



BAKER INSTITUTE FOR ANIMAL HEALTH

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Profiles

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To Improve **Animal Health**
Through Basic and Applied Research

64 YEARS OF
ideas
INTO **action** 

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A Message from the Director

Dear Friends,

It is my pleasure to update you on the exciting and innovative work going on at the Baker Institute for Animal Health in this, our 64th year. This past year, we have continued to focus on conducting groundbreaking research and transforming our discoveries into actions that improve the well-being of animals and the people who care for them.

The Institute has had a busy year. We have logged significant scientific achievements, expanded the ranks of our faculty, collaborated with researchers here at Cornell University and around the world, and strengthened our commitment to excellent teaching. We have also continued to expand upon our historical expertise in the study of immunology and the viruses that cause disease in animals and people. This work promises to not only improve our ability to diagnose, treat, and prevent infectious diseases, but it is also providing profound new insights into cancer and inflammatory diseases in animals and humans. Cancer and inflammatory diseases often arise as a result of the interplay between disease-causing pathogens and the host immune system, a complex exchange that many of our faculty members are focused on teasing apart. By understanding these relationships, both in health and in disease, we expect to unearth clues to preventing and treating these types of diseases in the future. None of this outstanding work could be done without the loyal support of you, our donors, and we are grateful for your support and encouragement as we work in partnership to achieve our goals.

Along with updates on current research activities, we celebrate several other notable events and facets of the Institute in this year's report, including the lifetime achievements of Dr. Leland "Skip" Carmichael, recipient of the Arthur F. North Jr. Canine Service Award, the accomplishments of our trainees, the dedication of two of our long-term staff, and the appointment of two new members to our Advisory Council. This has been an exciting year at the Baker Institute for Animal Health, to be surpassed only by the promise that our current faculty, students, and staff hold for the future benefit of animals and those who love them.

Once again, thank you most sincerely for your continued support, without which we could not continue to do what we do.

Best regards,



Colin R. Parrish, PhD
Director, Baker Institute for Animal Health



FACULTY PROFILES

Douglas F. Antczak, VMD, PhD | *Dorothy Havemeyer McConville Professor of Equine Medicine*

Dr. Doug Antczak's research program is focused on the health of horses, a passion of his from an early age. Through the Baker Institute's Equine Genetics Center, the Antczak laboratory group has a long history of advancing basic knowledge and applying that knowledge in equine genetics, immunology, and reproduction.

To support the Institute's studies of pregnancy immunology in the horse, Antczak has developed a unique herd of horses that all share similar immune system genetics, a commonality that makes them useful for a wide variety of investigations. Antczak's genetic selection and breeding of horses has led to his continuing involvement in the international Horse Genome Project. Horses from the Institute's experimental herd include the Thoroughbred stallion Bravo, the DNA donor for the equine Bacterial Artificial Chromosome library, and Twilight, the Thoroughbred mare whose DNA was the source for the horse genome sequence.

In another project, Antczak is working with equine herpesvirus type 1 (EHV-1), a highly infectious pathogen that causes

respiratory infections, abortions, and severe neurologic disease. Together with Dr. Klaus Osterrieder of the Free University of Berlin and Dr. Becky Tallmadge of the Department of Clinical Sciences at Cornell, Antczak is trying to determine how the virus interacts with the immune system to gain entry into horse cells. Using advanced techniques in cell and molecular biology, Antczak's team has been able to identify which molecules enable the virus to enter the cell and to discern how efficient they are compared with other receptors that allow the virus to enter. These distinctions, which are based in genetics, can help determine why some animals and some humans are more susceptible to herpesvirus infections than others, and can point the way to preventive therapies to keep herpesvirus from grasping these receptors, entering the cell, and making an animal or human sick.

Although most of the animals Antczak works with are close to campus in Ithaca, New York, some of the animals he studies are on the other side of the planet, in Qatar. The Dromedary camel, together with the Arabian horse and the Arabian oryx, represent three iconic mammals of the Arabian Peninsula, and

Judith A. Appleton, PhD | *Alfred H. Caspary Professor of Immunology*

As long as there have been animals, there have also been parasites. Dr. Judy Appleton's research focuses on exploring parasitic diseases of animals, including the ways in which the body fights (or fails to fight) infection with the worm *Trichinella spiralis* and the immune response to the "brainworm", *Parelaphostrongylus tenuis*. Appleton's work to understand the basic facts about these infections could eventually lead to methods for treating or preventing these infections.





with support from the Qatar National Research Foundation, Antczak's lab is sequencing and exploring the genomes of these three species. By gauging the diversity of these genomes within species and identifying commonalities between different species, Antczak hopes to identify genomic regions that contain novel pathways for survival in an arid environment and gain insights into how these species might survive in a future in which climate change further diminishes water resources on the Arabian Peninsula.

The immune response to *T. spiralis* has been a special focus of Appleton's work. Long recognized as the foodborne cause of trichinellosis, *T. spiralis* is found in pigs, rodents, and other animals. Trichinellosis infection rates are waning in developed countries, but the parasite remains common in impoverished communities and in places where uncooked meat or home-smoked sausages are consumed. For many years, scientists who studied *T. spiralis* thought that the body defended itself by sending an army of eosinophils (white blood cells) to an infection site to fend it off. However, by using a strain of mice that lack eosinophils, Appleton and her colleagues have shown that this is not the case, that eosinophils actually help the parasite in certain ways. At the beginning of an infection, eosinophils prevent an animal's own tissues from producing toxic nitric oxide that would otherwise kill off the parasite. They also help the parasite to grow by another mechanism that has yet to be elucidated. The discovery that eosinophils don't always defend the body against *T. spiralis* has prompted researchers to reexamine their assumptions about interactions between eosinophils and other types of parasites, and it could lead to more effective treatments for *T. spiralis* infections.

Another worm under the lens in the Appleton lab, *P. tenuis*, has a complicated life cycle and poses a difficult problem for farmers in the Eastern half of the United States. The worm is carried by white-tailed deer that shed the larvae in the environment where they may be picked up by terrestrial snails. Inside the snail, larvae develop into their infectious form, then leave the snail and cling to vegetation where they can be picked up by horses, cattle, sheep, alpacas, or llamas. The spread of the worm from deer makes the parasite very difficult to control in a farm setting, so livestock farmers are seeking a vaccine that can protect herds from infection. However, it's unknown what sort of immune reaction these livestock species can mount naturally against the worm, making it difficult or impossible to design a vaccine to augment that response. Together with a collaborator, Dr. Michael Thonney, Appleton's lab is working to define the immune response to *P. tenuis* in sheep and determine whether being infected with the parasite once offers immune protection if an animal encounters the parasite again in the future. If so, vaccines might well offer some promise for controlling this difficult parasite.

Scott Coonrod, PhD | *Judy Wilpon Associate Professor of Cancer Biology*



Cancer is the out of control growth of abnormal cells in the body, and it is known to strike almost every species of animal, including dogs, cats, horses, and, of course, humans. The current focus in Dr. Scott Coonrod's lab is breast cancer, referred to as mammary cancer in animals. Coonrod, who is the Judy Wilpon Associate Professor of Cancer Biology, is searching for ways to stop breast cancer cells from developing by specifically turning off genes in the cancer cells that are required for cell growth.

