible populations."

In addition to researching how estrogen and testosterone regulate genes and behavior, as well as the roles of estrogen, testosterone, and androgen receptors, Dr. Handa studies fetal alcohol effect (a less severe form of fetal alcohol syndrome) and pesticide exposure, especially as to how these affect developing reproductive systems and fertility in females. He also is conducting research into estrogen receptors, particular ER Beta, a novel form of estrogen receptor, to determine where in the brain these receptors are found, what types of neurons they are found in, and how they move through a cell's nucleus.

"We are finding these receptors in areas that are not repro-

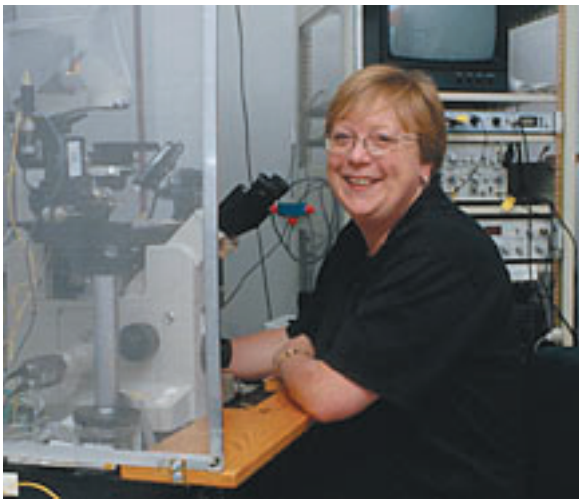
continued on page 11

Laboratory Looking at New Drugs to Improve Brain Function in Stroke Victims

In the Anatomy/Zoology Building at Colorado State, there is a laboratory that one day may give new hope to stroke sufferers, helping them to make more of the healthy brain tissue they have left. With funding from the American Heart Association and the National Institutes of Health, Dr. Kathryn Partin and her team of investigators are trying to better understand how cognitive enhancing drugs actually work inside the brain. The questions they answer one day may help drug companies design better compounds that improve the quality of life for those suffering with the after-affects of stroke.

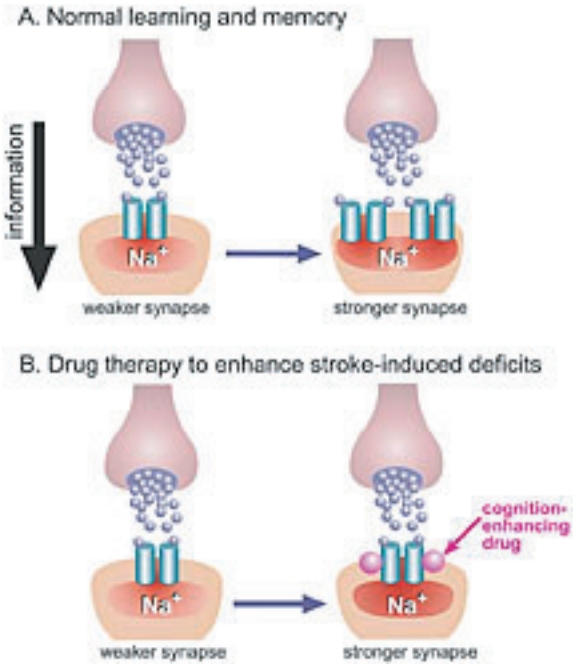
Dr. Partin, who is an associate professor in the Department of Biomedical Sciences, didn't start out nosing around neurons. She actually majored in history in college, but a course in science for non-majors sparked her interest in biology, and she went on to pursue graduate degrees in molecular microbiology. After a postdoctoral appointment to Duke University and the Howard Hughes Medical Center, Dr. Partin worked in Dr. Mark Mayer's laboratory at NIH. There, she undertook an education in neuroscience and began to explore a career that would lead her to Colorado State in 1996.

"Coming here as a junior faculty member was exciting, but somewhat overwhelming," Dr. Partin said. "I had never taught or written grants or served on faculty committees, so it was kind of intense. But the department has a wonderful mentoring program for junior faculty, and I couldn't believe how generous people were with their time and ideas. It's a very supportive atmosphere."



Dr. Kathryn Partin

Each year, more than 600,000 Americans suffer a stroke. Of those, 165,000 die, making stroke the third-leading cause of death. Currently, there are about 4.6 million stroke survivors.



Dr. Partin now enjoys a balance of teaching (which she has come to love), advising (especially young women looking to explore their own careers in science), and research (both basic and applied). Her laboratory is focusing on two areas of research: understanding how cognitive enhancing drugs work on glutamate receptors in the brain to improve cognitive function, and using a rat model to better understand what happens to the brain after a stroke.

Stroke is like a thief that comes in the night, but it steals life. From some of its victims, it takes almost everything, rendering them helpless. From others, it takes part of their memories or part of their ability to speak, walk, or talk. Stroke can signal its presence loudly with a sudden onset of symptoms or subtly with a soft passage through the brain. Each year, more than 600,000 Americans suffer a stroke. Of those, 165,000 die, making stroke the third-leading cause of death. Currently, there are about 4.6 million stroke survivors.

