Leadership Program
for Veterinary Students

1993 Program
LEADERSHIP PROGRAM

FOR

VETERINARY STUDENTS

College of Veterinary Medicine
Cornell University
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Program Overview

For the past four years the College of Veterinary Medicine at Cornell University has hosted a Leadership Program for Veterinary Students. The program combines faculty-guided research with research-related activities and other experiences designed to enhance the problem solving skills of the participating students, to promote in them high ethical standards and a commitment to a research career. The program has three major objectives: 1) to acquaint the participants with career opportunities in which research is a major element of the individual's professional activities; 2) to develop their leadership skills and awareness of relevant ethical issues, and 3) to establish a professional network that will benefit the students long after their formal education has been completed.

The 1993 program was sponsored jointly by the Richard King Mellon Foundation, the Merck Foundation, and the Robert W. Woodruff Foundation. In addition, The Wellcome Trust provided fellowships that enabled three students from the United Kingdom to take part in the program. The Auxiliary to the New York State Veterinary Medical Society contributed to the success of this initiative by providing each of the participants with a copy of a program source book as well as several book prizes.

The program roster included 24 students from thirteen different veterinary colleges in the United States, Canada, Australia, the United Kingdom, and the Republic of Estonia. The diversity enriched the program and afforded an opportunity for the students to compare their professional school experiences and to gain insight into career opportunities and the challenges of veterinary medicine worldwide. Carol Miltenberger, a third-year student in the College of Agriculture and Life Sciences at Cornell served as program coordinator.

"Class of 1993"

The program spanned ten weeks during the months of June, July, and August. Student fellows were assigned research projects which enabled them to explore a variety of subjects, to learn new investigative techniques, and to gain insight into the manner in which a research laboratory utilizes its professional and material resources.

The Leadership Program is first and foremost a research experience. It is much more than that, however. It includes a variety of activities calculated to assist the students with their career decisions, to heighten in them an awareness of ethical considerations and the meaning of leadership, while simultaneously improving their critical capacity and communication skills. Salient features of this year's program are described below:

Career Day: Career counseling is an important feature of the program. Counseling occurred informally and frequently while the program was in session; however, Career Day afforded a special opportunity for the students to focus on their future training. Four veterinarians who have achieved distinction as research scientists and administrators, or have only recently completed training comparable to that expected of program graduates, met with the students for an entire day. The following individuals took part:
The proceedings began the evening prior to Career Day when the students and counselors met to develop a meeting agenda. The latter included introductory statements by the students and comments by the counselors on their own careers. The presentations were followed by breakout meetings in which the students and individual counselors discussed various aspects of career planning. A social gathering and dinner that evening enabled the students to entertain their visitors, representatives of the program sponsors, and other invited guests.

**Group Discussions:** Three group discussions were held in conjunction with the 1993 program. A discussion of research and residency training was led by Professor Robert M. Lewis, Professor of Pathology and Professor Brian R.H. Farrow, Chairman of the Department of Clinical Sciences. The discussion leaders identified factors that prospective trainees should consider in selecting a residency; they explained how the national placement service operates; how one can arrange for advanced training in research before completing a residency, and how clinical experiences are integrated into many advanced training programs.

Dr. Ari van Tienhoven, Emeritus Professor of Animal Physiology and one of Cornell’s finest teachers, organized a “project” in biomedical ethics. During the ten-week period in which the program was in session, the students investigated, acted out, and reported on a major ethical issue that captured public attention several years ago. The students were provided with copies of several key articles and editorials, including the original paper which lay at the center of the controversy. They also received copies of the congressional testimony connected with the case. After several weeks of independent study, the students met to discuss the issue from the perspectives of twelve individuals who were immediately affected by these events. Students who did not represent one of the protagonists, prepared a report documenting how, in their opinion, such matters should be managed.
The third discussion focused on aspects of leadership identified by John Gardner in his book, *On Leadership*. The moderator, Dr. Robert D. Phemister, Dean of the Veterinary College, and two internationally respected leaders in higher education, Mr. Frank H.T. Rhodes, President of Cornell University, and Dame Leonie Kramer, Chancellor of Sydney University, engaged the students in wide ranging discussion of the subject.

Radiation Safety: Radioisotopes are used frequently in research; yet many individuals who are at an early stage in their training are unfamiliar with procedures connected with the proper acquisition, use and disposal of these materials. Participants in the 1993 program received four hours of instruction on such matters. The presentations were arranged by Cornell’s Radiation Safety Officer, Mr. Thomas J. McGiff.

Site Visits: Three visits to other institutions known for the excellence of their research were held in conjunction with this year’s program. The students and several members of the participating faculty visited the research facilities of Merck and Company in Rahway New Jersey, the National Institutes of Health (NIH), and the Beltsville campus of the United States Department of Agriculture (USDA), both in the Washington, DC area. The visits enabled the students to grasp the scope of research and opportunities for advanced training in the host institutions. Agendae for the three visits are reproduced below.

**Merck Research Laboratories**

**June 29, 1993**

**Creating New Products for Animal Health**

9:10 a.m.  Dr. Dan Farrington, Senior Director, Animal Science Research  
*“Field Operations North & South America”*

9:30 a.m.  Dr. Gerry Hickey, Assistant Director, Animal Drug Evaluation  
*“Basic Animal Science Research”*
9:50 a.m.  Dr. Linda Rhodes, Research Fellow, Biochemistry
10:10 a.m.  Dr. Srinivasa Prahalada, Senior Investigator, Safety Assessment
10:30 a.m.  Laboratory Discussions:
            Dr. Lynn C. Anderson, Director, Laboratory Animal Resources
            Dr. Wesley L. Shoop, Senior Research Fellow, Animal Drug Evaluation
            Dr. Kenneth L. Mohn, Research Fellow, Animal Drug Evaluation
            Dr. Dennis M. Schmatz, Director, Parasite Biochemistry and Cell Biology
12:30 p.m.  Lunch
1:30 p.m.  Dr. Jane Eagleson, Associate Director, Animal Science Research
           “Project Development”
1:50 p.m.  Dr. Janice Nicol, Assistant Director, Animal Science Research
           “Field Operations Eastern U.S. & Canada”
2:10 p.m.  Dr. Mark Soll, Executive Director, Merck AgVet, Central Marketing
           “Technical Services”
2:30 p.m.  Open Discussion
3:00 p.m.  Dr. Harold D. Hafs, Vice President (Retired), Agriculture and Animal Health Research and
           Development
           “The Merck Commitment to Animal Health”
3:30 p.m.  Closing Remarks

Leslie Triplett (left), Dr. Schlafer (center) and Marjorie McIsaac examine autopsy specimens at the National Cancer Institute (NIH).

National Institutes of Health
July 8, 1993
Research and Research Training at the NIH

8:30 a.m.  Dr. Marlene Cole, Director, Veterinary Research Resources Program
           “Overview of NIH, NCRR, and Veterinarians at NIH”
9:00 a.m.  Dr. Robert Carolan, Chief of Research Animal Branch, Veterinary Resources
           Program, National Center for Research Resources
           “PHS Commissioned Corp”
9:45 a.m.  Laboratory Visits:
           Dr. Ritva P. Evarts, NCI Laboratory of Experimental Carcinogenesis
           Dr. Kevin Gardner, NCI Laboratory of Pathology
United States Department of Agriculture  
(Beltsville Campus)  
July 9, 1993  
Research Programs of the USDA

8:30 a.m.  Dr. G.C. Marten, Associate Director, Beltsville Area  
"Overview of Beltsville Agricultural Research Center"

8:45 a.m.  Dr. T.J. Sexton, Institute Director, Livestock and Poultry Sciences Institute  
"Overview of Livestock and Poultry Sciences Institute"

9:00 a.m.  Dr. R. Fayer, Research Leader, Zoonotic Diseases Laboratory  
"Cryptosporidiosis"

9:30 a.m.  Dr. J. Urban, Research Leader, Helminthic Diseases Laboratory  
"Research on Parasitic Diseases"

10:00 a.m.  Break

10:30 a.m.  Dr. Robert Wall, Research Physiologist, Gene Evaluation and Mapping Laboratory  
"Transgenic Animal Research"

Student Presentations: Before leaving Cornell, the students reported on their research activities in an open forum to which faculty and administrative staff of the College of Veterinary Medicine were invited. The presentations were uniformly good, and some were outstanding. In the reports which follow, the students introduce themselves and describe their individual and collective experiences.
Dr. Gerry Hickey (left), representing Merck & Co., one of the program’s sponsors, exchanges thoughts on the program with Dr. Leland (Skip) Carmichael (center), and Dr. Douglas McGregor (right).

Carol Miltenberger (far right) organized the Career Day dinner. Her parents, representing the Richard King Mellon Foundation, were among the program guests.

The students took advantage of their visit to the NIH to learn more about opportunities for advanced training in that prestigious institution.

I am now halfway through the veterinary curriculum at Cornell, and the approaching reality of graduation was an impetus to participate in the Leadership Program. I perceived the program as a way to look more closely at research as an alternative career.

I completed my undergraduate studies at Cornell in Natural Resources, with an emphasis in tropical agriculture and development policy. I spent the next four years in and around dairy farms in New England, working with a large commercial herd, with a smaller integrated farming system, and also as an artificial insemination technician. My experience strengthened my interest in small-scale agriculture, particularly dairying, both in tropical countries and here at home. I decided to pursue a career in veterinary medicine, as a means to participate more broadly in farming—veterinary medicine offered me not only a solid scientific base and skills, but also an opportunity to apply those skills to practical problems of animal agriculture.

Several events during the past year demonstrated to me the critical role of research on problems peculiar to tropical and sub-tropical countries, and suggested a more specific career possibility. Last summer I visited and worked at the Uganda Trypanosomiasis Research Organization, where I took part in epidemiological field surveys of both the human and animal disease. The experience introduced me to the joys and frustrations of field research, and it opened my eyes to the realities of infectious disease in a country where parasitic disease is a part of daily life and death. The importance of infectious diseases to the health of animals and humans, and to society in the broader sense, was echoed in coursework in parasitology, infectious diseases, and foreign animal diseases during the second year of the veterinary curriculum. Infectious disease research appeared as another means to effect change in tropical agriculture, and suggested that a veterinary degree could serve as the foundation for advanced training in research, if I chose to pursue a research career. The Leadership Program enabled me to examine that possibility more closely.

As a Merck Foundation fellow, I worked in Professor Edward Pearce’s laboratory in the Department of Microbiology, Immunology and Parasitology. Professor Pearce’s principal research interest is in the immune response to infection with the trematode helminth Schistosoma mansoni. Schistosomiasis is among the most prevalent infectious diseases, affecting some 200 million people and countless domestic livestock in developing countries. The disease in most of these cases is chronic in nature, but it carries a mortality rate of 5-10%. Pathology due to infection is mainly the result of the host’s own immune response to parasite eggs, which become trapped in the liver and intestine where they induce the formation of granulomata.

Schistosome eggs are highly immunogenic. They provoke both B and T-helper (Th) cell activation with the T cell response being skewed in the type 2 Th (Th2) direction. Th2 cells, when activated, synthesize a discrete subset of cytokines, including IL-4 and IL-5 but neither IFN-γ nor IL-2. Responses of the Th2 type have been noted in several helminthiases, with IL-4 and IL-5 controlling the elevated IgE levels and the eosinophilia associated with these infections. In contrast, Th1 cells (which often constitute the response to intracellular pathogens) produce IFN-γ and IL-2 but not IL-4 or IL-5.

