Equine Genetic Diseases
Genetic Testing for Horses: What is available and when to use it

Stephanie J Valberg DVM PhD, Dipl ACVIM, ACVSMR

The selective breeding of animal populations may give rise to a common founder that can disseminate a genetic trait to many thousands of related offspring within a few years. The number of DNA mutation is gradually increasing and there will likely be many more identified in the near future with the rapid development of genetic tools specific for horses.

The pattern of inheritance of these traits is either autosomal dominant or autosomal recessive. **Autosomal dominant traits:** Require only one copy of the mutant gene to cause disease. Breeding of an affected heterozygous horse (one copy of the defective gene) to a normal horse results in a 50% chance of producing an affected horse. Breeding two heterozygous affected horses has a 50% chance of producing a heterozygous affected, 25% chance of a homozygous affected (2 copies of the defective gene) and a 25% chance of a homozygous normal being born. **Autosomal recessive traits:** Requires two copies of the mutant gene to cause disease. Breeding two affected horses results in a 100% chance of producing an affected horse. Breeding two carriers results in a 25% chance of producing an affected horse, a 25% chance of a normal horse and a 50% chance of a carrier. Breeding and affected and a carrier results in a 50% chance of producing an affected horse and a 50% chance of producing a carrier.

**Equine Genetic Diseases that have commercially available tests**

<table>
<thead>
<tr>
<th>Defect</th>
<th>Breed</th>
<th>Mode of inheritance</th>
<th>Genetic test available</th>
</tr>
</thead>
<tbody>
<tr>
<td>HYPP</td>
<td>QH, Paint, APP</td>
<td>A-Dominant</td>
<td>yes</td>
</tr>
<tr>
<td>GBED</td>
<td>QH, Paint</td>
<td>A-Recessive</td>
<td>yes</td>
</tr>
<tr>
<td>HERDA</td>
<td>Quarter Horses</td>
<td>A-Recessive</td>
<td>yes</td>
</tr>
<tr>
<td>MH</td>
<td>Quarter Horses</td>
<td>A-Dominant</td>
<td>yes</td>
</tr>
<tr>
<td>PSSM type 1</td>
<td>20 breeds: QH, Paints, Morgan, Belgian, Percheron, some Warmbloods………</td>
<td>A-Dominant</td>
<td>yes</td>
</tr>
<tr>
<td>OLWS</td>
<td>Paint, Pinto</td>
<td>A-Recessive</td>
<td>yes</td>
</tr>
<tr>
<td>JEB</td>
<td>Belgian</td>
<td>A-Recessive</td>
<td>yes</td>
</tr>
<tr>
<td>JEB</td>
<td>Saddlebred</td>
<td>A-Recessive</td>
<td>yes</td>
</tr>
<tr>
<td>SCID</td>
<td>Arabian</td>
<td>A-Recessive</td>
<td>yes</td>
</tr>
<tr>
<td>Lavender foal syndrome</td>
<td>Arabian</td>
<td>A-Recessive</td>
<td>yes</td>
</tr>
<tr>
<td>Cerebellar atrophy</td>
<td>Arabian</td>
<td>A-Recessive</td>
<td>yes</td>
</tr>
<tr>
<td>Fell Pony Syndrome</td>
<td>Fell Pony Syndrome</td>
<td>A-Recessive</td>
<td>yes</td>
</tr>
</tbody>
</table>

**Genetic Disorders of Quarter Horses**
Five genetic diseases have been found in Quarter Horses that have genetic tests commercially available. The 5 known genetic mutations in Quarter Horses include Hyperkalemic Periodic Paralysis (HYPP), Glycogen Branching Enzyme Deficiency (GBED), Hereditary Equine Regional Dermal asthenia (HERDA), type 1 Polysaccharide Storage Myopathy (PSSM1) and Malignant Hyperthermia (MH). Information is available on our website -- [http://www.cvm.umn.edu/umec/lab/home.html](http://www.cvm.umn.edu/umec/lab/home.html). In my opinion this breed distribution reflects the larger number of Quarter Horses in the USA relative to other breeds, a tendency to line breed, and the openness and dedication of the Quarter Horse Association to finance and support investigation into equine genetics. As of Feb 1 2012 the AQHA began offering a panel test that includes HYPP, HERDA, MH, GBED, and PSSM1.