Proper treatment immediately following stroke can vastly improve outcomes for many patients, but loss of some brain function is almost certain for all patients. That is where Dr. Partin is hoping to make a difference. She and her research team are investigating drugs that may enhance cognition.

"We are specifically interested in enhancing neuron-to-neuron interaction," said Dr. Partin. "After a stroke, the brain has fewer neurons which express fewer glutamate receptor proteins.

Glutamate receptors are neurotransmitters essential for neuronal signaling."

Glutamate receptors are aqueous integral membrane proteins receptors. When the receptor is open, sodium rushes in and allows the cell to know that other cells are communicating. The quality of the information depends on the strength of the signal. If the receptor can be forced to stay open for a longer period of time, the quality of the signal will improve, enhancing cognitive function.

"We do have drugs now that bind to the glutamate receptor and make the pores stay open longer, but we don't understand how they work," said Dr. Partin. "One of the problems is that if we overstimulate glutamate receptors, the result can be seizures. We want to better understand these drugs and develop others so we can improve on their performance and improve the lives of stroke patients without creating additional health problems."

Dr. Partin said she and her research team work closely with drug companies; they provide the drug compounds, and the research team publishes their results. Currently, the CSU team is investigating four separate compounds – two are proprietary, and two are strictly for research purposes and won't be used for treatment. Most of the studies are done using a rat model to better understand what happens to the brain after stroke and how many glutamate receptors are functioning using controls or the drug compounds.

Dr. Partin is collaborating with Drs. Ed Dudek and Phil Williams in working with the animal model for stroke.

"Understanding the basics of the brain and the effect of stroke is reductionist science, and I find that really intriguing," said Dr. Partin. "It's part of the puzzle, me and nature, trying to figure it out. The other part is, can we make a better drug using molecular biology and animal models? My passion for this work is fueled by both the people aspect – developing a better drug – and the puzzle. I find that balance very fulfilling." ■

When It Comes to Males and Females, Hormones Make All the Difference

continued from page 9

"We look at how factors in the environment can negatively affect function – factors like alcohol, stress, and pesticides – and how different compounds, like 'designer steroids,' may be able to counter those negative factors. The work we do is excruciatingly meticulous, but working with the brain is never boring."

ductively associated," said Dr. Handa. "So we assume they must have some role in cognitive function, an association with stress responses, or they play any of a number of other roles. The importance here is that targeting these various receptors with 'designer steroids' (steroids designed to fit with specific receptors) may allow us to modulate specific functions – something like the affect we see when we give tamoxifen to women. A positive side effect is that the drug seems to help in cognition, targeting a receptor that we don't quite understand yet."

With so much going on in his laboratory, it would seem that Dr. Handa and his research team could use some of their own cognition enhancement to keep up with everything, but Dr. Handa wouldn't have it any other way.

"We are working in some really fascinating areas where what we learn could have a real impact on our understanding of steroid hormones and brain function," said Dr. Handa. "We look at how factors in the environment can negatively affect function – factors like alcohol, stress, and pesticides – and how different compounds, like 'designer steroids,' may be able to counter those negative factors. The work we do is excruciatingly meticulous, but working with the brain is never boring."

Dr. Handa is collaborating on some of his studies with Dr. Mel Anderson, in the Department of Environmental and Radiological Health Sciences, and Drs. Kathryn Partin and Ed Dudek, with the Department of Biomedical Sciences. His work is funded through the National Institutes of Health, the National Science Foundation, and the American Chemical Council. ■

Researcher Looks at Gene Therapy as Possible Treatment for HIV Infection

HIV and AIDS have quietly left the front pages of America's newspapers. The nightly news no longer features AIDS activists protesting for increased money for HIV research. Celebrities, eager to move on to the next crisis, have changed the color of their ever-present ribbons. You might think that the crisis is behind us. And you would be dead wrong.

It is true that incredible advances have been made over the past 15 years in HIV/AIDS prevention education, diagnosis, and treatment in the United States and other developed countries. For cultural and financial reasons, these strides have not been as impressive in Third World countries. But even in developed countries, HIV treatment is expensive, becomes less effective over time, and often has debilitating side effects. The fact is, HIV still leads to AIDS, and AIDS is still a fatal disease. Infection rates once again are increasing in the United States, while HIV infection on the sub-Saharan African continent has reached epidemic proportions.

Dr. Ramesh Akkina

So while the American public may have moved on to other health crises, researchers in laboratories across the nation and around the world continue their battle against a chameleon-like virus that always is changing its biological profile to evade capture and defeat. At Colorado State University, Dr. Ramesh Akkina and his research team are at the forefront of cutting-edge investigations that are looking at gene therapy as a possible long-term treatment for HIV infection. The goal is one day to help those infected with HIV to manage their disease in much the same way people with diabetes manage their illness – not yet a cure, but hope for a more normal life.