My research project was directed towards elucidating why schistosome eggs induce Th2 as opposed to Th1 responses. Recent studies have indicated that naive precursor Th cells can differentiate into either Th1 or Th2 cells depending in part upon which cytokines are present in the environment in which they are stimulated. In the case of the Th1 response, recent studies have linked the initial release of IL-12 by antigen presenting cells (APC) interacting with antigen, to the eventual production of IFN-γ by NK cells and the differentiation of naive Th cells into Th1 cells. Much less is understood of the Th2 differentiation pathway, but IL-4 is known to have a key role. The initial source of IL-4 and the stimuli leading to its production remain to be elucidated, though mast cells and/or basophils, which produce a similar series of cytokines to Th2 cells, are considered to be its most likely source. I examined the hypotheses that schistosome egg antigens (SEA): 1) directly activate mast cells to make IL-4, and 2) activate macrophages to produce a cytokine which activates mast cells. Our candidate for the activating cytokine was MCP-1 (macrophage chemotactic protein),
which is produced by activated macrophages and is reported to be highly effective in inducing histamine release from mast cells.

The cell types used in these studies included a mouse macrophage cell line (P388D), a mouse mast cell line (CFTL-12), and non-elicited mouse peritoneal macrophages. The cells were incubated with schistosome eggs or SEA, alongside unstimulated cells and cells incubated with known mitogens. RNA was recovered from the cells and reverse transcribed into single-stranded cDNA. Cytokine gene transcripts were then amplified using cytokine-specific oligonucleotide primers in a semi-quantitative PCR. Initial comparisons of the cytokines produced after a 5-hour incubation with the antigen or mitogen suggest that the egg antigens do stimulate cytokine gene transcription in mouse macrophages and mast cells. Consistent with our hypotheses, SEA stimulated MCP-1 transcription in macrophages and IL-4 transcription in mast cells. Additionally, TNF-α transcription was observed in SEA-stimulated macrophages and TNF-α, IL-4, IL-10 and IL-13 were noted in the mast cells exposed to SEA. These results indicate that macrophages and mast cells can be directly activated by SEA to produce cytokines which may be involved in the complex message system that initiates a polarized Th2 response.

The Leadership Program allowed me to walk in “cold” to a research laboratory and begin to learn what “research” really means. I was able to learn several basic techniques, to focus in on some very particular questions, and to participate in meaningful studies that were already underway. Working closely with a scientist who was willing to teach, enabled me to share in his excitement and enthusiasm for his work. Talking with the others in the lab was particularly helpful, as it allowed me to begin to see more clearly the choices involved in research. I wish to thank Professor Pearce, Dr. Beth Sabin, and Mr. Mark Hulsebosch, for their patience, candidness, and sense of humor. Meeting so many other vet students from across the country and around the globe was also enjoyable. Many had similar questions but different experiences that balanced my own single view. The scheduled events this summer, particularly the visits to the National Institutes of Health, Merck, and the USDA, were also quite important in demystifying the references to the “NIH,” to “industry” and to “government,” which we so often hear when speaking of career possibilities. It was a busy summer! I feel I have learned a tremendous amount, and have been given information and experience to assist me in the decisions that I will make in the next few years.

John Benson
Washington State University

I enrolled in the Leadership Program after completing two years of veterinary medical training at the Washington State University College of Veterinary Medicine. It was during veterinary school that I first developed a strong interest in research. In the summer following my first year, I participated in several projects, each aimed at studying the equine enteric nervous system (ENS). The ultimate goal of the research was to identify the compounds and mechanisms involved in ischemic neurotoxicity of the ENS, a feature of many cases of equine colic. The nerve damage often is reflected in failure of the intestine to resume its normal peristaltic function following surgical colic correction. The aim of our research was to examine certain compounds in the ENS-VIP, substance P, glutamate, and nitric oxide, and to define their role in both normal and altered smooth muscle function. Methods employed in these studies included immunocytochemistry, in vitro myoelectric stimulation, and in situ hybridization techniques.

My experiences at Washington State lead me to examine a career in veterinary research more closely. I was particularly interested in learning about research opportunities in government and industry, and the Leadership Program was the perfect forum to accomplish that objective.

My research at Cornell was concerned with an interesting aspect of equine respiration. I worked in the laboratory of Professor Dorothy Ainsworth, where I took part in her studies of equine respiratory muscle recruitment during hypoxia, hypercapnia, and exercise. A long-term goal of the research is to determine whether diaphragmatic fatigue is a limiting factor in exercise in normal horses or in horses with respiratory tract disorders such as laryngeal hemiplegia or small airway disease.

My project focused on the recruitment pattern of both inspiratory and expiratory muscles in horses during treadmill exercise. Relevant data was acquired by implanting EMG electrodes in the costal diaphragm (inspiratory), transverse abdominal (expiratory), and external oblique (expiratory)
muscles. Such instrumentation techniques allowed the mean electrical activity of the muscles to be calculated and thus changes in muscle recruitment patterns to be determined as a function of the exercise hyperpnea. Other respiratory-related parameters measured during these studies were ventilation, (through a breathing mask) and thoracic and abdominal pressure changes (esophageal and gastric balloon catheters). Hence, we examined as many as seven physiologic parameters and arterial blood gases on a galloping horse which was quite a challenge! The results showed that both the diaphragm and transverse abdominal muscles exhibit significant increases in mean electrical activity as a function of exercise intensity. The external oblique muscle, however, produced a pattern suggesting that it serves a postural or locomotor function during exercise. Thus, the activation pattern of the external oblique seemed to correlate better with footplant than exercise intensity.

Once the normal recruitment patterns of these respiratory muscles during exercise have been established, we will examine the effects of added resistive breathing loads. It will be interesting to learn whether resistive loads, such as that induced by laryngeal hemiplegia, will produce a different muscle recruitment pattern. It is tempting to speculate that diaphragmatic fatigue is more likely to develop in these circumstances, and that muscles, such as the external oblique, may be more directly involved with respiration then they seem to be in normal horses.

Andrea Brown  
Auburn University

This fall I will begin my second year of veterinary school at Auburn University in Alabama. I have been interested in veterinary medicine since childhood, and worked for a small animal practitioner while in high school and college. I graduated from Samford University with a B.S. in Biology. It was during my undergraduate years that I was exposed to other career opportunities in science, and was chosen to participate in a drug toxicology study which resulted in a published report. After graduating from Samford, I postponed further university training to work in Spain. During that year, I also worked as a research assistant in two field projects, one involving livestock feed additives, the other studying native Hawaiian birds. I applied to the Leadership Program to gain more research experience, as well as to explore career opportunities in veterinary medicine.

My project this summer was conducted in Professor Max J.G. Appel’s laboratory at the James A. Baker Institute. The aim of my investigation was to adapt a colorimetric assay for use as a laboratory test for neutralizing activity of dog serum against the bacterium *Borrelia burgorferi*, the causal agent of Lyme disease. The colorimetric assay was described in the *Journal of Microbiological Methods*. It represents an important technological advance, for current methods for quantifying *B. burgorferi* rely on counting the bacteria in individual test samples, a very time-consuming process. The described assay was developed using mouse sera. Bacterial activity is reflected in the pH of the culture media as determined by an indicator, phenol red. Lactic acid produced by active *B. burgorferi* metabolism changes the color of the media from red to yellow. Serum lacking neutralizing activity does not inhibit metabolism of the bacteria; hence, the media becomes yellow. Serum with neutralizing activity retards or prevents this change, and the degree to which it does can be quantified using an absorbance reader.

My task was to adapt the assay for use with canine sera. Assays were prepared in 96-well microtiter plates. Changes in media color were determined daily. The first step was to culture the organisms in media alone to determine their rate of growth as reflected in the color of the media. Later experiments made use of sera from dogs infected with *B. burgorferi*. Unfortunately, we did not obtain the predicted results. Evidently, the assay may not be as easily adapted for use with dog sera as was hoped.

My experience this summer not only gave me the opportunity to work on a specific research project, but also allowed me to observe some of the ongoing investigations in Professor Appel’s virology laboratory. Excursions to Merck, NIH, and USDA afforded opportunities to learn about alternative career paths in industry and government, and events, such as Career Day, were not only informative, but also provided opportunities to talk informally with leaders in the scientific community. Best of all was the interaction with other program participants from other U.S. veterinary colleges and from colleges in other countries. I would like to thank Professor Appel and everyone in his laboratory as well as the Woodruff Foundation and the organizers of the Leadership Program for a memorable summer.
I began my veterinary training in 1985 in Kosice Slovakia, where I completed nearly two years of the course. Between 1987 and 1989, I had an unplanned "break" from my studies while escaping from my homeland to take up residence in a new country, Australia. It never occurred to me that emigrating would permanently impede my career plans, however. After passing exams in English proficiency, I began the first year of veterinary science at the University of Sydney. At the moment I am half way through my final year, and expect to graduate in December.

I want to start my professional career in a large private practice, preferably small animal or mixed. I feel that after completing veterinary training I need exposure to the "real world" in order to ground my theoretical knowledge and practical skills before continuing my formal education. In due course, however, I would like to pursue clinical sciences (medicine and surgery) as an intern or resident at an Australian veterinary school. Ultimately, a position at a university clinic seems quite attractive.

As a Mellon Foundation Fellow, I spent this summer in the Department of Physiology under the supervision of Dr. Curtis Fullmer. I became involved in his research on vitamin D metabolism and lead poisoning. Even today, when so much emphasis is placed on a cleaner, healthier environment, lead toxicity is still the most common preventable paediatric illness in the United States. Dr. Fullmer's research seeks to elucidate the mechanism of lead poisoning, and aid in its prevention.

Vitamin D affects the metabolism of lead in a manner similar to that of calcium. Indeed, calbindin D binds lead with an affinity greater than that for calcium. If lead is present in the diet, its absorption is similarly enhanced.

The project in which I was involved investigated the influence of dietary calcium deficiency, vitamin D deficiency, lead, and inorganic phosphate deficiency (alone or in various combinations) on vitamin D metabolism, in particular the effect of the above factors on the activity of renal 1-hydroxylase. Another renal enzyme, 25-hydroxy-vitamin D-24 hydroxylase also was investigated, although the physiological significance of its products (24, 25-di hydroxy-vitamin D and 1, 24, 25-trihydroxy-vitamin D) is poorly understood. Our experiments showed that calcium deficiency stimulates 1-hydroxylase, presumably by enhancing secretion of PTH which acts directly on the kidneys to promote production of the active metabolite, 1,25-dihydroxy-vitamin D.

A rachitic diet (deficient in vitamin D), in the absence of UV light, also stimulates the enzyme, primarily via the same endocrine pathway. Addition of lead to the diet elevates 1-hydroxylase activity, but the increase in circulating 1, 25-dihydroxylase-vitamin D and intestinal CaBP does not correspond to the level of increase of the enzyme. It is possible that the elevated 1-hydroxylase activity leads to exhaustion of the precursor, 25-hydroxy-vitamin D. Alternatively, there may be feedback stimulation of 25-hydroxy-vitamin D and/or 1, 25-dihydroxy-vitamin D catabolism by elevated 1, 25-dihydroxy-vitamin C. Although the mechanism of action of lead on the vitamin D metabolism is poorly understood, it does not appear to act via PTH. Clearly, more research is required to clarify these issues.

