James A. Baker Institute for Animal Health

College of Veterinary Medicine ▪ Cornell University

Advancing Veterinary Medicine Through Research

A Special Place in Veterinary Medicine

A mile or so across orchards and fields from the main campus of Cornell University's College of Veterinary Medicine, tucked in among woods and pastures mid-way up Snyder Hill, sits a place unlike any other in veterinary medicine: the James A. Baker Institute for Animal Health. Founded by Dr. Baker in September, 1950 as the Veterinary Virus Research Institute, the Baker Institute owes its physical remove to its beginnings as a virus isolation facility. It owes its unique status to a record of contributions to companion animal health and survival that is unsurpassed in veterinary medicine.

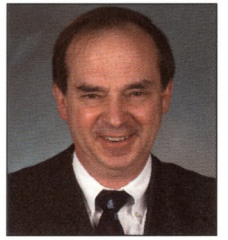
Along with its own campus, and perhaps because of it, the Baker Institute has a distinct atmosphere and personality. First, it is a place dedicated solely to veterinary research of the highest caliber and scientific merit. But it is also a place where every staff member feels a personal commitment to seeing the Institute grow and flourish. As Professor Emeritus Max Appel summed it up in a career memoir: "...the outstanding environment and camaraderie...created a fertile ground in which to do good work." The people of the Baker Institute are motivated by concern for the animals and human beings whom their research is intended to benefit, but also by their enthusiasm for the Institute itself, as a community of scholars and as a place of continual great promise.

Many thousands of companion animal owners, breeders, and veterinarians have shared that sense of mission; their financial support over the past fifty years has endowed the Institute with a measure of permanence that public grant funding can never provide. Along the way the Institute has also attracted many exceptional graduate students, postdoctoral researchers, and visiting scientists who have gone on to become veterinary school deans, academic department chairmen, industry leaders, and even university presidents. Three former graduate students – Drs. Carmichael, Appel, and Parrish – have achieved world renown in canine infectious disease research as members of the Institute's faculty.

A fiftieth anniversary is a fitting time to celebrate past accomplishments and set down a plan for the future. The pages that follow do just that, reviewing the Institute's achievements and history, its people, past and present, its active scientific programs, and its major goals and challenges. We invite both old friends and new acquaintances to turn the page, take a closer look, and see what makes the Baker Institute such a special place in veterinary medicine.

D F Antczak

Douglas F. Antczak
Director of the Baker Institute



James A. Baker Institute for Animal Health

James A. Baker Institute for Animal Health

1950 - 2000

Our Vision

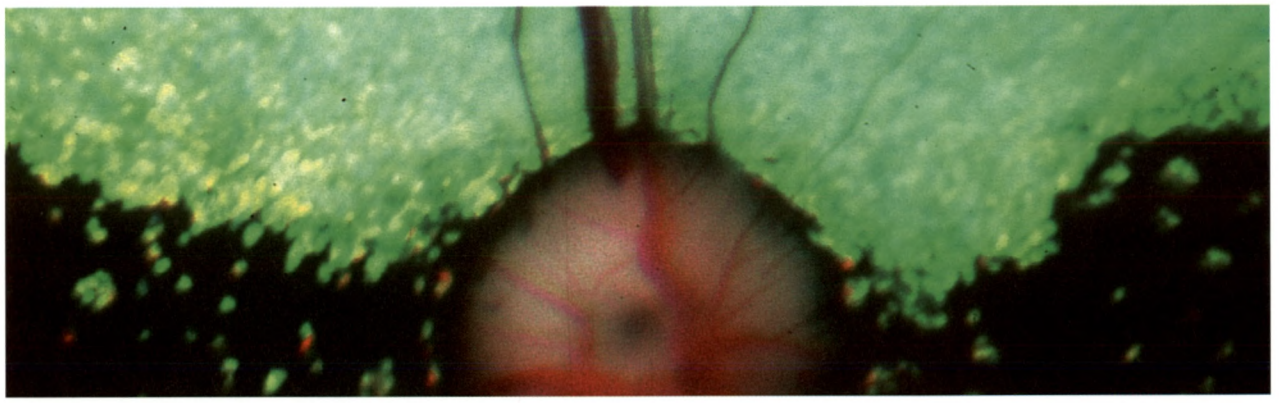
is to serve the animals that so
faithfully serve mankind.

Our Mission

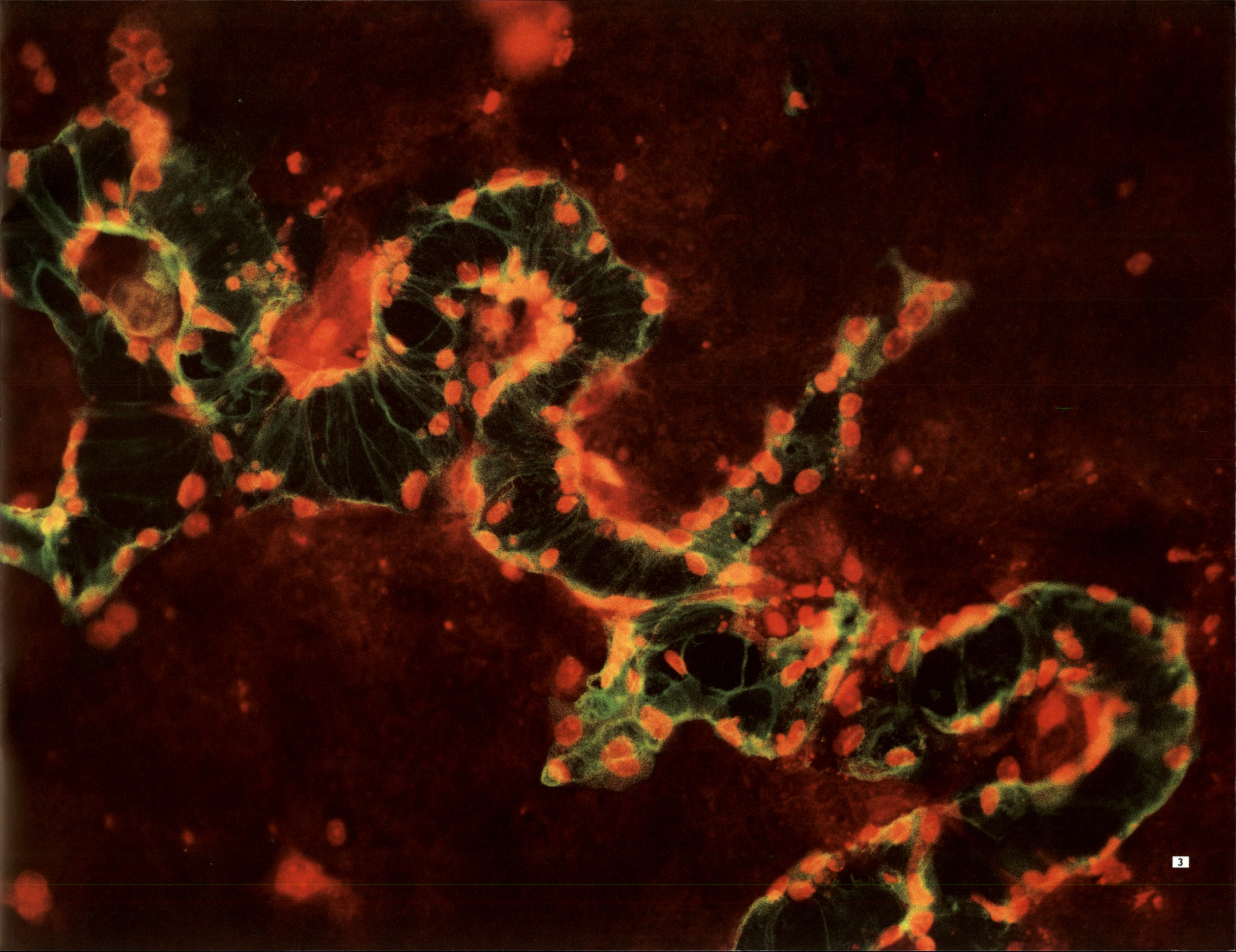
is to improve animal health
through basic and applied research.

Our Goal

is to be the leading academic
institution in animal health
research worldwide.

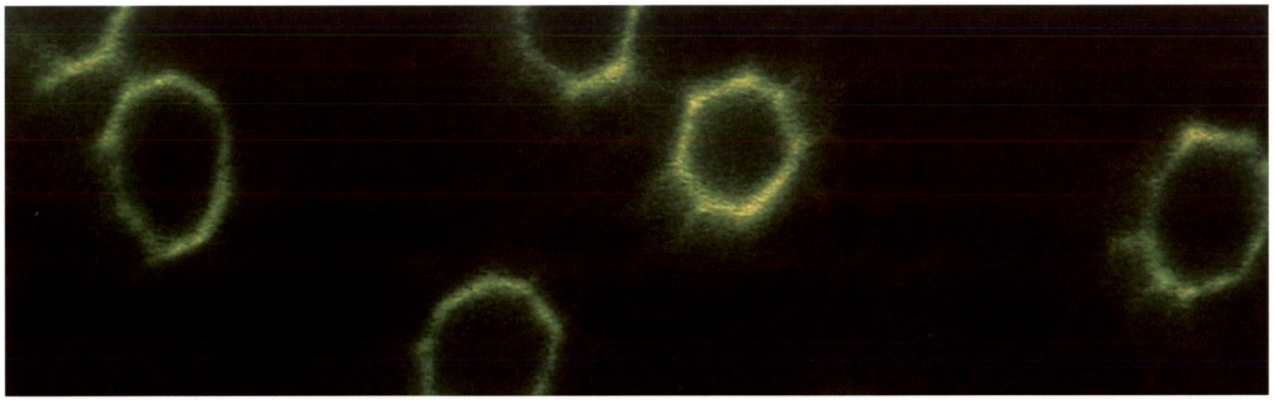


Advancing Veterinary Medicine Through Research



"He is the top man in his class, a versatile chap, interested in everything he does and good at practically everything he tries. He has plenty of energy and an unusual amount of curiosity, which leads him to try to get to the bottom of everything. Most unusual of all, he is critical, doesn't take anybody's word for anything and has ideas of his own."

Dean William Hagan to Dr. Carl Ten Broeck, March, 1940.
(Quoted by Ellis P. Leonard in *In the James Law Tradition*,
a history of Cornell's College of Veterinary Medicine.)

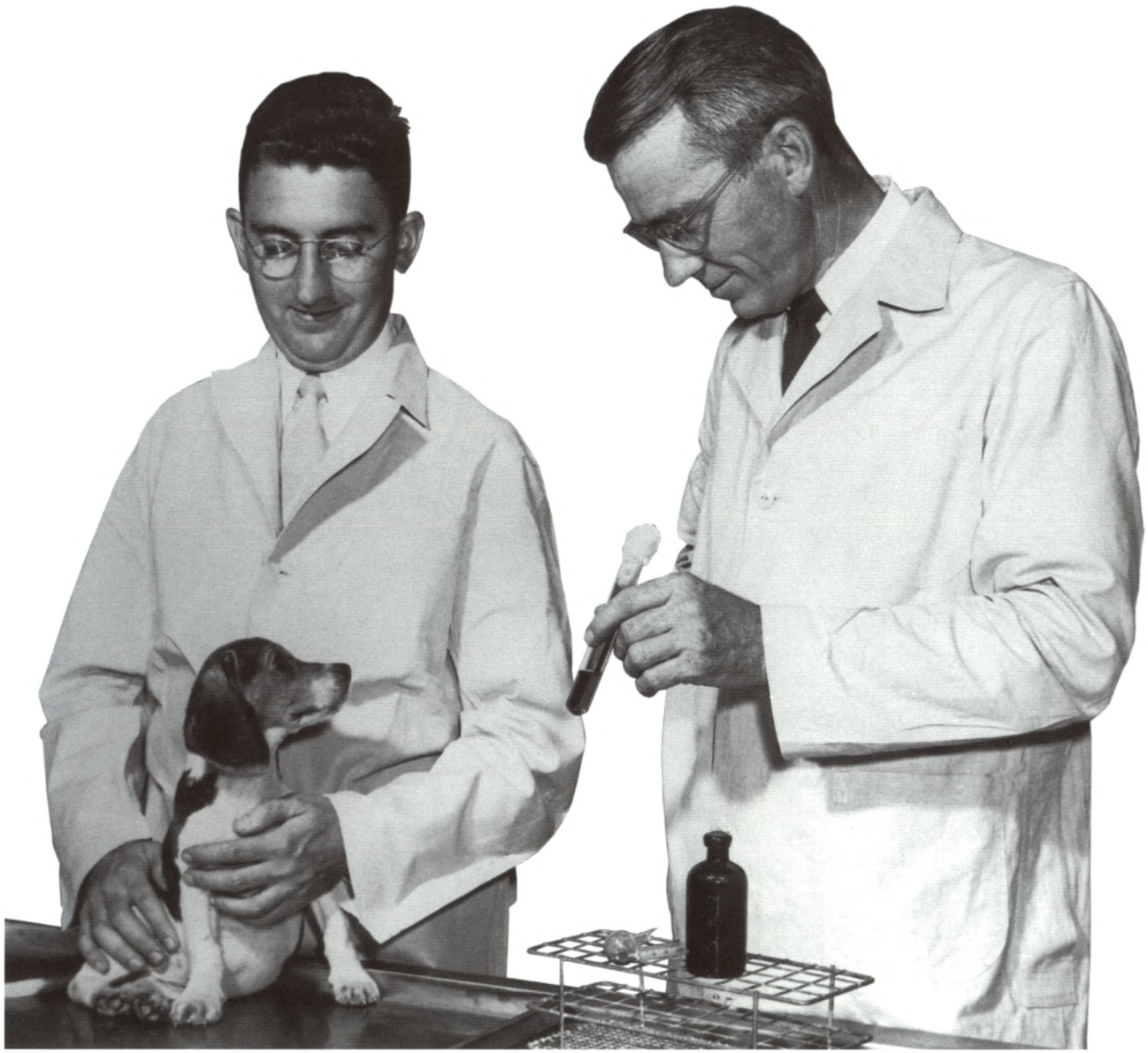


Advancing Veterinary Medicine Through Research

So wrote William Hagan in recommending James Andrew Baker for employment at the Rockefeller Institute in Princeton, New Jersey. Drew Baker had just completed a PhD in bacteriology while taking top honors in veterinary school, and the enthusiasm of Dean Hagan's endorsement was tempered by deep regret that he had no position to offer his exceptional protégé. When Hagan finally succeeded in bringing Baker back to Cornell as a full professor in 1947, the seasoned research scientist brought with him revolutionary new techniques for studying infectious disease agents – and visions of starting an institute of his own.

Baker was fascinated by animal viruses. At a time when they were not much studied, he and his staff investigated diseases in trout, swine, cats, deer, and cattle.

The Veterinary Virus Research Institute made major contributions in its first two decades to the control of diseases of livestock, including the discovery of the agent responsible for bovine viral diarrhea and the development of vaccines against hog cholera and transmissable gastroenteritis of swine. But Baker and his colleagues earned their most enduring renown for their pioneering and prolific work in the field of canine infectious diseases.



Dr. Baker with future Cornell veterinary dean Dr. George Poppensiek in 1952

Facilities Timeline

1950 Gaines Isolation Kennel constructed

1951 Cornell Research Laboratory for Diseases of Dogs (virus disease laboratory) dedicated

1953 Main laboratory and administration wing built

1954 First tissue culture laboratory for veterinary use established

In 1950 there were no effective means to control the two major scourges of dogs, distemper and infectious hepatitis. Fate stepped in when Cornell alumnus Walter Teagle, former president of Standard Oil of New Jersey, telephoned the president of Cornell University on behalf of his friend Robert Woodruff, the chairman of the Coca-Cola Company. Mr. Woodruff's prize pointer was ill, and Mr. Teagle wanted to know if anyone at Cornell could help. Cornell's President, Edmund Ezra Day, called Dean Hagan, and Dean Hagan put Dr. Baker on a plane to Atlanta.

