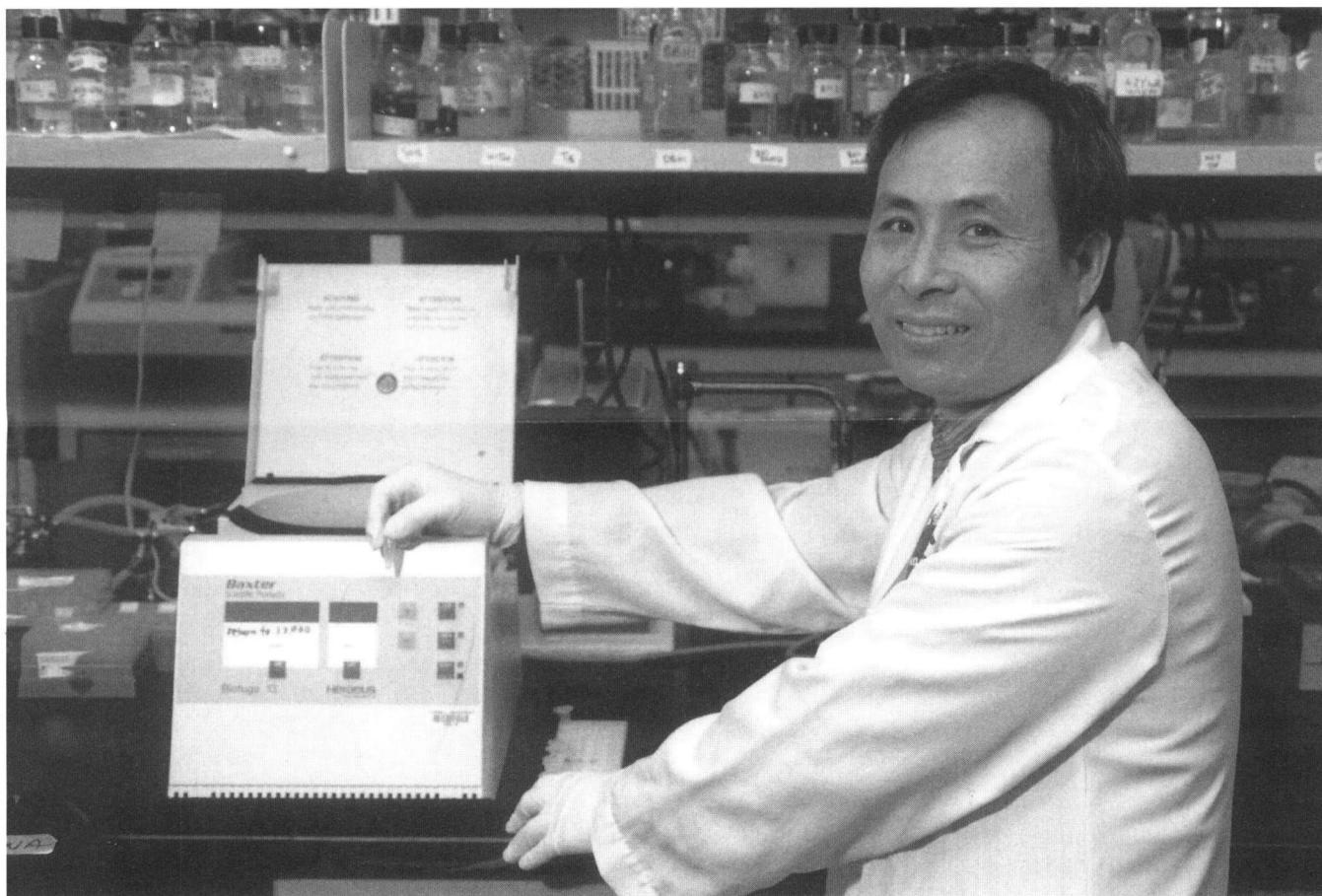


# Zweig

A report from the  
Harry M. Zweig  
Memorial Fund for  
Equine Research at  
the College of  
Veterinary Medicine  
at Cornell University

Memorial Fund News Capsule

No. 23 June 1997



ADRIANNA ROYERS

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### Dr. Yung-Fu Chang—Developing a Vaccine Against Equine Lyme Disease

**J**ust as Lyme disease has been afflicting ever more humans and dogs since it was discovered in the late 1970s, the disease has been spreading among horses as well. The most prevalent tick-borne disease in the country—and one of the most prevalent in the world—Lyme disease primarily hits horses in the Northeast, the upper Midwest, Texas, and California.