"Gene therapy has great potential to be an effective weapon in our HIV/AIDS arsenal," said Dr. Akkina. "Although we have made great strides in prolonging life with combination drug therapy, drug resistance remains a problem. Vaccination has long held the possibility of effective prevention, but to date we have yet to produce a viable vaccine. Both of these problems – drug resistance and ineffective vaccines – relate to the complex biology of this virus. It changes constantly in the body, making it very difficult to fight."

Dr. Akkina and his research team, with funding from the National Institutes of Health, are taking a different approach. With collaborators from the City of Hope research and medical center outside of Los Angeles, California, the researchers are looking to make the body's cells resistant to infection by the human immunodeficiency virus through genetic engineering. The idea does have a naturally occurring precedent. In the Caucasian population of European descent, approximately one percent of individuals have a slight genetic change that makes them resistant to HIV infection. They have a 32-base pair deletion in which the HIV co-receptor CCRV-5 is not present. Researchers discovered this anomaly when they found slower rates of infection in certain individuals within high-risk populations.

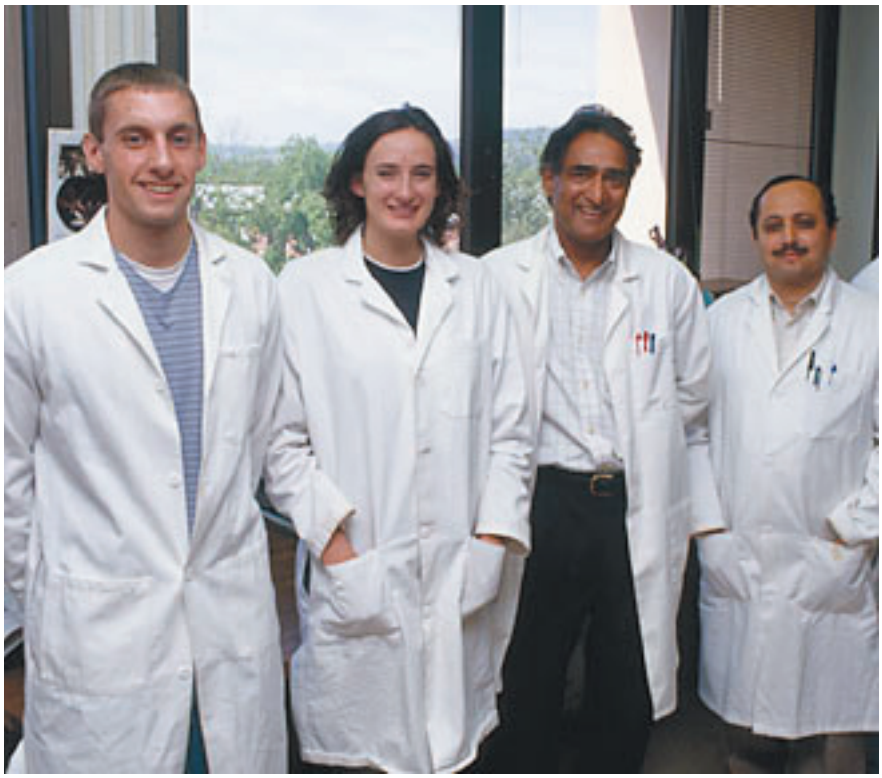
> Genetically engineered methods of fighting HIV/AIDS are most effective when used in stem cells, as stem cells are the factories that produce new cells including the all-important immune system players.

"In our particular approach, we are using genetic engineering to try to alter a cell's natural receptor mechanism," said Dr. Akkina. "Using specifically engineered virus vectors, we can deliver to the cell ribozymes that are designed to deactivate the host cell receptor for HIV. With this receptor disabled, HIV cannot latch onto or get into the cell, effectively blocking infection."

A second approach Dr. Akkina's laboratory is investigating involves using HIV to fight HIV. Using disabled HIV – all genes responsible for pathogenesis are removed, leaving behind genes respon-

sible for gaining access to the host cell – a designed ribozyme is introduced into the cell. That ribozyme destroys the HIV messenger RNA responsible for making the proteins necessary for HIV survival.

One of the challenges faced early on by researchers was that they were not able to retain large numbers of gene-modified cells in the long term. A new five-year grant is helping Dr. Akkina explore genetic engineering using stem cells. Genetically engineered methods of fighting HIV/AIDS are most effective when used in stem cells, as stem cells are the factories that produce new cells including the all-important immune system players. Both of the approaches currently under investigation in Dr. Akkina's laboratory use viruses to introduce DNA into the host cell. In vitro, both approaches are proving to be effective against HIV infection. In vivo trials have been underway using a special mouse model. In early HIV research, an animal model had been difficult to establish, as HIV only manifests itself in humans. Researchers, however, came up with a clever way around this dilemma. Using SCID-hu mice (severe combined immunodeficiency, and "hu" for human), researchers have been able to transplant human thymus tissue into the mouse surrogate, inject HIV, and create the disease in the transplanted human tissue. Because the mouse does not have the right receptors, HIV causes no disease in them.