Charles Danko, PhD | *Assistant Professor of Biomedical Sciences*

Genes are the basic blueprints for all living things, but how are those blueprints interpreted and turned into living, breathing organisms? That's the question our newest faculty member, Dr. Charles Danko, pursues in his work. Although the DNA tucked inside every cell provides a neat code for that cell to read and translate into RNA (ribonucleic acid) and proteins, the way those blueprint instructions are put into action often decides the difference between health and disease. In his studies, Danko is looking beyond simple linear sequences of genes and into the complex ways cells turn those instructions into action, through a process called gene regulation.

Breast cancer is one disease where gene regulation plays a big role, and it strikes humans as well as dogs and cats at alarming rates. In humans, roughly 75 percent of breast cancer cases are estrogen receptor-positive, meaning that the gene encoding the estrogen receptor alpha is "turned on" in those cells, a trait that may well be key to their ability to multiply almost endlessly. Danko is working to develop ways of analyzing the genome of breast cancer cells to quickly determine which genes are activated and therefore which drugs might be the

best choices for treating that individual cancer patient. The current methods for accomplishing this analysis are laborious and require ten or more assays to accomplish. Danko thinks with a single assay and computational technologies that he's developing for finding patterns in the data, he can accomplish the same goal quickly and efficiently. The work has the potential to help many animals and humans suffering from cancer of the breast and other tissues.

A heart disease called arrhythmogenic right ventricular cardiomyopathy (ARVC) strikes in both humans and in purebred boxers, a coincidence that could eventually help both humans and dogs overcome the condition. Danko is mapping the genome of affected and unaffected dogs to identify the genes responsible for ARVC and to unearth how those genes cause the disease to develop. Knowing the genetic basis of the disease will help breeders eliminate it from breeding lines and could eventually help develop drugs to treat the ARVC in humans.

From skin cells to bone cells to blood cells, the cells in the body can be wildly different but they all share the same genetics.

The genes encoded on a strand of DNA represent blueprints for how to make the myriad proteins a cell needs. If stretched out from end to end, the DNA from a single human or animal cell would stretch two meters long, so the cell keeps DNA organized and compacted by wrapping it around a series of hockey puck-shaped proteins called histones, forming a strand of chromatin that resembles a string of beads. Epigenetic modifications to the puck-shaped histones or to the genes themselves mark the genes according to how much that particular protein will be needed to keep the cell functioning properly, targeting the gene/protein for greater or lesser production as necessary. In cancerous cells these signals are flawed, leading to out of control cell growth and putting the animal's life at risk.

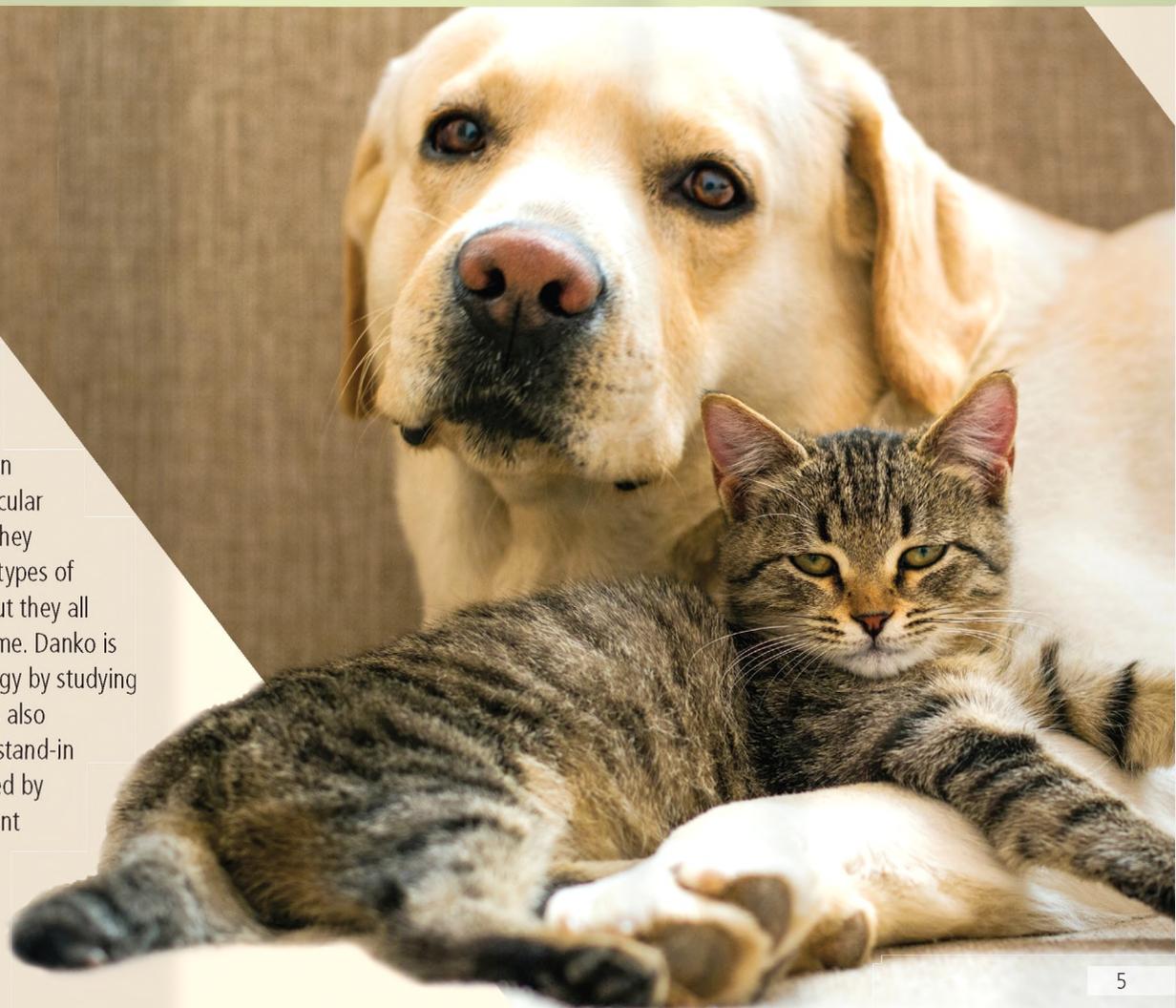
The Coonrod lab is currently focused on a small family of enzymes called PAD that apply these signals, or "marks", to histones. Coonrod recently found that one member of the PAD family, PAD2, makes histone modifications that impact the expression of genes that are regulated by the estrogen receptor. Increased estrogen receptor activity is thought to cause up to 75 percent of all breast cancers and is, therefore, a major target for breast cancer therapies. The Coonrod lab found that PAD2 marks histones at estrogen receptor binding sites and that this novel mark appears to be required for

estrogen receptor binding and target gene activation. Hence, the ability of the estrogen receptor to bind to genes where PAD2 makes its mark on the histones is an important factor that may promote breast cancer progression.

