1997 ANNUAL REPORT

Leadership Program for Veterinary Students
For more information about the Leadership Program, including how to apply, contact:

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The College of Veterinary Medicine at Cornell University invites promising students of veterinary medicine to a ten-week summer program designed to crystallize their interest in a career in research. For some student fellows, the program offers their first sustained exposure to medical research. For others, it builds on earlier experience, nurturing an already-developing interest. Each fellow is assigned a research project in an area of the student's interest, which enables him or her to explore the subject in depth, acquire practical experience with investigative methods, and gain insight into the way a research laboratory utilizes its professional and material resources.

The program is open to students who have completed at least one year toward the degree of Doctor of Veterinary Medicine. Participants typically rank near the top of their class. The program's emphasis on excellence draws the best from around the world: its twenty-four fellows this year represented seventeen veterinary colleges in Australia, Germany, the Netherlands, New Zealand, the United Kingdom, and the United States.

Regardless of background, each of the fellows in this highly selective program is recognized as having the ability and motivation to become a future leader of the veterinary profession or animal agriculture. The experience of the leadership program clarifies and strengthens their career goals.
### 1997 Students at a Glance

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Cornell undergraduate Michael Uber served as program coordinator. Antony Clements of Bristol University, Jonathan Happold of Sydney University, and Deborah Pratthley of Massey University were elected program representatives.
1997 Leadership Program Activities

The Leadership Program for Veterinary Students combines independent, faculty-guided research with a variety of activities, including career-related field trips and discussions, professional-skills development workshops, and interactive, student-directed learning.

**Leadership Development**

Discussion of the responsibilities of leadership and exercises to develop leadership skills are an important feature of the program. Among the activities this year was a panel discussion on qualities of leadership, with Dame Leonie Kramer, chancellor of the University of Sydney; Mr. Frank H. T. Rhodes, president emeritus of Cornell University; and Dr. David Fraser, dean of faculty of Veterinary Sciences at the University of Sydney, who served as chair.

Throughout the ten-week session, fellows participated in an exercise that applied the principles of the scientific method to the design of experiments and review of manuscripts. Led by Dr. Ari van Tienhoven, emeritus professor of animal physiology at Cornell, fellows reviewed scientific reports from the perspective of a science journal editor, formed opinions, and defended them before their colleagues. Dr. van Tienhoven was assisted by Dr. Hollis Erb.

A new workshop on emerging infectious diseases was organized by Dr. Robert Shope, professor of medicine at the University of Texas, Galveston, and Dr. Colin Parrish, associate professor of virology at Cornell. Fellows were asked to select four diseases from a prepared list. They then divided themselves into groups, conducted library research on the selected diseases, and reported back to their colleagues.

The parallels between creativity in science and the visual arts was the subject of a workshop led by Dr. Marian Horzinek, professor of virology at the University of Utrecht. The discussion afforded an opportunity for fellows to reflect on the power of lateral thinking—the ability to make correlations with experiences in other disciplines.

**Career Exploration**

Informal counseling occurs frequently, but in addition an entire day of the ten-week program was set aside to explore career options for veterinary graduates—including international experience, research training, and graduate education.

“The Changing Role of the Veterinarian in the Biomedical Sciences” was presented by Dr. John Strandberg, director of the Comparative Medicine Program at Johns Hopkins University, who later explored the topic in an informal meeting with the fellows.

Dr. Gerard Hickey, senior director of basic animal science research at Merck & Co., spoke about research and administration at Merck. He discussed careers in industry, comparing research in an academic institution and at a major, research-intensive pharmaceutical company.

Discussions were facilitated by Cornell faculty members Drs. Douglas Antczak, Alex Brown, Laura Eirmann, James Flanders, Achim Gruber, Noa Noy, Fred Quimby, Don Schlafer, and Ton Schat.
Two affiliated programs were created last year with assistance from the U.S. Department of Agriculture—one at North Carolina State University (NCSU) and one at the University of Sydney (SU). The tripartite initiative is expanding and fostering student exchanges among the participating institutions. This year, Scott Munn of NCSU and Peter Bracken of SU enrolled in the leadership program at Cornell, and John Stein, a participant in last year’s program at Cornell, and Larissa Minicucci, a first-year Cornell veterinary student, enrolled in the companion program in Sydney.