Dr. Akkina and his team

"Both of these problems – drug resistance and ineffective vaccines – relate to the complex biology of this virus. It changes constantly in the body, making it very difficult to fight."

"CSU is one of the few places in the world where advanced technologies and the SCID-hu system come together to test anti-HIV candidates," said Dr. Akkina. "All of us working in this research are very hopeful that we will have something effective against HIV in the next five years. We are answering more and more questions about how the virus works and developing promising ways so that we can engineer cells to become resistant to infection."

Those answers cannot come quickly enough. At the end of 2001, the Joint United Nations Programme on HIV/AIDS reported 40 million people worldwide living with HIV/AIDS. In that same year, 3 million people died of AIDS, including 580,000 children. In the United States, the Centers for Disease Control reports 793,026 cumulative cases of HIV/AIDS, with almost half a million deaths since the disease first left its calling card in the early 1980s. The United Nations warns that this pandemic is devastating developing countries – where 95 percent of HIV/AIDS cases occur – and will continue to do so for generations to come. For those who thought the AIDS crisis was over, these numbers are a chilling reminder that we have a long way to go. ■

Keys to Unlocking Mysteries of Brain Found in Very Small Places

Almost every day at the office, Dr. John Rash is on the hunt. The territory he covers is vast, but you couldn't even begin to see it with the naked eye. He meticulously searches for his prey using a high-resolution transmission electron microscope, a steady hand, and a very patient mind. What he is finding is changing the very nature of human understanding of the brain and could one day help researchers better comprehend neuronal function and more effectively battle diseases of the brain such as epilepsy, Huntington's, schizophrenia, Parkinson's disease, and others.

"There is an infinite amount of work to be done to understand the brain," said Dr. Rash, who is a professor in the Department of Biomedical Sciences. "We just now have the tools we need to better understand what is happening on a subcellular level, and we are discovering things we have never seen before. What we are learning is challenging some of our most basic and accepted principles of neurobiology."

When Dr. Rash came to Colorado State in 1979, he found a laboratory ill-equipped to handle the research he was interested in pursuing. During a 10-year period, the laboratory went from an antiquated electron microscope to one of the most modern in the world. Using a technique called "freeze fracture," where cells are supercooled and split open, Dr. Rash and his research team were examining the signaling between neurons and looking at neurons and glia, the small cells that encircle and nourish neurons. During one of his forays through the electron microscope, Dr. Rash stumbled upon a gap junction, a type of signaling mechanism for neurons.

"It wasn't supposed to be there," Dr. Rash said. "Until 10 years ago, it was dogma that gap junctions don't occur between neurons in the mammalian brain. Lots of studies in goldfish showed how these gap junctions, primarily operating through electrical communication, are a valuable thing to have, but they hadn't been found in mammalian brains, and it was commonly accepted that they just weren't there except in a few 'primitive' regions."

Dr. John Rash

But they were, and Dr. Rash began an intensive search to find more. The discovery meant that the brain was operating in ways scientists didn't yet understand, but ways that could have a profound impact on potential treatments and cures for brain disorders. During a four-year period, through "sheer brute force," Dr. Rash found additional gap junctions, but the going was very slow.

"We didn't have a good way to mark the junctions, and searching for them was an excruciatingly slow process," said Dr. Rash. "Even though we are talking about areas that are measured in fractions of micrometers, when an area is under high magnification, we can only look at one square micrometer at a time in a field that is 4 million square micrometers large. Moving through these fields could take a lifetime. We needed a way to mark the gap junctions so that they would be easier to find."

Dr. Kazushi Fujimoto, a researcher from Japan, soon provided an important clue in developing the "search engine" that Dr. Rash was looking for – freeze-fracture replica immunogold labeling. In this technique, antibodies are coupled to gold beads to tag, quantify, and locate gap junctions. In addition to identifying gap junctions, immunogold labeling can be combined with a variety of antibodies to tag a variety of connexins – pathways through which cells communicate. Of 21 connexins, 10 now have been found to occur in the brain. Using the freeze-fracture replica immunogold labeling techniques, Dr. Rash and his team are

continued on page 16

During one of his forays through the electron microscope, Dr. Rash stumbled upon a gap junction, a type of signaling mechanism for neurons. "It wasn't supposed to be there. Until 10 years ago, it was dogma that gap junctions don't occur between neurons in the mammalian brain."

Research Holds Promise for Vaccine Development Against Parasitic Diseases

American military forces fighting in Afghanistan must be on constant guard against the foot soldiers of the Taliban and Al Qaeda. Unfortunately, these are not the only enemies they face. The tiny sand fly, endemic in Afghanistan, poses danger as well when it bites for a blood meal, sometimes transmitting the protozoan parasite *Leishmania* that the fly initially picks up from infected rodents.