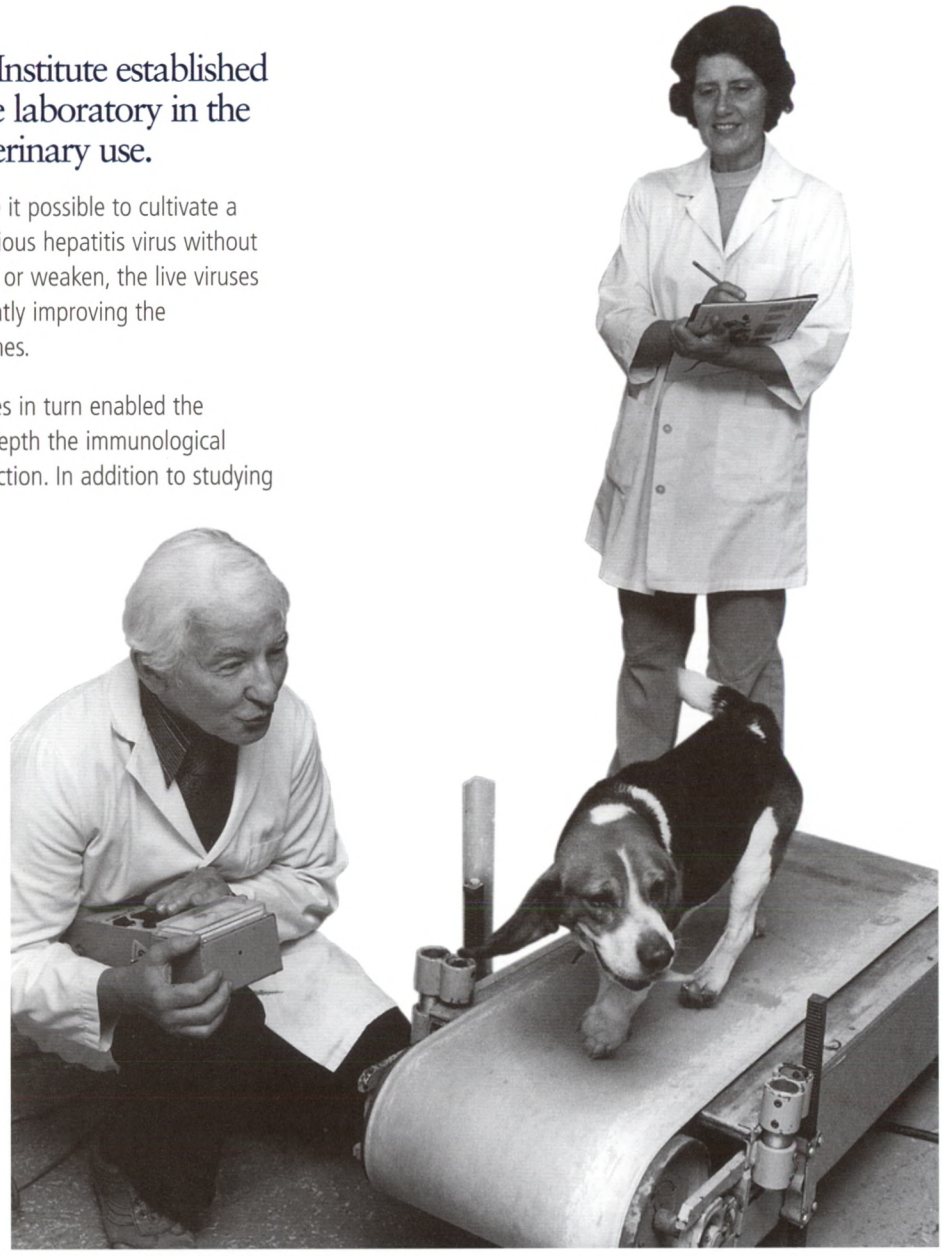
Dr. Baker did not give Mr. Woodruff the news he was hoping to hear. Instead he informed him that his dog would soon die of infectious hepatitis. Woodruff, who was accustomed to getting immediate results, expressed frustration when Baker explained that it would take time – and money – to do the research necessary to bring infectious hepatitis under control. Nevertheless, he listened, and then he approached the other industrialists in his social circle who kept kennels of hunting dogs. The story has it that they passed the hat around the tack room of Woodruff's plantation to provide Dr. Baker with start-up funds. When the Cornell Research Laboratory for Diseases of Dogs was dedicated at the Institute in January 1951, it was the first such facility in the world, and it was funded entirely by private donations.

In early 1952 Baker announced the development of the first experimental vaccine against canine infectious hepatitis. This had been combined with the now-famous Snyder Hill strain of canine distemper virus isolated at the Institute, thus becoming the first dual-virus vaccine for animals. More difficult than developing the vaccines was getting the attention of the marketplace, but after five years of public education efforts, the vaccine became commercially available, and the two greatest health threats then known to dogs soon receded into memory.

In the mid-1950s the Institute established the first tissue culture laboratory in the world for veterinary use.

This technological advance made it possible to cultivate a host-specific organism like infectious hepatitis virus without infecting dogs, and to attenuate, or weaken, the live viruses over time in culture, thereby greatly improving the predictability and safety of vaccines.

The ability to standardize vaccines in turn enabled the Institute's scientists to study in depth the immunological response to vaccination and infection. In addition to studying the transmission and pathogenesis of infectious diseases, the Institute set industry standards for vaccine production and diagnostic testing, and established the first definitive vaccination protocols for dogs and other animals. The discovery that maternal antibodies conferred through nursing could cause vaccination failures in puppies led Institute professor James Gillespie and consulting statistician Douglas Robson to chart the relationship between maternal antibody titers and the proper timing of vaccination. Use of their analyses in field trials of the dual distemper-hepatitis vaccine in 1959 and 1960 produced an unprecedented vaccination success rate of 98.8 percent.



Dr. Ben Sheffy conducting nutrition research with Ms. Alma Jo Williams in 1982

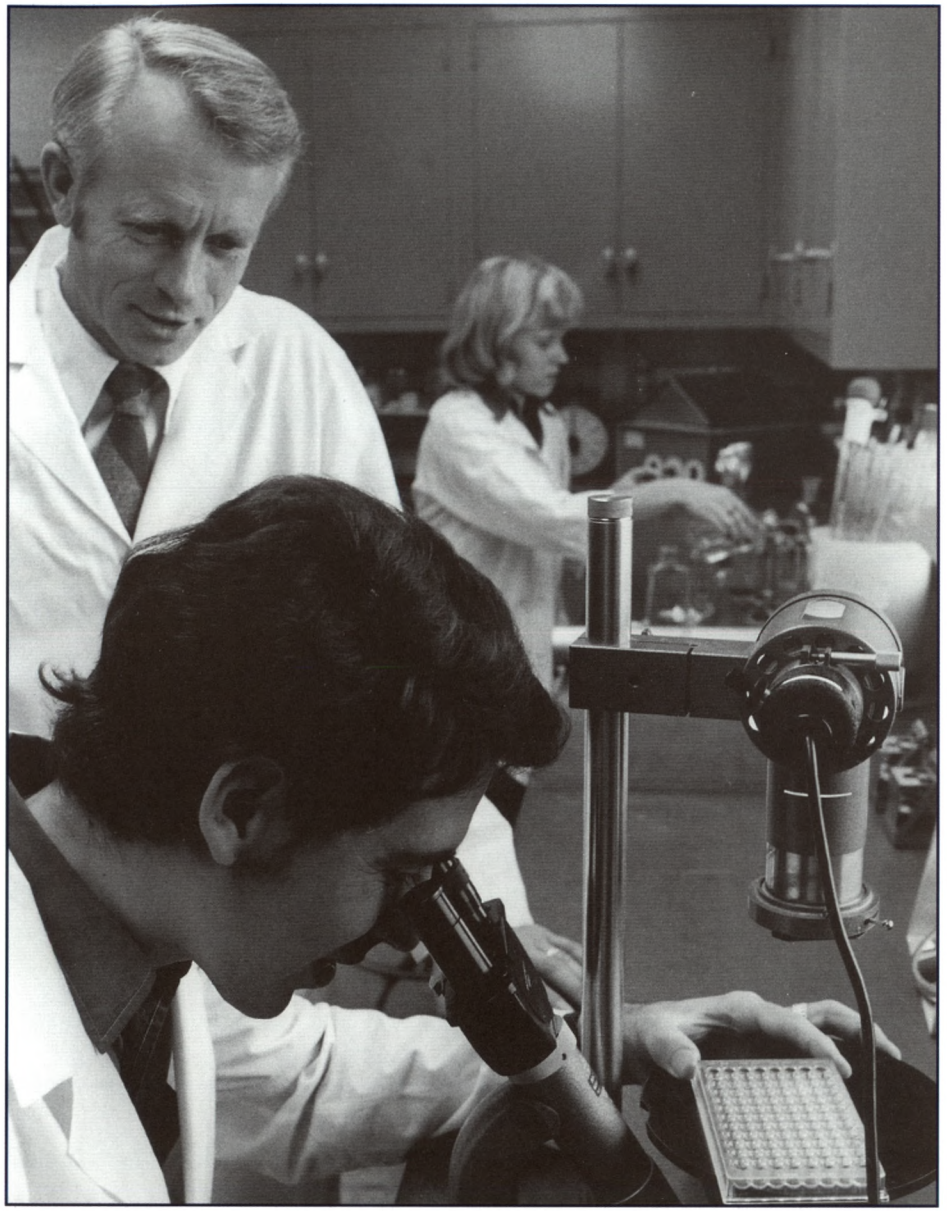
1960 Adele S. Colgate Tissue Culture Laboratory established

1968 Microbiology wing built

1978 Virus disease laboratory renovated

1979 First veterinary monoclonal antibody laboratory established

1984 Cornell's Mitchell Barn renovated and renamed as the Institute's Dorothy Havemeyer McConville Barn



Dr. Max Appel in 1975 with graduate student Ricardo Flores-Castro, who later became dean of veterinary medicine at the University of Mexico. In background is visiting scientist Dr. Liisa Sihvonen.

The foundation that Dr. Baker laid so carefully for the proper study of infectious diseases was put to the test three years after his death in 1975.

The sudden emergence of canine parvovirus (CPV) presented the Institute with its most urgent challenge since the early days of distemper and hepatitis. CPV erupted seemingly out of nowhere and spread rapidly across four continents. Within a few months of the first reports of mortality among dogs, scientists at the Institute had isolated the virus. Within three years, the work of Institute virologists Max Appel and L. E. Carmichael had culminated in the perfection of the modified live-virus vaccine that is still in use today. For many years, that discovery was Cornell's most valuable source of patent income.

Dr. L. E. Carmichael (right) on an FAO mission to Debre-Zeit, Ethiopia, in 1991 with Dr. Daouda Sylla (standing), director of the Pan-African Vaccine Control Laboratory and a former postdoctoral fellow at the Baker Institute.

The infamous parvovirus was not the first or last challenge to confront Carmichael and Appel. Their careers have been characterized by major advances against most of the viral and bacterial diseases known to pose a significant threat to dogs, including infectious hepatitis, herpesvirus, brucellosis, kennel cough, coronavirus, minute virus of canines, Lyme disease, and distemper, which has also cropped up repeatedly in wildlife species as diverse as the once nearly extinct black-footed ferrets of the American West and the lions of the Serengeti Reserve. Max Appel has played a prominent role in protecting exotic species from canine distemper, while Skip Carmichael occasionally lent his expertise to problems in livestock, discovering the agents responsible for *Mycoplasma bovis* mastitis in cattle and, with colleagues in Australia, *Mycoplasma ovipneumoniae* in sheep. Carmichael has also consulted for many years with Daouda Sylla, director of the rinderpest vaccine laboratory in the Republic of Mali in West Africa, under the auspices of the United Nations Food and Agriculture Organization.

Research Timeline

1951
Discovery of carrier state in canine hepatitis infections

2000
Groundbreaking for new laboratory building

1992
Vacant bovine facility renovated to house Center for Canine Genetics and Reproduction

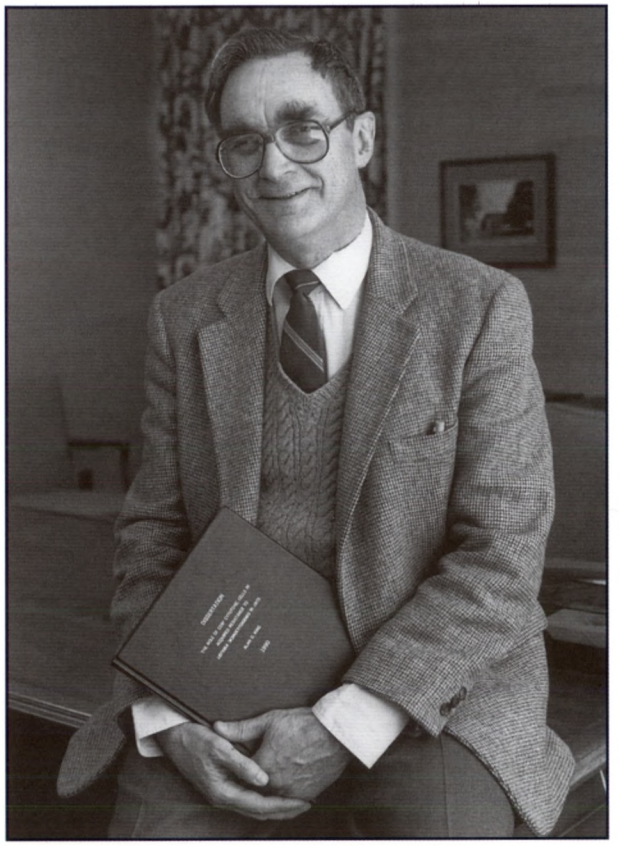
1988
Albert C. Bostwick Laboratory and associated molecular biology facilities completed

Once the Institute had defined its infectious disease control program it also became possible to devote resources to other kinds of problems in animal health.

At the urging of John M. Olin '13, a major founding benefactor and the first chairman of the Institute's Advisory Council, Baker in 1965 launched a new program to study canine hip dysplasia. He recruited physiological chemist George Lust in 1968 to head the program, which has grown under his direction to encompass molecular and biochemical studies of the genetics and pathogenesis of this condition. The biochemistry of osteoarthritis, the inevitable consequence of hip dysplasia, has also become an important focus of investigation at the Institute. Today both Nancy Burton-Wurster and Jamie MacLeod study this disease.

Mr. John M. Olin in 1968

In the 1970s immunology emerged as a separate discipline and an area of major interest in biomedical research. The Institute had always studied practical questions of immunology, such as response to vaccination, but the Institute's third decade saw a significant rise in basic research – and in funding from the National Institutes of Health. The transition was formalized with the recruitment of Douglas McGregor, a physician and immunologist from the Trudeau Institute, to lead the Institute into the post-Baker era. Robin Bell soon joined the faculty, followed in the early 1980s by Judy Appleton. The two professors of immunology study fundamental questions of host-parasite interactions that have led to a better understanding of mechanisms



Dr. Douglas McGregor in 1990

of immunity that operate in the intestinal tract. Those mechanisms are important for the development of control measures against intestinal pathogens as diverse as parasitic worms, bacteria like *Salmonella*, and canine parvovirus.

Doug Antczak, the present director of the Baker Institute, was also recruited to study basic immunological questions. His interest in the major histocompatibility complex, or MHC, of the horse has driven his research for over 20 years. The MHC is a genetic region in mammals that regulates intercellular communication affecting many aspects of immune response. Antczak's interest is in the host's interaction, not with an invading pathogen, but with a growing fetus, and his studies of equine pregnancy have served to bridge the Institute's longer-established programs in infectious diseases and immunology with the new studies in genetics, reproduction, and developmental biology that developed in the 1990s.

Colin Parrish, who distinguished himself as a graduate student in Professor Carmichael's laboratory during the parvovirus crisis, returned to the Institute in 1984 as a faculty member. His work has focused on the mechanisms that determine host range among closely related parvoviruses and, more recently, on the infection pathway taken by canine parvovirus once it penetrates the cell membrane.

In the last decade of this century, the Institute undertook a major expansion into molecular genetics research. Jamie MacLeod, Vicki Meyers-Wallen, Gus Aguirre, Greg Acland, and Jharna Ray all joined the faculty. With their recruitment, the genetic causes of inherited diseases of the eye, skeletal system, and reproductive system came under intense study at the Institute.

Technology has advanced at a continuously accelerating rate since 1950, and the work of the Institute has evolved along with it. Whatever the nature of the disease, however, or the approach taken to studying it, the Institute remains committed to its original purpose, to add to our understanding of animal diseases and to find the means to control their spread. In this the scientists of the Baker Institute have achieved remarkable success.

1952 First vaccine for infectious canine hepatitis

1955 Recognition of role of mycoplasma in kennel cough

1956 First combined vaccines for dogs

1958 Standardization of canine distemper virus serum neutralization tests

1960 Development of national distemper immunization program

Posts listed are the most current known or the ultimate achieved

Graduate Students

Albert L. Brown, PhD **1950-1951**
Chief Scientist, Bacteriology, SmithKline Beecham

Kyu Myung Lee, MD, PhD **1950-1956**
Professor of Microbiology, Cornell U.

Louise McBee, MS, PhD* **1950-1952**
Homemaker

Delbert G. McKercher, PhD* **1950-1952**
Professor and Head, Veterinary Microbiology, U. of California, Davis

Karl R. Reinhard, PhD* **1950**
Dean Emeritus, School of Veterinary Medicine, Oklahoma State U.

James I. Robinson, DVM, MS **1950-1951**
Veterinary Practitioner

M. S. Sabban, DVM, PhD* **1950-1953**
Director, Animal Health Institute, United Arab Emirates

Charles J. York, DVM, PhD **1950-1952**
Vice President, Research, Biologics Labs, Davis, California

Theodore Burnstein, DVM, PhD* **1951-1954**
Professor of Virology, Purdue U.

Andrew S. Greig, DVM, MS **1951-1953**
Principal Research Scientist, Animal Disease Research Institute, Ottawa, Canada

Manuel Moro, Jr., DVM, MS* **1952-1954**
Head of Department of Bacteriology and Virology, U. Nacional de San Marcos, Lima, Peru

Leland E. Carmichael, DVM, PhD **1956-1959**
John M. Olin Professor of Virology, Emeritus and Director, Cornell Research Laboratory for Diseases of Dogs, Baker Institute

Richard R. Gutekunst, MS, PhD **1956-1958**
Dean, College of Health Related Professions, U. of Florida

Peter H. Langer, VMD, PhD **1959-1962**
Chief, Veterinary Biologics, Ottawa, Canada

Leroy Coggins, MS, DVM, PhD **1960-1963**
Chairman, Department of Pathobiology, School of Veterinary Medicine, North Carolina State U.