Prizes
At the conclusion of the program, students report on their research activities. Book prizes are awarded to students with the best projects in molecular, cellular, and whole-animal research or integrative biology, and a Program Prize is given to the best overall project. This year, five students received awards:

Program Prize: Jonathan Happold, "Cardiovascular Adjustment to Exercise." Book award: Veterinary Medicine: An Illustrated History, Dunlop and Williams.


Summaries of their research, and those of their colleagues in the 1997 Leadership Program, are given in the next section of this publication.
DENNIS BAILEY
CORNELL UNIVERSITY

Signal Transduction
Isolation of novel signaling proteins that bind PAK

When I arrived at Cornell as an undergraduate, I was already confident in my decision to pursue a career in veterinary medicine. During my undergraduate education I became equally fascinated with molecular biology. As a result I am currently pursuing training in both clinical science and basic research.

Dr. Rick Cerione's lab is investigating pathways that regulate cell-cycle progression—in particular, signal transduction pathways involving CDC42, a monomeric G protein. In its active GTP-bound state, CDC42, interacts with several targets, including the serine-threonine kinase, PAK. This is the beginning of a cascade that eventually leads to the activation of Jun kinase. (Jun is a proto-oncogenic transcription factor.) At this time, the intermediate protein(s) linking PAK with Jun kinase are not known.

Working under Dr. Shubha Bagrodia, I tried to identify proteins in this cascade by first creating a fusion protein composed of glutathione-S-transferase linked to an SH3 domain-binding region of PAK. The fusion protein was purified by incubation with glutathione-agarose beads, and the bead-fusion protein complex was then incubated with whole cell lysates. Proteins that bound to the complex were isolated from the lysate by centrifugation and then run on an SDS-polyacrylamide gel. Using this technique, called affinity precipitation, I isolated two proteins that bind to PAK. At the moment, I am scaling up the procedure in order to purify enough of these proteins for sequencing.

The leadership program has been intense but highly rewarding: It has given me an excellent view of what basic research has to offer and has made me more excited about veterinary science than ever.

PETER BRACKEN
UNIVERSITY OF SYDNEY

Cellular Parasitology
LDH assay for Trichinella invasion

A fifth (and final) year student at the University of Sydney, Australia, I am interested in a research career in avian science but, prior to arriving at Cornell, had not had an opportunity to work in a research environment.

I conducted research in Dr. Judy Appleton's laboratory at the Baker Institute. It involved the study of Trichinella spiralis, a nematode that is parasitic in a wide variety of mammalian species. T. spiralis is important because it causes severe disease in both animals and man.

I used an in vitro technique to study the parasite as it migrates through and destroys cells on a monolayer. The level of cell damage was assessed by counting the number of dead cells (a very time consuming procedure). My goal was to develop an alternative method of quantitating cell death. To this end, I measured lactate dehydrogenase (LDH), which is contained within mammalian cells and is released when the cells die. I am currently trying to solve problems involved in recovering and measuring LDH levels from the in vitro parasite culture.

The leadership program has been a great experience for me. I have met many wonderful people from all over the world, and the experience gained from my research project has been enlightening. My immediate objective is to develop my clinical skills, but in the future I will not be content unless I am at the forefront of knowledge in a specific field.
ROGER BRALOW
UNIVERSITY OF QUEENSLAND

Signal Transduction
Role of lipid signal transduction in oncogenesis and metastatic spread

After completing an honors degree in Pharmacology at Melbourne University, I decided to pursue a career in veterinary science. I am currently in my final year of the veterinary program at the University of Queensland and will graduate in December.

My project with Dr. H. Alex Brown in the Department of Pharmacology focused on the activation of phospholipase D (PLD). This ubiquitous enzyme has been implicated in several forms of cancer, including human and canine breast cancers. The mechanisms of activation of PLD are unknown, but tyrosine kinases have been implicated in one pathway. My project involved co-expressing PLD with both receptor tyrosine kinases (e.g., neu, erbB3, EGFR1) and non-receptor tyrosine kinases (e.g., Src, FAK). These experiments involved quantification of PLD catalytic activity and alterations in tyrosine kinase specificity.

I also used a specific antibody for phosphotyrosine to determine which agents phosphorylate PLD. Subsequently I intend to ascertain whether phosphorylation causes changes in the activity of specific kinases. An ultimate goal of Dr. Brown's research is to produce a specific PLD antagonist to combat specific cancers.