Horses with Lyme disease, however, are often misdiagnosed and/or inappropriately treated because of the disease's variety of clinical manifestations. The clinical signs include fever, stiffness, chronic weight loss, muscle ▶

## Chang *continued from page 1*

tenderness, sporadic lameness and swollen joints, laminitis, and anterior uveitis. Neurological signs include depression, behavioral changes, loss of appetite, head tilt, and encephalitis. Veterinarians usually diagnose the disease based on the clinical signs, risk of exposure, response to antibiotics, and blood tests, which are not always reliable.

Information for the diagnosis, treatment, and development of a vaccine for Lyme disease in horses remains

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**"This information will allow us to develop a set of baseline criteria for Lyme infection in the horse."**

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very sparse, and experimental induction of the disease in horses has not yet been reported. A Cornell team of researchers led by veterinary microbiologist Yung-Fu Chang, D.V.M., Ph.D., is forging ahead with Zweig funding to study Lyme disease in horses with the ultimate goal of developing a vaccine against the disease.

Since this past January, Chang and his colleagues have been working on a horse model of Lyme disease. They infected ponies with the bacterial spirochete *Borrelia burgdorferi* by tick bite, a natural infection route in the field. For six months—and perhaps an additional four months if funding comes through—the researchers will observe the ponies for clinical signs of infection. They also will take monthly blood samples and skin biopsies to monitor the infection. At the end of the observation period, the ponies will be terminated and examined.

"We will seek to detect the organisms in different tissues using culture and modern molecular biologic techniques," explains Chang. "We also will look for signs of arthritis, central ner-

vous system damage, heart damage, and immunologic and pathologic responses typically seen in humans and other animals. This information will allow us to develop a set of baseline criteria for Lyme infection in the horse. No information is now available about the time course of infection, clinical signs, and pathologic and immunologic responses."

This information is essential for evaluating the efficacy and safety of an equine Lyme disease vaccine, Chang says. With this model of Lyme borreliosis in the horse, he and his colleagues can then proceed to evaluate the efficacy and safety of equine Lyme disease vaccines.

Chang is experienced in developing vaccines against the tick-transmitted disease. He was the principal investigator for the Cornell Lyme disease team of scientists who recently reported on developing a successful vaccine for Lyme disease in dogs. Their research, reported in the September 1995 issue of *Infection and Immunity*, showed that of 22 beagles vaccinated with a Cornell-developed vaccine, none developed Lyme disease when challenged by exposure to infected ticks. In contrast, 12 of the 13 control dogs exposed to infected ticks did develop the disease.

Ticks that carry the bacterial agents pick them up in their larval and nymphal stages when they feed on infected mice. Humans, horses, and other animals get the disease when infected tick nymphs or adult ticks feed and transmit the infection through the skin, particularly during the summer and fall, explains Chang, who also serves as the assistant director of the Microbiology Section of the Diagnostic Laboratory in the College of Veterinary Medicine at Cornell.

"Deer are not a reservoir for Lyme disease, as previously thought. Rather, deer are the host for the adult stages of the tick," he says.

After adult ticks feed and mate on deer during the fall and spring, the female ticks drop off and lay eggs on the ground. After several weeks, the eggs hatch into larvae, beginning a two year cycle.

Chang says the results of the research thus far have been encouraging.

"Because of our experience in developing a canine Lyme disease model, we approach this equine study with optimism," he says. ■

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## International Equine Neurology Conference to Honor John Cummings

A three-day, international conference on Neurologic and Behavioral Disorders of the Horse will be held at the College of Veterinary Medicine on July 11, 12, and 13. The conference is being co-sponsored by the Zweig Memorial Fund and honors Dr. John Cummings, who passed away unexpectedly in November 1996. Dr. Cummings had proposed the conference before his death.

The conference will bring together investigators with a wealth of clinical experience and research findings on the most troublesome neurologic and behavioral disorders in the horse. The conference format has been selected to present the most recent findings on each of the targeted disorders and to allow time for discussion of each.