Because of these sand flies, soldiers returning from Afghanistan may bring home more than wartime memories. Those unfortunate enough to contract leishmaniasis also may have scarring that forever will remind them of their time spent in that embattled country. But Dr. Richard Titus, a researcher at the College of Veterinary Medicine and Biomedical Sciences, is working to one day provide hope against leishmaniasis in the form of a vaccine.

Leishmaniasis is a parasitic disease spread by the bite of infected sand flies. The disease most often is found in tropical regions of South America and Africa, as well as the Middle East and southern Europe. There are several forms of leishmaniasis with the most common being cutaneous leishmaniasis, which causes skin sores that leave lifelong scarring. The number of new cases of cutaneous leishmaniasis each year in the world is thought to be about 1.5 million. In some cultures, the disfiguring scarring sometimes caused by the disease (often a result of inadequate treatment) can dramatically impact the lives of its victims – men are outcast from tribal groups and women are unable to marry. Two other types of the disease, visceral leishmaniasis (which affects some of the internal organs of the body) and mucosal leishmaniasis (which affects the linings of the nose and mouth) are less common but more dangerous.

Dr. Richard Titus

Leishmaniasis also is found in dogs, especially fox hounds that often live in close quarters and are somewhat aggressive. The sand fly is not the transmitter of disease in these cases, but rather the root causes are high levels of parasite in the skin and exchange of blood between fighting dogs. Recent outbreaks of leishmaniasis in Wisconsin and on the East Coast have highlighted the dangers of this disease to dogs.

Dogs also are the primary reservoir of infection to humans in more developed countries in South America and southern Europe, with the sand fly once again acting as intermediary. Outbreaks in these parts of the world are commonly controlled by destroying the local dog population. If researchers are able to develop and test a vaccine that will protect dogs, they will also be able to protect humans against infection from dogs and enhance the development of a human vaccine against leishmaniasis with the dog as a model.

Dr. Titus, a professor in the Department of Microbiology, Immunology, and Pathology, first became interested in leishmaniasis when he worked with the World Health Organization in Europe in the mid-1980s. In the 1950s, WHO had marked leishmaniasis for vaccine development, but like many other parasites, said Dr. Titus, *Leishmania* protozoans are very good at evading the immune response.

"We have taken a very different approach, an approach that several laboratories around the world are looking into to fight parasitic diseases such as leishmaniasis, malaria, and others," Dr. Titus said. "To date, we haven't been able to develop vaccines by directly attacking the organism, so we now are looking for a side door or a back door, some place else in the organism's life cycle that is vulnerable."

One very promising "door" Dr. Titus and his colleagues are attempting to pry open leads to saliva. When an infected sand fly bites, saliva is injected along with the parasite. The work Dr. Titus is doing, and the research of others, has shown than this saliva is extremely important to the establishment of the parasite in the host. The saliva contains proteins that prevent clotting, inhibit platelet aggregation, and actively dilate blood vessels. These proteins also prevent the induction of inflammation and inhibit the immune response of the host organism, giving the parasite time to multiply and establish an infection before

When an infected sand fly bites, saliva is injected along with the parasite. Mouse studies have shown that when the parasite is introduced without the saliva, the host mouse's immune system is able to ward off infection. When the parasite is introduced with the saliva, infection is practically guaranteed.

continued on page 16

Keys to Unlocking Mysteries of Brain Found in Very Small Places

continued from page 14

continuing to uncover which connexins go with which cell types in the brain and, in collaboration with scientists in Canada, are developing additional antibodies to further map out connexins in greater detail.

"I think the only thing holding us back right now is a lack of individuals who are trained in the techniques we use in the laboratory," Dr. Rash said. "The techniques we use here require many years of study and are time-and-labor intensive. But we hope shortly to expand our pool of graduate students who will be able to master these techniques and help us to move the work forward."

Dr. Rash and his research team recently received a boost from the National Institutes of Health to do just that. Now funded with three NIH investigator grants and one equipment grant, the laboratory will be expanding its staff and cranking up the rate at which it can further explore the realm of the human brain. For Dr. Rash, reinforcements can't come too soon.

"Having the right tools and the right people, we really can sort out the cast of characters in the brain," said Dr. Rash. "We'll be better able to figure out who is where, how many are there, and who they interact with. A clearer understanding of the most basic neuronal functioning will certainly bring us closer to clarifying normal brain behavior, while at the same time developing a better understanding of what might be going wrong when we see the brain functioning abnormally." ■

Research Holds Promise for Vaccine Development Against Parasitic Diseases

continued from page 15

the host can effectively respond. Mouse studies have shown that when the parasite is introduced without the saliva, the host mouse's immune system is able to ward off infection. When the parasite is introduced with the saliva, infection is practically guaranteed.

"We are working on identifying salivary proteins that will trigger an immune response to the proteins in sand fly saliva that are essential to establishing an infection by the *Leishamania* protozoan," Dr. Titus said. "Our results in mice have been very promising, and we would like to go on to clinical trials with dog populations."