After finishing my veterinary degree I would like to obtain clinical experience, either through practice or an internship. Later, I'd like to pursue my interest in pharmacology either through a Ph.D. or residency, or more likely both. My long-term goal is to successfully combine research with my clinical interests.

ANTONY CLEMENTS
BRISTOL UNIVERSITY

Canine Locomotion
Multiple force-plate analysis of canine locomotion

I will enter my final year at the University of Bristol this fall. I have only recently become aware of research opportunities available to veterinarians while pursuing an honors project, and I came to Cornell to increase my exposure to top-level research.

My project was conducted in the comparative biomechanics laboratory of Professor John Bertram, where I concentrated on multiple force-plate analysis of canine locomotion. We have a unique system that utilizes four force plates in series to allow simultaneous acquisition of data from contralateral limbs over three successive steps of trot. Unlike single-platform systems, this gives a complete description of the kinetics of that animal.

My goal was to characterize the parameters and variability of the canine trot in a normal Labrador. As well as looking at stride length, stride period, velocity, duty factors, impulse, and average force, we examined the way that the foot is loaded. Dysplastic dogs as well as normal counterparts were used with a view to establishing parameters that could differentiate a normal animal from an unsound subject.

As I look to the future I am leaning towards a large-animal internship followed by a residency in equine surgery. It is my expectation that these experiences will prepare me for a career in clinical research with performance horses, which are my main interest.
ALEXANDRA DÖRNATH
FREIE UNIVERSITÄT BERLIN

Reproductive Biology
Characterization of bovine trophoblast cell populations: parturition triggered by immune response

I was raised in Bremen, Germany, and studied veterinary medicine at the Tierspital in Zurich and Freie Universität Berlin. I applied to the leadership program for the research experience it offered, and for the opportunity to exchange thoughts and ideas with people from different parts of our world. I also wanted to look behind the scenes at the world-famous vet school at Cornell.

My research project involved the characterization of changes in trophoblast cell populations by flow cytometry during normal and abnormal pregnancies in cows. The immediate goals were to develop a procedure for isolating trophoblast cells; to optimize the histochemical identification of those cells with particular antibodies (MHC-I, MHC-II, CD-45); to improve their nuclear staining, and to compare and characterize—with the help of the immunofluorescence microscope and flow cytometry—trophoblast cell populations from different stages of pregnancy.

This project was conducted in collaboration with Dr. Christopher Davies, Dr. Donald Schlafer, and Mrs. Patricia Fisher. The main goal was to determine whether there are phenotypic changes in the chorio epithelium and the endometrium during pregnancy and if parturition is somehow triggered by these changes, and also whether placental retention occurs in the absence of these changes.

I am especially interested in aquatic medicine, and aspire to a career as a aquarium clinician. Long term, I see myself working as a director of a zoo or an oceanpark. The leadership program caused me to think about my future and increased my determination to realize the career goals that I have set for myself.

JONATHAN HAPPOLD
UNIVERSITY OF SYDNEY

Cardiovascular Physiology
Cardiovascular adjustment to exercise

An academic home environment in East Africa and Australia provided me with a love of animals, a fascination with biology and scientific research, and an interest in international affairs.

Under the enthusiastic and supportive guidance of Dr. David Robertshaw, I studied the cardiovascular responses to exercise in sheep. I “inherited” the project from a fellow Sydney student, Rachel Walker, who tragically was obliged to return home midway through the program. Together we investigated the physiological basis of exercise-induced lactate production. Lactate production may occur secondary to thermoregulation, with a redistribution of blood to the skin leading to hypoperfusion of certain tissues and subsequent partial anaerobic metabolism. Alternatively, the exercise-induced hyperventilation of panting animals, with resultant hypocapnia and respiratory alkalosis, may increase oxygen-haemoglobin affinity and impair oxygen transfer to the mitochondria.

The experiments involved exercising sheep on a treadmill at various intensities. Blood flow in the external iliac artery was measured using a surgically-placed flow probe. Central and rectal temperature and expired gas concentrations were monitored. Arterial and venous blood were sampled at intervals for analysis of O2 transfer and substrate metabolism.