Registration fees are \$150 before July 1 and \$225 thereafter. Blocks of rooms have been reserved at local hotels. For more information please contact Linda Schumacher at [lra2@cornell.edu](mailto:lra2@cornell.edu) or 607-253-3200. ■

## Unveiling Highlights Annual Zweig Committee Meeting

The unveiling of a painting by Corinne Kenney '62 of Long Valley, New Jersey, highlighted the annual meeting of the Zweig Memorial Fund Committee in November. The watercolor, a montage of racing scenes, now hangs in the waiting room of the vet college's Equine Farm Animal Hospitals.

Kenney gave up her veterinary practice six years ago to pursue her artwork full time, although she still does fill-in work as needed. In addition to watercolor, which she says is her "first love," she also works in oils and pastels. Horses are a frequent subject but she also paints landscapes, seascapes, and portraits. Her work has been widely exhibited, including shows at the annual yearling sale in Kentucky and at the Meadowlands sports complex in New Jersey during Hambletonian Week. She also has had two shows at the vet college.



Zweig Memorial Fund Committee member Anna Zweig (l.) and artist Corinne Kenney '62 unveiled Dr. Kenney's painting at November's committee meeting.

BARRY DILIBERO



The Zweig Memorial Fund Committee members visited the vet college for their annual meeting in November. From left: (row 1) Patricia Wehle, former College of Veterinary Medicine Dean Franklin Loew, Jean Brown; (row 2) John Jagar, Harry Snyder, Anna Zweig; (row 3) Paul Mountan, Charles Knauss, William Welsh; (row 4) Bruce Hamilton, John "Jack" Hardy.

BARRY DILIBERO

## Harry M. Zweig Memorial Fund for Equine Research—1997 Research Awards

**\$43,711** to Dr. Douglas Antczak and Dr. Christopher Davies for "The Horse Genome Project."

**\$61,453** to Dr. Alan Nixon for "Growth Factor Gene Expression Patterns in the Repair of Equine Articular Defects."

**\$40,000** to Dr. Dwight Bowman, Dr. Thomas Divers, and Dr. Hussni Mohammed for "EPM: Isolation of *S. falcatula*, PCR for Sporocysts, and Immunization of Horses."

**\$57,376** to Dr. Y-F Chang for "Vaccination Against Lyme Disease in the Horse, Part 1. Experimental Induction of Lyme Disease."

**\$32,959** to Dr. Patrick Concannon and Dr. Peter Daels for "Induction of Reproductive Function in Anestrous Mares Using a Dopamine Antagonist."

**\$20,000** to Dr. John Cummings, Dr. Thomas Divers, and Dr. Hussni Mohammed for "A Special Cornell Conference/Workshop on the Neurological and Behavioral Disorders of the Horse."

**\$9,700** to Dr. Douglas McGregor for "Career Development Training for Equine Research Scientists."

Total Zweig Funds Awarded—**\$265,199**

## A Look Back at 18 Years of Zweig-Funded Research

Since the Zweig Fund was established in 1978, many equine researchers at the New York State College of Veterinary Medicine have received support for studies that benefit both equine health and New York State's racing industry. This is the second of a series of articles that will look back at some of their accomplishments.

## Zweig-Funded Accomplishments in Orthopedic Medicine

Performance horses pound the track with tremendous force. And just like human athletes, they suffer from a host of bone and joint problems. Among the most devastating are tendon ruptures, bone fractures, cartilage problems, and arthritis. Learning better ways to treat such injuries and prevent them in the future has been a high priority of Zweig funded research since 1978.

### Repairing Cartilage Damage And Preventing Arthritis

For more than seven years, Dr. Alan Nixon, an equine orthopedist and director of the Comparative Orthopedics Laboratories at the College of Veterinary Medicine, has been systematically developing a procedure to restore healthy cartilage that has been damaged by fractures, knee and fetlock chips, infection, osteochondritis disease (OCD), or overuse. His novel technique has been used successfully on more than 45 experimental and clinical cases. It also has enormous potential for use in human joints, helping to repair problems early and thereby, largely prevent the development of arthritis.

Nixon and his team began their research by developing methods to harvest immature cartilage cells (chondrocytes) from foals and culturing them to increase their size, number, and productivity. The next step was to evaluate various techniques for safely preserving the live cells so they could be used on demand when needed in clinical cases.

The next challenge was to find a vehicle for secure delivery of the cartilage cells to joint surface defects. Fibrin, a natural component of blood clots, was found to be the ideal substance. It can be readily obtained from the blood of a candidate horse

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and injected during surgery to literally glue the transplant cartilage cells into the damaged joint surface.