Coonrod has found that blocking PAD2 and the epigenetic changes it makes prevents the estrogen receptor from binding to the relevant genes and prevents estrogen receptor-positive breast cancer cells from dividing. This makes PAD2 a very promising target for treating breast cancer, so Coonrod and his lab are investigating ways to stop the spread of cancer by shutting down PAD2.

Coonrod's work has the potential to uncover some powerful new ways for treating breast cancer – and preventing its return. Breast cancer survivors today who are at high risk for recurrence are administered the drug tamoxifen for years following their diagnosis and treatment, but most women become resistant to this therapy within five years. PAD2 inhibitors could represent a potent new therapy for those who are no longer responsive to tamoxifen therapy. Given that most cases of mammary cancer in dogs are estrogen receptor-positive, Coonrod hopes that, once developed, PAD2 inhibitors will also represent a new therapeutic option for canine mammary cancer.

Danko is also interested in the ways that cells accomplish these differences through gene regulation. He's collaborating with Dr. Avery August of the College of Veterinary Medicine on a project to study T-cells, a particular kind of immune system cell. As they mature, T-cells acquire different types of abilities and roles in the body, but they all maintain exactly the same genome. Danko is hoping to learn about immunology by studying this maturation process, but he's also thinking about the process as a stand-in for how development is controlled by gene regulation, creating apparent diversity from cells that are genetically identical.



Vicki Meyers-Wallen, VMD, PhD, DACT | *Associate Professor of Genetics and Reproduction*

Dr. Vicki Meyers-Wallen is working to identify the genetic causes behind inherited disorders of sexual development, or DSDs, conditions that impair the normal development of reproductive organs in animals and humans alike. Inherited disorders of dogs have long plagued dog breeding because, in many cases, it is difficult to tell which dogs carry the mutations related to the condition and which do not, an ambiguity that enables the mutation to continue to be passed down through the generations.

This ambiguity is true of the particular form of DSD that Meyers-Wallen is currently studying, "XX DSD", which causes infertility (impaired ability to reproduce) and sterility (the incapacity to reproduce) in 28 breeds of purebred dogs. And like other inherited conditions, XX DSD can't be eliminated from a population unless all the dogs that carry the mutations for the condition are identified and are prevented from reproducing and carrying the condition to the next generation. Similar conditions also occur in humans, but the genetics and the mode of inheritance of these conditions are often difficult or impossible to tease apart.

Dogs that are affected with XX DSD have normal female chromosomes but instead of developing ovaries, they develop testicles or combination ovary-testes called ovotestes, which produce testosterone and promote male features in the remainder of internal and external genitalia. Genetically speaking, these dogs are female because they have two X chromosomes, but since they have some features of male external genitals, they can appear to be males or females. Early investigations of the disorder focused on a gene called SRY, which is responsible for initiating male sex determination in humans, but Meyers-Wallen's lab put that possibility to rest by showing that SRY isn't present in XX DSD-affected dogs.

In order to determine the real cause, Meyers-Wallen is applying whole genome sequencing, computational tools, and careful analysis to solve the riddle of XX DSD. The search has been narrowed down to a small region in the genome where affected dogs differ from dogs who definitely do not carry the mutation for the disorder. Further testing lies ahead to determine which mutation is responsible for testes development in XX DSD dogs.

John S. L. Parker, BVMS, PhD | *Associate Professor of Virology*



Once Meyers-Wallen has identified the mutation responsible for XX DSD, a test can be developed to identify dogs that carry the mutation. Determining the genetic cause of XX DSD would not only help dogs. A better understanding of the normal pathways of sexual development may also help humans by pointing the way to genetic tests that can help families with a history of these disorders of sexual development make family planning decisions.



Dr. John Parker studies viruses and the ways in which animals respond to viral infection, laying the basic science groundwork for ways to improve disease diagnosis, treatment, and prevention. His lab is focused on viruses that infect humans and animals, including feline calicivirus, and the results of his projects can be broadly applied to benefit the health of both animals and humans.

The Parker lab is studying the ways feline calicivirus escapes attack by the immune system. Feline calicivirus often causes upper respiratory tract infections – commonly called “cat flu” – but more virulent strains of the virus can cause severe pneumonia, liver necrosis, pancreatitis, and other complications. Infection with these more virulent strains is fatal for 50-60 percent of cats. Parker and his colleagues are investigating the differences between the less virulent and highly virulent strains of calicivirus that might explain these varying effects. The results of these studies can help cats, but they will also hold lessons for human disease. Feline calicivirus is closely related to human norovirus, a virus notorious for causing widespread outbreaks of gastrointestinal illness. Since norovirus is difficult to study in the lab, much about this common human pathogen remains a mystery. Studies of feline calicivirus strains and the ability of the host to neutralize

these viruses can offer valuable insights that not only save cats, but may also help guide efforts to bolster the human immune response to norovirus.

Pathogenic viruses like calicivirus and norovirus cause incredible mortality and suffering among animals and humans, powerful effects that belie their relative smallness and genetic limitations. Recent studies show that another pathogen, cytomegalovirus, produces more protein products than would be predicted from the small number of genes it possesses, a finding that helps to explain how the virus is capable of achieving a great complexity of interactions and effects from seemingly meager genetic tools. Parker’s lab is tallying the protein products of such viruses as herpes simplex virus, influenza, and reovirus during infection to determine whether this phenomenon applies to other kinds of viruses. Aside from the interest to basic biology, the results will also help to identify whether there are a core set of proteins that all viruses employ during infection, a sort of common arsenal shared among viruses of many types. If so, those proteins might be used as an indicator to diagnose viral infections of many kinds, even infections caused by emerging viruses that haven’t been thoroughly characterized in the lab, an increasingly common public health concern.

Colin R. Parrish, PhD | *John M. Olin Professor of Virology*

Certain viruses have a troubling habit of moving from one species of animal into another. Dr. Colin Parrish's lab is working on understanding the principles behind how these viruses manage the jump and emerge to cause epidemics in new hosts. His current projects explore the evolution of canine parvovirus and control measures that might one day eradicate canine influenza, efforts with the potential for a significant impact on the health of dogs, cats, horses, and wildlife.