The leadership program was a wonderful experience in many ways. My research was stimulating, challenging, and enjoyable; the interactions with program participants and academics were truly inspiring, and I will value my fellow leadership students as both friends and colleagues for years to come. The program encouraged me to pursue a career in biomedical research on a global scale, and I am greatly indebted to all that have made this experience possible.
HAYDN JAMIESON  
MASSEY UNIVERSITY

Reproductive Biology  
_Mechanisms of gonadotropin-releasing hormone action regulating the glycoprotein hormone in a subunit gene in pituitary cells_

I am currently in my final year of the veterinary program at Massey University. I joined the leadership program to gain experience in areas that would assist me in pursuing a career in equine clinical research.

My research, conducted in Professor Mark Roberson’s laboratory, concerned the regulation of gene expression in the pituitary gland. Specifically, the project focused on how proteins within the nuclei of gonadotrophic cells interact with gene sequences that stimulate the promoter of the gene that codes for the alpha subunit of LH, a glycoprotein hormone. I wish to know whether interactions occur between proteins (one of which we already know stimulates the alpha subunit gene promoter) that result in enhanced binding of the DNA binding protein, LHx2. The answer to this question will be a step toward understanding gonadotrophic cell function with respect to stimulation by gonadotrophin-releasing hormone (GnRH).

I used a variety of molecular biological methods, including electrophoretic mobility shifts to detect protein DNA interaction and transient transfection studies of gonadotrophs.

The program has opened my eyes to fields of veterinary science that I was unfamiliar with and hence I have learned a lot. The exposure to molecular biology has been invaluable and memorable. My career, which will certainly include horses, is headed toward work in an academic institution.

ESTHER KORNALIJNSLIJPER  
UNIVERSITY OF UTRECHT

Sperm Motility  
_The influence of the oviduct on bull sperm motility hyperactivation_

Earlier in my studies I took a year off to do research on the endocrinology of pseudopregnancy (hydrometra) in goats. This was a great experience, and I was thrilled by the idea of spending a summer among people who do not think onderzoek is nix voor echte veeartsen (research is unimportant to real vets).

I worked with Dr. Susan Suarez in the department of anatomy and studied sperm motility hyperactivation. It was previously demonstrated that hyperactivation confers upon sperm an advantage in achieving fertilization. The main goal of my project was to determine whether a product of the ampulla of the preovulatory oviduct induces this distinct movement pattern that is characterized by highly asymmetrical flagellar bending.

To test our hypothesis, oviducts associated with large preovulatory follicles were obtained from a slaughterhouse. The isthmus and ampulla were separated for preparation of epithelial explants. After incubation either capacitated or incapacitated sperm were added. Free-swimming sperm were videotaped for motility analysis. I also studied the effect of amiloride, a calcium ATPase inhibitor, on bull sperm motility in both frozen-thawed and fresh semen. This pharmacological agent may act by raising intracellular calcium, which is needed for hyperactivation.

This program has been an even greater experience than I had expected. For the near future I am seriously interested in a career in research on reproductive biology. Further graduate training, as well as gaining clinical skills, will be my next step.
TANYA LEROITH
VIRGINIA-MARYLAND COLLEGE OF VETERINARY MEDICINE

Collagen Expression in Osteoarthritis
Characterization of the alternate splicing pattern of the COL2A1 gene in normal and osteoarthritic equine cartilage

I am a rising junior at the Virginia-Maryland College of Veterinary Medicine. I have been involved in biomedical research since my sophomore year of college. Having worked in the same institution for five years, I came to Cornell to get a new perspective and learn some new techniques.

It was my good fortune to work with Dr. Alan Nixon, director of the Comparative Orthopaedics Laboratory, studying osteoarthritis in the horse. During the 10-week period that the program was in session, I looked for re-expression of an embryonic collagen protein in osteoarthritic cartilage as the damaged tissue begins to heal.

Using quantitative polymerase chain reaction (qPCR), and in situ hybridization, I compared the expression of type IIB collagen (present in abundance in normal tissue) to re-expression of the alternate splice form, type IIA. Information on how the body attempts to heal damaged tissue is an important clue to understanding joint disease and what can be done about it. As rewarding an experience as the research aspect has been, I also gained valuable experiences in other aspects of the leadership program. It gave me the opportunity to meet interesting new people and the confidence to pursue my goals without hesitation.

Before coming to Cornell, I had a very limited idea of the opportunities available in veterinary medicine. I feel that the best way for me to take full advantage of the options is to stay in academia. I intend to finish my veterinary degree and apply for a graduate program.