Using an arthroscope to keep the incisions small—just a quarter-inch long—the researchers attached their surgical implant to one of two defects in twelve experimental horses. By embedding the cartilage cells into the fibrin matrix and then attaching the implant to bone with two resorbable tacks, the surgeons successfully discovered how to keep the cartilage cells from washing away in the joint fluid. The result was new and better cartilage. Successful studies then opened the way for the first clinical trials in 1995. To date, the transplant has been used to repair cartilage disease in the stifle, shoulder, fetlock, and knee.

Since then, many of Nixon's projects have centered on making the implant system better. These new Zweig-supported studies have used natural hor-



Alan Nixon

mone-like agents called growth factors to bolster the transplant cell response even further. Two potent growth factors have been evaluated extensively and one of these, insulin-like growth factor, was found to be particularly useful in promoting cartilage synthesis. Over the last year, it has been added to the fibrin and chondrocyte transplant, providing a stimulus to the new cells.

After five years of evaluating the long-term effects of the artificial implants, Nixon is pleased.

"I believe we are finally starting to make some progress in getting this essential but tardy tissue to regrow," he says. "The aversion of arthritic changes means added comfort in the short term and extended athletic careers over the long haul."

The challenge, however, is far from over. In the past, nothing could return a horse's already arthritic joint back to function.

"Most of the calls we get about cartilage cell grafting are for horses with advanced arthritis, and regrettably, there is little we can offer," says Nixon. However, his research group is progressing further toward being able to help these horses, with better timing of growth factor administration and the promise of growth factor delivery using gene therapy.

"I believe the future in joint repair rests in biologic and sustained facilitation of the natural healing responses," says Nixon. "Gene therapy provides our best avenue to provide this impetus, and much of our research will focus on this through the year 2000. Because of Zweig support, we're closer to offering a routine clinical method for horses and humans that could not only repair cartilage problems early on but help prevent the development of crippling arthritis later."

### **Preventing The Early Changes that Lead to Osteoarthritis**

Dr. James MacLeod, a veterinary molecular geneticist, has been using Zweig funding to study the traumatic joint problems so common in race horses. Painful, hot, and swollen

joints are often attributed to overexertion and the excessive stresses and strains placed on joints during heavy training and racing. If recognized early, before any physical damage to the articular cartilage occurs, most of these joints will heal completely with proper therapy and sufficient rest.

"Unfortunately, however, horses are often returned to active training after only short rest periods and the injuries commonly recur," points out MacLeod. "Over time, structural damage to the joint cartilage and

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**"These results provide strong evidence that very early events play critical roles in the development of degenerative arthritis, even though joint cartilage damage may not become clinically apparent for weeks or even months."**

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chronic degenerative osteoarthritis can develop."

Traumatic injury to the joint causes synovitis—an inflammation of the joint capsule and synovial membrane. As a result, inflammatory factors are released into the synovial fluid and diffuse into the cartilage.

"These factors are believed to cause metabolic dysfunction at the molecular and biochemical level within the articular cartilage and induce degradation of the cartilage matrix," says MacLeod. "This degradation of the matrix then predisposes the cartilage to structural failure if the horse continues to race or exercise strenuously."

To better understand the molecular mechanisms that link synovitis to cartilage degeneration, MacLeod focuses on early changes in the expression of specific genes and their relationship to abnormal metabolic and structural changes in cartilage matrix proteins.

"Initially, we concentrated on generating equine-specific genetic (DNA) probes for our research that enabled us to study the expression of individual genes, taking full advantage of contemporary molecular biology techniques," MacLeod explains. "These methods enable changes in gene expression to be identified with a level of specificity and sensitivity that was not previously possible."

MacLeod and his colleagues have shown that both synovitis and intra-articular corticosteroids do indeed induce rapid changes in the expression of some cartilage matrix proteins. They have found a major change in the expression of type II collagen, a protein that is very important for the molecular structure and tensile strength of cartilage. Both synovitis and corticosteroids significantly alter the synthesis of type II collagen relative to baseline values. Synovitis increases its expression, while corticosteroids decrease expression.

*continued on page 6*



James MacLeod

"These results provide strong evidence that very early events play critical roles in the development of degenerative arthritis, even though joint cartilage damage may not become clinically apparent for weeks or even months," says MacLeod.