Canine parvovirus first appeared in 1978 in a global pandemic that killed dogs by the hundreds of thousands. Although it's related to feline panleukopenia virus, which is specific to cats, canine parvovirus now appears to infect most carnivores worldwide (members of the Order Carnivora), including carnivores native to North America, many of which are critically endangered. Genetic evidence indicates it all started when a single feline panleukopenia virus mutated and gained the ability to attach to receptors on the cells of dogs. Parrish and his colleagues are studying how the virus has evolved since 1978, tracking the spread of new variants of the virus and the ways they differ from their predecessors. This natural variation

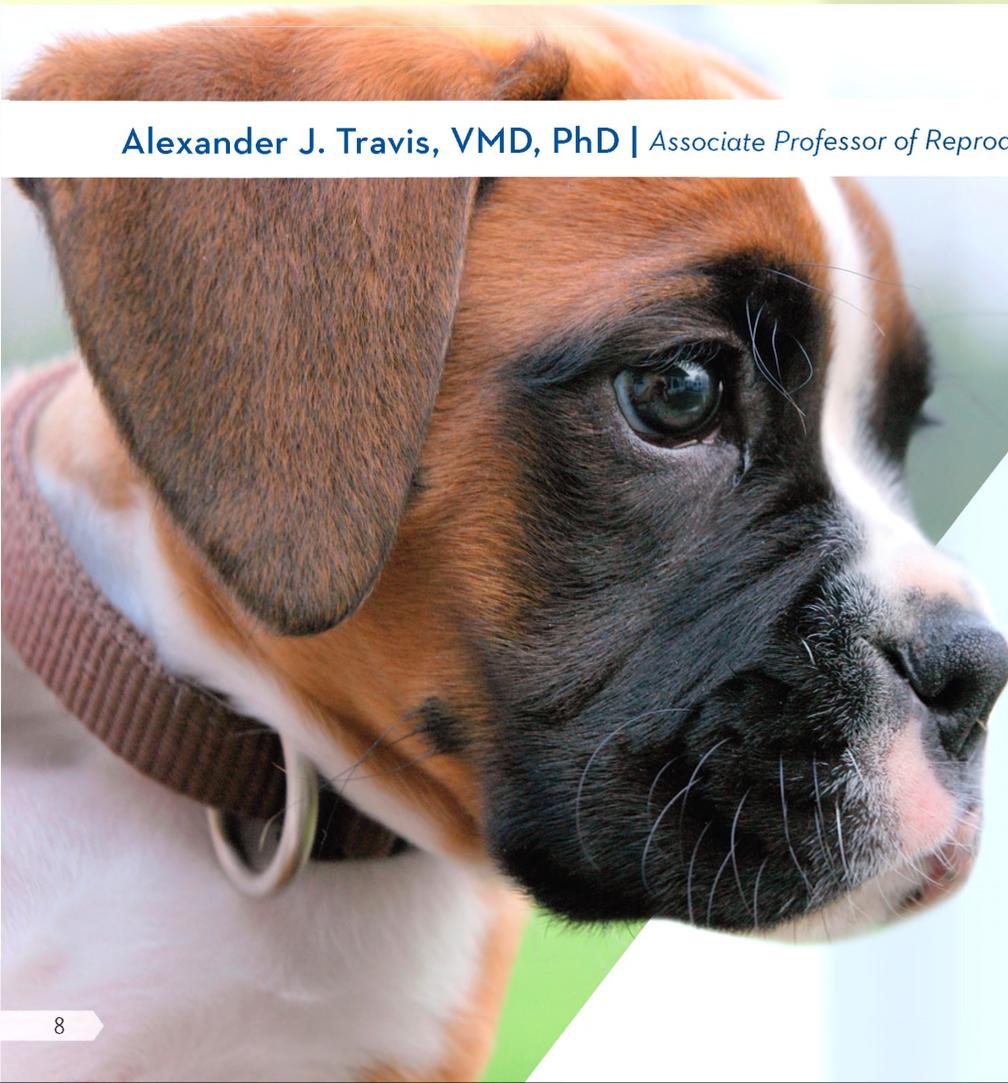
in the virus over time could make problems for vaccination efforts, so they're also taking a close look at the structure of the viral surface and how the virus attaches to host antibodies and to the receptors on the surface of dog cells. This will allow them to determine whether the vaccine for parvovirus is still a good match for the strains that are in circulation, and if the vaccine and the virus are mismatched, it may be time to update the parvovirus vaccine.

Influenza is one virus that's particularly well-known for crossing between different species. Parrish's lab is studying H3N8, a flu strain that jumped from horses into dogs in 1999 and led to a widespread outbreak in the following few years, but today seems to be maintained only in dogs at a handful of large animal shelters. It's not well understood why, after 14 years of continuous circulation, "dog flu" hasn't spread widely among the general dog population. Parrish and his colleagues are studying the genome of the virus and modeling the rate at which it moves from dog to dog to determine why H3N8 has died out in many locations and how control measures might be used to further limit spread. Their early results show the virus is

Alexander J. Travis, VMD, PhD | *Associate Professor of Reproductive Biology*

Dr. Alex Travis's lab explores a diverse set of subjects, ranging from technologies based on the very smallest biological machines to inquiries in wildlife conservation and sustainability at the landscape scale. Much of Travis's work stems from his studies of reproduction and the function and preservation of sperm.

In one recent success in assisted reproduction, the Travis lab was the first group in the Western Hemisphere to successfully perform embryo transfer using a frozen dog embryo. They also claim the title of first to successfully perform spermatogonial stem cell transplantation in a dog, a procedure in which the sperm-making stem cells from the testes of one dog are transferred into another dog. After the procedure, the recipient dog is capable of



not very transmissible, and that to maintain disease in a population each infected dog would have to have contact with two or three other dogs during the short period when the animal sheds significant numbers of viruses. These results indicate that control measures should be possible to eradicate dog flu, an accomplishment that would represent a rare achievement in animal health.



creating sperm that carry the donor dog's genetic material. By trying new techniques for assisting reproduction in dogs, Travis and his colleagues expect to learn more about how these approaches might be used to aid reproduction in humans and in non-domesticated species that are closer to extinction, including rare wolf species (See PhD student Jennifer Nagashima's profile on page 19).

In other work related to reproduction, the Travis lab is putting sperm tails to work in tiny nanodevices. Building on their past studies of sperm's energy-making enzymes, Travis and his colleagues are working to mimic the way these enzymes are organized in the tail (flagellum), to create enzyme machines powered by sugar. These tiny powerhouses could eventually be integrated into implanted hybrid biological/mechanical medical devices, where they would run on the sugars available in the body. Although those applications sound like science fiction, there are also more immediate uses for these tethered enzymes. For example, the Travis lab is exploring how enzymes attached to nanoparticles could be used as the basis for hand-held devices that could diagnose strokes or traumatic brain injuries.

Travis's interest in biology extends beyond cell and molecular studies into wildlife and landscape-scale approaches to conservation, work that calls on his veterinary training. As the Faculty Director for the Environment at Cornell's Atkinson Center for a Sustainable Future and the Director of the Cornell Center for Wildlife Conservation, Dr. Travis collaborates with researchers from around Cornell and the world to study large-scale interventions aimed at conserving wildlife and fighting human poverty and hunger by promoting sustainable agriculture and natural resource management. In one ongoing project, Dr. Travis's lab is collaborating with the non-profit business COMACO to develop egg layer facilities in remote rural communities in Zambia that will make chicken eggs more available in an area with persistent poverty and hunger. Over 50 percent of the children in this area show signs of chronic malnourishment and families have historically relied on bushmeat when they did not have enough food. One of Travis's students is currently measuring the impacts that local egg production might have on the health and nutrition of mothers and children, while simultaneously relieving pressure on wildlife.

Dr. Gerlinde Van de Walle focuses her studies on three general areas: how herpesviruses cause disease in dogs and cats, the causes of breast cancer in animals, and how stem cells might be used to treat injuries in horses. All of these studies in companion animals can also help to improve human health, and in each of these projects, Van de Walle relies on model systems that represent the fundamental facts about a disease or condition, but that lack unnecessary complexities.