MONICA MASON
CORNELL UNIVERSITY

Molecular Parasitology
Cloning and expression of Schistosoma mansoni BiP

Originally from St. Louis, Missouri, I graduated from Rockhurst College in Kansas City in 1995 with a B.S. degree in biology. That fall I began the challenging pursuit of a combined D.V.M./Ph.D. degree in immunology at Cornell.

I was pleased to participate in the leadership program and work on a project that is a continuation of my graduate research. The focus of my summer project was the molecular parasitology and immunology of Schistosoma mansoni, a helminth parasite that infects over 200 million people worldwide.

S. mansoni males and females reside in the mesenteric vasculature of mammalian hosts, producing thousands of eggs throughout their adult lives. The organisms also secrete several antigenic proteins. One of these molecules is a S. mansoni binding protein (SmBiP). It is a 68 kDa protein originally fractionated from S. mansoni egg antigens and known to induce type 2 immune responses in mice. The aim of my project was to express a recombinant 20 kDa fragment of SmBiP in vitro, and to purify large quantities of the protein fragment by affinity chromatography. The purified protein was then tested as an immunogen to induce antibody and splenic T lymphocyte responses in naïve mice.

After completing my graduate work, I hope to pursue a research career in public health. Ideally, I would like to study tropical zoonotic diseases, preferably at the NIH or CDC.
Muscle Disease

Immunohistochemical characterization of cellular infiltrates in muscle disease

I am a twenty-five-year-old student from the University of Sydney in my final year of a bachelor of veterinary science degree. I joined the leadership program for greater exposure to research.

My summer project was pursued in Dr. Barry Cooper's laboratory. It involved the characterization of cellular infiltrates in canine diseases of muscle, including polymyositis, Duchenne-type dystrophy, and masticatory myopathy. This was achieved by staining frozen sections of muscle with monoclonal antibodies against canine leukocyte antigens.

The goal of my research was to facilitate rapid diagnosis of polymyositis in dogs with lesions that are difficult to distinguish histologically from Duchenne-type dystrophy. Monoclonal antibodies were used to determine whether various subpopulations of T cells, and/or B cells, and macrophages are present. It is hoped that the research may contribute to knowledge about the pathogenesis of the diseases under study.

The leadership program enabled me to better evaluate the career options open to me on graduation, and has given me the additional research experience I wanted. It has also brought me in contact with a great group of people. While I am unsure of the future direction of my career, a residency program is attractive at the moment.
JODI NOVAK
CORNELL UNIVERSITY

Histocompatibility
Polymorphism in the major histocompatibility complex of the donkey

This summer, I had the privilege of working at the Equine Genetics Center, where a primary goal is to better understand the immunological relationship between mother and fetus during pregnancy. Interspecies matings between horses and donkeys are performed to increase the genetic disparity between maternal and fetal tissue. A key player in this relationship is a complex of genes responsible for producing cell surface antigens.

One objective of my research was to further classify donkey histocompatibility antigens. For this, I helped to perform a skin graft experiment followed by lymphocyte booster. A second goal was to determine whether the limited polymorphism of antigens in donkeys maintained at the center is in fact reflective of a larger donkey population. Testing more than forty blood samples collected from various donkey farms across New York and Pennsylvania, my results reaffirmed a much greater homogeneity in donkey antigen alleles compared to other species.

Participating in the leadership program proved to be an excellent opportunity to not only expand on my previous research experience, but also learn from the experience of other veterinary students with similar interests. My vision of an ideal career has begun to shift from private practice to the challenge and stimulation of research. Dr. Doug Antczak and his dedicated research team enabled me to have an unforgettable experience.

PATRICIA PESAVENTO
UNIVERSITY OF CALIFORNIA, DAVIS

Parasitology
Behavior of Trichinella on a myoblastic cell line

I will enter my second year at the University of California at Davis, where I am involved in a research project (which gets too little attention during classes). My main interest will be emerging infectious diseases, and I will devote special attention to pathogen identification and isolation.

In the laboratory of Dr. Judith Appleton, whose research explores the mechanisms of invasion by and immunity to the parasitic nematode Trichinella spiralis, I studied the interaction of T. spiralis with in vitro cultured myoblastic cells. In vivo, adult parasites living within the gut epithelium shed newborn larvae that migrate to muscle. The larvae invade myocytes and transform this multinucleated cell into a "nurse cell" in which the larvae live until the muscle tissue is consumed by a second animal. We found that proteins secreted by larvae are specifically taken up into the cytoplasm of the muscle cells. Many questions remain about how the secreted proteins actually enter the cells, where they are localized once inside, and their mode of action.