The Leadership Program gave me an opportunity to gain experience in something I have never done before: research. It has been a valuable experience and one which made me think about the many career opportunities there are for veterinary graduates. I very much enjoyed meeting so many interesting people, and learning at least a little bit about America. I would like to thank the Mellon Foundation for making it possible for me to participate in the program, and also Dr. Fullmer and his colleagues for their guidance, patience and friendliness.
Virginia Fajt  
Auburn University

I have completed two years of the veterinary course at Auburn University College of Veterinary Medicine. Prior to that, I received a B.A. with a major in Psychology from Kalamazoo College in Michigan. After graduating from Kalamazoo, I spent two years working as a legal assistant in a law firm in Denver, Colorado. During that time, I spent several weeks as a volunteer at Heifer Project International’s Livestock and Learning Center in Arkansas as a ranch hand. It was during this period that I first became interested in livestock. I decided to go back to school to earn a Bachelor’s degree in Animal Science at Colorado State University. I spent two years taking undergraduate science and animal science courses, but discontinued my studies to move to Florida. There, I worked for a trade association which represented fertilizer and agrichemical manufacturers. While in Florida, I spent several months working as a technician in a small animal clinic, and then decided to obtain a veterinary degree. Since moving to Auburn, I have worked in the USDA Parasite Research Lab studying intestinal parasites of cattle. I also spent a summer at the Plum Island Animal Disease Center on Long Island, studying Foot and Mouth Disease Virus.

When I learned about the Leadership Program at Cornell, I concluded that it would provide a good opportunity to learn more about research, and to be exposed to research at another institution. The other activities of the program such as the trips to Merck, NIH and USDA, and the ethics project, sounded like a way to investigate alternative careers in veterinary medicine.

As a Woodruff Foundation Fellow, I joined Dr. Vicki Meyers-Wallen’s laboratory at the James A. Baker Institute. The principal interest of Dr. Meyers-Wallen’s research is in the area of canine genetics and reproduction, and particularly the genetic basis of abnormal sexual development. I investigated XX sex reversal in a family of German Short Haired Pointers.

The sex of an animal is determined in three stages: chromosomal, gonadal or phenotypic. Chromosomal sex is determined at fertilization as XX or XY. During gestation, gonadal sex is determined. Initially, the gonad is undifferentiated. If the gene for testis determination is present, i.e., if the animal is a chromosomal XY, the gonad differentiates into a testis. Hormones produced by the testis determine male sexual characteristics, hence testis determination is the critical event in the development of the phenotypic male. In the absence of the Y chromosome, the gonad develops into the ovary, and a phenotypic female results.

In the case of sex reversal, the chromosomal and the gonadal sex of the animal do not agree. In the affected German Short Haired Pointers we were investigating, the animals had a 78, XX chromosome constitution and bilateral ovotestes, and a uterus. They also exhibited some degree of masculinization of the external genitalia, such as an enlarged clitoris. Since the animals have some degree of masculinization yet do not have a Y chromosome, we attempted to determine whether the gene for testis determination was present in these animals, i.e., whether the gene had translocated to a chromosome other than the Y.

To determine whether the gene was present, we electrophoresed samples of DNA on agarose gels, then transferred the DNA to a nylon membrane (Southern blotting). The gene for testis determination in mice has been isolated as the Sry gene. Therefore, by probing the Southern blots with the mouse Sry probe, we could determine if the Sry gene was present in the affected animals, which would indicate that the translocation of the gene for testis determination from the Y to another chromosome is the reason for sex reversal of the XX animals.

Towards the end of my project, I also employed the polymerase chain reaction (PCR) to look for a translocated gene for testis determination. PCR is a method of making many copies of a particular sequence of DNA. Since the sequence of the Sry gene is not known for the dog but is known for the mouse, one can look for the Sry homologue in the dog by using the sequence for the mouse gene as PCR primers. If the sequence is present, it will be amplified by PCR, and the product can be examined by gel electrophoresis and other techniques. The control Sry primers used with template DNA containing the mouse Sry genomic sequence yielded the expected 237 bp product. Time did not permit analysis of dog genomic DNA as a PCR template.
I am about to begin my sixth and final year at Cambridge University. Like the majority of students in my course, I took a Bachelor of Arts degree at the end of my third year, receiving it in Pathology. For my dissertation, and over the adjacent two summer vacations, I participated in a project investigating the effect of Theiler's Murine Encephalomyelitis Virus on mice. The infection has been proposed as a model for multiple sclerosis in humans. My task was to investigate the expression of interleukins and interferons in the central nervous system following infection. While pursuing this research, I became interested in the pathology, immunology and control of infectious diseases, and have since been considering further work in this area. I have an interest in diseases of importance in the developing world and particularly in zoonoses and public health problems.

My reason for applying to the Leadership Program was that I was looking for experience in aspects of infectious disease other than molecular pathology and thought it would provide an excellent opportunity to explore various career options. I received a Wellcome Trust Fellowship which enabled me to work with Professor Yrjo Gröhn in the Section of Epidemiology. Professor Gröhn is interested in quantifying the relationship between disease in dairy cattle and milk production. He has developed a model which can predict the expected milk yield of an individual cow in the absence of disease, based upon the current level of production of that cow. Expected milk yield can then be compared with the actual production of the cow, and deviations can be identified and analyzed to determine various associations with disease.

It is now generally accepted that to “survive,” dairy farms must operate as businesses. This necessitates thorough understanding of all sources of expense and income and determination of optimum input for maximum output; in this case, milk production.

My project was designed to investigate economic aspects of production diseases in dairy cattle. Specifically, it entailed quantifying total annual veterinary medical and preventive costs for a sample of New York State dairy herds and expressing this expense in terms of milk yield. Associations between medical expenses and yield could then be calculated and used as a guide to the optimum level of medical management. By the end of my project, the following results had been obtained. Average annual direct medical costs were found to be $75 per cow and $.35 per hundred weight of milk produced by the farm. Total costs were categorized under various headings and the proportions of the total cost calculated, as illustrated in the diagram below.

The most significant “exposure condition” was displaced abomasum; it accounted for more than 25% of the total cost within the disease category. Overall average annual medical costs represented only 3% of the value of the gross income from milk sales.

Further analysis is required to fully investigate any relationship between disease cost and milk yield. A major goal is to more accurately quantify the total cost of disease to dairies, and to consider at what level disease should be tolerated, and which methods of control, treatment or prevention are the most profitable.

I found my project this summer to be valuable, because I was introduced to an area in which I had little formal training yet one that is directly relevant to my interest in disease control. It has encouraged me to consider disease as a multifactorial system, which operates at a population, rather than at an individual level. In addition, the visits to NIH, USDA, and Merck & Co. provided insight into the work of national research and health organizations.
also enjoyed both the academic and social aspects of my time at Cornell and would recommend the experience to anyone not intent upon entering private practice.

Brain Kraje
Virginia-Maryland Regional College

I graduated from Virginia Tech in 1992 with a B.S. in Animal Science, and a double major in Biochemistry and Nutrition. During my senior undergraduate year, I developed a ninhydrin-based spectrophotometric assay for ovine cytosolic dipeptidase activities. During my first year at the Virginia-Maryland Regional College of Veterinary Medicine, I became involved in a study characterizing the sequelae of trigeminal nerve damage on prehension performance and growth in neonate rats. My plans are to work in a mixed practice for a couple of years following graduation, and then pursue residency training in internal medicine.

I was privileged to have participated in the 1993 Leadership Program as a Woodruff Foundation Fellow, under the supervision of Professor Jun-Lin Guan, a member of the Cancer Cell Biology group in the Department of Veterinary Pathology. The Guan laboratory is currently focusing on the function of an intracellular protein tyrosine kinase—pp125fak (or Focal Adhesion Kinase) in cell adhesion and tumor cell metastasis. The transduction of biochemical signals from the extracellular matrix (ECM), through such adhesion receptors as the integrins, activates intracellular protein tyrosine kinases, such as FAK. Activation of these enzymes may trigger downstream events, resulting in cell adhesion, motility, and differentiation.

To understand the role of FAK in integrin-mediated cell adhesion, Professor Guan and his associates are seeking to identify cellular proteins that interact with FAK. Recombinant FAK was expressed in a baculovirus system and used to identify the interacting proteins, using a filter binding assay. My work entailed cloning cDNAs encoding the interaction proteins.

Using a lambda-gt11 library (a lambda expression cDNA library made from mouse embryo, and purchased commercially), I transformed Y1090r-bacteria. The latter possess flagella which are required for viral transformation. A lambda expression library can be used to produce proteins which can be screened with appropriate probes for subsequent cloning and amplification of desired products. I initially incubated bacteria and phage together, in cationic buffer to allow entry of the virus. I then plated the colonies on agar and incubated the cultures at 42°C to "force" the virus into the lytic phase. Thereafter, the plaques were incubated for varying intervals in the presence of isopropyl thio-B-D-galactoside to drive expression of the proteins. Finally, after transferring the expressed proteins onto a nitrocellulose membrane, I screened them using a crude cell lysate containing FAK. In order to accomplish this, I had to radiolabel tyrosine residues on FAK with 32P-ATP, hybridize the probe with the nitrocellulose-bound proteins, and look for "positive" clones after exposing of the membranes to photographic film. Selecting "positive" clones, retransformation, and increasing levels of stringency should, in due course, result in isolation of the plaques producing the FAK-interacting protein. After screening over 165,000 colonies, I focused on several dozen putative positives. Further work will entail their subcloning, sequencing, and comparative analysis to known intracellular proteins.

Of all of the program's attributes, I found most appealing the responsibility of the participant to make things happen on individual initiative. In both the trips to industry and government, and in day-to-day interactions at the veterinary college, I was continually grateful for the consideration shown to us by our mentors and colleagues. Establishing a career in research-based medicine, at any level, involves actively DOING something, and this program is certainly a jump start.

Christopher Laing
University of Sydney

I graduated from high school in 1988 with the aim of extending my studies in veterinary science. I applied to both Melbourne and Sydney Universities, but decided in the end to enroll at Sydney. I am currently midway through my fourth year, having
spent a year in 1992 conducting research in order to earn a B.Sc. (veterinary) degree. I spent the year examining the vitamin D system in squamate reptiles, including the plasma transport system for vitamin D metabolites. I undertook this research through Sydney University, in collaboration with the Taronga and Melbourne Zoos, and the Gosford Reptile Park. The experience motivated me to further explore the possibilities of a research career, and was the reason I applied for admission to the Leadership Program at Cornell. I was accepted as a Mellon Foundation Fellow, and had the opportunity to pursue research at the James A. Baker Institute as part of a team headed by Professor Gus Aguirre. However, I worked closely with Professor Jhama Ray.