**HYPERKALEMIC PERIODIC PARALYSIS** (HyPP)

**Breeds affected:** Quarter horse-related bloodlines  
**Bloodlines:** Horses descendant from Impressive.  
**Prevalence:** 3% of the Quarter Horse breed is affected, 60% of halter horses  
**Age affected:** Signs usually begin by 2 to 3 years of age.  
**Clinical signs:** Range from asymptomatic to intermittent muscle tremors and weakness. Horses homozygous for HyPP may present with difficulty swallowing or respiratory distress.  
**Mode of inheritance:** Autosomal dominant.  
**Mutation:** A point mutation that results in a phenylalanine/leucine substitution in a key part of the voltage-dependent skeletal muscle sodium channel alpha subunit that controls channel activity (SCN4A).  
**Testing:** Veterinary Genetics Laboratory at the University of California, Davis on mane or tail hair roots.

**GLYCOGEN BRANCHING ENZYME DEFICIENCY** (GBED)

**Breeds affected:** Quarter horse-related bloodlines  
**Bloodlines:** Horses descendant from Zantanon and King  
**Prevalence:** 8% of the Quarter Horse breed. And 28% of Western pleasure are carriers  
**Age affected:** Signs usually present in utero or at birth  
**Clinical signs:** Abortion or stillbirth, may be born alive and are weak at birth. With supportive care may live to up to 18 weeks of age. Death may be sudden when exercised on pasture, associated with weak respiratory muscles or the result of euthanasia due to persistent recumbency. Treatable flexural deformities of all limbs and recurrent hypoglycemia (low blood sugar) and seizures occur in some affected foals.  
**Mode of inheritance:** Autosomal recessive.  
**Mutation:** A point mutation in exon 1 changes a tyrosine to a premature stop codon in the glycogen branching enzyme gene (GBE1) that is expressed in numerous tissues.  
**Testing:** Histopathological tissue samples (muscle and heart) stained for Periodic acid Schiff’s (PAS) show a variable amount of abnormal PAS positive globular and crystalline intracellular inclusions. Genetic testing is done by Veterinary Genetics Laboratory at the University of California, Davis or Vetgen in Michigan on mane or tail hair roots or Animal Genetics, or Progressive Molecular Diagnostics.

**HEREDITARY EQUINE REGIONAL DERMAL ASTHENIA** (HERDA)
Breeds affected: Quarter horses  
Bloodlines: Working cow and cutting horses  
Prevalence: 3.5% of the Quarter Horse breed and 28% of cutting horses are carriers.  
Age affected: Signs usually begin by 1.5 years of age  
Clinical signs: Wounds or sloughing skin, loose easily tented skin that does not return to its original position, scars, and white hairs at areas of hair re-growth found along the back and saddle area or areas with trauma. Healing is slow.  
Mode of inheritance: Autosomal recessive.  
Mutation: Point mutation that results in a glycine to arginine substitution in the equine cyclophilin B gene (PPIB) that plays a role in the processing of collagen for the anchoring of the skin to underlying tissue.  
Testing: University of California at Davis tests for this mutation.

Type 1 POLYSACCHARIDE STORAGE MYOPATHY

Two forms of PSSM appear to exist type 1 and type 2 PSSM. We have found the mutation for the type 1 in the GYS1 gene, the cause or causes of type 2 PSSM are under investigation but not yet known.  
Type 1 PSSM

Breeds affected: Quarter horse-related bloodlines, Belgians, Percherons, Morgans, Mustangs and some Warmblood breeds.  
Bloodlines: Present in founders of QHs and therefore widespread in all types of QHs with highest prevalence in halter and pleasure horses.  
Prevalence: 36-50% of Belgians and Percherons, 8% of the Quarter Horse related breeds, 30% of halter horses  
Age affected: Signs usually begin by 2 to 3 years of age but may occur in Weanlings. Some horses are subclinical.  
Clinical signs: Firm painful muscles, stiffness, skin twitching, sweating, weakness and reluctance to move with light exercise. Sometimes gait abnormalities, mild colic and muscle wasting. Serum CK and AST activity elevated except in Drafts.  
Mode of inheritance:  Autosomal dominant.  
Mutation: Point mutation that results in an arginine to histidine substitution in the GYS1 gene that codes for the skeletal muscle form of the glycogen synthase enzyme.  
Testing: Muscle biopsy samples evaluated for presence of amylase-resistant crystalline polysaccharide. Genetic testing on mane or tail hair roots, or unclotted blood samples at the Neuromuscular Diagnostic Laboratory at the University of Minnesota.  
http://www.vdl.umn.edu/vdl/ourservices/neuromuscular.html

MALIGNANT HYPERTHERMIA

Breeds affected: Quarter horse-related bloodlines  
Bloodlines: High frequency in one or two QH families often co-exists with PSSM  
Prevalence: 0.1% of the Quarter Horse breed is affected.  
Age affected: Adults  
Clinical signs: High temperature, metabolic failure and death under anesthesia. Tying up and fever. Signs of PSSM are more severe when both mutations are present. Sudden death
Mode of inheritance: Autosomal dominant.
Mutation: Point mutation that results in an arginine to glycine substitution in the RYR1 gene
Testing: Genetic testing at Neuromuscular Diagnostic Laboratory at the University of Minnesota. [http://www.vdl.umn.edu/vdl/ourservices/neuromuscular.html](http://www.vdl.umn.edu/vdl/ourservices/neuromuscular.html) Or through Monica Aleman at UC Davis

SUMMARY TABLE: Observed percentages of horses carrying a disease-causing allele for whole breeds (QH and APH) and for elite competitive subgroups.