My commitment to a career in research is strong, and one reason I enrolled in the Cornell program was for a focused and intensive individual research experience. Less obvious to me when I arrived in June was how important the interactions with other students would be. Our arguments and agreements were provocative, and the workshops and seminars exploring the role of the veterinarian in research provided rich material for ongoing conversations.
PAUL PLUMMER  
UNIVERSITY OF TENNESSEE  

Molecular Virology  
*Development of a PCR assay for detection of duck virus enteritis caused by a herpes virus*

I am a second-year veterinary student at the University of Tennessee. I have a strong interest in veterinary medical research and veterinary virology in particular. Hence, I joined this program seeing in it an opportunity to gain experience in a high-quality lab as well as a chance to interact with very knowledgeable scientists in a research setting.

I worked in the lab of Dr. Karl Schat in the Department of Microbiology and Immunology. My project concerned Marek's disease virus, particularly a glycoprotein known as gK. My goal was to clone the gene for the glycoprotein into a eukaryotic expression vector. The gene was amplified from genomic viral DNA using polymerase chain reaction and cloned into the vector. The vector will be used to transfect a REV-transformed lymphoblastoid cell line that expresses major histocompatibility complex 1 (MHC-I) and can present antigens to primed cytotoxic T lymphocytes. Cells will be selected for expression of this protein using a fusion protein, and ultimately used in a chromium release assay to determine if exposed chickens develop cell mediated immunity to this particular glycoprotein.

I also had the opportunity to work on a second project, which involved the development of a diagnostic PCR procedure for detecting duck viral enteritis in infected birds.

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DEBBIE PRATTLEY  
MASSEY UNIVERSITY  

Cardiology  
*Precordial lead mapping and circumstances of ventricular tachycardia in two canine models of sudden arrhythmic death*

Spending ten weeks exploring career paths and collaborating with people of various nationalities, as well as getting a taste of the research world, helped provide me with insights for future vocational decisions.

The Cornell cardiology crew involved me in many of their activities—from attending to German Shepherd puppies with inherited ventricular arrhythmias to applying feline Holter monitors. My principal activity involved analyzing data from ECG recordings of horses in atrial fibrillation, looking for evidence supporting mechanisms of the arrhythmia and characterizing subsequent conversion to sinus rhythm.

I return down under with a variety of experiences to draw on in pursuing my career goals. For the immediate future, I expect to participate in an equine/large animal internship.
JENNIFER SPRAGUE FRYER  
NORTH CAROLINA STATE UNIVERSITY

Hip Dysplasia  
*Analysis of hip laxity measurements for the prediction of hip dysplasia in Labrador retrievers*

During my first year at North Carolina State College of Veterinary Medicine, I began to discover that opportunities for veterinarians are not limited to clinical practice. Since I have a great fondness for bacteria, I applied to the leadership program to explore the possibilities of a career as a microbiologist.

My research at Cornell had a significantly different focus, however. Instead of working on bacteria, I pursued a study of the genetic basis for canine hip dysplasia (CHD). In order for progress to be made in this area, it is imperative that a dog predisposed to CHD be identified as soon as possible. Hip laxity is a relatively constant characteristic of CHD which can be quantitatively measured based on radiographs at a young age.

I analyzed the Norberg Angle and Distraction Index measurements from serial radiographs of young dogs in order to determine when these measurements stabilize and at what age these indices can be used to determine a dog's predisposition to CHD. Not only will this information bring CHD researchers closer to their ultimate goal, the information will be useful to breeders for early identification of dogs at risk of this debilitating disease.

DIANA STANTON  
UNIVERSITY OF TENNESSEE

Signal Transduction  
*Cytokine responses during murine toxoplasmosis*

I wanted a summer experience that would enable me to conduct basic research while deepening my understanding of the molecular basis of disease. The leadership program offered me these experiences as well as opportunities to visit other centers of scientific excellence and to reflect on career options.

My research project focused on host cell signal transduction pathways triggered by the intracellular protozoan pathogen, *Toxoplasma gondii*. First, I identified unique post-infection protein phosphorylation patterns in human endothelial cells, one of the first host cell-types encountered after natural infection. Anti-phosphotyrosine immunoblotting and immunoprecipitation following infection revealed unique early (12 hour) and late (72 hour) protein phosphorylation patterns.

