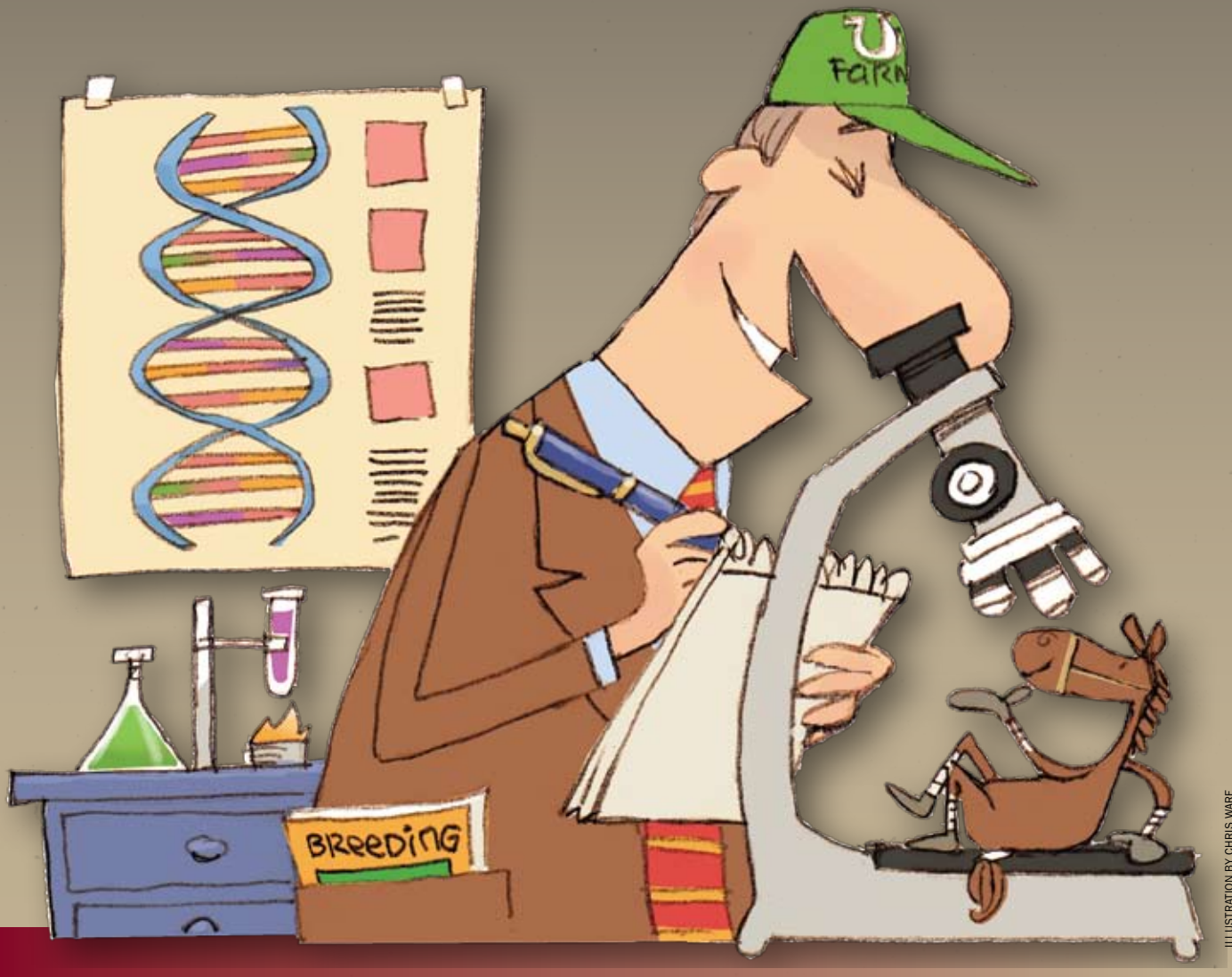
Researchers are making great headway with their understanding of genetics; here's why this area of study is both important and applicable for horse health

Genetics

What Does it All Mean?



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Researchers are beginning to objectively define physical and genetic contributors to racing performance, with the goal of helping breeders and owners maximize their horses' potential.