The project in which I became involved was concerned with a group of inherited diseases of dogs characterized by a deficiency of lysosomal enzymes and the storage of products caused by that abnormality. My research focused on the disorder known as Mucopolysaccharidosis VII (MPS VII). MPS VII is a storage disease that occurs in humans and mice, as well as in canines. It is caused by a deficiency of the lysosomal acid hydrolase, beta-glucuronidase, an enzyme that is responsible for metabolic breakdown of glycosaminoglycans (GAGs). A deficiency in the activity of the enzyme results in massive accumulation of GAGs in all affected tissues. The clinical manifestations of the disease are extensive and varied; they include mental retardation, bone deformities and hepatomegaly.

MPS VII is an autosomal recessive disorder. Several point mutations and one full exon deletion may contribute to the disorder in humans. The mutated gene produces mRNA, and also the enzyme itself, but the enzyme is abnormal, resulting in low activity. While the cDNA for beta-glucuronidase (GUSB) has been cloned and sequenced in the human, rat and mouse, a comparable study has not yet been made of the canine gene.

The aim of my project was to develop conditions under which regions of canine cDNA homologous to human GUSB cDNA could be detected, amplified by PCR (polymerase chain reaction). The PCR amplified canine DNA fragment could be used to clone canine GUSB cDNA from the cDNA library and to identify mutations of the gene. The project involved cross-species Reverse Transcription (RT)-PCR of canine RNA with oligomers derived from the closely related gene in humans. Oligonucleotides from the human cDNA were chosen on the basis of their homology with rat and mouse genes. RNA was extracted from retinal pigment epithelial (RPE) cell cultures. RPE has advantages over other cells in this particular study: it grows in culture as a monolayer, and also the level of expression of GUSB is quite high. RPE was obtained from both normal and clinically affected dogs. The RNAs were extracted and cDNA templates were made by RT using 3'-oligonucleotides. The cDNAs thus produced were amplified by PCR using both 5' and 3'-oligonucleotides and Taq polymerase. The PCR amplified DNA fragments were then analyzed by determining their migration on a polyacrylamide gel. Visible bands representing the individual fragments were then compared with bands in concurrently run cDNA controls. The presence of the same size bands was taken as evidence of homology of the canine and human genes in that region.

By participating in this project, I acquired some knowledge of molecular biology, a discipline in which I had no previous experience. I became familiar with the PCR technique as well as with other procedures for studying RNA.

Outside the laboratory, there were many useful experiences. The trips to Merck and to the USDA and NIH were interesting, affording as they did an opportunity to compare the research conducted in those institutions with that pursued in a university setting. Meeting veterinary students from around the world also was an interesting aspect of the program. Overall, I found it a valuable experience and would highly recommend it to students who are considering a research career.
research, with an element of teaching. I was interested to learn of The Leadership Program for I perceived in it the opportunity to clarify my ideas while simultaneously learning about a wide range of career options open to individuals with a veterinary degree. I found the program and the various trips connected with it helpful in this regard, and now am more sure of the direction in which to head.

As a recipient of a Wellcome Trust Fellowship, I was able to work with Professor Robert Oswald in the Department of Pharmacology. The work in this laboratory is concerned with the study of ligand-gated ion channels, primarily the nicotinic acetylcholine receptor (nAChR). Acetylcholine activated channels are by far the most studied neurotransmitter-gated channels. They also were the first channels whose unitary ionic currents were recorded by Neher and Sakmann using their revolutionary patch clamp technique, an achievement which gained them The Nobel Prize in 1991. The technique is now widely used for electrophysiological studies and was the main one I employed in my research this summer.

Much is known about acetylcholine receptors. They are thought to be composed of five subunits with an axial hole present to allow ionic flux. The complete amino acid sequence of a number of these subunits has been determined, and this in turn has led to predictions about the secondary, tertiary and quaternary structure of the molecule. Much is still to be investigated and proven, however. The definition of receptor topology can be expected to provide better understanding of receptor function and regulation. Correlation of structure with function is the main aspect of Professor Oswald’s research on acetylcholine receptors. A diverse range of techniques are being used to address this matter. One approach is to study the structural elements of cholinergic agonists that influence binding to and activation of the receptor, and modulation of channel function. It is hoped that by using systematically modified agonists and performing single channel recording using the patch clamp technique, microscopic changes in channel kinetics may be correlated with the structural modifications of the compounds. These investigations can be further enhanced by generating site-directed mutations in channel structure, then correlating the induced changes with channel function and agonist interaction. Information gained in this way should help to elucidate both channel structure and the regulatory sites, and is potentially of relevance in the generation of new cholinergic drugs.

My project involved an investigation of cholinergic agonist function using muscle subtype nACh receptors expressed by BC3H1 cells, a mouse brain tumor line, as the subject of study. The agonist series used were derivatives of the compound, 1-dimethyl-acetylpiperazinium (HPIP). The individual agonists differed in the number of carbon atoms present in a side chain attached to the amide group of the molecule. Their effect on channel function was discerned using the cell attached variant of the patch clamp technique. HPIP has previously been found to be a potent agonist.

Diagram showing traces of ion channel openings made using the patch clamp technique and the three agonists, HPIP, EthylPIP and PropylPIP. The traces display voltage against time.

The principal finding in the study I performed was that the sequential addition of carbon atoms to the side chain resulted in a marked reduction in the time the channel spent in its open state. The effects these modifications have on agonist affinity and channel closed time have yet to be analyzed from the data.

Graph demonstrating the change in average open time of channels as the length of side chain increases.

The summer was rewarding both intellectually and socially, and would thoroughly recommend it to others. I found it particularly interesting to meet other students, many of whom are interested in careers other than general practice, and to hear about veterinary training in their various countries. I would like to thank my supervisor, Professor Oswald, the program organizers and the Wellcome Trust for the chance to take part in the program.
This fall I enter the second year of the four year program at Iowa State University that will lead to the realization of my life-long dream: becoming a veterinarian. Before entering the College of Veterinary Medicine, I completed two years of an animal science degree, also at Iowa State.

The summer after I graduated from high school, I obtained my first research experience as an intern for the USDA in biological control of corn insects. I worked in biological control for two summers, my second year working on my own project. This project included identifying various weeds that contain the fungus *Beauveria Bassiana*, isolating this fungus, and testing its efficacy against the European Corn Borer. In my second year of college, I worked in a ruminant nutrition laboratory assisting in formulating a better bypass protein (a protein that is not broken down in the rumin) through varying pellet ingredients and frying/cooking methods.

My laboratory experience this summer as a Merck Foundation Fellow has taken me into an entirely different area of study. Only a few months ago, I could not understand why someone would enter the field of engineering. The physics and mathematics seemed overwhelming. After a summer of working in John Bertram’s Biomechanics Laboratory, my understanding and appreciation for engineering changed. Engineering and anatomy were the foundations for my project that was concerned with the modeling of growing bones.

On my first day, I learned to solder wires onto a strain gauge using a dissecting microscope. These strain gauges would become the basis for my research. A strain gauge contains three minute wire grids each oriented in a different direction and having a resistance of 120 ohms. When the gauge is deformed, the resistance of the grids change allowing one to identify the direction and magnitude of the deforming force. All materials deform under load, including bones.

Using the forces detected by the strain gauges and histologic techniques of circularly polarized light and fluorochrome bone labels, we tried to recreate a “picture” of the forces acting in a single plane of bone at midshaft. By attaching the gauges to the bones of growing goats, we could determine the manner in which the bones are used. In order to do this, we implanted three gauges — lateral, medial, and cranial — on both the radius and metacarpus. The gauges enabled us to monitor the forces we were interested in measuring. We used three sites at a plane of the bone in order to reconstruct the stress state of the bone deep to the surface (gauges can only be attached on the surface). Using fluorochrome labels and circularly polarized light, we could determine patterns associated with bone growth and internal fiber orientation, respectively. By combining these three sets of data, we could infer the forces acting internally on the growing bone. When the study is complete, new information will be provided on the response of the bone to experimentally altered stress levels indicated by varying exercise regimes.

The subject of our experiments were Nubian goats. They were suitable because of their small size and long legs. To collect force data, the gauges were surgically implanted after which the goats were allowed to recover for three days. Then, by running the goats on a treadmill, the strain gauge data could be collected on a computer. For three days following recovery, the goats ran daily on the treadmill before being sacrificed. The bones, which had been labeled with tetracycline HCL and Calcein at predetermined intervals before surgery, were then sectioned and studied under ultraviolet light and circularly polarized light.

Although this process seems quite straightforward, it entails many details that take a long time to perfect. My task was to work out all practical problems connected with the project. I constructed the gauges, determined the optimal way to protect the gauges from body fluids using protective materials, determined the best surgical approach to the mid-shaft of the bones, trained the goats to run on the treadmill, designed and made the circuits from the goats’ bones to the computer. I was provided with information from other projects and received lots of help from everyone in the lab; yet, I encountered many problems. Constructing gauges that would function in the animal for a week was a major problem. Figuring out solutions to these problems was frustrating, but also gratifying especially when everything came together and began to “work”. We made progress as the summer progressed. Buddy was our first research goat. His bones were not
marked and none of his gauges worked; hence we failed to collect any useful data. By comparison the bones of our last goat, Casper, were well labeled and almost all of the gauges attached to his bones functioned as expected.

Although this project will continue for at least two more years, I had the satisfaction of knowing that I made a significant contribution by developing the techniques that will be used by others. My experience at Cornell has been valuable. This Leadership Program provided an opportunity to participate in many aspects of a research project. I initiated the project, resolved problems, collected data and analyzed it. Working in one of the few biomechanics laboratories in the United States was a fascinating and exciting experience. I also have the pleasure of now owning a Nubian goat -- Buddy.

Marjorie McIsaac
Ontario Veterinary College

My interest in pursuing studies in veterinary medicine stems from a love of science and a growing fascination with the questions and challenges that lie therein. After completing an honors degree in science at the University of Ottawa (1990), I was faced with the decision to choose between graduate studies in oncology or a professional, medically-oriented program. Hailing from a family of veterinarians and aware of the abundance of career choices available, I chose to join my father and brother in this profession and entered the DVM program at the Ontario Veterinary College in Guelph. It was either that or I'd probably end up marrying a vet, like my sister.

Prior to beginning veterinary training, I spent the summer working between the PCR machine and gel box in the molecular genetics section of the Animal Research Centre in Ottawa. The following summer, I put the pipetman away and worked in regulatory veterinary medicine at Agriculture Canada and assisted veterinarians from the animal health and meat hygiene divisions. I also worked as a teaching assistant, bartender, waitress, tour guide and a myriad of other jobs. Not only did this pay the bills, it also helped me to pursue a lifelong dream to visit Africa where I worked at the International Laboratory for Research on Animal Diseases (ILRAD), in Nairobi, Kenya. My project involved the isolation and application of microsatellite markers for use in genome mapping and in the study of the trypanotolerance trait. It was exciting and fulfilling to work with a group of individuals from various disciplines that are devoted to the eradication of two major livestock diseases in Africa - trypanosomiasis and East Coast Fever. The experience has shaped my future goals and has shown me the various contributions that veterinarians can make in developing countries in tropical veterinary medicine and in the control of infectious disease. I would like to focus my future research endeavors in these areas where my work may be of human benefit.

