Galloping into the Future:
Genetic Tips and Tools for the Horse Owner

What is a genome?

Each genome contains the sum total of the instructions needed to perform the functions of life. These instructions are encoded in genes and maintained in sets of chromosomes, much like the multiple volumes of an encyclopedia. The genome of the domestic horse is similar in size to that of humans; approximately 2.7 billion bases. Of these 2.7 billion, only ~3% contains the instructions for building proteins, enzymes and other cellular components. The remaining 97% we can't fully decode, although it likely contains much of the crucial information on when, where and how each gene product should be used.

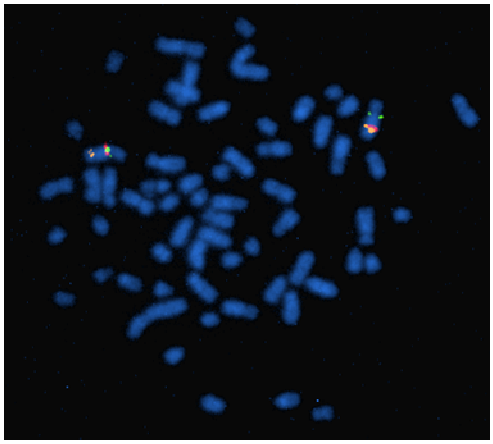

Figure 1. Equine chromosomes from a single cell stained with a fluorescent blue dye and viewed under a microscope. Three individual genes on one pair of chromosomes are marked with green, orange and red dye.

The equine genome is organized into 31 pairs of "autosomes" and two sex chromosomes, an X and Y, just as in humans (Figure 1). Most cells contain two copies of the genome, giving a total of 64 chromosomes (a convenient mirror to the 46 chromosomes in man). This "diploid" organization of the genome within the cell allows each individual gene to be present in two full copies. Thus if one copy acquires a detrimental mutation (a new "allele") the other will be able to continue to make a functional version of the gene product. The system of duplicate genes also introduces a variety of effects created when these two copies are inherited together. At the most basic level these interactions are described as "recessive" or "dominant". Should an individual possess two different copies of a gene (a "heterozygous" genotype), only the effect of the dominant allele will be visible. By the same logic, in order for the effect of a recessive allele to be visible the horse must possess two recessive copies. If an individual carries two identical alleles for a gene, be they recessive or dominant, the genotype is said to be "homozygous" for that locus.

Armed with knowledge of these patterns of inheritance for a given trait, you can predict the likelihood of obtaining a foal with this trait from a mating of two horses of known genotype. Geneticists use a tool called a Punnett Square to predict the results of a breeding for a single gene trait. Each parent has an equal chance to pass on either of the two alleles for a given gene. For example, if both parents are heterozygous the distribution of possible genotypes in the resulting offspring will be the same as the result of flipping two coins; three possible combinations of alleles (Figure 2).

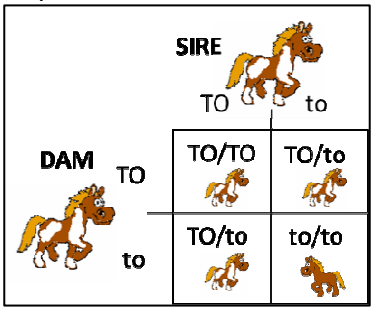

Figure 2. This example of a Punnett Square predicts the likelihood of obtaining a spotted foal from a breeding of two parents heterozygous for *Tobiano,* a dominantly inherited spotting pattern. Adding up the possible allele combinations shows that one out of four foals from such a cross will not be spotted.

How do you determine the genotype of a horse?

For some traits there are guidelines (and myths!) for making an educated guess regarding genotype. However, with the completion of the horse genome sequence in 2009 and accelerated research efforts, we can now test for more alleles in the horse than ever before. A brief list of currently available genetic tests in the horse is presented in Table 1 (reviewed in Bailey et al., 2013). These tests can be very effectively used by breeders to improve their foal crop and therefore increase the profitability of their operation, or to decrease the frequency of tragic and costly genetic conditions. However, their use is not yet widespread in the industry.

Why? First, many of these are recent discoveries and we don't have an efficient system in place to get this information out to the industry. Second, the cost of testing can be a significant deterrent. For each trait, in each horse, testing costs on average $20-$50. However, strategic testing can minimize the number of horses that need to be examined and emerging technologies will begin to rapidly decrease the cost per test.

What should I breed for?

Choosing a stallion for your mare can be a fun experience, as well as the most important business decision of your breeding program. The first step should always be a careful evaluation of the qualities, and faults, of the mare including any relevant genetic testing. If you know your mare carries an allele for a recessive condition in advance then avoiding the production of a sick foal is as simple as utilizing a stallion free of that allele. Identifying a list of desired traits in your foal crop will aid in the selection of relevant tests as tools and will organize your thoughts regarding stallion selection.