HEATHER SMITH THOMAS

When we think of genetics in horses, we generally think in terms of color inheritance—whether a foal will be bay, gray, chestnut, or have the splashes of color that we desire in our particular breed group. However, advances in the field of genetics reach well beyond coat color and are especially beneficial to owners and breeders that are trying to understand—and avoid—genetic diseases.

Ernest Bailey, PhD, immunogenetics and genomics researcher at the University of Kentucky's (UK) Gluck Equine Research Center, explains that there are basically two aspects of genetic study—creating tests and creating knowledge. Scientists have developed tests to determine if a horse carries certain traits (both desirable and undesirable) such as color, performance, or disease. And by understanding genetics better they are creating knowledge for improved management of horses.

"For example, some horses are thrifty keepers and may get laminitis on lush pasture," Bailey explains. "We generally don't think of this as a genetic problem, mainly because we don't want to address this by genetic selection." However, if an owner has already chosen a horse for other desired traits, he or she might want to find ways to treat or manage the horse predisposed to laminitis so he doesn't founder. Understanding the horse's genetics can help the owner achieve this.

How Can Genetic Research Help Horse Owners?

Researchers are gaining knowledge constantly about genetic traits of interest. They now are familiar with the genes to avoid or eliminate genetic defects such as severe combined immunodeficiency (SCID), overo lethal white syndrome (OLWS), hereditary equine regional dermal asthenia (HERDA), and hyperkalemic periodic paralysis (HYPP), among others, and have provided that information to breeders.

However, according to James MacLeod, VMD, PhD, John S. and Elizabeth A. Knight chair, professor of veterinary science, and director of UK's Equine Initiative, "Recessive (in which the horse must inherit a defective copy of the gene from each parent for the trait to manifest) and single-gene traits keep emerging in horse populations; some of which may have existed for decades before they are recognized. By this point, carriers may be widespread in a breed. Developing tests for newly recognized defective traits continues to be important."

While tests and knowledge can help horse owners and breeders avoid specific harmful traits, on the flip side they can also select for desired characteristics, as mentioned, from coat color to performance. With this ability, however, comes great responsibility.

"We can use it constructively or abuse it, like any other powerful technology," says MacLeod. As far as the latter, "An example might be the commercialization of genetic tests or services based on claims that are not supported by scientific knowledge, or only a limited understanding of the issue. Another potential scenario might be aggressive selection by breeders for a specific genotype (genetic makeup regulating a given physical trait) perceived to be highly desirable—before we fully understand whether genetic diversity in that region of DNA is important for the population."

Responsible Breeding

Knowing which of their horses carry unwanted genetic traits has already helped many breeders avoid producing foals with certain defects. "Diagnostic tests have been created for many different diseases (see list of testable equine genetic diseases on page 28)," says Bailey, and can identify exact disease-causing mutations. "We've

known these traits are hereditary, but until recently could not do a molecular test for the trait and identify carriers."

On the other hand, "A carrier of a deleterious trait may also have desirable qualities or express a whole spectrum of good characteristics we don't want to lose or eliminate," explains MacLeod. "Knowing the genetic keys, we might still be able to utilize these animals in a breeding program to maintain the desirable traits, while specifically avoiding the possibility of producing individuals that double up on an unwanted disease-causing recessive gene."

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> DR. JAMES MACLEOD

Bailey concurs, noting that undesirable traits that have cropped up and wreaked havoc within breed groups, such as lavender foal syndrome and SCID in Arabians and HERDA, HYPP, and polysaccharide storage myopathy (PSSM) in Quarter Horses, "are devastating, but we now have the capacity to identify the genes responsible for any new deleterious trait that shows up and can devise tests for these. This allows breeders to continue their programs and to select for traits they want, with confidence that we can guide them around these icebergs (emerging single-gene traits) that might otherwise wreck their breeding programs."