As a Mellon Foundation Fellow, I had the privilege to work with Professor Roy Levine, a member of the Cancer Cell Biology group in the Department of Veterinary Pathology. The efforts of this laboratory are focused on identifying growth and differentiation-specific genes in fetal rat lung. Lung alveoli are lined by two types of epithelial cells, alveolar type I and II cells. Type II cells are highly differentiated cells that produce and secrete surfactant proteins which combine with phospholipids to reduce surface tension in the lung. Surfactant deficiency is clinically associated with respiratory distress syndrome (RDS), the leading cause of infant mortality in developed countries.

In the final days of the 22 day gestation period, the fetal rat lung undergoes marked changes in growth and differentiation. Using a technique called mRNA differential display, developmentally regulated genes that may be involved in coordinating these events have been identified. To this end, RNA from 17 and 21 day rat fetal lung was reverse transcribed using an oligo-dT primer containing two additional randomly selected bases 3' to the poly T tail. cDNA was then PCR-amplified in the presence of radionuclides using the same oligo dT primer described above plus a random 10mer as the upstream primer.

A novel gene encoding a 4.5 kb mRNA (DD-5) expressed at 21 but not 17 days of fetal lung development was previously identified in this laboratory. In order to further characterize this gene at the genomic level, restriction analysis and Southern blotting were performed. Results indicate that the gene is present as a single copy. A fragment of this clone was radiolabelled and used to probe a rat genomic library to isolate the promoter region of the gene. Two positive clones were identified, purified, and analyzed by restriction digests and Southern hybridiza-
tion to identify fragments homologous to the cDNA probe. Appropriate fragments were subcloned into Bluescript and sequenced. We identified regions of the genomic clone that are homologous to the 5' region of the cDNA clone and are continuing to sequence this clone in the hopes of identifying the cis acting regulatory elements that control its transcription.

In order to assay potential promoter elements, we are using a luciferase reporter gene linked to the CMV promoter in test transfections. Transfection conditions were optimized for two different cell lines - a lung adenocarcinoma cell line and an immortalized fetal rat lung epithelial cell line. Lung explants isolated from 17 day fetuses were transfected with this reporter plasmid, but only low levels of luciferase activity were detected. Future endeavors will involve the transfection of plasmid constructs containing the DD-5 promoter region linked to the luciferase gene.

In the final part of my project, I used the differential display technique to identify genes which are expressed at day 16 and turned off at day 21. We are in the process of analyzing these clones by Northern blotting to determine if they are indeed developmentally regulated.

I am indebted to Professor Levine and the members of his laboratory for their unending patience and for providing an enjoyable environment that is conducive to learning. I also would like to thank Linda Griswold and Carol Miltenberger for coordinating the many activities and wonderful visits to NIH, Merck, USDA and for ensuring that we were all well taken care of. Finally, I would like to thank Dr. McGregor for his commitment and dedication to the future of our profession that has resulted in the inception of the Leadership Program. The program exposed us to excellence in research, allowed us to explore career possibilities and forge many new friendships.

Claire Micklethwaite
University of Sydney

Having spent my childhood surrounded by a menagerie of animals, it seemed only logical to pursue a career in Veterinary Science. I am now halfway through the fourth year of the five year Veterinary Science program at the University of Sydney. Last year, I completed a B. Sc. (Vet) in the Department of Pharmacology. My project involved studies of glial uptake of glutamate in animal models of chronic hepatic encephalopathy. Glutamate is the main excitatory neurotransmitter in the central nervous system, and alterations in its synaptic levels may have a role in the pathogenesis of hepatic encephalopathy. While I had taken part in a number of research projects, both at school and while in university, this was my first opportunity to design my own project and be responsible for its implementation. As such it was my first in-depth view of the world of research. I have not yet formed my long-term career plans, although I would like to combine clinical practice with research, possibly in an academic environment.

As a recipient of a Woodruff Foundation Fellowship, I spent this summer working with Dr. Benn Hershfield at the James A. Baker Institute. Research in this laboratory focuses on canine genetics. Molecular genetic methods are being used to define genetic similarities between dogs and humans as well as the genetic basis of various dog breeds. In addition to these general questions, Dr. Hershfield's research concentrates on hereditary retinal degenerations.

The project in which I became involved concerned a novel hereditary retinal degeneration in Huskies known as X-linked progressive retinal atrophy (XLPRA). It is the first animal model of a similar condition in humans. The genetic mutation responsible for this condition is unknown and is the subject of ongoing research.

Genetic studies of XLPRA rely on the presence of an informative pedigree which is bred and maintained in association with this laboratory. The mode of inheritance results in mainly males being clinically affected, although obligate heterozygous females may have patchy disease. Ophthalmic changes may be seen as early as 6-12 months of age. They progress rapidly so that generalized retinal atrophy is evident by 18 months.

My project had two specific aims. The first was to determine whether several human X chromosome probes could be successfully cross-hybridized to canine DNA samples in a Southern blot. Second, if cross-hybridization occurred, DNA from the subject dogs could be examined for possible restriction fragment length polymorphisms (RFLPs). If polymorphisms were found, the pedigree would be examined to determine linkage between polymor-
phisms and XLPRA.

My first step was to culture, prepare and label cDNA probes for use in the cross-species hybridization experiments. I chose two probes both of which cross-hybridized successfully. The pGDP probe binds to the long arm of the human X chromosome. The ZFX probe binds to the short arm in the region of a number of retinal genes in the human genome. Enzyme digests were systematically investigated for possible polymorphisms. Both are still being investigated for RFLPs. The laboratory will continue mapping the canine X chromosome using these and other probes which successfully cross-hybridize. The ultimate aim is to determine the genetic location of the defect by RFLP linkage analysis.

My time at Cornell has been an invaluable experience both personally and in terms of future career decisions. The tours, discussions, challenges and, most crucial of all, the people, combined to make this a rewarding and unforgettable summer.

Benedict Mohit
Tuskegee University

I am a senior student in the School of Veterinary Medicine at Tuskegee University. After completing the DVM degree, I would like to pursue an internship followed by a residency as preparation for Board Certification in Internal Medicine-Oncology. Alternatively/subsequently, I plan to continue postdoctoral studies in Pathology-Oncology. My ultimate career goal is to be a professor in a clinical department of a veterinary college.

I completed a B.S. (Honors-1982) in Agricultural Sciences majoring in Agricultural Engineering at UWI. As a veterinary student, I participated in clinical research at SmithKline Beecham-Animal Health. There I investigated the effects of intraperitoneal and subcutaneous minipumps as a continuous delivery system for GHRP-6 and its analogs. In addition, I worked on applications of clinical knowledge base couplers in the small animal clinic at my college. More recently, I completed a senior veterinary externship at the Animal Medical Center in New York City.

As a Woodruff Foundation Fellow, I worked with Professor Andrew Yen in the Department of Pathology-Cancer Biology. My research area concerned control mechanisms regulating cell proliferation and cell differentiation. The studies employed genetically engineered HL-60 cells, a promyelocytic leukemia cell line carrying a c-fms transgene. My task was to investigate the in-vitro effects of a src family kinase inhibitor [Radicicol] on cell proliferation and differentiation in c-fms transfected cells. The potential regulatory role of the retinoblastoma tumor suppressor gene in mediating this process was examined.

Proliferation and differentiation of this cell line depends on a function of their CSF-1 receptors, a 70kD transmembrane glycoprotein with intracellular tyrosine kinase activity encoded by the c-fms gene. Radicicol is a fungal metabolite with an C18 macrocyclic ring containing an epoxide residue, a chlorine, and two phenolic hydroxy groups. It appears to be a novel and specific protein-tyrosine kinase inhibitor suggesting its potential use in the analysis of cell differentiation and kinase mediated signal transduction, because src-like kinase activities are downstream of the CSF-1 receptor, itself a tyrosine kinase. Consequently, this metabolic cascade may be sensitive to the pharmacological modulation of src-like enzymes.

Results to date indicate: 1) Radicicol inhibits cell proliferation and targets src-like activities during the G1 phase; 2) the effects of retinoic acid on cell proliferation and differentiation are sensitive to src-like activities targeted by Radicicol and, 3) Radicicol appears to promote the differentiation pathway. In addition, Radicicol had a narrow pharmacological range of 0.1 - 0.3 ug/ml with 0.5 ug/ml showing marked toxicity.

In carrying out these studies, I acquired basic skills in mammalian cell tissue culture and flow cytometry. I became aware of the role of a team player in a research laboratory. I learned to recognize and extend the courtesies of sharing equipment, maintaining cultures, reagents etc. in sterile and ordered arrangements, and how to plan my activities within the framework of these shared resources. It was a challenge and the results I obtained were very encouraging.

The Leadership Program provided me with the opportunity to work with distinguished researchers and to meet veterinary professors whose books I had become familiar with during my training. I was impressed by the facilities and the research and clinical work conducted at Cornell. Extracurricular activities included visits to the NIH, USDA and Merck and Company. These events gave me a better
appreciation of veterinary medicine, the pharmaceutical industry and other research environments. The ethics project that we worked on individually and as a group stands out as the single most important experience for me this summer.

Career guidance sessions, which are features of the program, came at an optimal time for me as a senior student. They were informative and will become an integral part of my rationalization process for the choices I will make as my career unfolds. The encouragement and motivation I received were second to none.

I wish to thank the Robert W. Woodruff Foundation for sponsoring my fellowship and the program. I also would like to thank my mentor, Professor Andrew Yen, for defining my research project, obtaining the Radicicol I used form Tokyo University, and for his guidance and encouragement. Also, I wish to express my gratitude to Mrs. Susi Varvayanis for her unlimited patience in teaching me the necessary laboratory techniques and for tolerating my total ignorance of molecular biology. Finally, I wish to thank the Selection Committee for their confidence in me. I hope that I have at least met their minimum expectations.

As recipient of a Woodruff Foundation Fellowship, I had the good fortune to pursue research in the laboratories of Professors James N. MacLeod and Cornelia E. Farnum at Cornell University. My project involved cellular and molecular studies of long bone growth in mice. The three strains I used are genetically identical except for the genes controlling the production of growth hormone. Because of the alteration of expression of this single gene, the mice grow at different rates and reach different sizes at maturity. The parameters I examined were body weight, chondrocyte proliferation and cartilage matrix production in the proximal tibial growth plate, and hepatic IGF-1 gene expression.

The mice were studied from birth to five weeks of age. At this age, body weights were approximately 10, 17, and 21 grams for the dwarf, normal, and giant phenotypes, respectively. The enhanced growth of the “giant mice” was achieved using transgenic technology. Mouse eggs were microinjected with cloned copies of the rat growth hormone (rGH) gene. Three copies of rGH successfully integrated as a tandem repeat into the mouse’s genome. Progeny of this mouse have a 50% chance of inheriting the transgenes. In addition to their large size, individuals that inherited the rGH transgenes can be identified experimentally by dot blots or Southern blots of their DNA. To do these experiments, I amplified a plasmid containing rGH probe in E coli. The plasmid DNA was then purified and the rGH insert isolated by restriction enzyme digests and agarose gel chromatography. The dwarf mice have a normal growth hormone gene, but contain a mutation in the gene that encodes hypothalamic growth hormone releasing factor. As a result pituitary growth hormone production and release are greatly suppressed.