Another, possibly related, signal transduction pathway we examined involves NF-kB. The latter is a transcription factor found in most immune cells. NF-kB regulates the induction of many cytokine genes but it is not yet known whether it has the same function in endothelial cells in response to toxoplasma infection. To test this possibility, I attempted to visualize NF-kB in uninfected and infected cells using immunofluorescence microscopy.

The leadership program allowed me to participate fully in research projects under the mentorship of a fine researcher, Dr. Eric Denkers. It also included travel to such prestigious research centers as the NIH, USDA, and USAMRIID and opportunities to talk with top field specialists. These experiences have given me insight into previously unknown career opportunities in biomedical research for veterinarians. My future plans now definitely include a laboratory animal medicine residency combined with a Ph.D. degree.
COLORADO STATE UNIVERSITY

Genome Mapping

I have completed two years of veterinary school at Colorado State University. My goal after veterinary school is to combine equine medicine with clinical research.

In Dr. Doug Antczak's laboratory at the James A. Baker Institute, I pursued research aimed at mapping the genome of the horse. My work involved identifying and characterizing equine microsatellites. This was accomplished by screening an equine genomic library, sequencing positive clones, and making polymerase chain reaction (PCR) primers in the flanking regions of the microsatellites. The ultimate goal is to combine a linkage map and a physical map of the horse genome to provide equine scientists, clinicians, and horse breeders with an invaluable tool for studies of the genetic basis of normal growth and development, for molecular-based diagnosis and management of disease, and for the development of improved breeding strategies.

The equine genome project was an ideal way to discover the challenges of bringing laboratory and animal research together on a daily basis. In addition, the leadership program gave me new insight into career opportunities. This came not only by way of workshops and seminars but also through personal discussions with guest speakers and other members of the leadership group.

TRISTAN WEINKLE
CORNELL UNIVERSITY

Molecular Virology

I am entering my third year at the Cornell College of Veterinary Medicine. I became interested in research as an undergraduate while working in a molecular virology laboratory. As a veterinary student I continued research on salmonellosis in reptiles. I enrolled in the leadership program in the hopes that it would allow me to study a new disease system while strengthening my skills in molecular biology.

I studied a retrovirus (VRV) isolated from an endangered viper species, Vipera russelli. My goal was to understand the relationship this virus holds to other retroviruses. To do this I used RT-PCR to amplify a highly conserved 900 base-pair region within the retroviral protease and reverse transcriptase genes. After cloning this region into the pBluescript vector, I will sequence the fragment. Using this data, and sequence data already collected from other retroviruses, I will be able to construct a phylogenetic tree of these viruses. Using the same clone as a probe, I will then perform Northern blots of viral RNA to determine genome size.

The leadership program allowed me to realize the goals I had upon entering the program while combining my interests in herpetology and virology. The greatest benefit, however, was the career-exploration aspect of the program. With two years of veterinary school to go, I am unclear about the future. Ultimately, however, I would like to fuse my interests in research and molecular biology with my interests in zoo and exotic-animal medicine and pathology.
**JONATHAN WERNER**
**TUFTS UNIVERSITY**

**Molecular Virology**
*Herpes simplex virus DNA packaging*

I am enrolled at Tufts Veterinary School, where I will start my third year this fall. Over the past few years I have been involved in several research projects, and this summer I wanted to find out how a veterinary degree can be combined with research to make a satisfying career.

My project involved the study of Herpes simplex I viral proteins and their interactions with other proteins. By using a technique called the yeast two-hybrid system, we were able to identify protein-protein interactions. This method utilizes the GAL-4 transcriptional activator, which has been divided into its separate binding and activation domain gene sequences. Each is fused to either viral or host gene sequences. The plasmids containing these sequences are then co-transformed into yeast, which produce the fusion proteins. If there is a protein-protein interaction between these fusion proteins, then the GAL-4 transcriptional activator is reconstituted and can subsequently activate two reporter genes.

In the future I plan to complete a residency in pathology, after which I would like to pursue graduate studies leading to a Ph.D. degree in either virology or microbiology.