*deceased

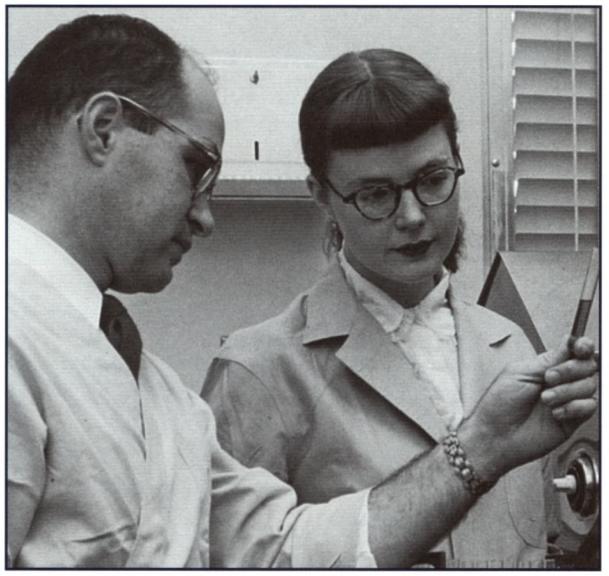
M. Taher A. Fouad, BVSc, MSc, PhD **1961-1964**
President, Biotron Laboratories, Centerville, Utah

Robert F. Kahrs, DVM, MS, PhD **1961-1965**
Dean, College of Veterinary Medicine, U. of Missouri-Columbia

Max J. G. Appel, DVM, PhD **1964-1967**
Professor of Virology, Emeritus, Baker Institute

F. Jerry Volenec, PhD **1966-1969**
Director, Project Development, Orquest, Inc., Mountain View, California

James A. House, DVM, PhD **1965-1970**
Head, Reagents and Vaccine Services, Foreign Animal Disease Diagnostic Laboratory, USDA, APHIS, Greenport, New York



Marilyn A. Menegus, PhD **1968-1972**
Director, Microbiology Laboratories, Strong Memorial Hospital, Rochester, NY

Philip A. Pickerill, DVM, PhD **1968-1970**
Area Veterinarian in Charge, USDA, APHIS, Jackson, Mississippi

Lisle W. George, DVM, PhD **1970-1974**
Professor of Large Animal and Internal Medicine, U. of California, Davis

Douglas Hugh Davies, BVS, PhD **1971-1974**
General Manager, New Zealand Animal Health Reference Laboratory and Exotic Disease Response Centre, Upper Hutt, New Zealand

Charles A. Banta, MS, PhD **1972-1975**
Principal Research Nutritionist, ALPO Petfoods, Allentown, Pennsylvania

David A. Bemis, PhD **1973-1977**
Associate Professor, Department of Comparative Medicine, U. of Tennessee

Douglas R. Miller, PhD **1974-1977**
Professor of Biochemistry, Louisiana State U.

Earl F. Bloch, MS, PhD **1974-1978**
Professor, Department of Microbiology, Howard University

William R. Shek, DVM, MS, PhD **1974-1979**
Director, Diagnostic Services, Charles River Laboratories, Wilmington, Mass.

Ricardo Flores-Castro, DVM, PhD **1975-1978**
Dean, School of Veterinary Medicine, U. of Mexico

Thomas O. Manning, DVM, MS **1977-1980**
Assistant Professor of Dermatology, North Carolina State U.

Brian A. Summers, DVM, PhD **1976-1980**
Professor of Pathology, Cornell U.

Shaw-chien Tsai, MS, DVM, PhD **1976-1980**
Berkeley, California

Chung-sung Chen, DVM, MS **1977-1978**

Marc H. Langweiler, DVM, MS, PhD **1977-1980**
Technical Specialist in Flow Cytometry, Dartmouth-Hitchcock Medical Center

Geoffrey Letchworth, III, DVM, PhD **1977-1980**
Professor of Virology, U. of Wisconsin

David J. Dueland, MS, MD **1978-1981**
Surgeon, Geisinger Medical Center, Danville, Pennsylvania

Roy V. H. Pollock, DVM, PhD **1978-1981**
President, IDEXX Informatics, Eau Claire, Wisconsin

Paul C. Meunier, PhD **1979-1983**
Head of Pathology, duPont Merck Pharmaceutical Co.

Joseph M. Friedlander, DVM, MS **1980-1982**
Veterinary Practitioner, Brick, New Jersey

John M. Olsewski, MS, MD **1980-1982**
Chief, Orthopaedic Spine Surgery, Montefiore Medical Center, Bronx, New York

1965 **Discovery and isolation of canine herpesvirus**

1966 **Isolation and characterization of *Brucella canis***

1970 **Definition of the pathogenesis of canine distemper**

1974 **First practical test for diagnosis of canine brucellosis**

1977 **Description of pathogenesis of *Bordetella bronchiseptica* infection in dogs**

Colin R. Parrish, PhD **1980-1984**
Associate Professor of Virology, Baker Institute

Ching-hua Wang, MD, PhD **1981-1986**
Associate Professor, U. of California, San Bernardino

Anne Crump Avery, PhD, VMD **1982-1989**
Assistant Professor, Department of Pathology, Colorado State U.

Daniel H. Sajewski, MSAGR, MS **1982-1992**
Anesthesiologist and Director of Pain Management, Roslyn, New York

Christopher J. Davies, DVM, PhD **1983-1988**
Assistant Professor, Microbiology and Immunology, Cornell U.

William J. Mitchell, DVM, PhD **1983-1987**
Assistant Professor, College of Veterinary Medicine, U. of Missouri-Columbia

Harry Leipold, PhD **1984-1989**
Senior Scientist, Emisphere Technologies, Tarrytown, New York

Ali Ahmad, PhD **1985-1989**
Assistant Professor, Centre of Research, Ste. Justine Hospital, Montreal, Quebec

Duzhang Zhu, PhD **1985-1989**
Senior Research Scientist, Lederle-Praxix Biologicals, West Henrietta, New York

Melissa S. Carlisle, BVSc, PhD **1986-1990**
Veterinary Pathologist, Veterinary Pathology Services, Brisbane, Queensland, Australia

William Donaldson, BVSc, PhD **1986-1989**
Associate Director, International Regulatory Affairs and Planning, Pfizer Animal Health, New York, New York

Capt. Alan D. King, DVM, PhD **1986-1989**
Birmingham, Alabama

Catherine Y. Linder, DVM, MS **1986-1988**

Julio G. Oriol, DVM, MS **1986-1988**
Vice-President, Victoria Hoteles, Playa Dorado, Puerto Plata, Dominican Republic

Chong-hui Zhang, MS, PhD **1986-1992**
Instructor in Medicine, Division of Tumor Immunology, Dana-Farber Cancer Institute, Harvard Medical School

John Angelos, MS, DVM **1987-1992**
Resident, Large Animal Medicine, U. of California, Davis

1978 Isolation of canine parvovirus-type 2 (CPV-2)

1979 First vaccines for CPV-2

1981 Perfection of attenuated vaccine for CPV-2

1982 Discovery of greatly increased fibronectin in early-osteoarthritic cartilage of dogs

1984 First successful transplantation of horse embryos into mules

Maria Fernandez-Maillo, DVM, MS **1987-1989**
Madrid, Spain

Rory J. Todhunter, BVSc, PhD **1987-1992**
Associate Professor, Clinical Sciences, Cornell U.

Laura K. Hanson, PhD **1988-1993**
Research Fellow, Department of Microbiology, Eastern Virginia Medical School

Shwu-fen Chang, MS, PhD **1989-1992**
Associate Professor, Graduate Institute of Cellular and Molecular Biology, Taipei Medical College, Taipei, Taiwan

Theodore Llana, III, PhD **1989-1993**
Graduate Student in Business Administration, Georgetown U.

Juli K. Maher, DVM, PhD **1989-1994**
Veterinary Practitioner, VetSmart Corporation, San Diego, California

Orisetimeyin Otubu, MS, MD **1989-1991**
Medical practitioner, Anderson, South Carolina

Anthony T. Vella, MS, PhD **1989-1990**
Assistant Professor, Department of Microbiology, Oregon State U.

Gabriele Grünig, DVM, PhD **1990-1994**
Assistant Professor of Pathology, St. Luke's Roosevelt Hospital Center Health Science Institute, Columbia U.

Lauri Ellis Neyer, PhD **1990-1994**
Research Scientist, Bayer Corp., Berkeley, California

Dai-wei Zhang, MD, PhD **1990-1994**
Resident in Radiology, Nassau Medical Center, Long Island, New York

David Peters, DVM, PhD **1991-1996**
Project Leader, Schering-Plough Animal Health Corp., Elkhorn, Nebraska

Dina Barbis Tresnan, DVM, PhD **1991-1995**
Senior Research Scientist, Pfizer Central Research, Animal Health Biodiscovery, Groton, Connecticut

Deborah Negrao-Correa, MS, PhD **1992-1997**
Assistant Professor of Immunology, Federal U. of Minas Gerais, Brazil

Clarissa L. Santos Kao, MS **1992-1995**
San Francisco, California

Reinhard Straubinger, DVM, PhD **1993-1997**
Research Associate, Baker Institute

Lisa A. Fortier, DVM, PhD **1994-1998**
Senior Research Associate, Department of Molecular Medicine, Cornell U.

Michael Olivier, MS, PhD **1994-1997**
Research Associate, Department of Genetics, Stanford U.

Matthew C. Stewart, BVSc, PhD **1994-1998**
Senior Research Associate, Department of Orthopedics, Case Western U.

Weiquan Wang, MD, PhD **1994-1999**
Surgical Internship Program, Brown U.

John S. L. Parker, BVMS, PhD **1995-1999**
Postdoctoral Fellow, Baker Institute

Dai Wang, PhD **1995-2000**
Postdoctoral Associate, U. of Medicine and Dentistry of New Jersey

Wen Yuan, MS **1995-present**

Caroline J. Zeiss, BVSc, PhD **1995-1999**
Assistant Professor of Pathology, Yale University

Jessica M. Baker, PhD **1996-2000**
Research Fellow, Department of Immunology, Dana-Farber Cancer Institute, Harvard U.

Fuliang Du **1996-present**

Rina Gendelman **1996-present**

Paige Adams, DVM, MS **1997-present**

Hao Chen **1997-present**

Julia Flaminio, DVM, MS **1998-present**

Gloria J. Matthews, DVM **1997-present**

Karsten Huffer, DVM **1999-present**

Rebecca Tallmadge **1999-present**

Postdoctoral Associates, Research Associates, and Consultants

Erskine Morse, DVM, MS, PhD* **1950-51**
Dean, College of Veterinary Medicine, Purdue U.

Vincent Marshall, DVM **1954-58**
President, Swine Vaccines, Inc., Omaha, Nebraska

Hadley Stephenson, DVM* **1954-76**
Professor Emeritus of Veterinary Therapeutics and Small Animal Diseases, Cornell U.

Chintamani Singh, GBVC, MS, PhD **1956-57**
Director, Indian Veterinary Research Institute, Izatnagar, India

Douglas Robson, PhD **1957-75**
Professor Emeritus of Biometrics, Cornell U.

Robert C.T. Lee, DVM, PhD **1958-61**
President Emeritus, National Chung Hsing U., Taiwan, Republic of China

Alexander Zeissig, DVM, MS, PhD* **1969-70**
Director, Veterinary Diagnostic Laboratory, Cornell U.

Gustavo D. Aguirre, VMD, PhD **1971-72**
Caspary Professor of Ophthalmology and Director, Center for Canine Genetics and Reproduction, Baker Institute

Helen A. Greisen, MS, PhD* **1972-83**
Electron Microscopist, Baker Institute

Thomas W. Jungi, MS, DPhil **1976-78**
Professor of Immunology, Institute of Veterinary Virology, U. of Berne, Switzerland

Urban K. Forsum, MD, PhD **1978-79**
Professor of Bacteriology, U. of Uppsala, Sweden

Melissa C. Woan, MS, PhD **1978-85**

Christine San Hui-Chou, PhD **1979-80**

Steven J. Zoha, PhD **1979-81**

Rodger V. Allhands, DVM **1980-81**
Professor of Physiology, U. of Illinois

Mark J. Newman, MSc, PhD **1981-83**
Vice President, Infectious Disease Program, Epimmune, San Diego, California

Sara Louise Cosby **1985**
Senior Lecturer in Molecular Pathology, The Queen's U. of Belfast, Northern Ireland

Masataka Korenaga, PhD **1985-87**
Associate Professor of Parasitology, Kochi Medical School, Nankoku City, Kochi, Japan

Juergen Steinmeyer, PhD **1988-90**
Associate Professor, Orthopadische Universitatsklinik, Med. Zentrum fur Orthopadie und Physikalische Medizin, Giessen, Germany

Karen Munkenbeck Trotter, PhD **1988-90**
Teaching Support Specialist, Veterinary Microbiology and Immunology, Cornell U.

Prema Arasukavalar, MS, PhD, DVM **1990-94**
Assistant Professor, North Carolina State U.

Beata Marchewka-Mizak, DVM, PhD **1990-91**
Assistant Professor and Department Head, Carnivore and Fur Animal Diseases, National Veterinary Research Institute, Pulawy, Poland

Anthony Farquhar, MS, PhD **1991-94**
Assistant Professor, Mechanical Engineering, U. of Maryland

Richard E. Goodman, PhD **1991-93**
Scientist, Monsanto Corporation, St. Louis, Missouri

Allen Gruenberg, MS, PhD **1991-94**
Scientist, New Zealand Pastoral Agricultural Research Institute, Wallaceville Animal Research Centre, Upper Hutt, New Zealand

Patricia L. Lucia, PhD, DVM **1991-93**
Veterinary Practitioner, Lafayette, New York

Uwe Truyen, DVM **1991-93**
Associate Professor, Institute for Medical Microbiology, Ludwig-Maximillians U., Munich, Germany

Da-Nian Gu, MS, PhD **1992-present**
Research Associate, Baker Institute

Kalyanasundaram Ramaswamy, BVSc, MVSc, PhD **1992-94**
Assistant Professor, U. of Illinois

*deceased

1991 **Discovery of CPV-2b**

1991 **First cloning of horse histocompatibility genes**

1992 **First identification of a candidate gene for an inherited eye disease of dogs, rod-cone dysplasia**

1993 **First cloning of horse gamma interferon**

1994 **First DNA blood test for an inherited eye disease of dogs, rcd-1**

A.T. M. Wahid, MD **1992-1995**
Resident Physician, Allegheny U. Hospitals, Philadelphia, Pennsylvania

Kathryn Gropp, DVM, PhD **1993-1995**
Pharmaceuticals Division, Proctor and Gamble Company, Miami Valley Laboratory, Cincinnati, Ohio

Laurel E. Southard, MS **1993-1995**
Director, Hughes Undergraduate Research Program, and Coordinator, Undergraduate Research, Biological Sciences, Cornell U.

Anona Bamford, PhD **1994-1995**
Bio-Rad Laboratories Ltd., Hemel Hempstead, England

Hsi Liu, MS, PhD **1994-1996**
Centers for Disease Control, Atlanta, Georgia

Vesna Novosel, DVM **1994-1995**
Project Leader, Viral Vaccine Production, Institute of Immunology, Zagreb, Croatia

Alix F. Straubinger, DVM **1994-present**
Research Associate, Baker Institute

Luc Haerter, PhD **1995-1997**
Laboratory Chief, Department of Surgery, U. of Zurich, Switzerland

Martha Harding, DVM, PhD **1995-1997**
Senior Research Scientist, Pfizer Central Research, Animal Health Biodiscovery, Groton, Connecticut

Trenna ManWarren, DVM **1995-1996**
Veterinary Practitioner, Muncy, Indiana

Catherine S. McVay, MS, PhD **1995-1997**
Assistant Professor, Department of Microbiology and Immunology, Texas Technical U.

Maria E. Verdugo, MD **1995-present**
Research Associate, Baker Institute

Barbara A. Butcher, MS, PhD **1996-1999**
Senior Research Associate, Department of Microbiology and Immunology, Cornell U.

Chih-Tung Chen, MS, PhD **1996-1999**
Laboratory for Soft Tissue Research, Hospital for Special Surgery, New York, New York

Weikuan Gu, MS, PhD **1996-1998**
J. L. Pettis V. A. Medical Center, Loma Linda, California

Christine M. Schweizer, DVM **1996-1997**
Lecturer, Veterinary Clinical Sciences, Cornell U.