Cellular studies of the tibial growth plate included an estimate of matrix production using oxytetracycline labeling visualized by epifluoroscopy. Chondrocyte proliferation was determined using bromodeoxyuridine, a thymidine analog that is incorporated into the replicating strands of DNA. I had technical problems with the oxytetracycline labeling, but chondrocyte replication seemed to change in parallel with altered growth rates. My most dramatic and exciting finding came from an investigation of liver IGF-1 gene expression. IGF-1, or somatomedin C as it was originally termed, is a growth factor that mediates at least some of the biological effects of growth hormone. Consistent with the absence of pituitary growth hormone production, the dwarf mice did not transcribe the IGF-1 gene in their livers. This was determined by
Northern blotting, a technique in which RNA is electrophoretically separated in an agarose gel, blotted onto a nitrocellulose or nylon membrane, and then probed with a radiolabeled cDNA fragment. I became quite proficient at isolating liver RNA of high quality.

The Leadership Program has been an invaluable experience for me. I am now convinced that I made the right choice among the other options I had this summer. I gained valuable insights into potential careers in veterinary medicine that are different from the traditional areas of clinical practice. I was able to make several new friends from different countries and to better appreciate their training programs and personal views on ethical issues associated with the proper conduct of research. Based on my experiences, I strongly recommend this unique program to any veterinary student who has aspirations for training beyond the DVM level and is interested in a career other than private practice.

Penny Olson
Ontario Veterinary College

I have wanted to be a veterinarian from a very early age. Fortunately, I have been able to pursue my goal. After two years of a B.Sc. Zoology program at the University of Toronto, I was accepted into the veterinary program at Ontario Veterinary College at the University of Guelph. I will enter the second year of the program this fall.

My involvement with scientific research began the summer after I finished high school when I was awarded a Summer Research Fellowship at the University of Guelph in a lab studying the reproductive physiology of seals. The following summer I had a job in public education at the Huntsman Marine Science Centre in Eastern Canada. The summer before entering veterinary school, I pursued my interest in reproductive biology through a research position at the Ontario Veterinary College’s Animal Biotechnology-Embryo Laboratory. In studying the effect of semen extenders on bovine oocytes, I found that certain extenders, combined with the semen of some bulls, can cause fragmentation and parthenogenesis. Last summer I had the opportunity to participate in a joint project of the Metro Toronto Zoo and the Ontario Veterinary College. My research concerned the development of feline oocytes; information that is needed to develop in vitro fertilization techniques for the preservation of endangered species.

As a Mellon Foundation Fellow this summer, I was fortunate to work with Professor James Casey and Professor Paul Bowser who are studying retroviruses in fish. Our research focused on Walleye Dermal Sarcoma Virus (WDSV) which has been implicated in multifocal, benign, cutaneous tumors found on adult walleye. A seasonal periodicity of tumor prevalence has been observed: tumor prevalence is higher during the spring and fall months than during the warm summer months. We also studied the viruses associated with plasmacytoid leukemia of Chinook Salmon, and hematopoietic tumors in Northern Pike. My part of the project involved extracting and purifying the viruses from piscine tissues using sucrose density gradients. Reverse transcriptase assays were used to determine if virus was present in the extracted material. I also participated in a transmission study in which fingerling walleyes were inoculated with extracts from tumors taken from walleyes affected in the spring and the fall. Two groups of walleyes were inoculated with the salmon plasmacytoid leukemia virus and the northern pike virus. Time did not permit this study to be completed during my stay. It remains to be seen whether artificial infection occurs and whether pathological lesions develop in the experimental fish.

Our main endeavor was to sequence a DNA clone of the WDSV through the use of sequencing gels. Analysis of the viral genome provides information about genetic relationships between retroviruses. The WDSV is a new model for oncogenesis that is expected to provide insight into the processes of tumor induction and tumor regression. The people with whom I worked were friendly and enthusiastic. In addition to learning several new techniques, I learned a great deal about genetics, virology and oncogenesis.

The Leadership Program also is a worthwhile experience outside of the lab. Through trips to Merck and Co., the National Institutes of Health, and the U.S. Department of Agriculture, and discussions held on Career Day, my eyes were opened to the varied and exciting opportunities available to veterinarians in academic, industrial and governmental settings. These experiences helped to clarify my career goals. After graduation, I plan to enter private practice for a few years. Therefore, I will seek
advanced training in the form of an internship or residency, or perhaps a clinically oriented research training experience.

One of the most memorable aspects of the program was living and working with veterinary students from around the world. It was interesting to compare educational systems and personal aspirations. There were ample opportunities to socialize, travel, and pursue individual interests. I would like to extend my gratitude to my supervisors and their lab groups, the Mellon Foundation and all who made this program possible. The Leadership Program was as an invaluable part of my veterinary education.

Joanne Rainger
University of Sydney

In 1989 I enrolled in a Bachelor of Veterinary Science degree at Sydney University. This had been a life-long goal for me stemming from an interest as a child into what made animals “tick.” Prior to entering Sydney University, I had worked in local veterinary clinics on a voluntary basis. In 1992, I completed a Bachelor of Science (Vet) degree studying Lactate in Exercising Horses. The degree required preparing a thesis, making an oral presentation, and defending my thesis. I found this first exposure to research, enjoyable and interesting.

Once qualified, I would like to obtain an internship or enter a mixed private practice followed by a residency. Hopefully, I will be able to undertake some of this work in an overseas institution. Eventually I would like to be involved in research examining exercise physiology or clinical disease.

As a Woodruff Fellow, I was fortunate to participate in research with Dr. Sydney Moise and her cardiology research team in the Department of Clinical Sciences. My project involved working with a colony of German shepherd dogs who suffer from inherited ventricular arrhythmias and are prone to die suddenly and unexpectedly, often during sleep.

Previous work with these dogs demonstrated that those which died suddenly were subject to polymorphic nonsustained ventricular tachycardia. The episodes of ventricular tachycardia often were associated with bradycardia and a preceding pause. Dogs often died during sleep or while resting after exercise. The dogs died between 4 to 30 months of age, with the highest frequencies of severe ventricular ectopy occurring between 20 to 30 and 40 to 50 weeks of age. Post-mortem examination of the hearts of dogs that failed to reveal any histopathological abnormalities.

The young age, lack of cardiac pathology, and common death during sleep suggest that the ventricular arrhythmias have features in common with some cases of sudden infant death syndrome (SIDS). The association of ventricular ectopy with bradycardia and death during sleep suggest a possible mechanism for some cases of SIDS. Our hypothesis was that perturbations to the autonomic nervous system can trigger the arrhythmias. It is believed that the arrhythmias are potentiated by alterations that cause bradycardia (increased parasympathetic tone) in conjunction with bursts of increased sympathetic tone.

This summer we conducted two experiments to determine if the clinical arrhythmia was 1) associated with sleep, and 2) increases in parasympathetic tone. To answer the first of these questions, we performed a 24-hour video analysis of the activity of the dogs with simultaneous electrocardiographic monitoring. To answer the second question, we conducted baroreceptor sensitivity tests on dogs exhibiting ventricular arrhythmias by injecting a bolus dose of phenylephrine which due to vasoconstriction resulted in an increase in blood pressure. The increase in blood pressure was followed by a decrease in heart rate, a response initiated by the baroreceptor reflex. During the baroreceptor sensitivity test surface and intracardiac electrocardiographic responses, systemic blood pressure and phases of respiration were recorded on a Gould electrophysiograph. To assess the involvement of sinus pause and bradycardia in the potentiation of ventricular arrhythmias in the injection of phenylephrine was repeated during pacing. The inherent sinus rate was determined after treatment with propanalol amd atropine.

Analyses of the behavior and electrocardiographic activity of severely affected dogs over a period of 24 hours suggested that the dogs had more arrhythmias during periods of inactivity (sitting, sleeping) than periods of activity. The ventricular arrhythmias may have been triggered by a decrease in heart rate, an irregularity in sinus rhythm, and/or an increase in
parasympathetic tone.

Following injection of phenylephrine, the dogs showed an increase in ventricular ectopy. However, when the atrium was paced following the injection of phenylephrine, there was no ventricular ectopy present. The results suggest that heart rate or the type of rhythm (regular versus irregular) may be the trigger for the arrhythmias.

To assess the degree with which dogs were affected with ventricular arrhythmias, 24-hour ambulatory electrocardiographic monitoring (Holter monitoring) of the dogs was conducted. I was involved with the placement of the recorders and the reading and recording of data from the tapes.

As the most severe forms of ectopy are seen in young dogs, the maintenance of a proportion of puppies was a high priority in the work I did this summer. I was involved in monitoring the females oestrus cycles of pregnant bitches, semen evaluation, and care of puppies. I have thoroughly enjoyed my project as it has afforded me the chance to learn about cardiology and canine reproduction while gaining research and practical clinical skills.

The Leadership Program through activities such as trips to Merck, the National Institutes of Health, and the USDA revealed many career options to veterinarians. This information will help me make more informed career decisions in the future. The program has also enabled me to meet many wonderful people from all over the world and gain a more international view of my profession.

Ashley Reynolds
Cornell University

In 1992, I obtained my B.S. degree in Animal Physiology and Neurosciences from the University of California, San Diego. While an undergraduate, I had the opportunity to serve as a teaching assistant in physiology courses. I also completed an academic internship in an equine surgery practice and researched the topic of "Exercise-Induced Pulmonary Hemorrhage in Thoroughbred Racehorses." My participation in an independent research project studying the effects of trace metals on the autooxidation of beta-hemoglobin provided additional research exposure. These experiences demonstrated the joys and challenges of teaching and research and strengthened my desire to pursue a career in academia, preferably teaching physiology in a college of veterinary medicine.

As a Merck Foundation Fellow, I had the opportunity to pursue research under the guidance of Professor Robert H. Wasserman and Dr. Thomas L. Pannabecker. My project focused on transepithelial calcium transport in a short-circuited toad bladder, and included the hormonal effects of 1,25-dihydroxy vitamin D3 on calcium transport. After mounting a sheet of intact toad bladder epithelium between the two halves of a cylindrical hollow tube (Ussing chamber), bicarbonate-buffered Ringer's solutions of equal concentrations were circulated from reservoirs connected on either side of the epithelium. Voltage-monitoring electrodes and current-introducing electrodes connected to a voltage clamp apparatus served to monitor the transepithelial potential difference and reduce the potential difference to zero by passing current across the epithelium, thus short-circuiting the membrane. Diffusion of ions such as calcium due to transepithelial chemical and electrical gradients was eliminated in order to study active transport of electrolytes across the epithelium. Radiolabelled calcium was added either to the mucosal or serosal side of the epithelial membrane and unidirectional mucosal to serosal or serosal to mucosal transport of calcium was measured. Transport in both directions was determined simultaneously by utilizing two pieces of bladder from the same animal mounted onto individual Ussing chambers.

We found that there is a net secretion (serosal to mucosal movement) of calcium into the lumen of the bladder under control conditions — i.e., without addition of 1,25 dihydroxy vitamin D3 (1,25(OH)2D3).
When the latter was added to the serosal compartment, a striking inhibitory effect occurred which was most pronounced after three hours. This finding suggests that vitamin D₃ has an effect on gene expression, perhaps leading to increased activity of the calcium pump and/or increased numbers of calcium pumps inserted into the basolateral membrane.