In addition, the researchers have recently identified a unique and previously undiscovered variant of an important matrix protein called fibronectin. A major characteristic of the new isoform is that high levels of expression occur only in cartilage, in contrast to other forms of fibronectin that have a wide tissue distribution throughout the body. MacLeod notes that this discovery provides an important opportunity to better understand the functional role(s) of fibronectin in cartilage and how changes in fibronectin expression might contribute to the pathogenesis of osteoarthritis.

"I am very grateful for the support we have received from the Zweig program," MacLeod says. "The funding was awarded during the project's early development. Results from these initial experiments were very helpful in our successful efforts to obtain grants from national funding agencies. These additional grants have enabled our research in these important areas of cartilage biology and joint disease to continue."

### **Improving Orthopedic Surgery Techniques**

The most common injury suffered by racehorses is a an internal rupture of a tendon, commonly called a bowed tendon. Although a surgical procedure called a proximal check ligament desmotomy can sometimes correct the problem, it fails in more than 50 percent of cases.

Dr. John Bertram, the only biomechanics specialist at Cornell's College of Veterinary Medicine, has been using Zweig funding to improve the procedure by studying the distribution of forces in the flexor tendons before and after surgery. He has been able to conduct these studies on animals

running on the treadmill, in cadaver limbs operated by testing machines that replicate the motion of the limb during running, and in detailed computer models.

"Our primary purpose is to use the muscular system of the digital flexor system in the horse as a general model for studying the interaction of muscles and tendons and how a mammal adapts to changes in the muscles that occur in injuries and as a result of surgery," says Bertram.

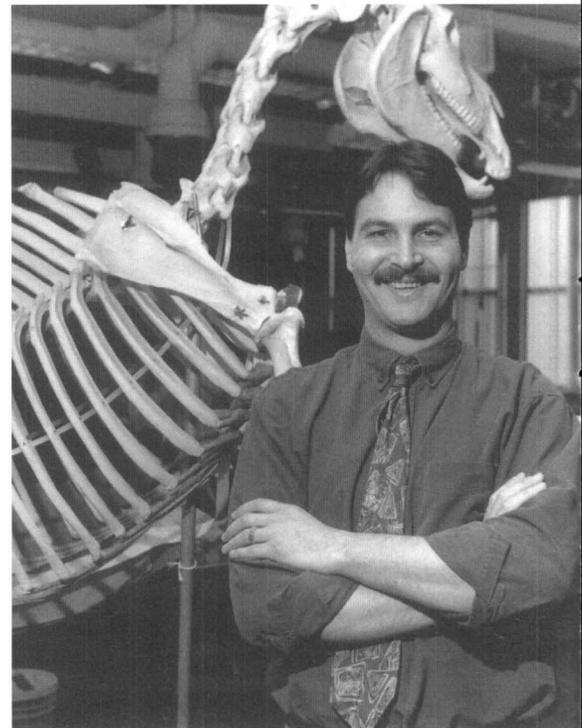
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Bertram also has used electromyographic analyses (EMG) to compare muscle activity patterns during motion both before and after surgery and to see how the various tendons and muscles are affected. Three-dimensional high-speed video gait analyses have given him a deeper understanding of the subtle changes in joint position and angle in running horses before and after surgery. These analyses have allowed him to determine that the muscles operating the digital flexor tendons provide quite different functions in the running horse, and likely have different functional limits as well.

When a horse is running, a series of muscles apply forces with similar direction at the fetlock. From a superfi-



*John Bertram*

cial perspective this may not seem a very good design, because there are several muscles positioned to do a job that could be accomplished by just one. However, these muscles have different effects under different running circumstances. In a sense, they work much like the gears in an automobile, where each gear is appropriate over a given range of speeds. This also appears true for the flexor components. Unfortunately, fatigue in one of these components is likely responsible for overloading the other; the system is forced to run in an inappropriate gear and trouble can result.

Thanks to initial support from Zweig, Bertram and his colleagues are beginning to discover the mechanical complexities of the horse limb and can provide a new perspective on this serious problem. ■

One of the recent additions to the Zweig Committee is Dr. Paul C. Mountan, 54, who has been an equine veterinarian for some 30 years.

