Zweig

Memorial Fund News Capsule

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

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INSIDE

Zweig Committee Looks Down the Road Twenty Years

During their annual gathering on November 11, 1999, members of the Zweig Committee shared their thoughts on the fund's expectations and goals for the next 20 years.

"The Zweig Fund realizes that equine research will probably be much more international in years to come, more global due to advances in communication; there will be more cooperation between researchers, among colleges. The level of the projects has really risen since the original proposals. The fund has fulfilled our initial plans, plus." *Anna Zweig*

"As members of the committee, we see such a progression, a structured reality. Technology has allowed equine researchers to go further than we ever thought possible. I most enjoy seeing how the research develops on a ▶

Zweig Committee

continued from page 1

practical, day-to-day basis—following it from the lab to the field. The projects we fund are a nice strong blend of research and clinical science." *Jean Brown*

"Some of the interactions of animal medicine with human medicine are interesting—fixing torn joint cartilage in race horses, fixing the same types of tears in football players." *Paul Mountan, DVM*

"The research at Cornell is on the cutting edge. For example, equine gene therapy may become a reality because of some of the projects funded by this committee. . . . We are preparing for the future.

"It's kind of a neat deal to see the tremendous influence Dr. Zweig had in putting the fund together, to see what's happened in the last 20 years. And now we're talking about trying to do something for equine health in perpetuity.

"Just a couple of years ago it got to the point where, if it wasn't molecular, a project didn't get much notice. Now it's moving back to a mix of cutting-edge and practical projects." *John Jagar, DVM*

"We would hope that the next 20 years would be as productive as the last. One of the strengths of the committee is that you have laypeople like me and veterinarians like John [Jagar] and it makes for a good mix, a good exchange of ideas." *Bruce Hamilton*

"There's always been a frank exchange between the fund and the college—when we've agreed, we've agreed; when we've disagreed, we've said so. This has been valuable to furthering the projects funded. We're trying to develop a permanent endowment so that the work of the fund will continue." *Charles Knauss*

"It's amazing that we have a powerful brain trust here [in the committee, in the researchers at Cornell]—I don't think we've even begun to tap it." *Philip Trowbridge* ■

New York State Thoroughbred Breeding and Development Fund

Each year, the New York State Thoroughbred Breeding and Development Fund gives 2 percent of its total annual revenue to the Harry M. Zweig Memorial Fund. That contribution usually means more than one-quarter of a million dollars for research at Cornell that benefits the equine industry. In 1997, for example, eight faculty members from the College of Veterinary Medicine received grants from $11,000 to $80,000 for research ranging from chronic obstructive pulmonary disease and the horse genome project to equine vaccines for Lyme disease and gene therapy for equine cartilage repair.

The fund was established in 1973 to promote thoroughbred breeding and racing in New York State and to expand the agricultural land used for producing and improving the quality of thoroughbred race horses in New York State. A public benefit corporation of New York, the New York Thoroughbred Breeding and Development Fund provides incentive awards each year amounting to about $32 million to breeders and owners of registered New York–breds or registered New York State–based stallions, including purses earmarked for New York–breds. For example, a breeder earns an award every time his registered New York–bred wins a pari-mutuel purse for first through fourth place at Saratoga, Belmont Park, Aqueduct, and Finger Lakes.

"One of the major factors considered when the fund was created in the early 1970s was the need to preserve the great 'green belt' of this strong agricultural state," says William A. Levin, chair of the Board of Directors of the fund corporation. "Our record shows that we're doing just that—today, there are 380 active thoroughbred farms in New York—that's a far cry from the less than 200 in existence 20 years ago. These farms range from small family farms to large commercial breeding operations and are producing more horses of higher quality than ever before."

The fund's annual report for 1997 shows how the fund's efforts are paying off in other ways, too. In that year, New York–bred thoroughbreds earned a total of more than $44 million throughout North America, putting New York among the top four states in the nation.

The Zweig Memorial Fund and the Thoroughbred Breeding and Development Fund share as members Harry D. Snyder of the New York State Racing Commission; Michael J. Hoblock, chair of the Racing & Wagering Board; and Philip Trowbridge, manager, Gallagher's Stud Farm. ■

Stay Up to Date Via the Web

For the latest information on equine research supported through the Harry M. Zweig Memorial Fund click on its new Web site: **http://www.vet.cornell.edu/public/research/zweig/.**

The site includes articles on research now under way, a list of current Zweig committee members, a history of the fund, and an archive of back issues of the Zweig News Capsule.