Maria M. Viveiros, MSc, PhD **1996-1998**
Postdoctoral Research Scientist, Jackson Laboratory, Bar Harbor, Maine

Qi Zhang, MS, MD, PhD **1996-present**
Research Associate, Baker Institute

Sarah Bacon, MA, PhD **1997-1999**
Assistant Professor, Department of Biological Sciences, Mt. Holyoke College

Peter Bracken, BVSc, DVM **1997-1998**
Large Animal Intern, U. of Georgia

Ari Correa, MS, PhD **1997**
Faculty member, Instituto de Ciencias Biologicas, Brazil

Duska J. Sidjanin, MS, PhD **1998-present**
Research Associate, Baker Institute

Anna Kukekova, MS, PhD **1999-present**
Postdoctoral Associate, Baker Institute

Fernanda Romaris, MS, PhD **1999-present**
Postdoctoral Fellow, Baker Institute

Maija Vihinen-Ranta, PhD **1999-present**
Postdoctoral Fellow, Baker Institute

Barbara Zangerl, MS, PhD **2000-present**
Postdoctoral Associate, Baker Institute

Visiting Scientists

Arif Celiker, DVM, MS, PhD **1952-1954**
Chief, Bacteriology Lab, Pendik Institute, Istanbul, Turkey

Grayson B. Mitchell, DVM **1952-1954**
Veterinary Practitioner, Kings Ferry, New York

Hugo Stunzi, DVM **1952-1953**
Director, Veterinary Pathology Institute, U. of Zurich, Switzerland

Sureyya Aygun, MS, DVM, PhD **1953**
Turkish Government Officer

Alan O. Betts, MA, PhD, MRCVS **1955-1956**
Principal and Dean, Royal Veterinary College, U. of London

Omer Erturk, DVM, PhD* **1955**
Veterinary College, U. of Ankara, Turkey

Hans Keller, DVM **1955**
Ag Veterinaria, Zurich, Switzerland

Bernd Liess, DVM **1956-1957**
Professor and Head, School of Veterinary Medicine, Hannover, Germany

Ahmed Shimi, DVS **1956-1957**
Teheran U., Iran

B. S. Pomeroy, DVM **1958**
Professor of Veterinary Bacteriology, U. of Minnesota

John A. Roberts, BVSc, PhD **1963-1964**
Principal Research Officer, CSIRO, Australia

Daouda Sylla, DVM, Dip.Bact.Ser. **1965**
Director, Pan-African Vaccine Control Laboratory, FAO, Dakar, Senegal

Donald L. Croghan, DVM, MS **1966-6198**
Section Head, National Veterinary Services Laboratory, USDA

Helen H. Lee, PhD **1969**
Professor of Parasitology

Toby D. St. George, DVM, DVSc **1974-1975**
Principal Research Officer, CSIRO, Long Pocket Laboratories, Brisbane, Australia

Liisa Sihvonen, DVM **1974-1975**
Professor and Head, Department of Virology and Epidemiology, National Veterinary and Food Research Institute, Helsinki, Finland

Hui-Qing Bai, MD **1988-1989**

Xiu-Feng Lu, MD **1988-1989**
Research Scientist, Phyton, Inc., Ithaca, New York

Françoise Sacuto **1988-1989**

Akira Hashimoto, DVM, PhD **1989**
Professor, Laboratory of Pathobiology, Graduate School of Veterinary Medicine, Hokkaido U., Sapporo, Japan

Gerald J. Pijanowski, DVM, MS, PhD **1989-1990**
Associate Professor, Veterinary Biosciences, U. of Illinois

Han Tie-Yan **1989-1990**

Eliane Marti, DVM **1991**
Postdoctoral Fellow, Institute of Animal Breeding, U. of Berne, Switzerland

Marion Tischner, DVM, PhD **1991**
Professor and Head, Department of Animal Reproduction, U. of Agriculture, Krakow, Poland

*deceased

1994 **Cloning and expression of canine erythropoietin (EPO)**

1996 **Demonstration that articular cartilage contains a unique isoform of fibronectin**

1996 **Successful clinical trial of recombinant canine EPO therapy**

1997 **Development of an accurate, early diagnostic test for canine hip dysplasia**

1997 **Identification of interleukin-8 as an initiator of arthritis in dogs with Lyme disease**

Susan Fubini, DVM 1994-1995
Professor of Clinical Sciences, Cornell U.

Theo Van Veen, PhD 1997
Professor, Gothenburg U., Sweden

Susan Carpenter, PhD 1998
Associate Professor, Department of Veterinary Microbiology and Preventive Medicine, Iowa State U.

Brian Farrow, BVSc, PhD 1999
Professor of Clinical Sciences, U. of Sydney

Zuohua Mao, MD, PhD 1999-present
Associate Professor, Shanghai Medical U.

Institute Faculty

James A. Baker, MS, DVM, PhD* 1950-1975
Director, Baker Institute

James H. Gillespie, VMD 1950-1963
Professor and Chairman, Veterinary Microbiology, Cornell U.

George C. Poppensiek, VMD, MS 1950-1955
Dean Emeritus and James Law Professor of Medicine, Emeritus, Cornell U.

Ben E. Sheffy, MS, PhD 1954-1985
Caspary Professor of Nutrition, Emeritus, Baker Institute

Leland E. Carmichael, DVM, PhD 1959-present
John M. Olin Professor of Virology, Emeritus and Director, Cornell Research Laboratory for Diseases of Dogs, Baker Institute

Max J. G. Appel, DVM, PhD 1967-present
Professor of Virology, Emeritus, Baker Institute

George Lust, PhD 1968-present
Professor of Biochemistry, Baker Institute

Ronald D. Schultz, MS, PhD 1973-1977
Professor and Chair, Department of Pathobiological Sciences, U. of Wisconsin, Madison

Robin G. Bell, PhD 1976-present
Professor of Immunology, Baker Institute

Douglas D. McGregor, MD, DPhil 1976-1991
Associate Dean for Research and Graduate Education, College of Veterinary Medicine, Cornell U.

*deceased

Douglas F. Antczak, VMD, PhD 1978-present
Director and Dorothy Havemeyer McConville Professor of Equine Medicine, Baker Institute

Nancy Burton-Wurster, MS, PhD 1981-present
Senior Research Associate, Baker Institute

Judith A. Appleton, MS, PhD 1982-present
Professor of Immunology, Baker Institute

A. Dwight Lopes, VMD 1982-1983
Consultant, Groton, Connecticut

Colin R. Parrish, PhD 1984-present
Associate Professor of Virology, Baker Institute

Gregory M. Acland, BVSc 1992-present
Senior Research Associate, Baker Institute

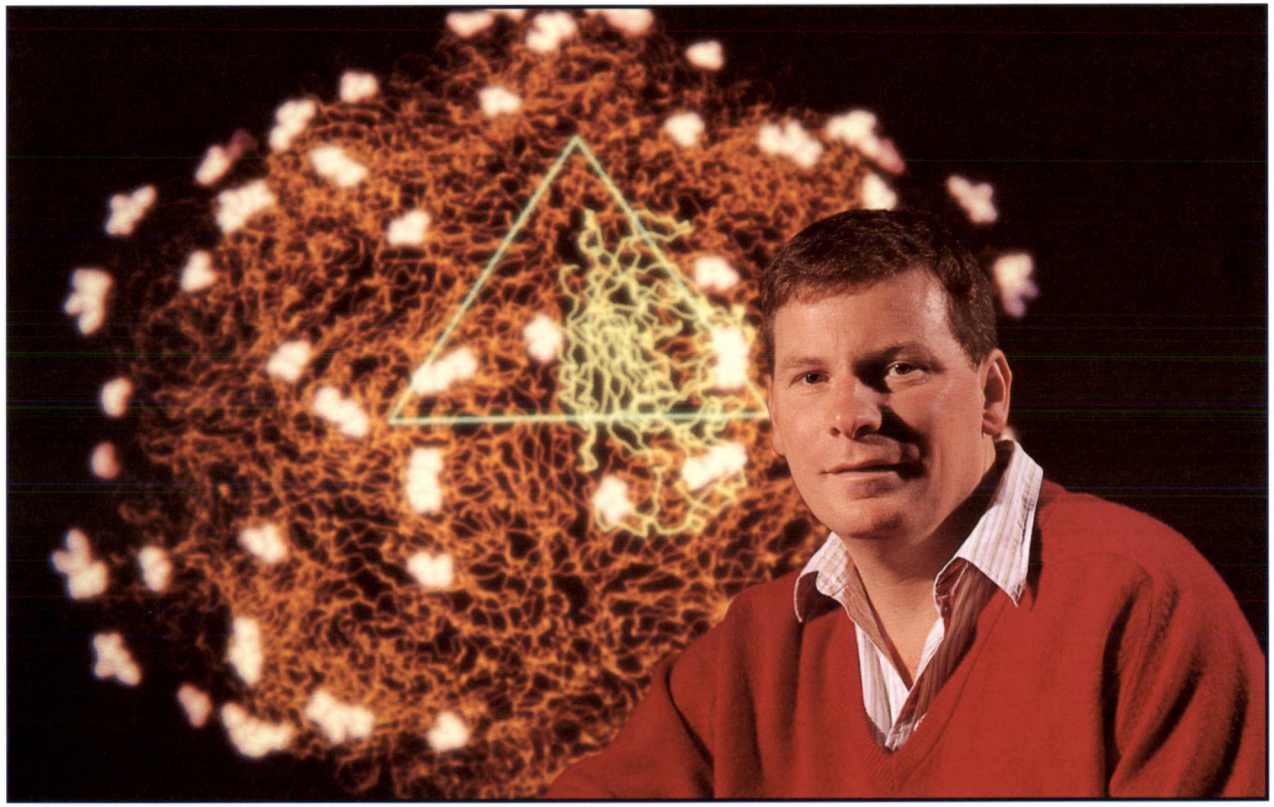
Gustavo D. Aguirre, VMD, PhD 1992-present
Caspary Professor of Ophthalmology and Director, Center for Canine Genetics and Reproduction, Baker Institute

James N. MacLeod, VMD, PhD 1992-present
Associate Professor of Molecular Genetics, Baker Institute

Vicki N. Meyers-Wallen, VMD, PhD 1992-present
Associate Professor of Theriogenology, Baker Institute

Jharna Ray, MS, PhD 1992-present
Assistant Professor of Molecular Genetics, Baker Institute

Kunal Ray, MS, PhD 1993-1998
Assistant Director, Indian Institute of Chemical Biology, Calcutta, India



1997 First publication of a linkage map of the canine genome

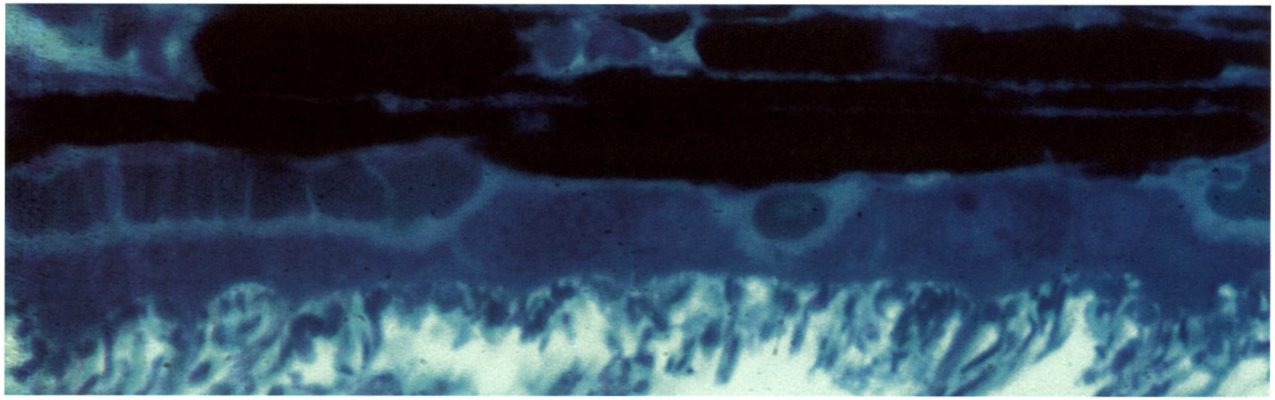
1998 Successful *in vitro* gene therapy to correct disease in retinal cells

1998 Identification of the mutation causing MPS VII in dogs

1998 Linkage mapping of the locus for progressive rod-cone degeneration in dogs

1998 Development of first practical diagnostic tests for the minute virus of canines

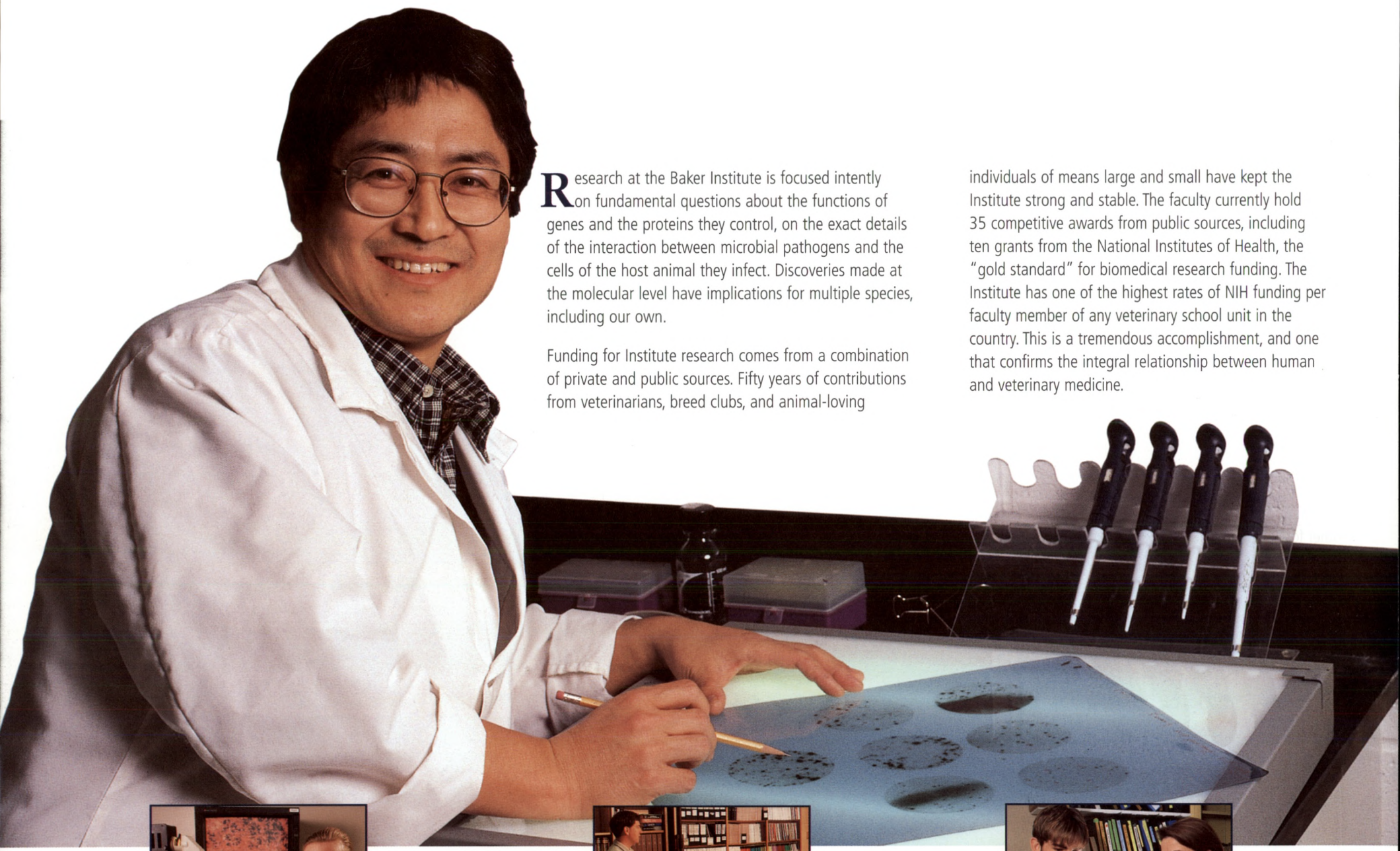
Although the technologies employed by the Baker Institute have become dramatically more sophisticated since 1950, the essential aim remains the same: to combine basic research and advanced training for veterinary and biomedical scientists with practical, service-oriented programs that can have a profound influence on veterinary medical practice.

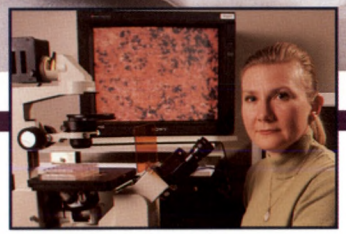


Advancing Veterinary Medicine Through Research

Research at the Baker Institute is focused intently on fundamental questions about the functions of genes and the proteins they control, on the exact details of the interaction between microbial pathogens and the cells of the host animal they infect. Discoveries made at the molecular level have implications for multiple species, including our own.

Funding for Institute research comes from a combination of private and public sources. Fifty years of contributions from veterinarians, breed clubs, and animal-loving individuals of means large and small have kept the Institute strong and stable. The faculty currently hold 35 competitive awards from public sources, including ten grants from the National Institutes of Health, the "gold standard" for biomedical research funding. The Institute has one of the highest rates of NIH funding per faculty member of any veterinary school unit in the country. This is a tremendous accomplishment, and one that confirms the integral relationship between human and veterinary medicine.





Canine genetic mapping and linkage studies

The primary aim of our research is to identify and map the genes involved in a range of canine hereditary disorders that affect the eye. This information helps us to understand the biology of these disorders and to develop genetic tests that can identify carriers and affected dogs before they are bred. A second area of our work is the testing of potential therapies for canine hereditary retinal disorders.

We have recently mapped genes for cone degeneration, a form of day blindness, in Alaskan malamutes, and for two forms of progressive retinal atrophy (PRA), progressive rod-cone degeneration and early retinal degeneration. Genetic tests have been developed for PRA in Portuguese water dogs, Chesapeake Bay retrievers, Labrador retrievers, and cocker spaniels; and for congenital stationary night blindness in Briards. Disorders currently under study include several other forms of PRA and of day blindness, two forms of oculoskeletal dysplasia, and collie eye anomaly.

As part of this effort we have collaborated with several other investigators, particularly Dr. Elaine Ostrander at the Fred Hutchinson Cancer Research Center, to develop and expand the canine genome map. This has also led to the establishment of the Canine Reference Family DNA Distribution Center, a collaborative arrangement between Cornell and Ralston Purina to make available to the international community of canine genetics researchers a panel of DNA samples forming the reference families for the canine map.