"We are working on identifying salivary proteins that will trigger an immune response to the proteins in sand fly saliva that are essential to establishing an infection by the *Leishamania* protozoan. Our results in mice have been very promising, and we would like to go on to clinical trials with dog populations."

Dr. Titus foresees the development of a leishmaniasis vaccine "cocktail" that will contain agents to induce an immune response against proteins found in saliva, against the protozoan itself, and against the sand fly vector. Such a vaccination could prove very effective in the prevention of leishmaniasis in human and canine populations. Additionally, the vaccine could prove a valuable model for other parasitic diseases vectored by blood-feeding arthropods.

As a complement to the vaccine work, Dr. Titus' research laboratory also is examining the immune response to the *Leishmania* protozoan in mice. He works with two types of mice that have very different responses to infection by *Leishmania*. The white mouse, known as a BALB/c mouse, dies from the infection while the black mouse, C57BL/6, lives.

"This model is literally black-and-white, live-or-die," Dr. Titus said. "We have to ask ourselves, what is going on here? It's vital to first understand that the most important immune mechanism in response to infection is the induction of T-lymphocytes. A robust response means antibodies are produced and the infection can be dealt with. When challenged with *Leishmania*, the C57BL/6 mouse produces the TH1 cell with interferon gamma – these mice are able to kill the parasite. The BALB/c mouse, on the other hand, has a TH2 response, no interferon, and the parasite lives and divides quite happily in the macrophage cells. This is an extreme example, but provides us with a fantastic research tool for studying the immune response to this disease."

Dr. Titus has collaborated extensively with Dr. Jose Ribeiro of the National Institutes of Health and others in his leishmaniasis studies. His work is funded by the NIH. He hopes to procure additional funding to support a vaccine study in dogs, which one day may lead to a viable vaccine for both dogs and humans. ■

$6 Million In Gifts Fund Research Chairs in Cancer and Orthopaedics

Two gifts totaling $6 million will establish endowed chairs at two internationally known centers of veterinary and biomedical research at the College of Veterinary Medicine and Biomedical Sciences, the College recently announced.

A private gift of $3 million from Mrs. Barbara Cox Anthony will endow a chair with the Orthopaedic Research Center, and another $3 million from the James M. Cox, Jr. Foundation of Atlanta, Georgia, will establish a chair with the Robert H. and Mary G. Flint Animal Cancer Center.

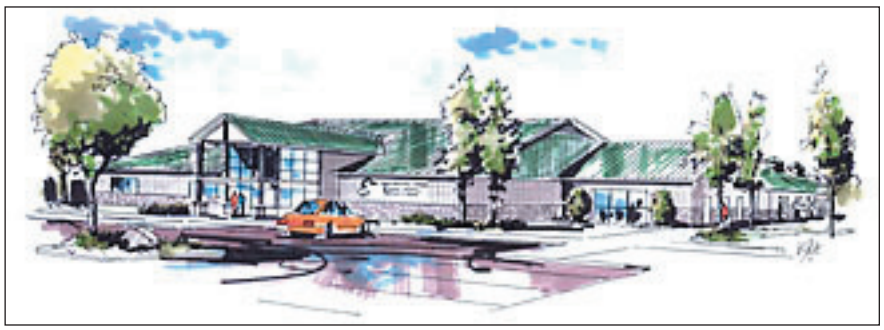
"This is an easy investment to make. The veterinary scientists who are engaged in the kind of research that will ultimately benefit both animal and human health are deserving of our support," said Mrs. Anthony, president of the James M. Cox, Jr. Foundation. "These are marvelous facilities conducting important and extraordinary work. The Orthopaedic Research Center and the Animal Cancer Center are engaged in scientific pursuits that are making a significant impact on the world of medicine."

Dr. Lance Perryman, dean of the College, said the generosity of Mrs. Anthony, and that of the James M. Cox, Jr. Foundation, will greatly enhance clinical, teaching, and research programs at the two centers.

"Without the private support of individuals such as Mrs. Anthony and foundations such as those dedicated to the memory of her brother, much of the work we do here simply would not be possible," said Dr. Perryman. "We are very proud of what we have been able to accomplish, but also realize the debt of gratitude we owe to pioneering people like Mrs. Anthony who have a vision for our future and see the possibilities that lie ahead. Working together, we can accomplish so much."

The Orthopaedic Research Center is dedicated to conducting research into the treatment and prevention of musculoskeletal problems occurring in equines and humans. During the past 17 years, research done by the orthopaedic research team at the College has not only benefited horses but also advanced human orthopaedic treatments. Current projects include using gene therapy to treat arthritis, defining fluid markers that predict orthopaedic disease, and using computer joint modeling to research fractures and prevention methods.