In addition, it offers direct links to four professional organizations and societies; 14 other sites of special interest to practitioners and breeders; and the home page of the Cornell College of Veterinary Medicine. ■

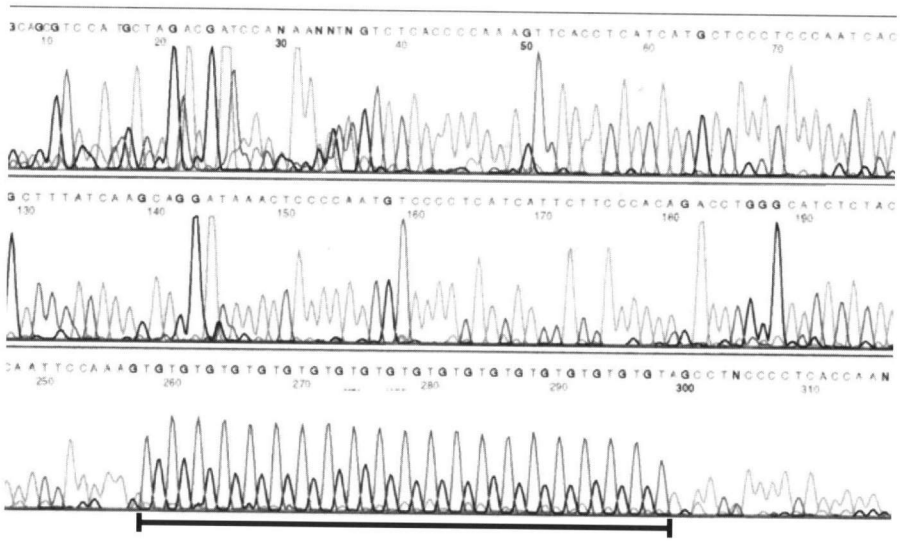
The Genetic Gender Gap: All Genes Are Not Created Equal

The springboard to equine research of the future is supported by the knowledge generated from futures past. Each advance occurred as researchers made new connections between the basic knowledge of the day and biological observations, then proposed a new theory to test and refine. That's what the Austrian monk Gregor Mendel did 135 years ago when he developed the fundamental laws of inheritance, and that's what Douglas Antczak D.V.M., Ph.D., director of the James A. Baker Institute for Animal Health, is doing today as he moves forward with the Horse Genome Project and links it to a whole new rule of inheritance.

Mendel taught us that offspring receive half of their genetic heritage from each parent. Dominant genes are expressed in the offspring while recessive genes, such as light coat, just get passed down to the next generation. When the recessive gene finally gets paired up with a recessive gene for the same trait from the other parent, the grandchild will have the light coloring. But which parent contributes particular genes has never mattered until recently. Antczak thinks it's going to matter a lot to geneticists in the next millennium.

Ten years ago, he noted a curious practice of horse breeders: they not only charted how well racehorses did as sires but they also how they did as sires of broodmares. Horse breeders said they had observed how some award-winning stallions became outstanding sires of broodmares but not of performers.

Antczak was puzzled; the phenomenon didn't make any sense according to any known laws of genetics. But then in 1986, a British researcher, Azim Surani, brought to light a genetic observation that had languished in the literature for 20 years. He startled the genetic world when he published findings stemming from impregnating mice with two sets of chromosomes from the same parent (instead of one set from the mother and one set from the father). All the fetuses failed but in new, predictable ways depending on whether the double set came from the mother or the father. For the first time, a genetic gender gap has been detected. Surani proposed that the outcomes of the pregnancies were predictable if you accepted that some genes get switched "on" and "off" depending on the gender of the parent contributing the genes.



Microsatellites—repetitive elements within a horse's DNA—serve as mileage markers that help scientists identify the location of genes controlling important functional traits. They also make it possible to tell which traits were contributed by the mother and which by the father.

> "Some genes are transmitted either in an active or inactive form, like a light switch that's either on or off, depending on which parent they come from. . . . Can we ultimately learn how to switch some beneficial genes on?"
>
> Dr. Douglas Antczak

"His experiment showed a whole new paradigm of inheritance that we hadn't imagined or expected. For the first time, scientists realized that it sometimes mattered whether particular genes came from the mother or father," Antczak said. "Evidently, some genes are transmitted either in an active or inactive form, like a light switch that's either on or off, depending on which parent they come from."