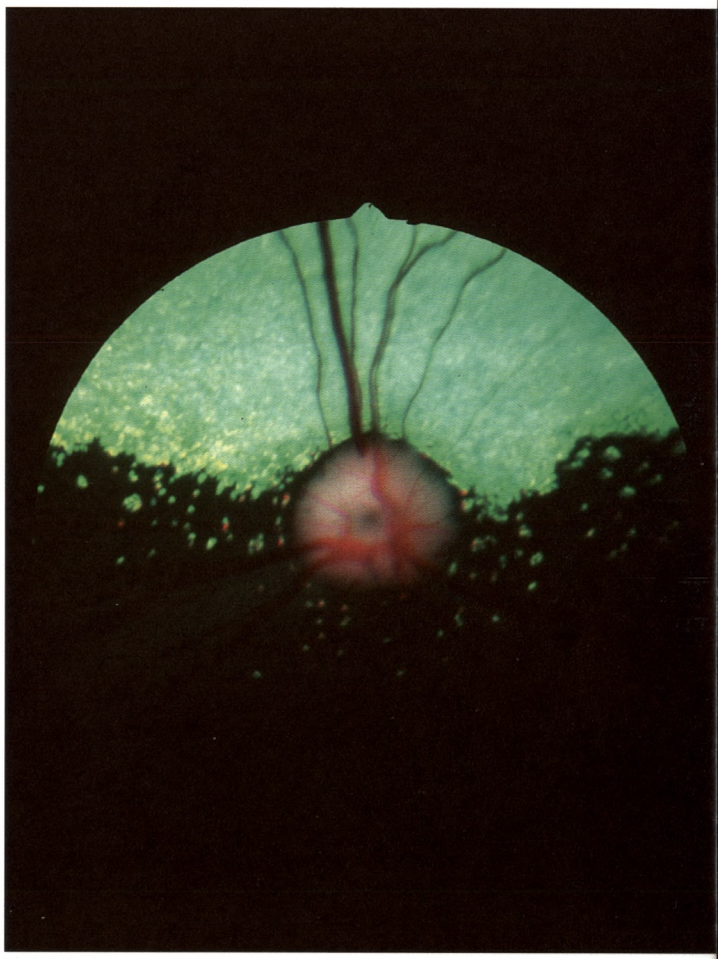
Selected Publications

Acland, G., Ray, K., Mellersh, C., Langston, A., Rine, J., Ostrander, E., Aguirre, G. A. 1999. Novel Retinal Degeneration Locus Identified by Linkage and Comparative Mapping of Canine Early Retinal Degeneration. *Genomics* 59:134-142.

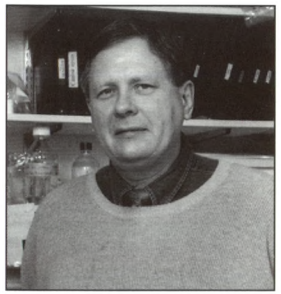
Dudus, L., Anand, V., Acland, G. M., Chen, S.-J., Wilson, J. M., Fisher, K. J., Maguire, A. M., Bennett, J. 1999. Persistent transgene product in retina, optic nerve and brain after intraocular injection of rAAV. *Vision Research* 39:2545-2553.

Werner, P., Mellersh, C. S., Raducha, M. G., DeRose, S., Acland, G. M., Prociuk, U., Wiegand, N., Aguirre, G. D., Henthorn, P. S., Patterson, D. F., and Ostrander, E. A. 1999. Anchoring of Canine Linkage Groups with Chromosome Specific Markers. *Mammalian Genome* 10:814-823.

Acland, G., Ray, K., Mellersh, C., Gu, W., Langston, A., Rine, J., Ostrander, E., and Aguirre, G. 1998. Linkage analysis and comparative mapping of canine progressive rod-cone degeneration *(prcd)* establishes potential locus homology with retinitis pigmentosa (RP17) in humans. *Proceedings of the National Academy of Sciences USA* 95:3048-3053.



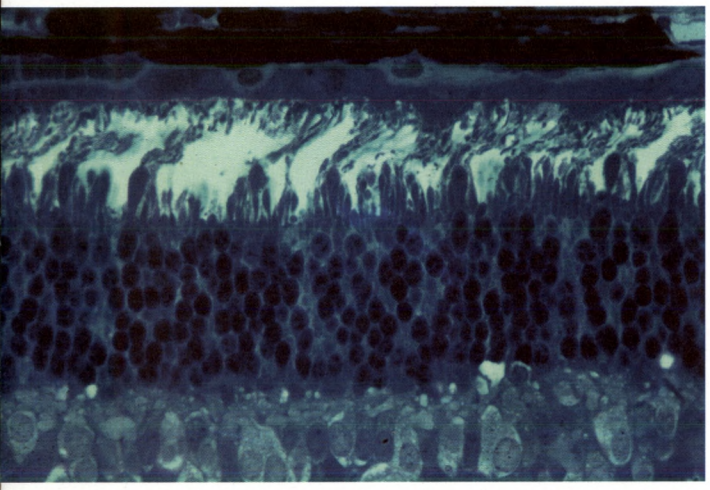
Retinal fundus photo of a Briard affected with congenital stationary night blindness. As is typical in this disease, the retina appears completely normal when viewed with an ophthalmoscope.



Gregory M. Acland

Senior Research Associate: BVSc, University of Sydney, 1965
Diplomate, American College of Veterinary Ophthalmologists

Canine genetics/genomics; ophthalmic genetics



Canine rod and cone cells showing early-stage damage from progressive retinal atrophy.

Our laboratory is actively engaged in multiple research projects relating to the inheritance of retinal degenerations in dogs, humans, and other mammals. These include efforts to identify the genes and locate the mutations associated with several separately inherited forms of progressive retinal atrophy (PRA), a significant disease of dogs that is also the genetic analog of retinitis pigmentosa, a group of retinal degenerations inherited in human families. Forms of PRA currently under study include photoreceptor dysplasia in the miniature schnauzer, rod-cone dysplasia 2 in the collie, X-linked PRA in the Siberian husky, and progressive rod-cone degeneration, a late-onset form of the disease known to affect five breeds (poodles, Labrador retrievers, American and English cocker spaniels, and Portuguese water dogs) and suspected to occur in many other breeds as well.

I also collaborate with colleagues within and outside the Baker Institute in the study of macular degeneration, a disease of humans, and the MPS (for mucopolysaccharidosis) group of lysosomal storage disorders, which affect humans, dogs, cats, and mice. Our group has also been collaborating with Elaine Ostrander's group at the Fred Hutchinson Cancer Research Center in the construction of a linkage map of the canine genome. Given the striking number of inherited diseases that are common to dogs and humans, this map promises to be a boon to genetic studies in both species.

Selected Publications

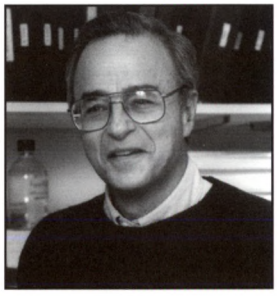
Aguirre, G., Baldwin, V., Weeks, K., Acland, G., and Ray, K. 1999. Frequency of the codon 807 mutation in the cGMP phosphodiesterase ß-subunit gene in Irish setters and other dog breeds with inherited retinal degeneration. *Journal of Heredity* 90:143-147.

Gu, W., Ray, K., Pearce-Kelling, S., Baldwin, V., Langston, A., Ray, J., Ostrander, E., Acland, G., and Aguirre, G. 1999. Evaluation of the APOH gene as a positional candidate for *prcd* in dogs. *Investigations in Ophthalmology and Visual Science* 40:1229-1237.

Acland, G., Ray, K., Mellersh, C., Langston, A., Rine, J., Ostrander, E., and Aguirre, G. 1999. A Novel Retinal Degeneration Locus Identified by Linkage and Comparative Mapping of Canine Early Retinal Degeneration. *Genomics* 59:134-142.

Acland, G., Ray, K., Mellersh, C., Gu, W., Langston, A., Rine, J., Ostrander, E., and Aguirre, G. 1998. Linkage analysis and comparative mapping of canine progressive rod-cone degeneration *(prcd)* establishes potential locus homology with retinitis pigmentosa (RP17) in humans. *Proceedings of the National Academy of Sciences USA* 95:3048-3053.

Aguirre, G. D., Baldwin, B., Pearce-Kelling, S., Narfström, K., Ray, K., and Acland, G. M. 1998. Congenital stationary night blindness in the dog: common mutation in the RPE65 gene indicates founder effect. *Molecular Vision* 4:3.



Gustavo Aguirre

Alfred H. Caspary Professor of Ophthalmology: VMD, University of Pennsylvania, 1968
PhD, University of Pennsylvania, 1975; Diplomate, American College of Veterinary Ophthalmologists

Equine immunology, genetics, and reproduction

For 20 years our program has focused on the biological interactions that take place between a mother and fetus during pregnancy. In particular, we are concerned with how the placenta and fetus avoid recognition and destruction by the maternal immune system. This is an intriguing question that has broad applications to many areas of biology and medicine, including organ transplantation and cancer biology. In the course of these studies our laboratory has acquired expertise in three important areas of equine medicine: immunology, genetics, and reproduction. The immunological assays we have developed for our research are also used to characterize immune system defects in horses admitted to the Large Animal Hospital at Cornell. Our reproductive studies have led to new ways to study the growth and function of the placenta. Finally, our genetic studies have been fundamental to the international collaboration of the Horse Genome Project.

Because of the laboratory resources that we have developed here at the Baker Institute, we are in a unique position to investigate the complex interactions between mother and fetus. Our studies are of relevance not only to horses, but also to other animals and to human health.

Selected Publications

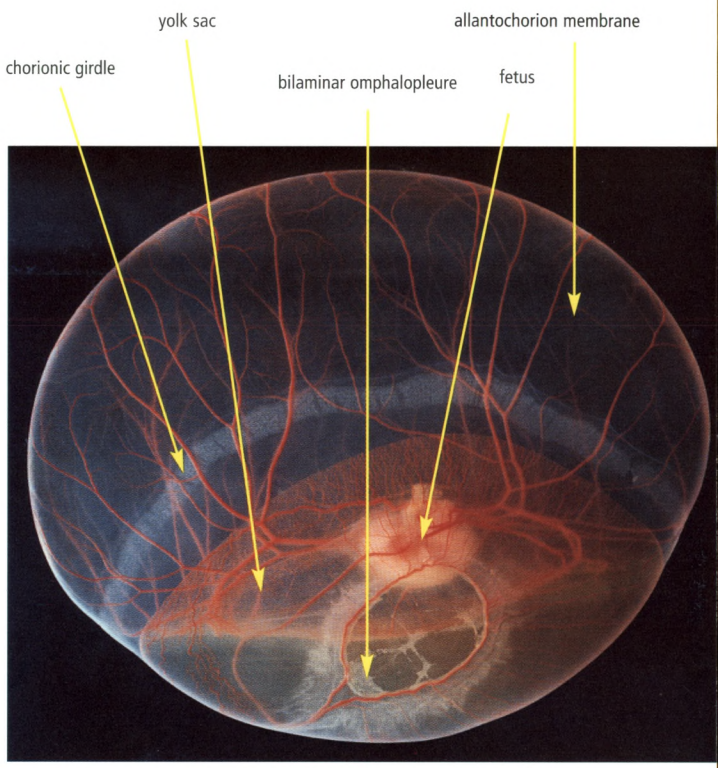
Baker, J. M., Bamford, A. I., and Antczak, D. F. 1999. Modulation of allospecific CTL responses during pregnancy in equids: an immunological barrier to interspecies matings? *Journal of Immunology* 162:4496-4501.

Römer, I., Grützner, F., Winking, H., Haaf, T., Niveleau, A., Orth, A., Skidmore, L., Antczak, D., and Fundele, R. 1999. Global methylation in eutherian hybrids. *Nature* 40:131-132.

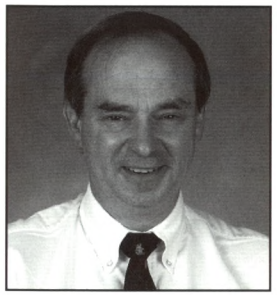
Tallmadge, R.L., Evans, K.G., Hopman, T.J., Schug, M.D., Aquadro, C.F., Bowling, A.T., Murray, J.D., Caetano, A.R., and Antczak, D.F. 1999. Equine dinucleotide repeat loci *COR081-COR100. Animal Genetics* 30:470.

Maher, J. K., Tresnan, D. P., Deacon, S., Hannah, L., and Antczak, D. F. 1996. Analysis of MHC class I gene expression in equine trophoblast cells using *in situ* hybridization. *Placenta* 17:351-359.

Grünig, G., Triplett, L., Canady, L.K., Allen, W.R., and Antczak, D. F. 1995. The maternal leukocyte response to the endometrial cups in horses is correlated with the developmental stages of the invasive trophoblast cells. *Placenta* 16: 539-559.



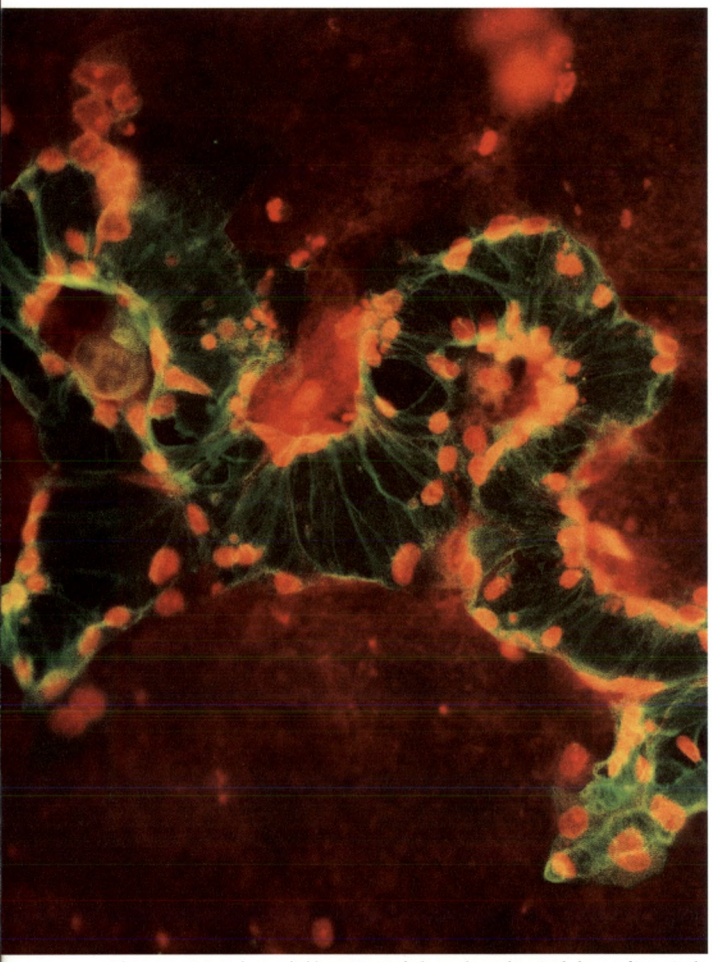
A day 33 horse conceptus, showing the principal components of the developing placenta. The invasive band of cells of the chorionic girdle are poised to migrate into the uterus at day 36-38 to establish the dramatic structures of the endometrial cups. The cup cells are the sole source of equine chorionic gonadotrophin, and they also provide a strong immunological stimulus to the mare at this critical stage of equine pregnancy.



Douglas F. Antczak

Dorothy Havemeyer McConville Professor of Equine Medicine
VMD, University of Pennsylvania, 1973; PhD, Cambridge University, 1978

Mucosal immunity, host-parasite interactions



The serpentine path traveled by a *T. spiralis* larva through a single layer of intestinal epithelial cells can be traced in the fluorescently labeled tyvelose it deposited in its wake. There are no parasites visible in this field. The nuclei of dead cells stain intensely and uniformly red or, where they overlap with tyvelose, yellow. Nuclei of the live cells in the surrounding monolayer are very lightly fluorescent.

Roundworms, or nematodes are important causes of disease in animals, yet relatively little is known about how they sustain themselves in the animals that they infect. Our research aims to elucidate and exploit the ways by which the host's immune response interferes with parasitism by nematodes. We are currently studying two important pathogens, *Trichinella spiralis* and *Parelaphostrongylus tenuis.* The latter organism is a significant cause of disease in sheep, goats and llamas in the Northeast. Our goals for the *P. tenuis* work are twofold: first, to develop an antigen detection test for use in diagnosis, and second, to design vaccines to prevent infection. Our interest in *T. spiralis* concerns the most fundamental question in infectious disease, specifically, how does one organism parasitize another?

The larval stage of *Trichinella spiralis* initiates infection in a susceptible host when it invades and then travels through intestinal epithelial cells. Our experimental approach relies upon an *in vitro* model of invasion that we have developed. We hypothesize that the processes of invasion and intercellular transit are facilitated by glycoproteins that are disgorged by infectious larvae. These glycoproteins bear complex glycans that are capped with a novel sugar called tyvelose. Tyvelose-specific antibodies are able to protect epithelia from invasion and cause established *T. spiralis* larvae to abandon their niche. These antibodies interfere with the niche of the larva in several ways, the outcome being a failure of the worm to develop in its animal host. Currently, our aim is to investigate the molecular basis for establishment of the epithelial niche of *T. spiralis*.

Selected Publications

Peters, P. J., Gagliardo, L. F., Sabin, E. E., Betchen, A. B., Ghosh, K., Oblak, J. B., and Appleton, J. A. 1999. Dominance of IgG2c in the anti-phosphorylcholine response of rats infected with *Trichinella spiralis. Infection and Immunity* 67:4661-4667.

McVay, C., Tsung, A., and Appleton, J. A. 1998. Participation of parasite surface glycoproteins in antibody-mediated protection of epithelial cells against *Trichinella spiralis. Infection and Immunity* 66: 1941-1945.

Ellis, L. A., McVay, C. S., Probert, M. A., Zhang, J., Bundle, D. R., and Appleton, J. A. 1997. Terminal b-linked tyvelose creates unique epitopes in *Trichinella spiralis* glycan antigens. *Glycobiology* 7:383-390.