While the popularity of a stallion can increase the value of his foals, choice of a stallion based solely on the marketability of his name is risky. Overuse of popular stallions and the associated increase of linebreeding or inbreeding can have a detrimental effect on the long term health of the breed. For example, the American Quarter Horse is the world's largest breed, and well-known for the diversity of activities it excels at. However, within specific subgroups of the breed a popular sire effect has led to increases in the frequency of genetic conditions. ***HYPP,*** was the first mutation discovered in the horse, and a test for this allele has been available since 1992 (Rudolph et al., 1992). At that time the frequency of the disease in halter-bred Quarter Horses was ***22%***. Despite the availability of a genetic test permitting selection of breeding stock free of the disease, the frequency of ***HYPP*** increased to ***56.4%*** in the halter-bred Quarter Horse in just 17 years (Tryon et al., 2009). The genetic test was used primarily to reduce the clinical signs by avoiding production of homozygous foals. Consequentially, the number of heterozygous carriers has increased dramatically. This strategy capitalizes on a short term gain for the horse operation, but leads to a long-term loss for the quality of the breed as a whole. It is also important to remember that while the popularity of a stallion may rise and fall, the value of a sound, healthy, and quality horse is fundamentally stable. In the end, a trendy pedigree may mean nothing for a foal affected with a genetic condition.

What is next for genetic tools?

To date, research has focused on single gene conditions and colors. With improved tools provided by the horse genome sequence we can begin to attack more complex traits like performance, conformation and behavior. These same tools will also change the way we approach genetic testing. Currently, genetic tests are offered for just one allele at a time or a small bundle of two to three alleles. Novel methods like DNA sequencing enable testing of many genes, or even a whole genome for a fraction of the cost. While these services are not yet available in the horse, they are now seeing widespread use in human testing and are under development.

Genetic testing isn't just for the horse breeder. Tests for conditions like ***HYPP*** and ***PSSM1*** can be utilized as a diagnostic tool, providing you and your veterinarian the answers you need to make key management and treatment decisions to improve the health and well-being of your horse. Genetic testing may also be used for educational purposes, for example, in determining the precise color or pattern of your horse. Products to determine the breed of a mixed-breed dog are now commonplace, and are both fun and educational. While not yet available in the horse such a service may be available soon.

Unlike other animal diagnostic tests, genetics in the horse is often investigated by the owner and not the veterinarian. It is important for the horse person to keep this in mind and to carefully consider integrating genetic testing into their management and breeding programs. Research in this field has provided many exciting discoveries over the years. Hopefully, the field of equine genomics will continue to be a front runner in the creation of new and valuable tools for the horse industry.

Table 1. Commercially Available Genetic Tests For the Horse.

Trait	Symbol	Breed?	Year
Hyperkalemic Periodic Paralysis	HYPP	Quarter Horse, etc.	1992
Chestnut	E	Many	1996
Severe Combined Immunodeficiency	SCID	Arabian, etc.	1997
Overo Lethal White (Frame)	OLWS	Paint, etc.	1998
Black/Bay	A	Many	2001
Herlitz- Junctional Epidermolysis Bullosa	H-JEB	Belgian Draft	2002
Cream	CR	Many	2003
Glycongen Branching Enzyme Disease	GBED	Quarter Horse, etc.	2004
Malignant Hyperthermia	MH	Quarter Horse, etc.	2004
Sabino Spotting (1)	SB1	Many	2005
Silver (Multiple Congenital Ocular Anomalies)	Z	Many	2006
Tobiano Spotting	TO	Many	2007
Polysaccharide Storage Myopathy	PSSM1	Quarter Horse, etc.	2008
Grey	GR	Many	2008
Champagne	CH	Many	2008
Dominant White	W series	Many	2008+
Hereditary Equine Regional Dermal Asthenia	HERDA	Quarter Horse, etc.	2009
Junctional Epidermolysis Bullosa	JEB-2	Saddlebred	2009
Lavender Foal Syndrome	LFS	Arabian, etc.	2010
Cerebellar Abiotrophy	CA	Arabian, etc.	2010
Distance	MSTN	Many	2010
Fatal Foal Immunodeficiency Syndrome	FIS	Fell Pony	2011
Congenital Myotonia	CM	New Forrest Pony	2012
Loss of Canter (DMRT3)	SG	Many	2012
Splashed White	SW	Many	2012
Congenital Stationary Night Blindness	LP	Appaloosa, etc	2013

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