James L. Voss Veterinary Teaching Hospital



Orthopaedic Research Center

New facilities for the Orthopaedic Research Center, presently under construction, will house state-of-the-art surgery facilities, a visitor's center, a conference room with a view into surgery, administrative offices, and a high-speed treadmill. An attached equine care facility will house up to 32 horses and include paddocks and pastures for turnout. The Orthopaedic Laboratory, adjacent to the Center, now is being renovated. The new laboratory facility will include a biomechanics laboratory, a biomaterials and histology laboratory, a molecular biology/radiobiology room, and an image analysis room.

The Animal Cancer Center (ACC) is the second beneficiary of the recently endowed chairs. Since the 1960s, ACC researchers and veterinarians have conducted innovative cancer research and provided state-of-the-art treatment for companion animals, moving from research that identified the types of cancers affecting pets to the prevention, diagnosis, and treatment of cancer in animals.

The pioneering work done by the staff of the Robert H. and Mary G. Flint Animal Cancer Center at Colorado State has led to important advances in the treatment of human cancers, including the use of dietary supplements that support cancer treatments and the improved and refined use of surgery, chemotherapy, and radiation therapy for pets.

Soon to be housed in a new wing of the James L. Voss Veterinary Teaching Hospital, the Animal Cancer Center will include examination rooms, state-of-the-art research laboratories, a special multipurpose training and lecture room, tumor tissue processing and archiving, magnetic resonance imaging, and nuclear medicine capabilities. ■

New Departments in Place at College

As the College nears the end of its two-year reorganization effort, four new departments have taken shape and now are officially operational. The new departments are Biomedical Sciences, Clinical Sciences, Environmental and Radiological Health Sciences, and Microbiology, Immunology, and Pathology. The new departmental structure represents a merging of the seven former departments into streamlined organizations that provide a better fit for the College's current mission and future growth plans.

"Like any major change, this has been a long and difficult process, but I think that the College is better for it," said Dr. Lance Perryman, dean of the College. "The departments have a renewed sense of energy, and we will be better able to operate in today's research and academic environment."

The College's final structure is the result of an intensive process involving extensive input from faculty and staff members. Dr. Perryman said Joe Schwarz, the College's human resource officer, deserves much of the credit for helping the College make its way successfully through the reorganization.

"Joe worked extensively with each department in reorganizing its structure and re-allocating human resources to best fit each department's mission," said Dr. Perryman. "This was a huge undertaking, and Joe took it on with grace and the desire to get the job done right."

The scope of each of the departments is defined below.

The new departmental structure represents a merging of the seven former departments into streamlined organizations that provide a better fit for the College's current mission and future growth plans.

The **Department of Biomedical Sciences** houses many of the College's basic sciences programs including anatomy, neurobiology, and physiology.

The **Department of Biomedical Sciences** houses many of the College's basic sciences programs including anatomy, neurobiology, and physiology. The department provides a substantial portion of the first two years of the Professional Veterinary Medical Program curriculum as well as offering a full complement of graduate degrees. Undergraduate and graduate course work in the biomedical sciences offers students a comprehensive education to support further academic or career aspirations.

The department houses many of the College's premier research centers. These include the Animal Reproduction and Biotechnology Laboratory and the Program in Molecular, Cellular, and Integrative Neurosciences. Both of these are among the 14 University Programs of Research and Scholarly Excellence. The Department also participates in the Cell and Molecular Biology Program, the Electron Microscopy Center, and the Hypo-Hyperbaric Chamber Facility.

Faculty and students in the Department of Biomedical Sciences are involved in a wide range of research programs including nervous system disorders, neural communication, neural and muscular development and regeneration, genetic engineering of animals and microbes, numerous facets of fertility and reproductive health in humans and animals, and pulmonary hypertension and high altitude studies. The interim department head is Dr. C.W. Miller.

The **Department of Clinical Sciences** is the applied veterinary medical arm of the College and boasts a variety of unique research centers and service units.

The **Department of Clinical Sciences** is the applied veterinary medical arm of the College. Located at the James L. Voss Veterinary Teaching Hospital, the department provides most of the final two years of the Professional Veterinary Medical Program curriculum, clinical residency programs, and graduate programs targeted toward students with degrees in veterinary medicine.

The department is heavily involved in patient care at the James L. Voss Veterinary Teaching Hospital, as this is a fundamental part of the Professional Veterinary Medical Program. The department also has an extensive research program, focusing primarily on improving the diagnosis and treatment of animal disease. Numerous research projects within the department also benefit human medicine, garnering extensive support from the National Institutes of Health.

The Department of Clinical Sciences boasts a variety of unique research centers and service units. These include the internationally acclaimed Robert H. and Mary G. Flint Animal Cancer Center (a University Program of Research

and Scholarly Excellence), Center for Veterinary Epidemiology and Animal Disease Surveillance Systems, Equine Teaching and Research Center, Integrated Livestock Management Program, Medical Oncology Research Laboratory, and the Orthopaedic Research Center. The department also is breaking new ground with the inclusion of human-animal bond studies in the veterinary curriculum through the Argus Institute for Families and Veterinary Medicine. These programs also provide support and services to faculty, students, and hospital clients. Additionally, the department houses one of the nation's few complementary veterinary medical treatment and study centers, the Charles R. Shipley, Jr. and Lucia H. Shipley Center for Complementary Medicine and Natural Healing. Dr. Anthony Knight is the department head.