ManWarren, T., Gagliardo, L., Geyer, J., McVay, C., Pearce-Kelling, S., and Appleton, J. A. 1997. Invasion of intestinal epithelia *in vitro* by the parasitic nematode *Trichinella spiralis. Infection and Immunity* 65:4806-4812.

Judith A. Appleton

Professor of Immunology

MS, University of Georgia, 1977; PhD, University of Georgia, 1980

Intestinal and systemic anti-nematode immunity

For many years we have investigated mechanisms of immunity against *Trichinella spiralis*, a parasitic nematode, or roundworm, that infects the intestine. We have defined significant roles for immunoglobulin E (IgE) and, more recently, for IgA, in the rejection of *T. spiralis*. We have also recently begun to direct considerable effort to an analysis of systemic anti-nematode immunity. We are interested in learning how filarial worms and other systemic nematodes manage to avoid the effects of antibody, which is so effective against nematodes in the intestine. To investigate this, we have developed a model system in rats to study *Brugia pahangi*. This filarial nematode parasite is closely related to *B. malayi*, a species that causes significant morbidity in man. Adults of both *B. pahangi* and *B. malayi* live in the lymphatic vessels and lymph nodes at many sites in the body.

Most research conducted on *B. pahangi* has been done in humans, mice, or cats, and analysis in each of these systems has faced serious deficiencies. The view has developed that the long life-span of filariids in humans is due to a parasite-induced suppression of specific immune reactivity against the parasite. All of the studies of human lymphocyte reactivity to filarial antigens have been conducted on cells isolated from blood. Our preliminary findings in rats appear to show that this procedure is misleading with regard to overall reactivity.

Although rats display the same long-term characteristics of infection as humans, we have not found in rats an equivalent lack of reactivity to the parasites' antigens. However, we have found that lymphocytes circulating in the blood of infected rats are less reactive to parasite antigens than cells in the lymph nodes. This finding suggests that lymphocytes in different parts of the body may react differently to parasite antigens. We believe that this model will provide significant insights into mechanisms used by nematodes to avoid the effects of strong host immune responses.

Selected Publications

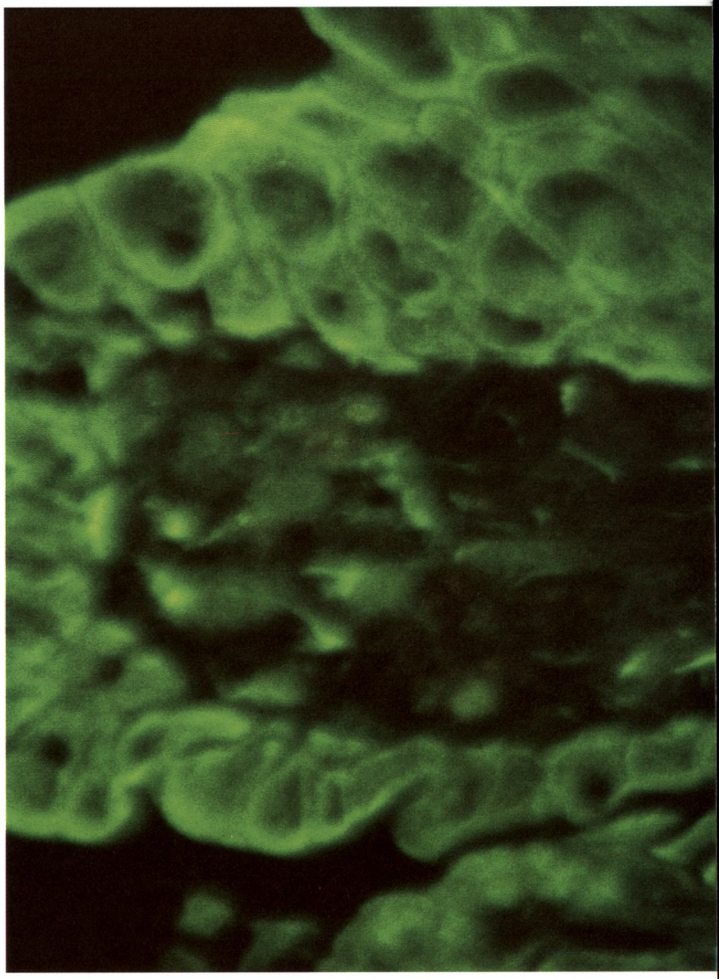
Bell, R. G., Adams, L., Coleman, S., Negrâo-Corrêa, D., and Klei, T. 1999. *Brugia pahangi:* Quantitative analysis of infection in several inbred rat strains. *Experimental Parasitology* 92:120-130.

Bell, R. G. 1998. The generation and expression of immunity to *Trichinella spiralis* in laboratory rodents. *Advances in Parasitology* 41:149-217.

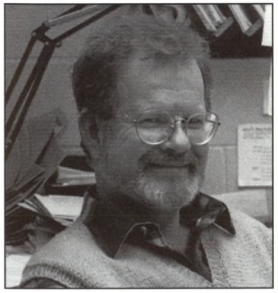
Ramaswamy, K., Negrâo-Corrêa, D., and Bell, R. G. 1996. Local intestinal immune responses to infection with *Trichinella spiralis*: Real time, continuous assay of cytokines in the intestinal (afferent) and efferent thoracic duct lymph of rats. *Journal of Immunology* 156:4328-4337.

Negrâo-Corrêa, D., Adams, L. S., and Bell, R. G. 1996. Intestinal transport and catabolism of IgE. *Journal of Immunology* 157:4037-4044.

Ramaswamy, K., Hakimi, J., and Bell, R. G. 1994. Evidence for a novel, IL-4 inducible, IgE-uptake and transport mechanism in the intestine. *Journal of Experimental Medicine* 180:1793-1803.



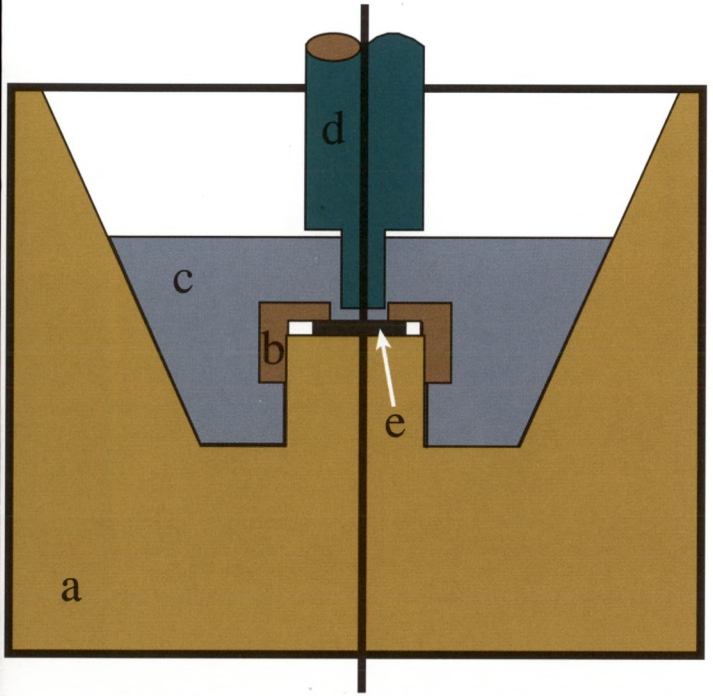
Binding of fluorescent-labeled immunoglobulin E (shown in green) to the epithelial cell layer of the intestine



Robin G. Bell

Professor of Immunology
PhD, Australian National University, 1971

Cartilage biochemistry and osteoarthritis



The apparatus used to apply mechanical loads to cartilage samples has three test chambers like the one shown here. A cartilage disk is held on the standing pin (a) by a hold-down ring (b) while being maintained in culture medium (c). The flat-ended indentor (d) applies stress to the core of the cartilage disk (e) by striking it rapidly at regular, frequent intervals.

Cartilage is a wonderfully resilient tissue that resists compression and minimizes friction from joint movement. The structural properties of cartilage are determined by the highly organized and spatially differentiated matrix that supports and is nourished by the cartilage cells. In dogs with hip dysplasia, cartilage is compromised early in the progression to osteoarthritis. We are particularly interested in the role in that progression of fibronectin, a glycoprotein that is an important constituent of cartilage matrix. As our laboratory was the first to demonstrate, the fibronectin content increases dramatically in osteoarthritic cartilage. With colleagues in the laboratory of Dr. Jamie MacLeod we have recently identified a previously unknown splice variant of fibronectin that is specific to cartilage. We are investigating its importance to the structure and function of a healthy cartilage matrix.

It has long been proposed that damage to healthy cartilage from mechanical impact can initiate the progression to osteoarthritic lesions. We have developed a means of modelling the early stages of cartilage degeneration in osteoarthritis by applying high levels of repeated-impact loads to disks of cartilage while they are maintained in a culture medium. The area of impact on these cartilage disks shows biochemical and metabolic changes similar to those documented in osteoarthritic lesions, including increased fibronectin and cell death. This model will facilitate understanding of the mechanisms of disease progression and may provide an efficient preliminary screen for treatment modalities. It is our hope that our studies will someday benefit both animals and humans who suffer from osteoarthritis.

Selected Publications

Chen, C.-T., Burton-Wurster, N., Lust, G., Bank, R. A., and Tekoppele, J. M. 1999. Compositional and metabolic changes in damaged cartilage are peak-stress, stress-rate, and loading-duration dependent. *Journal of Orthopaedic Research* 17:870-879.

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MacLeod, J. N., Burton-Wurster, N., Gu, D.-N., and Lust, G. 1996. Fibronectin mRNA splice variant in articular cartilage lacks bases encoding the V, III-15 and I-10 protein segments. *Journal of Biological Chemistry* 271:18954-18960.

Nancy Burton-Wurster

Senior Research Associate
MS, New York University, 1967; PhD, New York University, 1970

Hip dysplasia, osteoarthritis, articular cartilage physiology

For 30 years our research has addressed the cause, pathogenesis, diagnosis, and treatment of hip dysplasia and osteoarthritis in dogs. Multiple genes influence the inheritance of this disease, and environmental factors, especially the effect of food consumption on growth rate, can also play a part. Signs of disease occur not only in hip joints, but also in shoulder, knee, and lumbar vertebral joints, suggesting that hip dysplasia is only the most conspicuous manifestation of a more widespread disease. We recently devised a radiographic means, illustrated at right, to predict the development of hip dysplasia in young dogs by measuring the extent of dorsolateral subluxation, or displacement, of the femoral heads. Our current work is focused on identifying a genetic marker that correlates to either normal or abnormal displacement. To this end, we have developed a large, informative pedigree of disease-free and dysplastic dogs. Once we link a DNA marker to either a normal or abnormal phenotype we can begin studies to characterize the genes that control the expression of hip dysplasia.

Selected Publications

Todhunter, R. J., Acland, G. M., Olivier, M., Williams, A. J., Vernier-Singer, M., Burton-Wurster, N., Farese, J. P., Gröhn, Y. T., Gilbert, R. O., Dykes, N. L., and Lust, G. 1999. An outcrossed canine pedigree for linkage analysis of hip dysplasia. *Journal of Heredity* 90:83-92.

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Olivier, M., Breen, M., Binns, M. M., and Lust, G. 1999. Localization and characterization of nucleotide sequences from the canine Y chromosome. *Chromosome Research* 7:223-233.

Farese, J. P., Todhunter, R. J., Lust, G., Williams, A. J., and Dykes, N. L. 1998. Dorsolateral subluxation of hip joints in dogs measured in a weight-bearing position with radiography and computed tomography. *Veterinary Surgery* 27:393-405.

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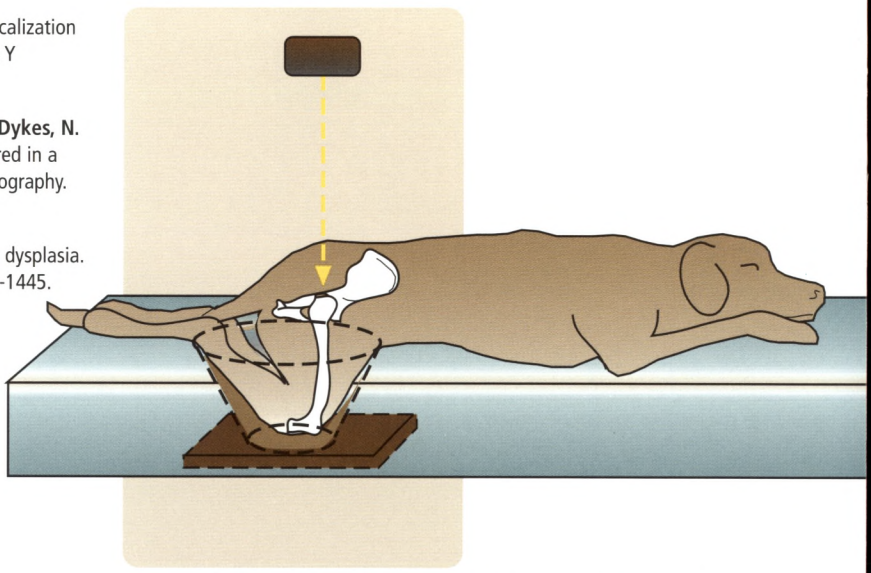
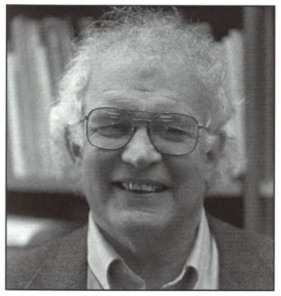
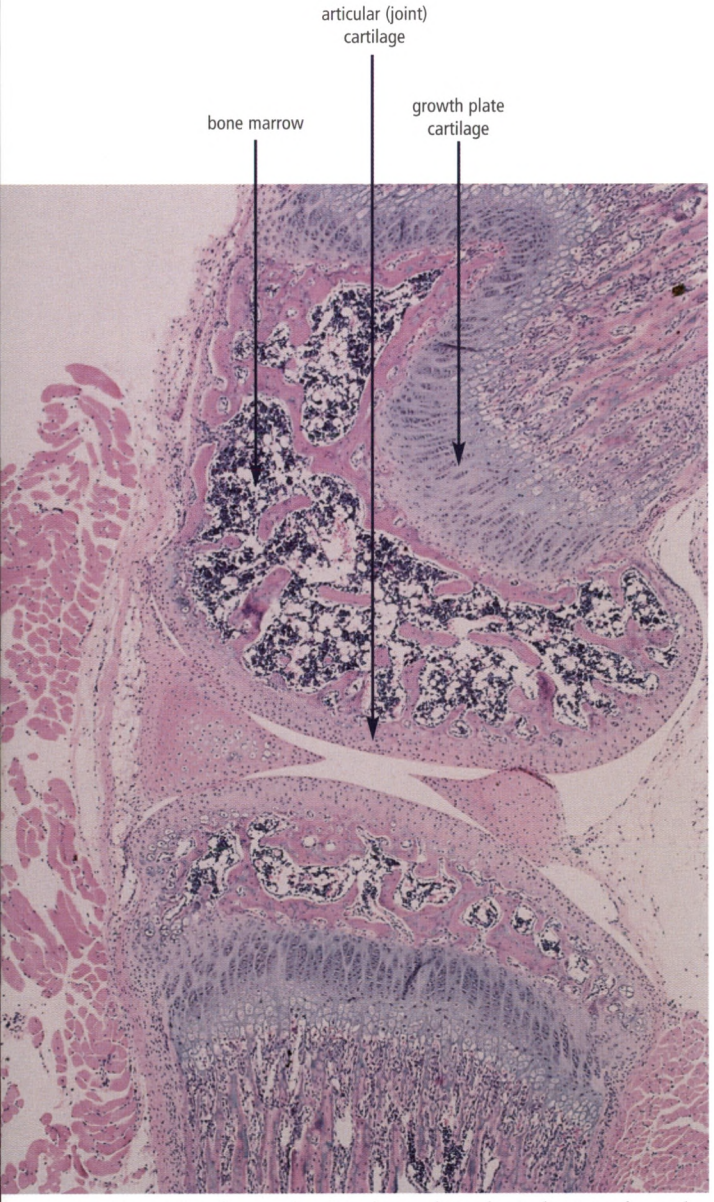


The dorsolateral subluxation test is performed by placing a tranquilized dog in a supported kneeling position on a foam-rubber pad. Dashed line and arrow indicate the path of the X-ray beam



George Lust

Professor of Physiological Chemistry
PhD, Cornell University, 1964



Cross-section of a mouse knee joint showing the cartilage at the joint surfaces and the growth plates of the bones. In the bone marrow, erythropoietin stimulates the precursors of red blood cells to proliferate and differentiate into red blood cells.

Cartilage, osteoarthritis, anemia

My laboratory has two major projects. The first project focuses on chondrocytes, cells that synthesize and maintain cartilage. There are several different types of cartilage in the body. Some cartilaginous tissues are stable throughout life, like joint cartilage and the structural cartilage in our noses and ears. Other types of cartilage, however, are transitional and convert into bone through a process called endochondral ossification. In our research, we compare the patterns of gene expression in chondrocytes from different cartilaginous tissues, at different developmental stages, and in different disease states. Our broad objective is to better understand the function of chondrocytes and how their unique properties are regulated. Important clinical conditions with direct relevance to our research include the progression and treatment of osteoarthritis, and abnormal growth or fracture repair in bones.

The second project in my laboratory focuses on a protein called erythropoietin that stimulates precursors of red blood cells in the marrow of bones. Erythropoietin is the primary regulator of red blood-cell production in animals, including humans. Chronic diseases such as kidney failure and cancer can result in anemia due to a deficiency of erythropoietin. Using recombinant DNA technology and cell culture-based methods of protein expression, we are working to make canine and feline erythropoietin available for therapeutic use by veterinarians.