To study infections with canine and feline herpesvirus (CHV and FHV), Van de Walle is developing a cornea model of infection that relies on donated tissues from dogs and cats that have died from unrelated causes, allowing her to study the eye disease in detail in the lab and try new ways of controlling these herpes infections. Many of the viruses that infect dogs and cats are closely related to viruses of humans, so studies of dog and cat viruses can benefit the health of both species. CHV and FHV are a case in point. Although they cause deadly infections in newborn animals and serious eye disease in older animals, they are alphaherpes viruses just like the one that causes cold sores in humans, so understanding

how CHV and FHV infect dog and cat tissues can lead to a better understanding of human disease and potentially to new antiviral therapies.

To model breast cancer in the lab, Van de Walle uses breast stem cells taken from dogs and horses to study the ways tumors develop – or don't develop. Although dogs and cats are quite susceptible to breast cancer, the condition is incredibly rare in horses, sheep, and cows, so the differences in their breast tissues may reveal new ways of preventing or controlling cancer. Mammary stem cells may hold the key: as the cells that create new breast tissue, many scientists now suspect they are also the source of breast tumors. Van de Walle has grown these stem cells in the lab to compare how dog cells and horse cells differ, and the study has revealed that differences in the substances these cells release may well affect tumor formation. Future work will look more closely at these substances to identify specific factors that suppress tumor formation in horses.

BICKNESE PRIZE

Leen Bussche, DVM

The Bicknese Family Prize was established in 2005 by Dr. Joanne Bicknese, '76, DVM '78, as an annual award to support research activities of a woman scientist-in-training. The award aims to provide support at a critical point in the trainee's academic development and to help launch her into a successful career. Bicknese, one of the Institute's most devoted and generous supporters, is a current member of the Institute's Advisory Council and served six years as chair through the Institute's 50th Anniversary and the building of the west wing. The fund honors her parents, Helen and Louis Bicknese, and her aunt and uncle, Grace and Carl Bicknese.

The 2013 Bicknese prize winner was Dr. Leen Bussche, a postdoctoral associate in Dr. Gerlinde Van de Walle's lab. Bussche was working toward her DVM at the University of Ghent in Belgium when she began working under Van de Walle's lab in the Department of Comparative Physiology and Biometry there, and when



Stem cells are also at the heart of Van de Walle's work with racehorse healing. Her lab is investigating the use of mesenchymal stem cells to heal important injuries in racehorses, a booming medical business built around promising techniques and products that haven't actually been proven to help these hardworking animals. Using cells grown in the lab, Van de Walle models the process of healing in horse tissue, testing whether stem cells or materials secreted by stem cells can help the process along. Insights about stem cells learned from these models could illuminate new and better ways to heal skin wounds and treat internal injuries in horses and in humans.

Van de Walle made the move to the Baker Institute in 2013, Bussche jumped at the chance to move her research to Cornell.

"I knew that Cornell and the Institute could bring the research to a higher level. The work done here is very high quality," says Bussche. "The project I'm working on is so novel that we need the support of other researchers to accomplish the work."

Bussche's project focuses on stem cells found in mammary tissue, malleable cells that give mammary tissue its remarkable abilities to meet the needs of motherhood over the course of an animal's life. Unfortunately, these cells can also multiply out of control in some circumstances, forming mammary gland tumors. Bussche says scientists speculate that stem cells may trigger tumor formation when they lose control over their stem cell properties.

Although unspayed dogs, cats, and many other animals are stricken with mammary cancer at rates similar to humans, horses, cows, and pigs almost never get mammary cancer, possibly because their mammary stem cells never lose their special stem cell properties - their stemness. Bussche has grown mammary stem cells from dogs and horses in the lab to compare how they differ, and she's found that differences

in the substances these cells release may well affect tumor susceptibility.

"I'm analyzing these secreted factors from horse cells and screening them to figure out if there's a factor that is responsible for maintaining the stemness and their resistance for tumor cell transformation," says Bussche. "My project is about identifying those factors, identifying possible candidate substances that might be used in cancer therapy."

Bussche has put the Bicknese prize money to good use in her career advancement, using some of the funds to travel to Belgium for an interview with the Belgian American Education Foundation (BAEF), an organization that promotes the exchange of scholars between the two countries. The interview helped Bussche secure a one-year fellowship from BAEF and has also provided her with the opportunity to network with scientists and career advisors from here in the U.S. and Belgium at a BAEF meeting in Brussels earlier this year.

"Without the Bicknese prize I wouldn't have had the opportunity to do the interview or the dinner, and I would never have been able to get my own funding, so it really helped me out," says Bussche.

New Advisory Council Members

Ms. Susanne Handler

Like many of our Advisory Council members, Susanne Handler came to know the Baker Institute through a personal connection. Handler, who has been a professional horse trainer and dressage judge for more than 40 years, learned about the Institute through her close friend and council member, Dr. Peggy Reed. Handler's love of animals, her desire to help support basic science to improve animal health, and the Institute's reputation spurred her to accept the offer to join the council.

"I feel very honored to be associated with such a prestigious place," she says.

Handler has trained horses all over the country, but works mostly near her home in Darien, Connecticut.

Handler's former husband, now deceased, was an alumnus of the College of Veterinary Medicine (Dr. Joseph A. Heissan, DVM '70), and she says they both felt strong ties to his *alma mater* and visited the campus and Ithaca often. Handler, who has shown Belgian sheepdogs in the past, says she's committed to supporting veterinary medicine and she hopes to contribute to the Institute with insight and advice at regular council meetings.

"I have always had a huge love for animals and a great interest in veterinary medicine," says Handler.





Keith Richter, DVM

New Advisory Council member Keith Richter, '78, DVM '81, now owns two veterinary specialty hospitals and a veterinary reference laboratory, but when he arrived at Cornell as an undergraduate animal science student in 1974 he had never even seen a cow. This self-described city boy from Long Island soon warmed to the relatively rural life in Ithaca and developed an enduring connection with his *alma mater* that continues today. Richter lives in the San Diego, California area.

Richter began his relationship with the Baker Institute and the Cornell Feline Health Center when he first started his own hospital in 1990 and began participating in the Clinic Memorial Giving Program. His clients Robert and Mary Jane Engman were particularly touched by his donation to the Institute following the death of their beloved dog, Mr. Emerson in 1997, and have since become supporters of the Institute. As the Engmans became more involved with the Institute and its leadership, so too did Richter, and when current director Colin Parrish invited him to join the Advisory Council in 2013, Richter gladly accepted.

"I am a clinician scientist, but I don't have a connection to basic science," says Richter. Participating on the council gives him the opportunity to lend a hand to basic research in animal science, a cause he firmly believes in. "My connection to Baker is a way I can support basic science," he says. "It's also a way of supporting the University".

"Cornell has a big place in my heart. My closet is full of Big Red t-shirts," he says.