The **Department of Environmental and Radiological Health Sciences** offers a wide spectrum of undergraduate and graduate opportunities, as well as providing a prime environment for research.

The **Department of Environmental and Radiological Health Sciences** offers a wide spectrum of undergraduate and graduate opportunities, as well as providing a prime environment for research. The two complementary facets of the department allow for an exchange of innovative ideas to create vibrant programs that address pressing needs in environmental health and advance research in radiology.

The department is home to two University Programs of Research and Scholarly Excellence: the Radiological Health Sciences and Cancer Research Program and the Center for Environmental Toxicology and Technology. Other research and service units include the Colorado Injury Control Research Center, Environmental Health Advanced Systems Laboratory, High Plains Intermountain Center for Agricultural Health and Safety, Institute for Rural Environmental Health, and OSHA Consultation Program.

The environmental health component of the department focuses on the study of potential human health impacts due to interactions between people and their environments. Students are prepared for careers in areas such as solid and hazardous waste management, disease prevention, and air and water quality management. Students often choose to continue their education, pursuing postgraduate degrees that allow them to specialize further. The radiological health section of the department offers graduate degrees in radiological health sciences and works closely with the Department of Clinical Sciences to research the role radiation plays in abnormal cellular development. The department also provides postgraduate and specialty certification in veterinary radiology and radiation oncology. Dr. John Reif is the acting department head.

The **Department of Microbiology, Immunology, and Pathology** is home to vibrant undergraduate and graduate education programs as well as some of the finest biomedical research centers in the nation. Graduate training in pathobiology, biomedical research, microbiology, and immunology are major missions of the department.

The **Department of Microbiology, Immunology, and Pathology** is home to vibrant undergraduate and graduate education programs as well as some of the finest biomedical research centers in the nation. Undergraduates have unequaled opportunities to work in research laboratories and contribute to some of the most important work in infectious diseases being done anywhere in the world.

Located within the department is the Program of Research and Scholarly Excellence in Infectious Diseases. This program encompasses several world-class research facilities whose laboratories focus on diseases caused by arthropod-borne viruses, mycobacteria, retroviruses, prions, and parasites, including those that cause malaria. Graduate training in pathobiology, biomedical research, microbiology, and immunology are major missions of the department. The department also provides postgraduate training and preparation for specialty certification in veterinary microbiology, anatomic pathology, and clinical pathology.

The department's highly active undergraduate program provides faculty mentors for undergraduate students and puts high value on placing students in faculty laboratories, where classroom lessons are translated into research practices. Many of the department's students go on to pursue postgraduate education or apply to veterinary or medical school. The comprehensive curriculum prepares students for a wide variety of careers in industry, government, or academic research settings. Dr. Steve Benjamin is the acting head of the Department of Microbiology, Immunology, and Pathology. ■

College Research Programs Garner Benefits of New University Funding

Two innovative College research programs are the beneficiaries of a new research fund at Colorado State University that provides grants to help turn specific University programs into world-class research centers.

Earlier this year, the Academic Enrichment Program (AEP) funded nine proposals from throughout the University for a total of $4.15 million. Within the College, two programs were funded. The two grants, valued collectively at $2.17 million, will support the development of a research program in genomics and proteomics – particularly in the purchase of technical equipment – and assist in infrastructure renovation and improvement of laboratories in the basic sciences.

"The AEP represents a pool of $32 million that President Albert Yates felt offered a once-in-a-lifetime opportunity to build the institution and create additional world-class programs. He felt very strongly that this money should be invested to build the University's future," said Dr. Tony Frank, the University's vice president for research.

Dr. Frank said the fund will award approximately $7 million in research grants each year for the next five years. In general, the fund is being used for proposals that are no less than $100,000. Dr. Lance Perryman, dean of the College of Veterinary Medicine and Biomedical Sciences, said the AEP will provide a much-needed boost to programs that are ready to explode in growth and development but need funding to light the fuse.

"This is truly a case of making an investment in the future of the University and the College," said Dr. Perryman. "Genomics and proteomics are two of the most exciting and innovative areas of research, and the College is poised to take its place in these two new fields. The AEP provides us with the seed funding to get these programs off the ground. Additionally, funding for infrastructure renovation and facilities upgrades in our laboratories will support our innovative work in the biomedical sciences and allow us the opportunity to compete more effectively in terms of research, education, and outreach." ■

NONPROFIT
ORGANIZATION
U.S. POSTAGE
PAID
Fort Collins, Colorado 80523
Permit Number 19

College of Veterinary Medicine and Biomedical Sciences
1601 Campus Delivery
Fort Collins, Colorado 80523-1601

Colorado State University