Selected Publications

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MacLeod, J. N., Burton-Wurster, N., Gu, D.-N., and Lust, G. 1996. Fibronectin mRNA splice variant in articular cartilage lacks bases encoding the V, III-15, and I-10 protein segments. *Journal of Biological Chemistry* 271:18954-18960.

James N. MacLeod

Associate Professor of Molecular Genetics
VMD, University of Pennsylvania, 1984; PhD, University of Pennsylvania, 1990

Canine developmental genetics and reproduction

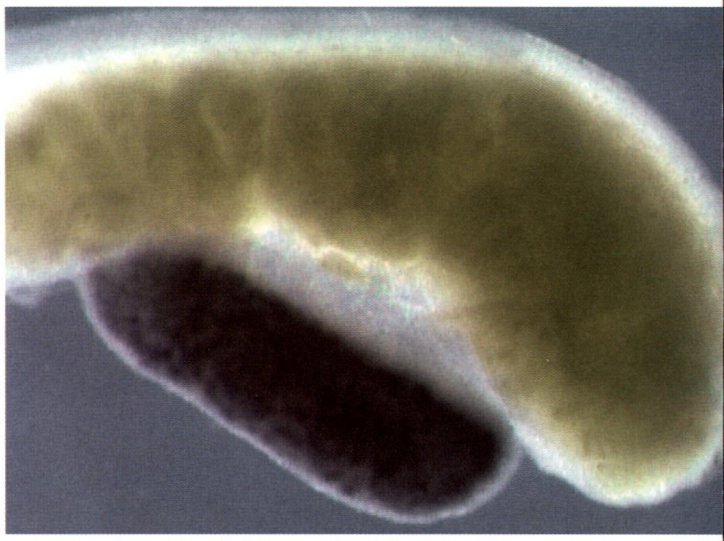
Our laboratory studies inherited reproductive disorders in dogs. I also have the opportunity to study these problems from the clinical perspective as a reproductive specialist at Cornell's Companion Animal Hospital. In order to treat or prevent these defects we need to understand the genetic basis for their development. Thus, we are studying the genetic control of the developing reproductive organs. Our laboratory is unique in that we study developmental genetics in dogs, rather than in mice or rats, to understand reproductive tract development. Results of our studies are directly applicable to dogs, but are also relevant to other domestic animals and to humans. We are cloning canine genes that control normal development of the testis, ovary, and uterus. Our laboratory recently identified, cloned, and sequenced the canine Sry gene, which is normally responsible for initiating testis development. By studying the expression of such genes we are beginning to understand how they control normal development of the canine reproductive tract and which genes are involved in abnormal development. A major goal of our studies is to identify the gene mutation that causes XX sex reversal, an autosomal recessive disorder that we have found to occur in 15 different dog breeds. Upon identifying a gene mutation that causes a reproductive abnormality, the next step is to design a practical and economical test to screen DNA and detect carriers and affected dogs. Such tests will be used to prevent the production of affected dogs and to eliminate the gene mutation from a breed without eliminating any particular line within a breed.

Selected Publications

Meyers-Wallen, V. N., Schlafer, D. S., Barr, I., Keyzner, A. 1999. Sry-negative XX sex reversal in purebred dogs. *Molecular Reproduction and Development* 53:266-273.

Meyers-Wallen, V. N., Palmer, V. L., Acland, G. M., Hershfield, B. 1995. Sry-negative XX Sex Reversal in the American cocker spaniel dog. *Molecular Reproduction and Development*, 41:300-305.

Meyers-Wallen, V. N., Bowman, L., Acland, G. M., Palmer, V. L., Schlafer, D., Fajt, V. 1995. Sry-negative XX Sex Reversal in the German shorthaired pointer dog. *Journal of Heredity*, 86:369-374.

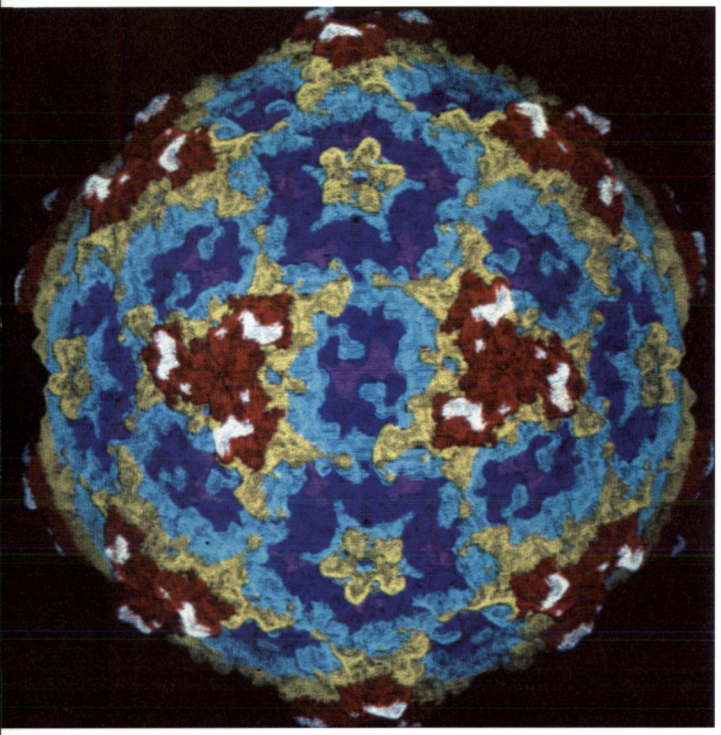


Embryonic canine testis (purple) and mesonephros (white) stained to show expression of Sox9 messenger RNA in the developing seminiferous tubules of the testis.

Vicki N. Meyers-Wallen

Associate Professor of Reproduction
VMD, University of Pennsylvania, 1976; PhD, University of Pennsylvania, 1986; Diplomate, American College of Theriogenologists

Canine virology and infectious diseases



A representation of the surface of the canine parvovirus capsid based on its atomic structure. The capsid is 20-sided, or icosahedral, in shape.

My laboratory studies viral diseases of dogs, cats, and their relatives, with a central focus on canine parvovirus (CPV) and its close relative, feline panleukopenia virus (FPV). We are examining both the most basic properties of the viruses and the applied problems associated with their infections in dogs and cats.

CPV emerged as a new disease in the late 1970s and spread around the world during 1978. Since then we have sought to trace the origin of CPV as a dog virus and its subsequent evolution in nature. We have used a variety of molecular biological approaches to understand the special properties of the new virus that allowed it to infect dogs, and we have used X-ray crystallography to examine the structural details of the virus particle that determine the differences in the virus-cell interactions. We are now using the techniques of cell biology to look for differences in virus uptake into cells that become infected and those that do not.

We are very interested in understanding how better to control CPV in dogs and cats and FPV in cats. In particular, our studies have revealed the existence of antigenic variation in naturally circulating CPV strains, knowledge that has allowed several companies to develop better and more specific vaccines. We have also shown that the more recent strains of CPV are capable of infecting and causing clinical disease in cats.

In other studies we have determined the genomic sequence of the minute virus of canines, a parvovirus that causes a variety of clinical outcomes. Infection in fetal or neonatal puppies causes disease that is often fatal. Our studies show that the virus is highly divergent from any other parvovirus and essentially unrelated to CPV. We are now developing two diagnostic tests, one molecular-based and the other a serological test using viral antigens prepared using molecular methods. We will be conducting surveys to determine the incidence of disease caused by this virus and the prevalence of the infection.

Selected Publications

Weichert, W. S., Parker, J. S., Wahid, A. T. M., Chang, S.-F., Meier, E., and Parrish, C. R. 1998. Assaying for structural variation in the parvovirus capsid and its role in infection. *Virology* 250:106-117.

Parker, J. S. L., and Parrish, C. R. 1997. Canine parvovirus host range is determined by the specific conformation of an additional region of the capsid. *Journal of Virology* 71:9214-9222.

Truyen, U., Gruenberg, A., Chang, S.-F., Obermaier, B., Veijalainen, P., and Parrish, C. R. 1995. Evolution of the feline-subgroup parvoviruses and the control of canine host range *in vivo*. *Journal of Virology* 69:4702-4710.

Agbandje, M., McKenna, R., Rossmann, M. G., Strassheim, M. L., and Parrish, C. R. 1993. Structure determination of feline panleukopenia virus empty particles. *Proteins* 16:155-171.

Colin Parrish

Associate Professor of Virology
PhD, Cornell University, 1984

Mucopolysaccharidosis, oculo-skeletal dysplasia, bleeding disorders

Our studies focus on the molecular genetic basis of inherited disorders in companion animals. Our aim is to understand the pathology of these disorders and to develop means to diagnose and treat them. The inherited diseases we study are also found in humans, and thus both animals and humans might benefit from this research.

Mucopolysaccharidosis (MPS) is the term for a group of related diseases whose effects may include blindness and other organ damage, mental retardation, and early death. We have identified the mutation responsible for MPS type VII, developed a diagnostic test, and achieved success in experimental gene therapy in retinal cell culture. Ophthalmologist Maria Verdugo has now developed an experimental surgical means to insert normal copies of the gene into the eye.

Oculo-skeletal dysplasia, a disease of Samoyeds and Labrador retrievers, is characterized by short-limbed dwarfism and potentially blinding defects such as vitreous dysplasia, retinal detachment, or cataracts. Colleague Gregory Acland demonstrated that a different gene controls the inheritance of the condition in Samoyeds than in Labradors, despite the similarity of disease phenotypes. Graduate student Fuliang Du is screening the canine genome to identify the molecular defects responsible for these diseases. He is also investigating the osteoarthritic potential of these dogs based on their cartilage morphology.

With Marjory Brooks from Cornell's Diagnostic Laboratory I am also seeking to determine the molecular defects present in hemophilia A and B. From this work we hope to develop diagnostic tests to prevent factor VIII- and IX-mediated bleeding disorders in dogs.

Selected Publications

Ray, J., Scarpino, V., Laing, C., and Haskins, M. 1999. Biochemical Basis of ß-Glucuronidase Gene Defect Causing Canine Mucopolysaccharidosis VII. *Journal of Heredity* 90:119-123.

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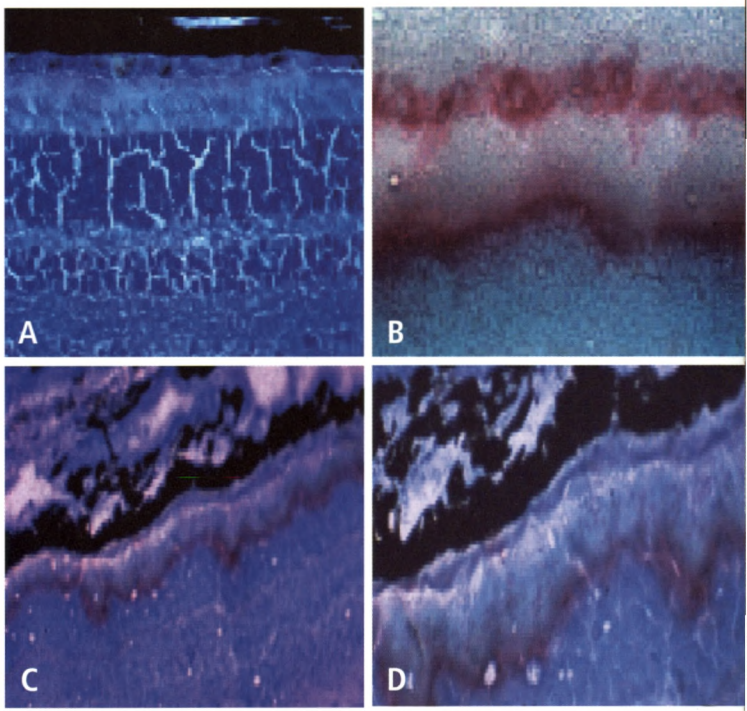
Ray, J., Haskins, M. E., and Ray, K. 1998. Molecular diagnostic tests for ascertainment of genotype at the canine mucopolysaccharide type VII locus. *American Journal of Veterinary Medicine* 59:1092-1095.

Ray, J., Wolfe, J. H., Aguirre, G. D., and Haskins, M. E. 1998. Retroviral cDNA transfer to the RPE: stable expression and modification of metabolism. *Investigative Ophthalmology and Visual Science* 39: 1658-1666.

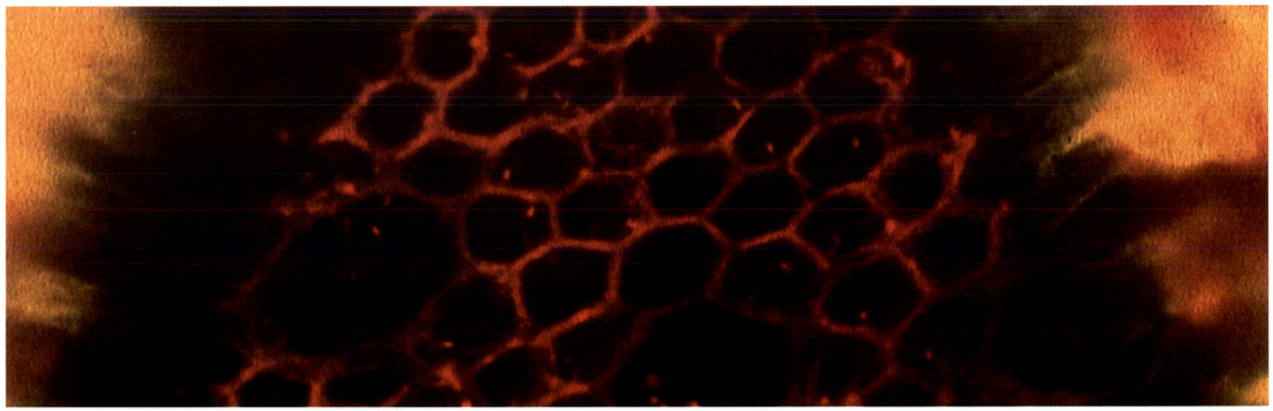


Retinal cells tested before and after gene therapy for the presence of beta-glucuronidase (GUSB). MPS VII is caused by a lack of this enzyme. A) An untreated affected eye shows no GUSB reaction. B) An untreated normal eye shows GUSB product, stained red. C and D) Affected eyes show GUSB reaction after treatment by subretinal transplantation of corrected retinal cells.

Jharna Ray

Assistant Professor of Molecular Genetics
MS, University of Calcutta, 1976; PhD, University of Calcutta, 1981

About 100 people – faculty, students, and technical, maintenance, and administrative staff – occupy the laboratories and other buildings on Snyder Hill and at the McConville Barn. The Baker Institute is now stronger and larger than at any time in its history, and the total staff numbers have grown about 40 percent during the past five years.



Advancing Veterinary Medicine Through Research

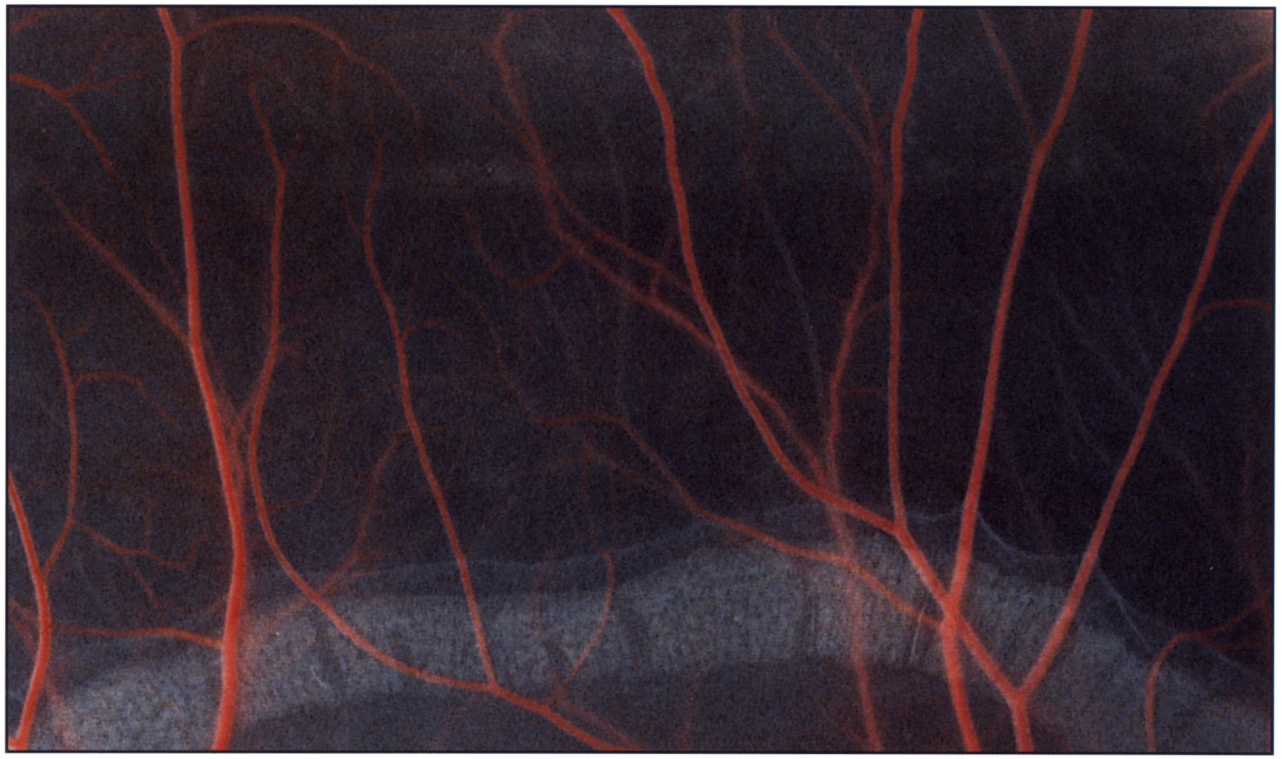
These are very exciting times in biomedical research. Veterinary medicine will be a full participant in the unfolding revolution in biology – making discoveries that both advance scientific knowledge and bring true benefit to our animal patients.