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**REBBECCA WILCOX**
**MELBOURNE UNIVERSITY**

**Molecular Parasitology**
*Mechanisms of immunity against the common fish parasite Ichthyophthirius multifiliis (Ich)*

I am completing a mid-course research year at the University of Melbourne School of Veterinary Science. I came to Cornell to gain experience in molecular biology as well as insight into research opportunities in veterinary science.

I conducted research on the immunological response of fish to the protozoan parasite, *Ichthyophthirius multifiliis* or “Ich.” Ich is of profound pathogenic and economic significance in freshwater fish, having been implicated in “white-spot disease” pandemics both in nature and aquaculture. The parasite completes part of its life cycle within fish skin, feeding on epidermal debris and causing devastating damage when it leaves the fish. Fish mortality is attributed to compromised respiratory, osmoregulatory, and excretory functions.

The molecular aspects of my project hinged upon the phenomenon of “immobilization” in vitro, and parasite exit from the host in vivo upon incubation with parasite-specific monoclonal antibodies (mAb). These mAb bind constitutively expressed “i” or “immobilization” antigens on the surface of the protozoan.

Employing SDS-PAGE, Western blotting, and protease assays, I began work aimed at elucidating the signal transduction pathways and protease secretion associated with mAb binding. Further work will involve experimental maintenance of the obligate parasite in vitro on immortalized fish epidermal cell lines, with modified cell culture media.

Ultimately, I wish to conduct research in wildlife disease and conservation. To achieve these goals I intend to complete a Ph.D. degree within an appropriate discipline, and subsequently apply this to the field of nondomestic animal medicine and research.
ESTHER WISSINK
UNIVERSITY OF UTRECHT

Oncology

Optimization of Lu-ECAM-1 expression in a heterologous cell type

I am a veterinary student at the University of Utrecht. I joined the leadership program for the opportunities it offers to gain skills in scientific research and to further explore career options for veterinarians.

My research project was conducted in Dr. Bendicht U. Pauli's laboratory in the Department of Pathology. It involved study of the lung endothelial cell adhesion molecule, Lu-ECAM-1. Lu-ECAM-1 mediates adhesion of metastatic melanoma cells to lung endothelium. The aim of my project was to augment gene delivery and expression of bovine Lu-ECAM-1 cDNA in the human embryonic kidney cell line HEK 293. The reasons were twofold. First, an adhesion assay can be performed with transfected HEK 293 cells to provide unequivocal proof that Lu-ECAM-1 acts by itself in mediating adhesion of the melanoma cells, eliminating other adhesion molecules on the endothelial cell surface from consideration. Second, since endothelial cells express only moderate levels of Lu-ECAM-1, transfected HEK 293 cells can be used as an in vitro model.

We evaluated the effectiveness of three receptor-mediated gene transfer methods, namely lipofectamine, SuperFect, and replication-deficient adenovirus, to augment the transfer and expression of Lu-ECAM-1 in HEK 293 cells.

My stay in the lab provided me insight in molecular biological research and made me aware of my appreciation of this type of research. Career counseling activities gave me a clearer perception of graduate schools and residencies. At this moment, I am thinking of pursuing either a Ph.D. degree or a residency.

NICOLETTE ZARDAY
UNIVERSITY OF CALIFORNIA, DAVIS

Molecular Virology

The cellular responses to parvovirus binding or infection

I have completed my first year of study at the University of California, Davis, School of Veterinary Medicine, where my purpose is to learn to approach scientific research with a broad understanding of the mechanisms of disease as well as basic animal biology.

The work in Professor Colin Parrish's laboratory concerns molecular mechanisms affecting the host range of viruses, primarily canine parvovirus (CPV), mechanisms of virus infection, and the evolution and emergence of CPV variants. My research focused on assessing the time course of death and viability of cells infected with CPV, as well as the cytotoxic effects of viral proteins.

I conducted in vitro studies infecting fibroblast- and lymphocyte-type cells with CPV and plotting the time course of cell survival and death. I also performed experiments using plasmids expressing viral proteins as well as a green fluorescence protein (GFP). These techniques enabled me to compare cytotoxic effects of nonstructural (NS) proteins, which are probably involved in viral replication, to effects of structural (VP) proteins.

After finishing veterinary school I plan to pursue Ph.D. studies in either cell biology or infectious disease. The leadership program helped solidify my interest in a career in research. It also broadened my perspective on the range of fascinating work in which veterinarians as scientists can participate and lead.
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