TABLE 1 EQUINE GENETIC DISEASES

Disease	Affected Breed(s)	Dominant/ Recessive	Test Available
Known Genetic Disorders Recognized by the AAEP			
Hyperkalemic Periodic Paralysis (HYPP)	QH-related breeds	Dominant	Yes
Hereditary Equine Regional Dermal Asthenia (HERDA)	QH-related breeds	Recessive	Yes
Polysaccharide Storage Myopathy Type 1 (PSSM1)	20 breeds: QH-related, Morgans, Belgians, Percherons, Warmbloods, others.	Dominant	Yes
Severe Combined Immunodeficiency Syndrome (SCID)	Arabians	Recessive	Yes
Overo Lethal White Syndrome (OLWS)	Paints, Pintos	Recessive	Yes
Glycogen Branching Enzyme Deficiency (GBED)	QH–related breeds	Recessive	Yes
Junctional Epidermolysis Bullosa (JEB)	Belgians, Saddlebreds	Recessive	Yes
Lavender Foal Syndrome (LF)	Arabians	Recessive	Yes*
Malignant Hyperthermia	QH-related breeds	Dominant	Yes
Suspected Genetic Disorders – Specific Genetic Tests Not Yet Available			
Polysaccharide Storage Myopathy Type 2 (PSSM2)	QH-related breeds, Thoroughbreds, Morgans, Warmbloods, Arabians, others	Unknown	No; muscle biopsy diagnosis
Recurrent Exertional Rhabdomyolysis (RER)	Thoroughbreds, Standardbreds, Arabians, Appendix QH	Dominant/Polygenic	No; muscle biopsy diagnosis
Cerebellar Abiotrophy (CA)	Arabians	Recessive	DNA marker test**
Congenital Stationary Night Blindness (CSNB)	Appaloosas	Recessive	No
Splash White Color Pattern (SW-1, SW-2, SW-3)	QH-related breeds, Paints, Tennesee Walkers, Icelandics, Shetland Ponies, Miniatures	SW-1: Unknown, SW-2, SW-3: Probably Recesssive	Yes***

QH-related breeds = Quarter Horses, Paints, Appaloosa, and their crosses.

**The gene for Lavender Foal has been identified and published, however has not yet been officially recognized by the AAEP.*

***The gene responsible has not been identified. A test for a DNA marker believed to be close to the region containing an abnormal gene is offered.*

****Only the color pattern genetic tests are available at this time. Only a portion of horses with these genes have blue eye and deafness phenotype. Additional research is needed to completely determine any genetic associations.*

A Basis for Performance

Nena Winand, DVM, PhD, a veterinary molecular geneticist at Cornell University, says another new development in equine genetics is testing for performance-based genes. This area of interest has been fueled by the recognition of sequence polymorphisms (normal variations in DNA sequences between individuals) in a particular gene—myostatin—that are associated with Thoroughbred racehorses' tendency for success at certain racing distances. "For example, if you want to breed horses to perform optimally over certain distances and are dealing with heterozygous mares (having inherited only one copy of the trait-causing gene), this testing might allow you to channel sire selection," she says. "By capitalizing on the available genomic tools, we are beginning to objectively define physical and genetic contributors to racing performance, with the goal of helping breeders and owners maximize performance potential of their horses."

Breeders must keep in mind, however, that performance is a combination of genetics and environment—things that happen to the conceptus from its beginning until after birth (more on this concept of epigenetics on page 38) in addition to how the horse is raised.

"Everyone wonders if we can make another Secretariat if we clone him, but one of the things we're learning about genetics is its limitations," says Bailey. "If you had 10 clones of Secretariat they would all be different (because they would all be gestated in and born into different environments). But you'd probably get more stakes winners out of 10 Secretariat clones than from 10 random Thoroughbreds," since you would at least be starting with proven genetic potential.

MacLeod further explains that performance is not a single-gene trait like coat color, which might have one or two primary genes and one or two modifier genes. "The things that come into play to make a successful athletic horse are much more complicated. Even if you find a gene that seems to be important for a specific characteristic of performance, there will still be many shades of gray around that. A given horse might not have inherited the specific form of that one gene, yet still be very successful in performance because it has the others, and vice versa."

Thus, unlike genetic tests for those diseases caused by a single deleterious gene, tests for performance are statements of probability within a large set of variables.