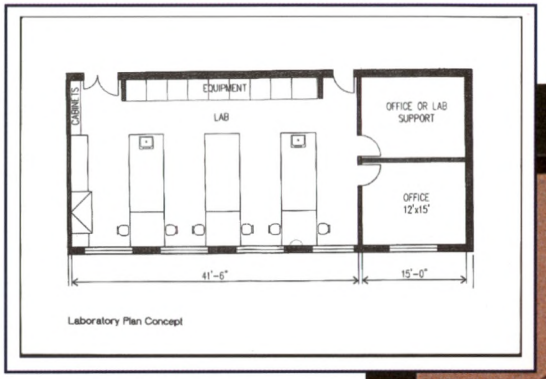
- Jamie MacLeod

The cutting edge is always a challenging place to work. As knowledge advances, so does the complexity of the questions remaining to be answered. Along with the difficulty, of course, comes the promise of greater and greater breakthroughs for animal and human health.

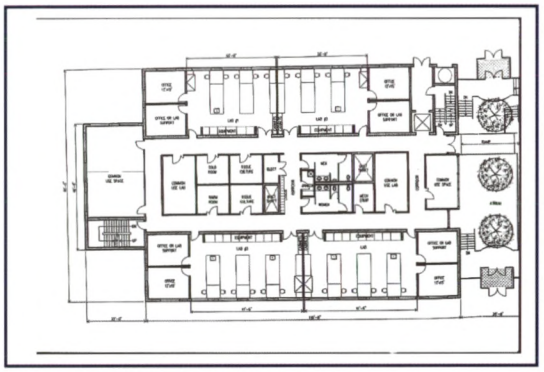
The worldwide effort to define the nucleotide order of genomic DNA in organisms both simple and complex – gene mapping – is progressing more rapidly than many people thought possible even five years ago. These gene maps will guide the first steps of a revolutionary quest – to learn to the last detail about every life function of complex organisms like dogs or human beings. This will be an enormous challenge, but it is within our grasp, and the knowledge it yields will surely refine our approach to disease prevention and treatment in ways that would seem miraculous to us now.

The Baker Institute, with its historic strengths in immunology and infectious disease research and its depth of expertise in molecular genetics and genomics, has the outstanding staff and programs in place to participate fully in the advances of the next decade. The Institute's twentieth-century facilities, however, are not equal to the increasing demands of modern technology. On the following pages we present our vision for the Institute in the twenty-first century.

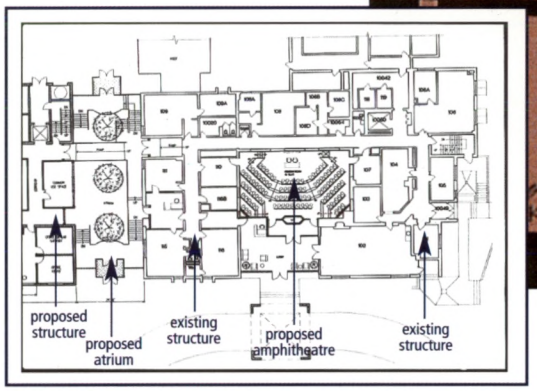




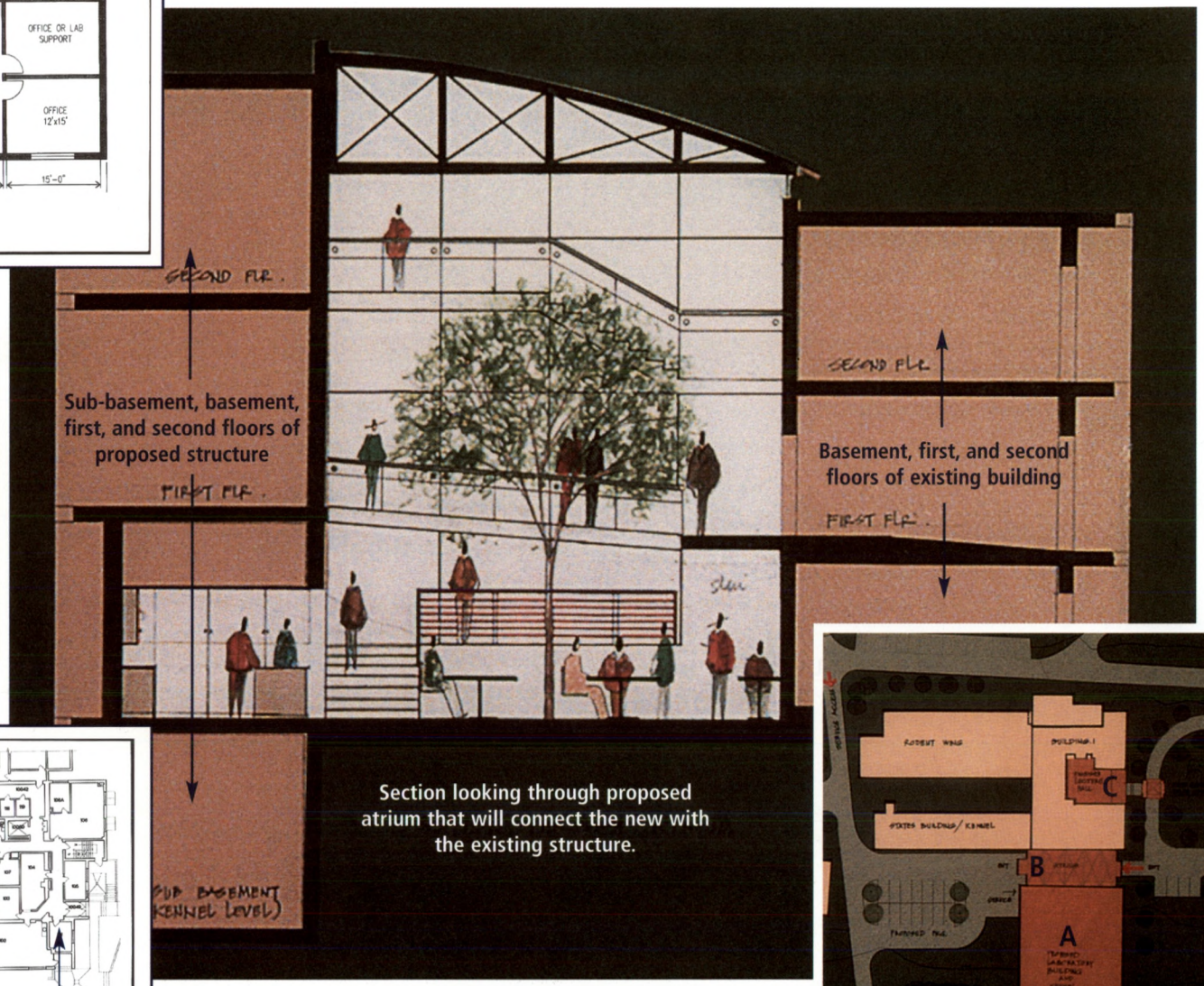
Proposed laboratory floor plan



Proposed first-level floor plan

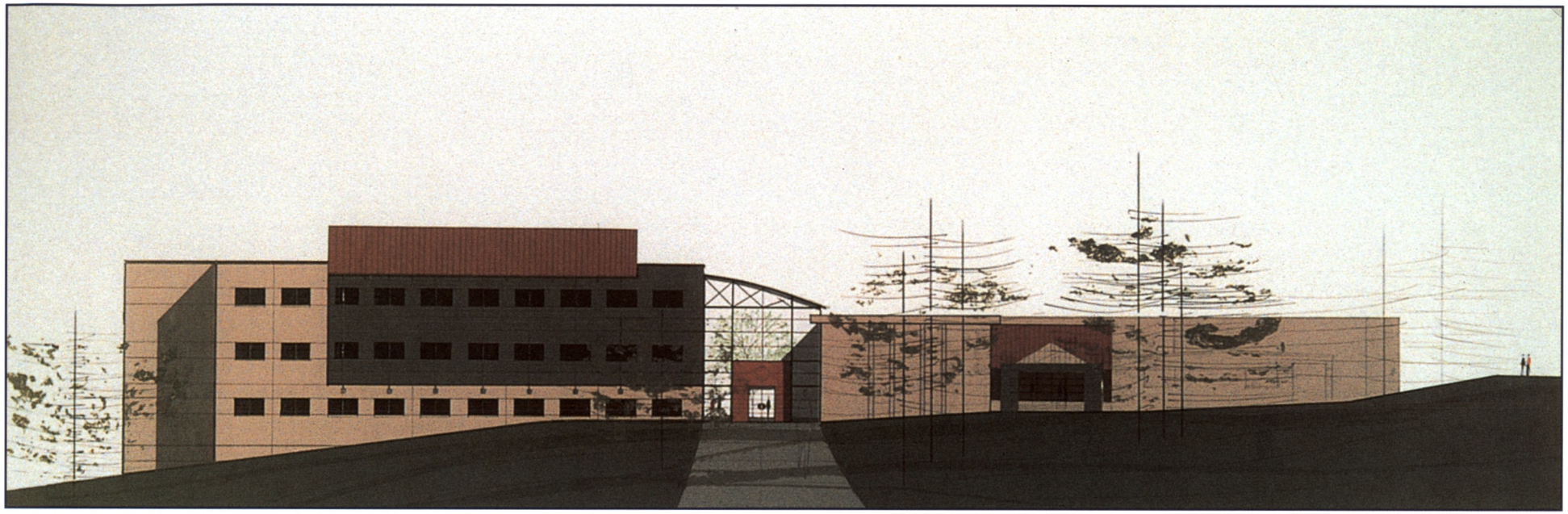


Floor plan showing proposed structure, proposed 100-seat amphitheatre, and existing building



Proposed map showing location of new structures in relation to existing structures. A) new laboratory wing B) atrium and main entrance C) 100-seat amphitheatre

Superior research facilities are needed to attract the best biom



Architect's rendering of the new building, viewed from the south. The existing building, on the right, and the proposed addition, on the left, will be joined by a glass-walled atrium that will serve as the main entrance to the Institute.

Modernization of the Baker Institute will enhance existing programs and enable the faculty to respond to emerging needs and opportunities in animal health research.

The James A. Baker Institute for Animal Health faces an exciting challenge in maintaining its leadership in biomedical research and advanced training of veterinary scientists. The Institute's very success in winning competitive funding is driving expansion of the research programs and staffing needs at a rate that can no longer be supported by our current laboratory facilities.

The complexity of contemporary research calls for large and interdisciplinary teams of investigators, technicians, and students working in concert with complex, automated technological systems too large to be housed in individual laboratories. The Baker Institute was not designed for these twenty-first century realities.

Starting in October 2000, construction will begin on a 47,000-square-foot building to adjoin the Institute's current facility. State-of-the-art laboratories and large common-use space will exist on each floor, serving a variety of specialized needs. Connecting the new structure to the existing building will be a glass-walled atrium. Rising three stories, this light-filled, open space will welcome staff and visitors alike to the Institute. The final component will be a 100-seat teaching amphitheater with global teleconferencing capabilities.

The new research wing will house twelve laboratories arranged around shared equipment and technical space. Laboratories will average 1100 square feet, in keeping with current industry standards, and include two adjoining offices. In contrast to the small existing laboratories, these spaces will be open and bright, fostering collaboration both within and between laboratories, and at all professional levels, including technical staff, students, and faculty.

edical scientists and enable them to achieve their full potential.

Realizing the Vision

I feel it is an honor and a privilege to be the chairman of the Advisory Council of the Baker Institute. As both a pet owner and a practicing veterinarian I appreciate the dedicated work these men and women do to enhance the lives of our animals and to make my job both easier and more rewarding.

As in any thriving venture there are several key factors needed to succeed. We need a constant supply of keen, inquisitive minds, a dedicated support staff, an environment conducive to discovery and thought, and economic support sufficient to allow the investigators to channel their energies in the proper direction – discovery.

The Institute, like families or other businesses, occasionally comes upon a major crossroad. We are approaching one of these milestones as the Institute readies itself for its second half century. The building that has served us so well needs help. As you have previously read, an exciting new structure is being planned.

I feel that it is our job as patrons of the Institute and beneficiaries of its work to help realize the vision of the new building. This need affords us the opportunity to participate and give back to the Institute that has so diligently worked for us for so many years.

Henry J. Travis

Henry J. Travis, DVM
Chairman, Baker Institute Advisory Council

Advisory Council

Credits

Writing and Editing
Jeanne Griffith

Design
Courtney&Co. design

Pre-press
The Image Press

Printing
Eastwood Litho

Photography

Charles Harrington
Maria Verdugo: front cover and p. 16
Sarah Bacon and students: pp. 11, 16
John Parker giving seminar: pp. 12, 16
Colin Parrish: p. 14
Qi Zhang: p. 16
Jharna Ray: p. 27

Dede Hatch
Baker Institute: inside front cover and pp. 1, 32
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faculty: pp. 20-26

Frank DiMeo
faculty: pp. 17, 18

Sol Goldberg:
Ben Sheffy and Alma Jo Williams: p. 6
Max Appel and Ricardo Flores-Castro: p. 7

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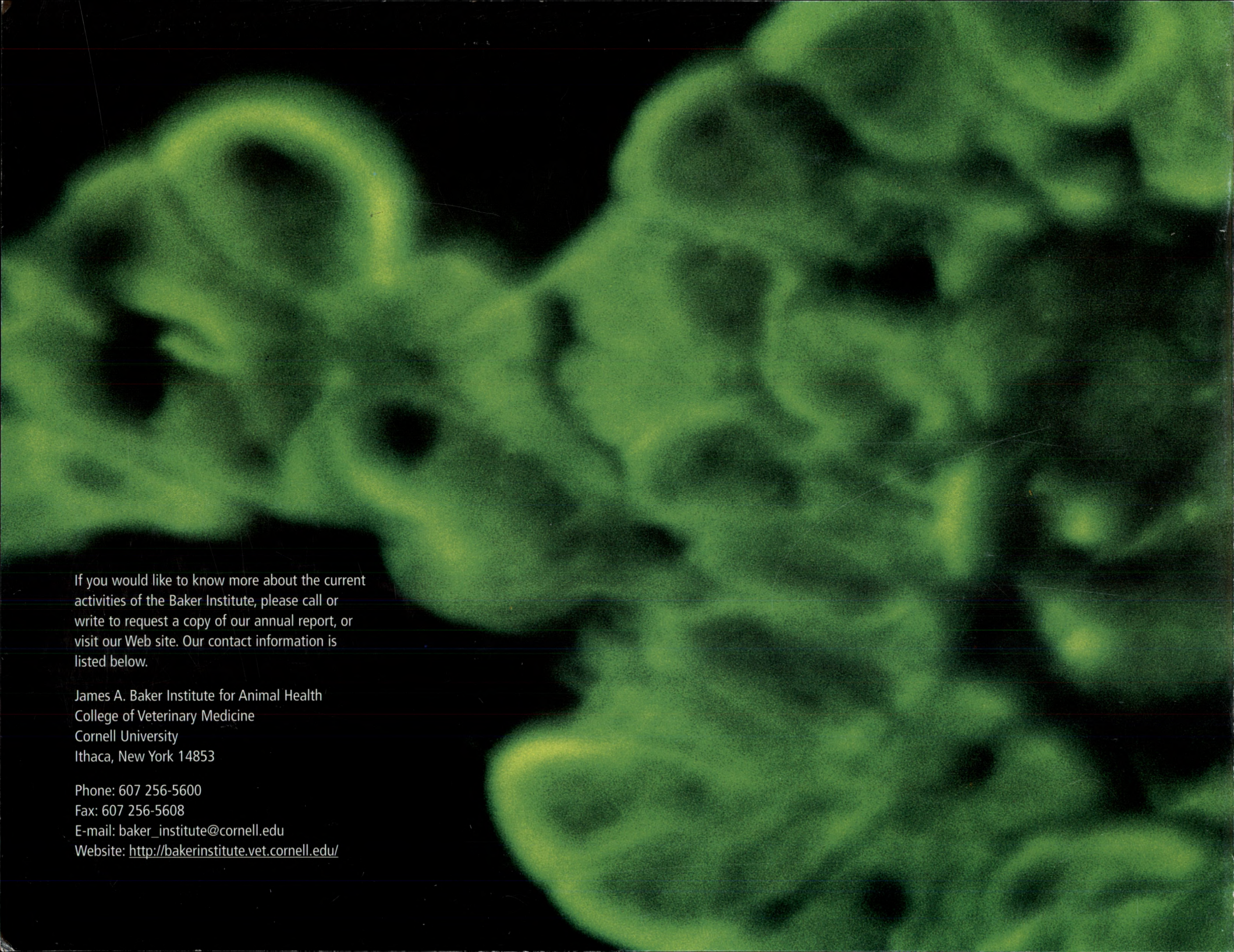

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James A. Baker Institute for Animal Health
College of Veterinary Medicine
Cornell University
Ithaca, New York 14853

Phone: 607 256-5600
Fax: 607 256-5608
E-mail: baker_institute@cornell.edu
Website: http://bakerinstitute.vet.cornell.edu/