Leland (Skip) E. Carmichael, DVM, PhD '59, receives the Arthur F. North Jr. Canine Service Award



For his scientific contributions to the health of dogs around the world, the Baker Institute has awarded Dr. Leland (Skip) Carmichael the Arthur F. North Jr. Award. One of the original graduate students at the Institute, Carmichael arrived straight out of veterinary school at the University of California, Davis in 1956, and eventually took a lead role in the development of the parvovirus vaccine that helped to significantly reduce the impact of that new disease in dogs in the early 1980s.

In addition to his work on parvovirus, Carmichael made great inroads against many formerly important diseases of dogs, including canine adenoviruses types 1 and 2, canine herpesvirus, and canine brucellosis, during the course of his long and productive career studying veterinary infectious diseases. When canine brucellosis began appearing among beagles in this country in 1966, he and his colleagues were the first to describe the disease and identify the bacterium responsible, work that eventually helped identify control measures for that infection.

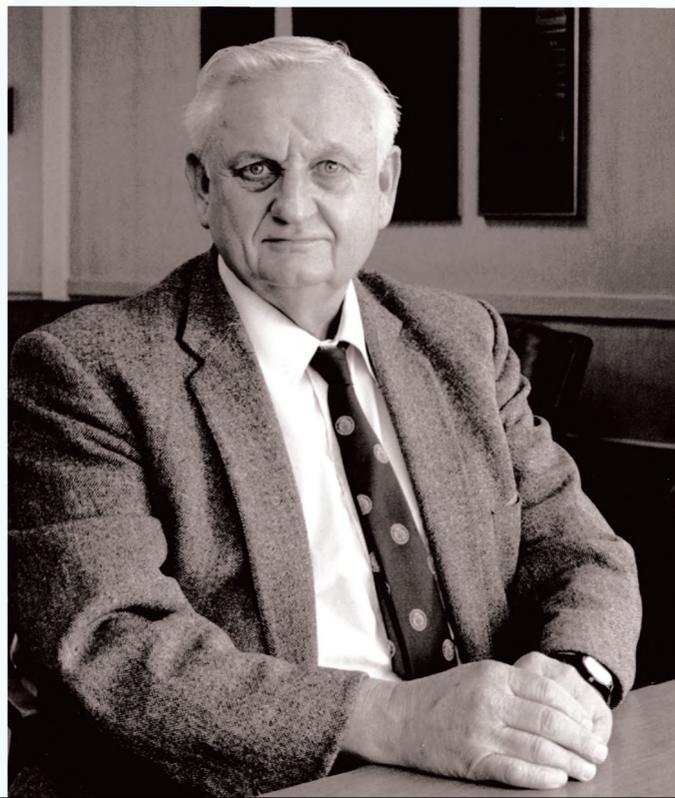
The sudden emergence of canine parvovirus in 1978 presented the Institute with an urgent challenge. Carmichael recalls that he was on vacation with his family on Cape Cod that summer when the outbreak first made headlines and his colleague Max

Appel, DVM, PhD, called him back to work on the catastrophe. Within three years, Carmichael had perfected the modified live-virus vaccine for parvovirus that is still in use today.

Carmichael says his career studying emerging infectious diseases in dogs was energizing for him because something new was always around the corner. "The joy of discovery is the 'wow', the moment when you find something you didn't expect. The causes of most of the recognized diseases out there seem to have been identified, but they keep coming up because life is predicated on change," he says.

Carmichael is now a Professor Emeritus. He lives in Ithaca with his wife of 57 years, Mary Margaret.

The Arthur F. North Jr. Canine Service Award was established in 1982 by friends of the late Dr. Arthur F. North Jr., DVM '35, in recognition of his services as a veterinarian and as an effective advocate of research to benefit the health of dogs. A 1935 graduate of Cornell's College of Veterinary Medicine, North established the Somerset Veterinary Group in Somerville, New Jersey in 1947. He was widely respected for his dedication, integrity, and keen interest in the progress of veterinary medicine, which he demonstrated as a medical and surgical innovator and as a strong proponent of veterinary research. The North Award recognizes those whose contributions to the improvement of canine health and well-being reflect this same spirit of concern for all dogs.





Upper Left: Carmichael in 1956, the year he started his PhD studies at the Baker Institute, then known as the Veterinary Virus Research Institute

Right: Carmichael and Roy Pollock, DVM '78, PhD '81 in 1979.

Left: Carmichael in 1997, the year of his retirement.

LONG-TERM STAFF HIGHLIGHTS

Lynne Anguish

When laboratory technician Lynne Anguish first came to Cornell, Jimmy Carter was president, a Bee-Gees song was #1 on the charts, and a gallon of gas cost 86 cents. She began work that spring of 1979 at the College of Veterinary Medicine, then in 1996 accepted a position in Robin Bell's lab at the Baker Institute. Today, Anguish is one of our longest-working employees, and after so many years at Baker, she says the collaborative, family atmosphere is a big reason she's stayed for so long.

In her first position at Baker, Anguish worked as a technician for one-time faculty member Robin Bell, studying *Trichinella* and *Brugia* parasites, the foodborne pathogen and the cause of elephantiasis, respectively. She worked with John Parker from 2003 to 2008, studying reovirus, a human pathogen that has the potential to be used in cancer therapies. Then in 2008, Anguish made the transition to Scott Coonrod's lab where she continues to work as laboratory manager.

In the Coonrod lab, Anguish is working to better understand the role of PAD enzymes in the development of breast cancer and squamous cell carcinoma, a form of skin cancer. The early evidence linking PAD2 to skin cancer in mice is startling, she says, and they'll be following up on the work in the coming year.

In addition to her work at the lab bench, Anguish keeps the lab running smoothly by ordering supplies, maintaining lab

equipment, keeping databases up-to-date, and writing scientific protocols that can help the trainees work more efficiently. She also helps Coonrod write grant proposals to support their research.

"Baker is a very unique place. It's like a family here, small enough that everybody knows everybody else," she says. "It's very collaborative, and Scott and I work well together. We're a good team."

Being a long-time employee, the trainees and newer staff also look to Anguish for advice with their projects. "I've worked in so many different labs and done so many different types of protocols, that people from all over the vet school come to me with questions," she says.

When she's not at work, Anguish keeps busy training and showing dogs, including her young black shepherd Wren. Lately she and her husband have also been spending time with two little people in their lives: their granddaughters, ages four years and six months.

It's been a rewarding career so far, says Anguish. "I like being able to use my creativity. Figuring out how to do things, how to make things work, playing with the instruments if they break, figuring out why they're not working," is gratifying for her and keeps her energized about her work.





Kevin Draiss

After graduating from Cornell in 1984, Kevin Draiss's first job was a summer landscaping position at the Baker Institute. His roles have changed since he started 30 years ago, and today he's a technician, caring for animals and keeping lab resources running smoothly. He says the personal connections that he's made at the Institute over the years have been important to him.

"What I enjoy about Baker are the people," says Draiss. He estimates that he's been acquainted with 60 percent of the people represented in the photo portraits that line the halls, and he still keeps up with friends he's made here who have since moved on to new posts all around the world.