In another experiment, the addition of ouabain, a Na⁺/K⁺ ATPase inhibitor, to the serosal compartment, reduced calcium secretion into the bladder lumen. It had no discernable effect on calcium absorption, however. From these data, we postulated that there is an apical membrane sodium/calcium exchanger and a Na⁺/K⁺ ATPase on the basolateral membrane. Previous studies, using immunohistochemical staining utilizing a peroxidase-conjugated double antibody technique, showed localization of the calcium pump in the region of the basolateral membrane of the toad bladder epithelial cells.

Our experimental findings suggest the existence of basolateral calcium pump and Na⁺/K⁺ ATPase, and an apical membrane sodium/calcium exchanger. Thus, mucosal to serosal movement of calcium occurs due to the action of the calcium pump translocating calcium across the membrane, out of the cell. The sodium/calcium exchanger extrudes calcium into the lumen of the bladder simultaneously with entry of sodium into the cell down its electrochemical gradient. This gradient, created by low intracellular sodium levels, would be maintained by the Na⁺/K⁺ ATPase removing sodium from the cell.

The inhibitory action of 1,25(OH)₂D₃ may be explained by the following mechanism: once calcium enters the cell via calcium channels within the basolateral membrane, the pump would immediately extrude the calcium back out of the cell. If the activity and/or number of calcium pumps increases, this process occurs even more quickly. Thus, because the calcium does not traverse the cell and enter the lumen of the bladder, net secretion of calcium is reduced. We propose that 1,25(OH)₂D₃ does not affect the rate of calcium movement from mucosa to serosa because calcium transfer across the apical mucosal membrane, unaffected by the vitamin D hormone, is a limiting step in the transport process. The overall effect of 1,25(OH)₂D₃ is to decrease secretion of calcium into the lumen of the bladder and thus make this calcium available for other body processes. A surprising finding of this research is that the rate of transepithelial calcium transport is not steady, but rather rises and falls with a regular periodicity.

Future experiments are required to examine these proposals and observations in more detail.

The Leadership Program allowed me the unique opportunity of having an intellectually challenging summer in a high caliber research laboratory while also establishing friendships with bright, personable veterinary students from all over the world. Professional enrichment activities such as Career Day and visits to the NIH helped me to examine the multitude of career possibilities available to veterinarians while providing guidance from successful veterinarians and researchers who have achieved the goals which someday I hope to match. I am grateful to all who have made this wonderful experience possible.

I am a fourth year veterinary student at the University of Liverpool in England. It has not been a lifelong ambition of mine to be a veterinary surgeon, but I was attracted by science and a strong interest in animals. From the beginning of the course I was eager to gain research experience. Having undertaken one computer based retrospective clinical study during my first summer vacation, I was keen to experience laboratory research. This opportunity arose when the Wellcome Trust sponsored me to take an intercalated degree in Biochemistry in the academic year 1992-3. My associated honors year project involved the characterization of a protein in
rodent urine called Meprin. It entailed the collection and processing of mouse urine samples through to enzyme assays, zymography, SDS-PAGE and Western blotting.

I was thrilled to be offered a place in the Leadership Program and was once again supported in this by the Wellcome Trust. This summer, I was warmly welcomed as a member of Professor Chang’s busy laboratory where I participated in the thrills and spills (literally!) of molecular genetics. The work has broadened my experience with laboratory techniques and has been an excellent complement to the protein biochemistry of my intercalated degree. There is much satisfaction to be gained from tackling real life practical problems associated with DNA manipulations described in standard course texts.

I focused on the genes encoding the toxins of *Actinobacillus Pleuropneumonia*, which are major virulence factors in porcine pleuropneumonia, a widespread disease of economic importance. The three toxin coding genes- ApxI, ApxII and ApxIII- have already been cloned. I participated in work aimed at developing a recombinant vaccine. Parts of the sequence of toxin gene ApxI from serotype 5 required clarification. I also started a “chromosome walk” using a radioactively labeled probe form the 5’ terminus of the same gene. This should allow sequencing of upstream regulatory regions. Quantitative toxin assays indicated that there was poor expression of the cloned genes ApxI and ApxII from their natural promoters in *E. Coli* hosts. Therefore I also helped in the processes of manipulating these genes to bring them under the influence of a strong host promoter. Toxin overexpression should provide a source of protein to work on further toxicity and immunoprotective studies. The work entailed Southern blotting, plasmid isolation and DNA purification, bacterial transformation, and M13 vector preparation of single stranded DNA for sequencing by the dideoxy method.

The Leadership Program provides insight into the world of veterinary science research, combined with an organized schedule of events highlighting different research career opportunities. At the end of the summer, I shall take home with me not only valuable research and technical experience, but happy memories of a group of fellow students from all over the world, with some of whom I hope to continue lasting friendships. I would like to offer my sincere thanks to Professor Chang for his time and enthusiasm, to the Wellcome Trust for its financial support and to Dr. McGregor and everyone else whose contributions have made this program so successful.
fourth day of treatment a luteolytic dose of prostaglandin F2α was administered. Cows were inseminated at the ensuing estrus. On day six (day of insemination was day zero), cows from the control group received a 10 ml intrauterine infusion of Ringer solution, while those in the experimental group received a 10 ml intrauterine infusion of 1% Oyster Glycogen, a compound previously shown to cause aseptic endometritis. On day seven, embryos were recovered and assessed morphologically (quality, stage of development and number of blastomeres). The experiment was not completed when the program ended, but preliminary results indicate that embryos recovered from heifers with endometritis are often degenerate and have changes in the Zona pellucida. Because these changes are much more severe than those caused by co-culture with neutrophils for 24 hours in vitro, it suggests that an aspect of inflammation other than a direct action of neutrophils may be important in mediating the detrimental effects on embryos.

The Leadership Program provided an excellent opportunity to gain experience in research. I would like to thank Cornell University for a great summer and the Mellon Foundation for its sponsorship.

Melinda Stewart
University of Sydney

I am currently in my fourth year of veterinary science at the University of Sydney, and have one more year of large animal clinical work to complete before graduating in December, 1994. I have always had an interest in scientific research, primarily influenced by members of my family. In 1992, after completing my third year of veterinary science, I took the opportunity to carry out research for a year in the Department of Veterinary Pathology. My work in the area of neuroimmunology (interactions between the nervous system and immune system in the G.I.T. of sheep), gained me a B.Sc(Veterinary) degree. I was able to continue this research, and apply it to vaccine development against intestinal helminths of ruminants during the following summer. I did so with the C.S.I.R.O as part of a studentship program funded by the Australian Wool Corporation. During my veterinary course, I also have tempered my interest in research with practical work in small animal clinics and at Taronga Park Zoo.

I applied for admission to the Leadership Program, seeing in it opportunities to further my experience in research and to gain experience with new research techniques. In addition, I wanted to develop a perspective on other career opportunities available to veterinarians and the avenues through which they can be pursued.

My summer was spent at the James A. Baker Institute, in the laboratory of Professor Colin R. Parrish. My fellowship was funded by the Mellon Foundation. It enabled me to study canine parvovirus and, specifically the antigenic properties of the viral capsid protein. In pursuing this project, I studied the manner in which viral epitopes are recognized by different antibodies. The project also provided an ideal opportunity to acquire a working knowledge of animal virology and molecular biology.

Canine Parvovirus (CPV) was first identified in 1978 as the cause of an often fatal enteric disease in dogs and myocarditis in puppies. Within two years the virus had spread to virtually all populations of dogs examined - both domestic and wild. Since then, two antigenically variants have appeared (CPV type-2a and CPV type-2b). Although antigenically distinct, each variant is virtually identical genetically.

Over the summer, I produced two separate clones of regions of the CPV capsid protein gene. The clones were then inserted into the bacterial expression plasmid, pMal-c2. This was achieved by digestion of both the viral genome and pMal-c2 with restriction endonucleases to yield specific cleavage fragments which could be ligated.

The pMal vector provides a method for expressing and purifying large quantities of a specific protein expressed by a cloned gene. Each VP-2 gene fragment was placed downstream from a strong “tac” promoter and the malE gene, which encodes the maltose binding protein (MBP). These were inserted into Escherichia coli as a suitable bacterial host, and induced to produce large quantities of the cloned capsid protein. The proteins were purified using affinity chromatography.

The fused proteins 9VP-2 sequence combined with MBP will be analyzed by Western blotting, and by ELISA using a variety of polyclonal sera and monoclonal antibodies against the CPV capsid.

My summer at Cornell has provided an invaluable opportunity to expand my views on veterinary career options and to focus my career goals. The unique combination of a research project, discussions, social interactions and an opportunity to travel abroad was a memorable step in my veterinary career.
Michele Terrelonge
Cornell University

I was born and raised on the island of Jamaica. I came to Cornell as an International Student Scholar in 1986 and graduated in 1990 with a degree in Animal Science. I then returned to Jamaica and worked as a Research Officer for "Jamaica Broilers", a company that is the largest producer of broiler meat and eggs in the Caribbean region. I enrolled in the Veterinary College at Cornell in 1991 and expect to graduate in 1995.

After completing my veterinary studies, I will probably enroll in a Ph.D. program in Immunology and Infectious Diseases at a medical school. I am especially interested in vaccine development and aim to pursue a career either at a veterinary or medical school or in an international agency. Five million people die each year from diseases that can be prevented; another five million people are crippled, blinded or mentally retarded as a result of the same diseases. Vaccines are the most effective way to control communicable diseases and provide the greatest hope for disease eradication. New developments in biotechnology have stimulated great interest in research using novel techniques for developing more effective vaccines at a price affordable by the poorest countries. Developing vaccines will be exciting because it is a multidisciplinary undertaking encompassing genetics, biochemistry, immunology, microbiology and epidemiology.

I love to travel and would enjoy an international career involving people and projects throughout the world. I was president of the MultiEthnic Veterinary Students Association at Cornell and have been active in efforts to increase minority enrollment with the overall goal of increasing diversity in veterinary medicine. Beside my professional goals, I have the equally important personal goal of working throughout my career to increase opportunities for minority students in science. I want to be a role model and mentor for the next generation of talented and energetic young veterinarians and scientists of the future who I hope will be more demographically representative in their racial and ethnic background.

As a Woodruff Foundation Fellow, I worked in the laboratory of Professor Bendicht Pauli in the Department of Pathology. Professor Pauli's research is in the field of cancer biology. When tumor cells metastasize, they often implant preferentially in certain organs. The major interest of the lab is to define the role of vascular endothelial cell adhesion molecules (ECAMs) in organ-specific metastasis. Professor Pauli and his associates have focused their research on a lung specific endothelial cell adhesion molecule (Lu-ECAM-1) localized on endothelia of distinct vascular branches of bovine lung. This molecule is the principal endothelial cell adhesion molecule for lung metastatic B16 melanoma cells. The Pauli group recently cloned and sequenced the Lu-ECAM-1 cDNA. Ms. Joanne Widom, a member of the group, is trying to identify, clone and sequence the gene for the human homologue of Lu-ECAM-1 from human DNA. My task was to collaborate with Joanne in trying to isolate the corresponding murine gene and, if successful, to clone and sequence it.