Improved Research

Equine genetic research currently under way worldwide will produce the data needed to build more genetic tools and tests for traits of interest to horse enthusiasts, along with uncovering clues to managing common diseases. Such research has been aided tremendously by the completion of the equine genome sequence in 2007, a map that can be applied to studies of genetic expression and hereditary variation, leading to a new level of understanding equine diseases. MacLeod, for instance, is studying joint cartilage—molecular and cellular details of how this important tissue develops and how treatments might modify the disease processes or influence cartilage's ability to repair.

"(Knowledge of the horse genome) may not directly provide the answers, but it gives me a more powerful set of research tools to investigate critical questions," he notes.

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>
> DR. ERNEST BAILEY

Just as access to the Hubble space telescope beginning in 1990 enhanced scientists' ability to study star systems, researchers like MacLeod—with access to the full equine genome—have been able to advance their research efforts on equine diseases more successfully.

"Those of us involved with equine genetics came into this because we are interested in particular systems (diseases, vaccines, management issues, etc.) and we needed the genetics tools in order to make important advances on these," says Bailey. "For example, Jim Mickelson (PhD) at Minnesota wanted the equine genome so he can study muscle physiology. Doug Antczak (VMD, PhD) at Cornell is interested in the immunology of pregnancy (i.e., how a mare's body responds immunologically to a developing fetus and doesn't reject it). Much of our use of genetic tools depends on a scientist's area of interest. I was

recently at a meeting where people working on infectious diseases, reproduction, sports medicine, and immunology were all talking about using genetics in their studies. It now pervades all areas of research."

In other words, access to the equine genome will likely enhance many fields of study. "We can use new approaches to study variables that impact growth mechanisms during pregnancy and in young horses," MacLeod says. "An example might be a better understanding of complex diseases such as developmental orthopedic problems. We'll not only gain insight into their cause, but hopefully develop diagnostic and management strategies to avoid them."

Another benefit of genetic knowledge will be improved research quality at a reduced cost. Consider a scientist who wants to study disease incidence in horses that are thrifty keepers. His or her research would benefit from an efficient way to identify 20 susceptible individuals for the project.

"Instead, we must begin by studying susceptible and resistant animals together, with very high costs, or wait until susceptible animals are already becoming affected," Bailey explains. "It would be cheaper, faster, and more effective if scientists who wanted to understand this condition could (accurately identify and) select a group of animals predisposed to this syndrome and compare them to a resistant group."

Another example of progress made possible by genetic knowledge can be observed through current research on equine arteritis virus (EAV), which seems to cause mild disease in Standardbreds but more serious clinical disease in Thoroughbreds. "The idea that this might be a genetic difference has been controversial, but we've recently found some genetic determinants," Bailey says. "Now we can compare susceptible horses to resistant individuals, and have better understanding how the virus causes serious clinical disease. This may enable us to make better vaccines and therapies."

Ultimately, the more scientists can understand the physiology of health and performance—all the way down to the molecular level—the better. Then horse owners can more successfully select horses for the traits they desire and, with a veterinarian's help, treat them to prevent problems.

LORI SCHMIDT

Identifying carriers of undesirable traits within breed groups helps avoid these conditions and increases the likelihood that a healthy foal will result.

Looking to the Future

"Many questions remain," says MacLeod. "Understanding genetics is not just a function of the linear sequence of DNA bases. At one point, I thought that if we could just understand the sequence of G, A, T, and C bases (guanine, adenine, thiamine and cystosine), we could just 'read the book' and all the knowledge would be there. Sequencing the equine genome has been a major step forward, but there is so much more to learn. For example, when, where, and how much of a given gene is expressed is important, as well as what regulates these parameters of gene expression."

Several other structural features of DNA modify and influence how the primary sequence (of a specific gene) is expressed. Researchers are discovering these additional layers of control and working to understand their importance.

Ultimately, all this new research and knowledge can help us become better horsemen, making more informed breeding and management decisions about our horses. "Doors are opening and the future is exciting, but we are just getting started," MacLeod concludes.

ABOUT THE AUTHOR

Heather Smith Thomas *ranches with her husband near Salmon, Idaho, raising cattle and a few horses. She has raised and trained horses for 50 years, and she has been writing freelance articles and books nearly that long, publishing 20 books and more than 9,000 articles for horse and livestock publications.*