Antczak, who has been spearheading Cornell's contribution—largely funded by the Zweig fund—to the Horse Genome Project, has always made it a little hobby "to look for kernels of scientific truth in the practical, everyday activities of animal breeders. When I read about Surani's research, I realized that this so-called genetic imprinting might explain what horse breeders had been observing for years: that greatness skips a generation and gets passed down

continued on page 4

Gender Gap *continued from page 3*

through daughters."

Secretariat is a prime example. His dam, Somethingroyal, had been sired by Princequillo, a leading sire of broodmares three decades ago. Secretariat was a racing superstar but not an exceptional sire himself; his offspring were disappointing performers. "But his daughters are some of the greatest broodmares in the world now," says Antczak. They've produced champions such as A. P. Indy, Summer Squall, Chief's Crown, Dehere, Gone West, and Storm Cat.

This is what geneticists now call the maternal-grandsire effect. Although most genes are "on" when they get passed down, or get expressed depending on their dominance or recessiveness, some get "switched off" when passed down through males. None of Secretariat's sons or the sons' offspring became exceptional performers. But when females passed the gene down, they somehow "reset" the gene, turning it on, and in this case it is evidently related to performance. And sure enough, Secretariat's daughters' offspring are, like their grandfather, outstanding athletes.

Antczak searches for markers that identify particular genes on equine chromosomes. Most of the imprinted genes discovered in several species so far are involved in early placental and fetal growth. In pigs, scientists have identified some imprinted genes that affect muscle and heart mass in utero. About 30 imprinted genes have been identified in humans and are linked to disorders such as Prader-Willi and Angelman syndromes (related to mental retardation), Turner's syndrome, Huntington's disease, bipolar depression, and schizophrenia.

"The activities of imprinted genes seem to be prenatal, affecting growth and in utero development, but their effects are significant enough to persist a lifetime. If we confirm that imprinted genes can affect muscle growth and heart mass in horses, for example, such knowledge could prove very important to racing and performance," said Antczak, pointing to Secretariat's heart for example. Although that racing superstar was of average size, his heart weighed 22 pounds, compared to the average 8.5-pound thoroughbred heart.

Antczak is currently studying four possible markers for imprinted genes in the horse, all that affect growth. Such research is now possible, thanks to Zweig funding of the Horse Genome Project, which is racing forward and allowing Cornell equine scientists to work on the worldwide frontiers of equine genomics.

"This funding provides us with a framework of genetic equine knowledge that we can use to identify markers for imprinted genes in the horse and to determine their effect on athleticism or other important physical traits," Antczak said.

On the cusp of a new millennium, we just might be facing a brave new world of equine genetics in which horse specialists will breed more efficiently for performance or bone and joint function and influence the incidence, for example, of allergic respiratory diseases such as COPD (chronic obstructive pulmonary disease), debilitating arthritis, and OCD (osteochondritis dissecans disease)—all of which have genetic components.

"We might also explore a range of questions," Antczak noted, "such as: Are there examples of placental failures that are due to inherited genes from sires? Do some stallions transmit genes for a superior prenatal environment which would enhance fetal growth? Do certain maternal genes determine the pattern for fetal growth which can influence performance? Can we ultimately learn how to switch some beneficial genes on?"

The answers to these questions just may become evident in the century ahead. ■

Harry M. Zweig Memorial Fund for Equine Research—2000 Research Awards

The following research awards were made by the Zweig Committee at its annual meeting in November.

Renewals

$55,679 to Dr. Douglas Antczak for "Horse Genome Project"

$28,771 to Drs. Norm Ducharme and Richard Hackett for "Spectro-Temporal Signature for Identification of Upper Airway Abnormalities in Exercising Horses"

$67,787 to Dr. Alan Nixon for "Growth Factor Gene Therapy Approaches to Equine Cartilage Repair"

Revised

$46,531 to Yung-Fu Chang for "Cloning of *L. interrogans* Serovar Pomona Type Kennewicki Immunogen Genes"

New

$37,730 to Dr. Dorothy Ainsworth for "Exercise-Induced Immunosuppression: A Cause of Illness and Vaccine Failures in Racehorses?"