After that summer job in landscaping, Draiss moved on to a permanent position at the Institute, working on landscaping and on various maintenance jobs when the weather allowed and working as an animal technician during the frigid Ithaca winters. When he first started, former Institute Director Douglas McGregor

had the idea to turn the overgrown former farmland around the labs into a leafy, park-like setting; a job that required a lot of hours and hard work, says Draiss, but he's proud to have been a part of creating the beautiful gardens at the Institute today.

"I can point to a lot of mature trees I planted over the years," he says.

In his current position, Draiss is a certified animal technician, and he keeps up on the numerous training courses necessary to do the job.

Although he no longer works on the grounds, Draiss still gardens at the Institute in his free time, keeping a large plot of tomatoes and asparagus beside the horse barn. In the harvest season, he often shares the bounty with co-workers at the Institute. He also enjoys fishing and motorcycling and describes himself as a Civil War buff, making regular summer trips to Maryland and Virginia to visit the battlefields there.

Postdoctoral fellow looking for the truth about viral pandemics

New pandemic diseases seemingly strike from out of the blue and Andrew Allison, PhD, wants to understand why. A postdoctoral fellow in Colin Parrish's lab, Allison is working to understand how canine parvovirus, a pathogen that is often deadly in puppies and vulnerable adult dogs, first emerged and is now adapting and changing over time. He's found that the virus is moving back and forth between domestic and wild carnivores, a pattern of spread that could give clues to how future pandemic diseases of humans or domestic animals may emerge.

Allison remembers when he first became interested in virology. A hantavirus outbreak in 1993 in the Four Corners region of the southwestern United States struck several previously healthy people, killing half of its victims within days of showing seemingly mild, flu-like symptoms. The suddenness of the outbreak and the lethality of the infection shocked and intrigued Allison. It also taught him to question long-held assumptions in science, because at the time scientists thought hantaviruses existed only in Asia and Europe and they initially discounted the possibility that a hantavirus could be causing the rash of illnesses.

"Hantaviruses had been in the New World all along and scientists never knew it. It was amazing to me that disease-causing viruses could be so widespread but no one ever knew," says Allison.

He's now finding that canine parvovirus is also extremely widespread. Allison has been looking for the virus in wild carnivores, a diverse group of mammals that includes dogs, wolves, cats, bears, raccoons, and seals, to see if they are infected with the virus and may effectively transmit it to other animals. The results were clear.

"Canine parvoviruses appear to be ubiquitous in the wild. Everywhere in the United States we looked we've found the virus in wild, free-ranging carnivores," he says.

Allison, Parrish, and their collaborators have also found evidence that the virus may spread differently among wild animals than it does among domestic dog and cats. Domestic animals pick up canine parvovirus from traces of feces from another infected animal, but by studying the genetic signatures of viruses in the wild, the team has found evidence that wild

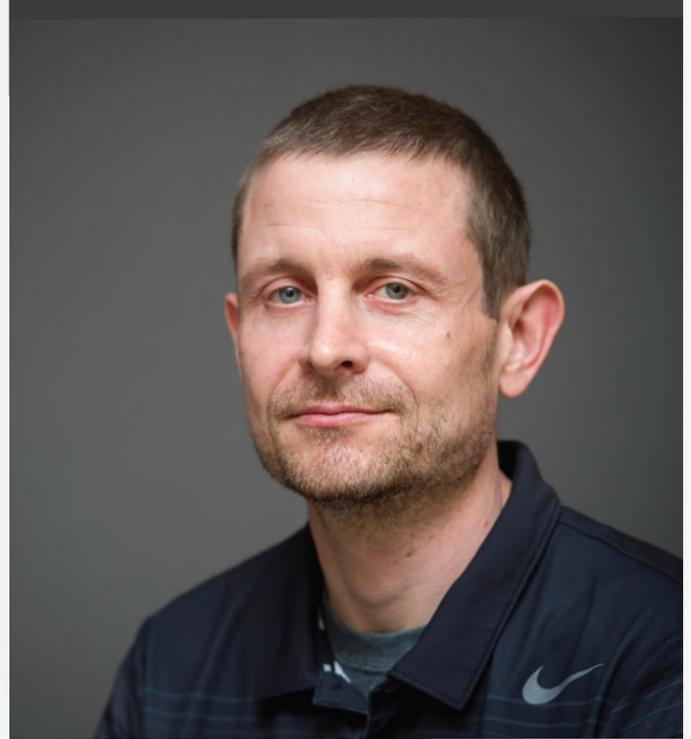


carnivores may be acquiring the virus by eating infected animals and scavenging on carcasses.

“It appears there may be continual back and forth transmission between domestic and wild animals. All these different hosts are infected, so it opens up the idea that the emergence of a pandemic virus like canine parvovirus could potentially come from the wildlife reservoir,” says Allison.

The fact that canine parvovirus is extremely prevalent in wild carnivores and can apparently be transmitted back and forth between wild animals and dogs also has implications for how the virus first emerged back in the mid-1970s. Since canine parvovirus is closely related to feline panleukopenia virus, scientists have long thought dogs must have acquired the virus from domestic cats, but Allison’s results have raised another possibility.

“This suggests that canine parvovirus may not have emerged directly from domestic cats. It may have emerged from some other unknown wildlife reservoir,” says Allison.



In future work with canine parvovirus, Allison says the Parrish lab will be collaborating with Dr. B.V. Venkataram Prasad at Baylor University to study the receptor protein (transferrin receptor) on dog cells that allows the virus to attach and get inside the cell. The structure of the dog receptor isn’t known and how it physically interacts with the virus is a mystery, he says, but it could reveal a great deal about how the virus infects cells and why there may be differences in the susceptibility of different carnivore species to various parvoviruses.

PhD student helping to improve the odds for endangered animals

Jennifer Nagashima is passionate about saving endangered species, and she's turning her commitment to helping these creatures into action. In her research at the Institute, the PhD student is focused on improving assisted reproduction techniques that can help endangered canids (dog-like mammals) like wolves and wild dogs reproduce in captivity. Nagashima is the first student to participate in the Cornell-Smithsonian Joint Graduate Training Program (JGTP), a shared graduate program in which she's doing half her research here at the Baker Institute and half at the Smithsonian Conservation Biology Institute (SCBI) in Front Royal, Virginia. Through this unique program, Nagashima benefits from the help of two advisors: Alex Travis VMD, PhD, of the Baker Institute, and Nucharin Songsasen DVM, PhD, of SCBI.

Nagashima discovered her interest in wildlife as a child. Watching an Animal Planet show on endangered tigers motivated her to do something to help endangered animals and she soon began volunteering at a zoo near her home in Palm Springs, California. She carried her interest in animals to Cornell, first as an undergraduate, and now as a graduate student.

Of the 36 species of wild canids in the world, seven are listed as threatened or endangered and two are near extinction. To help rebuild populations of these animals, zoos have made efforts to get captive wolves, foxes, and wild dogs to breed. However, the old fashioned way of making canid pups can fail

for any number of reasons, and distant institutions often want to breed their animals together without putting the animals through the stress of travel or upsetting their social packs. To overcome these hurdles, zoos need to be able to use *in vitro* fertilization techniques like those used to help infertile human couples, but this is no small task. Female canids are only fertile once or twice per year, and once the female produces an egg it undergoes a days-long maturation process before it can be fertilized. Canid sperm also undergo a maturation process, so efforts to bring together canid eggs and sperm are notoriously difficult and no one has ever successfully produced a puppy from any canid species using *in vitro* fertilization.