Horses have been "in his blood" since boyhood when he aspired to become an equine vet like his older cousin, Robert E. Cornell, D.V.M., who has a practice in Connecticut. Raised in Yorktown Heights in Westchester County, Mountan was the second of six children of David J. Mountan Jr., a corporate trial attorney, and Emma E. Mountan, a graduate of Columbia Presbyterian nursing school. Although not horse people, his parents supported their son's interest and purchased his first horse for him when he was 12.

Entering Cornell in 1960, Mountan was a proficient rider and soon joined the polo team. He was a member of the team that won the national intercollegiate championships in 1963, and was named Most Valuable Player at the national intercollegiate tournament in 1964. He still plays polo at his alma mater almost every year when he joins fellow alumni to take on the vet faculty during the annual vet conference.

To further his experience with horses, Mountan spent summers during college working as a groom and trainer at a polo club near home and then later at Hobeau Farms in Ocala, Florida. Working there with Elmer Hubeck, Jr., Mountan got his first taste of working with Thoroughbreds. Just out of veterinary school in 1966, he spent a year under the tutelage of Dr. M. B. Teigland, caring for Thoroughbreds and working the race tracks and farms in and around Miami.

"They were really my two mentors," recalls Mountan, "along with Cornell obstetrics professor and polo team coach, Stephen J. 'Doc' Roberts."

In 1967, Mountan returned to the Hudson River Valley, this time to the Dutchess County town of Rhinebeck where he's now the senior of four partners in the Rhinebeck Equine LLP practice. The area is home to many Thoroughbred farms, and his clients



STERLING PHOTOGRAPHY

**"My goal is to use my experience as a long time Thoroughbred breeder and equine veterinarian to help determine where funds would be most beneficial to equine health and the racing industry."**

include Gallagher's Stud, Thorndale, and Moonshadow Farms as well as Rojan and Buttonwood Farms.

Over the years, Mountan has served as a member of the Equine Practice Advisory Committee of the New York State Veterinary Medical Society as well as the Equine Advisory Committee of the New York State College of Veterinary Medicine at Cornell.

On the home front, Mountan enjoys playing tennis in his not-so-spare time. He and his wife, Dale, "a life-long horsewoman," have been operating their own small Thoroughbred breeding

farm for more than 20 years. Full Sail Farm is a 30-acre spread on which the Mountans keep three or four broodmares at any one time along with occasional race track lay-ups requiring his expertise.

"We've had good success with our mares," Mountan reports. "Our first foal, Right Approach, won \$150,000 back in the late seventies and was followed by many others, all of which made it to the track and, with the exception of two, were all winners. Now we concentrate on a few select boarding broodmares. Last year, a horse we foaled, Checkpasser, won \$121,000 as a New York Bred Stakes winner."

These days, with his two children off at college, (David graduated this spring from Ithaca College and plans to attend vet school. Daughter Cody just finished her freshman year at Cornell with intentions of a future in the equine industry), the Mountans still actively care for more than a dozen horses. Aside from the boarded Thoroughbreds, they have two of Dale's retired show horses, a Hackney pony, a hunter, and Cody's show jumper.

The Mountans also share their home with nine Jack Russell terriers. Dale publishes a Jack Russell Terrier Calendar and maintains a Web site devoted to the breed on the World Wide Web (<http://www.jack-russell.com>).

She works closely with a nationwide rescue service that takes in these often misunderstood little dogs from inappropriate situations and finds new homes for them. Placing more than 30 dogs a year, she has kept some of the "unadoptables" as part of the family.

Although on the Zweig Committee for only about a year, Mountan hopes his experience will help guide the direction of research projects. "My goal is to use my experience as a breeder and veterinarian to help determine where funds would be most beneficial to equine health and the racing industry," he says. "We're also working on further endowments so that the fund can continue to benefit equine research indefinitely." ■

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**T**he Harry M. Zweig Memorial Fund for Equine Research honors the late Dr. Harry M. Zweig, a distinguished veterinarian, and his numerous contributions to the state's equine industry. In 1979, by amendment to the parimutuel revenue laws, the New York State legislature created the Harry M. Zweig Memorial Fund to promote equine research at the College of Veterinary Medicine, Cornell University. The Harry M. Zweig Committee is established for the purpose of administering the fund and is composed of individuals in specified state agencies and equine industry positions and others who represent equine breeders, owners, trainers, and veterinarians.

### **1996 Harry M. Zweig Memorial Fund Committee**

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