$33,600 to Dr Robert Gilmour for "Ionic Basis of Repolarization in Equine Heart: Relevance to Atrial Fibrillation and Acquired LQTS"

$40,000 to Kevin Haussler for "Back Motion in Horses during Different Gaits: Effects of Back Injuries"

Total Zweig funds awarded—$310,098 ■

As a 12-year-old growing up in Charleston, South Carolina, one of the last things John Jagar wanted to do was to learn to ride horses.

"When my mother said I needed to take lessons for six months because riding horses was something I should know how to do, I fought her all the way," says Jagar, 46, a veterinarian in Millbrook, New York, and a member of the Zweig Committee for three years. "But then those six months turned into six years. I swallowed the hook and was caught."

Through his teens, Jagar showed hunters. "I was fortunate, however, to ride a very crummy horse," he laughs.

Huh?

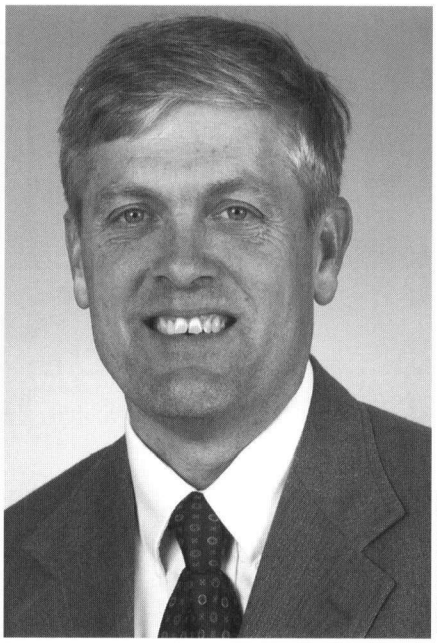
"I consider it fortunate because during a show in high school, Ellen Gleason, formerly of Rochester, New York, saw me and said I rode too well to ride something so terrible. So why didn't I come to her farm and ride *her* horses?"

It was on Gleason's trainer's horse farm in Atlanta that Jagar was first drawn to veterinary medicine. Intrigued by the work of her equine veterinarian, he decided that was the field he wanted to pursue.

After his sophomore year at the University of the South in Sewanee, Tennessee, Jagar worked as a groom on Claiborne Farm, which was owned by the family of a classmate. There he met veterinarians Colonel Floyd Sager and Jim Klyza, both alumni of the New York State College of Veterinary Medicine at Cornell.

"After meeting those two men, I decided Cornell was the only veterinary school in the world to go to."

Getting in was no easy task, however, because Cornell was—and still is—a statutory college and primarily accepts New Yorkers. Jagar found a friend, however, in Dr. Sandy Delahunta, then the chair of admissions, who stuck his neck out and got Jagar admitted.



ALEXIS WENSKI-ROBERTS

Jagar reads research proposals with an eye to their practical benefit.

"This committee has been the best I have ever served on. It's a great bunch of people doing a very worthwhile thing."

John Jagar

"I've redeemed myself since," Jagar says with a grin. "Although I was the token southerner then, I have since come back to live and practice in New York."

Before doing so, however, Jagar did an internship and residency at Auburn University and received a master's degree in large animal surgery. He returned to New York in 1980 to work as a resident veterinarian on a breeding farm in Ghent. In 1984, he opened a practice with two partners. They located the business—Millbrook Equine Veterinary Clinic, P.C.—in the Hudson Valley, which is the hub of the New York horse breeding industry.

In his free time, Jagar helps his 16-year old daughter, Ashley, prepare for and compete in three-day horse events. His 14-year-old son, Ross, on the other hand, is a "golf nut." With his wife, Suzanne, Jagar owns a thoroughbred broodmare, now with a weanling and a yearling still on the farm, a stallion share, and three dogs: a Labrador to hunt with and two "rug rats"—a terrier and a cocker spaniel, "which is a veterinarian's dream because they have every problem known to dog."

This past summer, Jagar volunteered as one of 60 veterinarians working at the Olympics. "I was assigned to fences 4, 19, and 20, and truthfully, there were very few veterinary problems. But we had a great time there for two weeks."

Jagar says he is elated to be a member of the Zweig Committee.

"This committee has been the best I have ever served on. It's a great bunch of people doing a very worthwhile thing. It allows me to read research proposals that are on the cutting edge of veterinary medicine. It gives me a chance to know what's going on and to provide some input to ensure there will be some practical end result from the research that will benefit horsemen." ■

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The 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 pari-mutuel 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.

2000 Harry M. Zweig Memorial Fund Committee