Nagashima is tackling this challenge in domestic dogs, an effort that she hopes will eventually help bring some endangered canid species back from the brink of extinction. She's getting help from Travis, who is guiding her work to optimize the preparation of sperm from male canids, and working with Songsasen on optimizing the preparation of eggs from female canids. Their results have been promising so far, says Nagashima, and she's planning to publish them soon so that other labs and zoos can learn from the advances.

"By improving understanding of both the male and female sides of fertilization, we've improved our ability to produce dog embryos. In the future I hope to apply this new knowledge to assisted reproduction efforts for endangered canids," says Nagashima.





Photo: Yehudi Hernandez



GIFT FUELS BASIC DISEASE RESEARCH

Memorial Gift Program kindles longstanding relationship with Baker Institute

For Robert and Mary Jane Engman, it all started 19 years ago on Mrs. Engman's birthday on the way back to work from a lovely lunch. Mrs. Engman's scream immediately shocked her husband into the realization that a Boston terrier had wandered into a busy intersection.

"Pulling over the car and coaxing him into the back seat was one of the better things I have done in my life," said Mr. Engman. "No one claimed him, so we brought him into Mary Jane's office, where he lay in a little bed looking very depressed as I argued that it would be too difficult for us to keep him since we work every day. When I saw the expression on Mary Jane's face it was obvious he'd just have to come to work with us."

They named the dog Mr. Emerson and soon he became closely bonded to Mrs. Engman; a high-tech electronics firm had a new employee. Years later, when Mr. Emerson developed heart trouble, the Engmans brought him to Dr. Keith Richter, '78. Under Richter's care, the Engmans enjoyed two more happy years with Mr. Emerson.

"When Mr. Emerson finally passed away, we were really touched to learn Dr. Richter made a contribution to Cornell's Baker Institute in Mr. Emerson's name through the Memorial Gift Program," said Mr. Engman. "We've contributed to Baker ever since, growing to learn more about the organization and what it does to advance animal health. It's a cause we really believe in - we've always loved dogs and cats and had several with diseases that have been helped along by research. If



Above: The Engmans' dogs, Ben and Amy

you've ever had a dog that's ill and you can get help for it, it's because research has been done at places like Baker."

Over the years the Engmans began to get to know more not only about Baker's mission, but its people. They became friends with Dr. Douglas Antczak, Baker's director at the time, from whom they learned more about Baker's work and what the Institute hoped to accomplish through research.

"Cornell is a good school, we like the people we've met there and know they do a great job," said Mr. Engman. "They do basic research, which we believe is one of the best ways to address health problems. We need to understand how things work on a cellular level. Every step along the way toward this understanding is a step toward making pets' lives easier."



**ACTIVE
AWARDS**

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► **Douglas F. Antczak, VMD, PhD | Dorothy Havemeyer McConville Professor of Equine Medicine**

NIH, *Immune Tolerance to Serial Trophoblast Transplants*, Mentor

Morris Animal Foundation, *Genetic Studies of Equine Sarcoid Tumors*, Principal Investigator

Qatar Foundation-Qatar University, *Comparative Genetics of Complex Diseases*, Principal Investigator

► **Judith A. Appleton, PhD | Alfred H. Caspary Professor of Immunology**

Cornell Atkinson Center for a Sustainable Future, *Small Molecules as Targets in Control of Nematode Infections in Animals and People*, Principal Investigator

► **John S. L. Parker, BVMS, PhD | Associate Professor of Virology**

Cornell Feline Health Center, *Mechanisms of Feline Calicivirus (FCV) Infection of Polarized Epithelial Cells*, Principal Investigator

Morris Animal Foundation, *The Role of Feline Junctional Adhesion Molecule A in Feline Calicivirus (FCV) Infection*, Principal Investigator

NIH, *Studies of the Global Translational Response to Human Virus Infection*, Principal Investigator

Winn Feline Foundation, *Identifying the Role of Allelic Variations of Feline Junctional Adhesion Molecule A in Susceptibility/Resistance to Feline Calicivirus Infection*, Principal Investigator

► **Colin R. Parrish, PhD | John M. Olin Professor of Virology**

NIH, *Structural Controls of Functional Receptor and Antibody Binding to Viral Capsids*, Principal Investigator

NIH, *The Evolutionary and Biological Bases of Host Switching in Viruses*, Principal Investigator

NIH, *Host Cell Receptor Variation and the Control of Viral Cross-species Transmission and Epidemic Emergence*, Mentor

► **Alexander J. Travis, VMD, PhD | Associate Professor of Reproductive Biology**

NIH, *Nanoscale Energy Production for Implantable Medical Devices*, Principal Investigator

Weill Cornell Medical College, *Developing a Multiplex Point-of-care Platform to Detect Multiple Stroke Biomarkers*, Principal Investigator

► **Vicki Meyers-Wallen, VMD, PhD, DACT | Associate Professor of Genetics and Reproduction**

NIH, *Identification of XX DSD Mutations by RNA-seq and Comparative Genomics*, Principal Investigator

► **Gerlinde Van de Walle, DVM, PhD | Assistant Professor of Microbiology and Immunology**

Cornell Cancer Biology Pilot Research Program, *The Effects of Tumor-Inducing Stimuli on Oncogenic Transformation of Mammary Stem Cells*, Principal Investigator

Cornell Feline Health Center, *Peptidylarginine Deiminase (PAD) Inhibitors: A Novel Class of Anti-Cancer Drugs for Feline*, Principal Investigator

Cornell Stem Cell Program, *Towards Cell-free Regenerative Therapies: Characterization of the Equine Mesenchymal Stem Cell (MSC) Secretome*, Principal Investigator

Morris Animal Foundation, *The Role of Citrullination in Canine Cancer Stem Cells: Opportunities for Novel Anti-Tumor Strategies and Biomarker Development*, Principal Investigator

Morris Animal Foundation, *Species with Variable Susceptibility for Mammary Cancer*, Principal Investigator

Research Grants Program in Animal Health, *The Air-Liquid Canine Corneal Organ Culture System: A New Tool to Study the Pathogenesis of Acute Alpha herpesvirus-Induced Ocular Disease*, Principal Investigator

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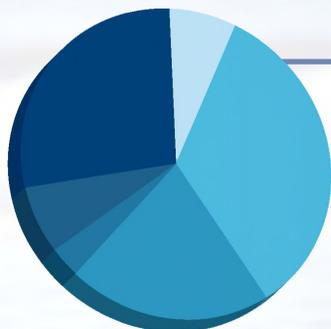
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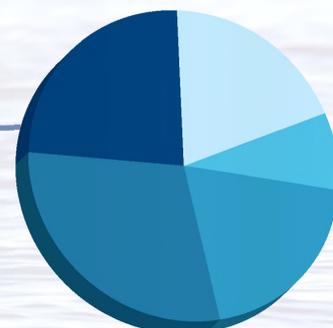


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