The first step was to obtain a fragment of DNA from the mouse/human homologue to use as a probe which could then be employed to isolate the cDNA from a library. Our approach was to use PCR to amplify a DNA fragment form genomic DNA or from a cDNA lung library. Degenerate primers were made based on the sequence of bovine Lu-ECAN-1 cDNA. Ms. Joanne Widom, a member of the group, is trying to identify, clone and sequence the gene for the human homologue of Lu-ECAM-1 from human DNA. My task was to collaborate with Joanne in trying to isolate the corresponding murine gene and, if successful, to clone and sequence it.

The experience I gained with molecular biological techniques will surely be useful in the future. I learned to appreciate that research is a slow, arduous process and that it is essential to acquire the ability to trouble-shoot effectively when things fail to "work." I truly enjoyed the time I spent in the lab and the people I worked with both in and outside of the Leadership Program. The program provides an invaluable opportunity to investigate career options that one would infrequently experience in the traditional veterinary curriculum. One can also avail
oneself of sound advice from top scientists in planning one's career. At the beginning of the summer, I was confused about the direction in which I was headed. I decided to become a veterinarian in order to work with people and animals and have an active lifestyle. After participating in this program, I have become firmly convinced that I am destined to pursue a career in research.

Leslie Triplett
Oregon State University

I graduated from Whitman College in 1990 with a Bachelor of Arts in French Literature and Language. Thereafter, I elected to expand my career options by taking an additional year of upper level science courses at Portland State University thereby fulfilling the requirements for entry into veterinary college. After considerable thought, I chose Oregon State University College of Veterinary Medicine, enrolling in the fall of 1991 as part of the Washington-Oregon-Idaho combined program. My decision to pursue a degree in veterinary medicine rather than a Ph.D. in French came from a lifetime family commitment as well as extensive work exposure to large animals on ranches and in clinics.

The summer following my first year in veterinary college, I was introduced to clinical and laboratory research as a Dorothy Russell Havemeyer Foundation Fellow in Equine Genetics at the James A. Baker Institute. This experience was beneficial in defining the niche in veterinary medicine that I wish to occupy. I developed a keen interest in reproductive research while studying the immune relationship between the conceptus and the dam.

All of the proceeding events led to my decision to seek additional academic research experience. This summer I had the great fortune to receive a Merck Foundation Fellowship. The award enabled me to perform research under the guidance of Dr. Peter W. Nathanielsz in the Laboratory for Pregnancy and Newborn Research (LPNR). The LPNR is an extensive network of laboratories and researchers devoted to all aspects of periparturient physiology. A broad spectrum of techniques, -e.g. immunohistochemistry, Northern blots, Western blots, microsphere studies and surgery are applied to better define the role of the fetus in parturition as well as other physiologic factors of the mother essential to this process. My summer research involved the use of surgically excised myometrium from third trimester ewes, dGA +/-120, as the basis for modeling the pharmacologic effects of synthetic E series prostanoid agonists destined for therapeutic use in pregnant women. Both circular and longitudinal layers of myometrium were placed in a superfusion system where they were tested for responsiveness to synthetic receptor-specific E prostanoid agonists (ranging form EP1-EP3 receptor agonists). The individual agonists were added to the system in progressively increasing concentrations. The objective was to develop contractile response curves (CRC) and EC50s for each agonist as a measure of its activity.

The study focused on three E prostanoid agonists: Iloprost, a potent EP1 as well as IP agonist; Sulprostone, a highly selective and potent EP3 and EP1 agonist, and Dinoprostone, a broad spectrum EP agonist involving EP1-EP3 and possibly EP4. The results revealed little difference in EC50 of the contractile response elicited by these highly efficacy-receptor-specific drugs for the E series prostanoids on longitudinal layers of sheep myometrium. The circular layers of myometrium had EC50s which were more variable, especially with regard to Iloprost. Iloprost had an irregular CRC that is the subject of ongoing study. The investigation is using an EP1 receptor-specific antagonist, AH6809, on sheep myometrial strips prior to and during their exposure to the synthetic agonist acting on multiple EP receptors. I hope to better evaluate the potency of this E prostanoid agonist when its reactivity is limited to only one receptor population.

The Leadership Program gave me the opportunity to delve further into the world of reproductive research and to do so in an academic setting. I especially want to thank Dr. Nathanielsz for the freedom and guidance that enabled me to independently design and execute my experiments together with my co-worker David DiPiazza. The LPNR, as well as the program, have the unique capacity to take a multiplicity of independent research efforts and pull them together in a rich union during laboratory presentations and discussions. These discussions created the impetus for innovative thinking and inter-laboratory cooperation. The program proved to be a valuable and enjoyable experience which brought together bright and motivated veterinary students from around the world.
Prior to entering the College of Veterinary Medicine at Cornell, I attended DePauw University in the booming metropolis of Greencastle, Indiana. While completing studies for a B.A. in biology, I obtained some research experience although very little that was relevant to clinical veterinary medicine. I worked as a microbiology TA and also completed a research project in which I transformed plant leaf tissue into root tissue by injecting the leaves with a plasmid bearing bacteria. I used medicinal and poisonous plants indigenous to Indiana and attempted to analyze their production of alkaloids. I also spent a summer as an intern at the Eli Lilly Company performing a drug trial on bisphosphonates suspected to have treatment potential for osteoporosis. Despite these varied experiences, I am still unsure of the area in which I would like to pursue research as a career. I perceived the Leadership Training Program as a means by which I could broaden my experience in research, especially in an area that is relevant veterinary medicine. At this time, I am looking for a way to integrate my research and clinical interests.

While participating in the Leadership Program, I collaborated with Dr. Dan Gamett in research in the Department of Pharmacology under the supervision of Professor Richard Cerione. The Cerione laboratory is broadly interested in cell signal transduction through the activation of receptor tyrosine kinases by growth factors. Depending on the cells and ligand, the former can be stimulated to either proliferate or differentiate. The cascade by which the signal generated at the cell membrane travels to the nucleus to influence gene activation is critical in this connection.

The project in which I was involved was a study of the subclass I growth factor receptor known as erbB2. This receptor protein is involved in human breast cancers as it is believed to regulate breast epithelial cell growth. A ligand for erbB2, known as heregulin (HRG), is currently under study. As part of my project, a rat pheochromocytoma cell line (PC12) which expresses erbB2 was transfected such that a second membrane protein, erbB3, was also expressed. Although erbB3 is not known to have tyrosine kinase activity, it is believed to form a heterodimer with erbB2 to increase the activity of the receptor. Besides the PC12 cells that were transfected with erbB3, two other cell lines were used. One of these were the parental PC12 cells that contain endogenous erbB2. The other PC12 cell line over-expressed erbB2 (as an outcome of transfection).

By Western blotting, we examined changes in the pattern of cytoplasmic and nuclear protein phosphorylation in response to varied growth conditions. These conditions included the presence or absence of dexamethasone (Dex) as well as the presence of varied growth factors. The latter stimulates an inducible promoter associated with the erbB3 gene.

We also examined the three cell lines for changes in neurite outgrowth in response to Nerve Growth Factor (NGF), HRG, HRG + Dex and Dex alone. Cells in which the erbB2 receptor and NGF receptor are activated begin to elaborate neurites and show a decrease in cell proliferation indicating that ligand/receptor interactions can induce neuronal differentiation. Cells in which this type of differentiation occurred were then examined for further phenotypic characteristics such as dopamine uptake.

The Leadership Program was an excellent means to gain research experience as well as to meet other students from different countries. I would recommend the program to any veterinary student interested in pursuing a career in research.

As a veterinarian want-to-be since the third grade, I have traveled a direct but wide path to my present status as a second-year veterinary student at Cornell. A childhood surrounded by family pets ranging from dogs to gerbils, and a public school education in Troy, NY laid the groundwork for the activities that led me to veterinary school. Among those activities was research, which made its first appearance in my life during high school in the non-animal form of tobacco plants.

While fulfilling my pre-veterinary requirements
at Dartmouth College, I enthusiastically pursued the multitude of opportunities the liberal arts environment provided. Four years passed rapidly in a whirlwind of studying in Europe, competing and traveling with a Division I track and field team, working at alumni reunions and in administrative positions in various student social groups. I tired of the passive learning required by lecture formats, and wishing to challenge my learning abilities, chose to pursue an honors thesis within my biology major. My research focus for one year was on the effects of food deprivation on the reproduction of a local invertebrate zoo plankton species, and its potential as an indicator species for acid stressed lakes. The development of my independent learning and thinking skills which arose through the exercises of experimental design, data collection and analysis, and presentation of the completed project made the experience highly satisfying.

After a year of simultaneously exploring career options, including laboratory animal medicine and physiologic research, and the Cascade mountain tops of the Pacific Northwest, I returned East to Cornell to begin my veterinary education. Since arriving, I have maintained my broad interests, and my first year activities included the organization of a new student group dedicated to providing a forum for discussion of current changes occurring in the veterinary field. In addition I volunteered in the Avian Clinic, and worked in the large animal clinic. My career path remains undetermined as I continue to explore the many options which exist.

The summer research project required by the Leadership Program allowed me to investigate the potential career path of veterinary research in the field of reproductive studies. For ten weeks I worked with Professor Barry Ball examining methods of imaging cortical granule distributions in equine oocytes. The importance of this research lies in understanding the potential role of cortical granules in equine infertility and successful in vitro fertilization techniques.

Normally, fertilization triggers the release of cortical granules from the oocyte into the perivitelline space. The contents of the cortical granules alter the surrounding zona pellucida proteins, preventing additional sperm from fertilizing the egg. Failure of cortical granule function could result in polyspermic fertilization of the oocyte, with subsequent abnormal development and embryonic loss in mares. Premature release of cortical granules and the hardening of the zona pellucida may be a factor in the low success rate of equine in vitro fertilization techniques.

In order to determine the potential role of cortical granules in equine oocytes, the normal distribution and function of these structures must first be known. In obtaining accurate images of the 200-600nm cell structures, we utilized two different techniques, epifluorescence microscopy and the recent technology of laser-scanning confocal microscopy. Confocal microscopy employs lasers to produce clear images at different focal planes within a specimen. From these images a computer can generate a 3-dimensional image of the entire cell, providing a more realistic picture of granule distribution than the 2-dimensional image produced by epifluorescence microscopy. In addition, the optical sections are significantly reduced in size, allowing greater resolution of microscopic structures and a reduction in background fluorescence.

Immature oocytes were collected from equine follicles by scraping the follicle wall. After in vitro maturation, the oocytes were stripped of their cumulus cells, and the zona pellucida was removed. The oocytes were then stained with fluorescein-isothiocyanate-conjugated Lens culinaris agglutinin (FITC-LCA) which bound to the cortical granules. In addition, the oocyte chromatin was stained with either Hoechst stain or propidium iodide, depending on the microscopic method chosen. These chromatin stains allowed the maturation state of the oocyte to be determined.

The small amount of material available for examination, the numerous steps required for preparation of the oocytes for microscopic evaluation, including exploration of mounting techniques for confocal microscopic viewing, was a challenge throughout the project. Together they limited the amount of data that could be collected over the ten weeks of the program. Work will continue within the lab because of the preliminary data collected shows the potential of these techniques to produce quality, accurate 3D images of CG distributions in equine oocytes.