<table>
<thead>
<tr>
<th>Population</th>
<th>HYPP</th>
<th>PSSM</th>
<th>GBED</th>
<th>HERDA</th>
<th>OLWS</th>
</tr>
</thead>
<tbody>
<tr>
<td>QH</td>
<td>1.5</td>
<td>11.3</td>
<td>11.0</td>
<td>3.5</td>
<td>NO</td>
</tr>
<tr>
<td>APH</td>
<td>4.5</td>
<td>4.5</td>
<td>3.9</td>
<td>1.7</td>
<td>21.3</td>
</tr>
<tr>
<td>Halter</td>
<td>56.4</td>
<td>28.2</td>
<td>5.1</td>
<td>0.8</td>
<td>NO</td>
</tr>
<tr>
<td>Western pleasure</td>
<td>1.1</td>
<td>8.6</td>
<td>26.3</td>
<td>12.8</td>
<td>NO</td>
</tr>
<tr>
<td>Cutting</td>
<td>NO</td>
<td>6.7</td>
<td>13.6</td>
<td>28.3</td>
<td>NO</td>
</tr>
<tr>
<td>Reining</td>
<td>NO</td>
<td>4.3</td>
<td>3.1</td>
<td>9.3</td>
<td>NO</td>
</tr>
<tr>
<td>Working cow horse</td>
<td>NO</td>
<td>5.7</td>
<td>9.5</td>
<td>11.5</td>
<td>NO</td>
</tr>
<tr>
<td>Barrel racing</td>
<td>1.2</td>
<td>1.4</td>
<td>1.2</td>
<td>1.2</td>
<td>NO</td>
</tr>
<tr>
<td>Racing</td>
<td>NO</td>
<td>2.0</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
</tr>
</tbody>
</table>

NO = Not observed in the dataset.

Genetic Disorders of Arabians

SEVERE COMBINED IMMUNODEFICIENCY (SCID)
Breeds affected: Arabian
Prevalence: 8% in USA CARRIERS
Age affected: < 6 months of age
Clinical signs: Recurrent infections, respiratory disease, eventual death.
Mode of inheritance: Autosomal recessive.
Mutation: 5 base pair deletion in the gene coding for DNA-dependent protein kinase (DNA-PK) catalytic subunit
Testing: Vetgen on mane or tail hair roots
LAVENDER FOAL SYNDROME (LFS)
Breeds affected: Arabian, higher prevalence in Egyptian Arabians
Prevalence: 8 – 17% CARRIERS
Age affected: Signs present at birth
Clinical signs: A dilute coat color and a range of neurological signs, including recumbency, opisthotonous, paddling movements and extensor rigidity leading to euthanasia
Mode of inheritance: Autosomal recessive.
Mutation: A single base pair deletion in the MYO5A gene, which codes for the protein myosin-Va
Testing: Veterinary Genetics Laboratory, University of California, Davis

CEREBELLAR ABIOTROPHY
Breeds affected: Quarter horse-related bloodlines
Prevalence: 19% CARRIERS
Age affected: Signs usually between 1 to 6 months of age
Clinical signs: Clinical signs of CA usually develop between the ages of 6 weeks and 4 months and include ataxia, hypermetria and intention head tremors
Mode of inheritance: Autosomal recessive.
Mutation: A single nucleotide polymorphism located adjacent to a potential binding site for GATA-2. GATA-2 is a transcription factor involved in expression of MUTYH, a post replication DNA glycosylase
Testing: Veterinary Genetics Laboratory, University of California, Davis, Animal Health Diagnostic Center at Cornell University.

Genetics Diseases in Other Breeds

JUNCTIONAL EPIDERMOLYSIS BULLOSA (JEB)
Breeds affected: Belgian drafts, Saddlebreds
Prevalence: 36% CARRIERS for Belgians, 3% CARRIERS Saddlebreds
Age affected: Signs usually present within a few days after birth
Clinical signs: Ulceration of skin and oral cavity lesions develop which become more extensive with age. Extensive oral ulcerations may also be present. Ulceration of the coronary band may proceed to sloughing of the hooves.
Mode of inheritance: Autosomal recessive.
Mutation: JEB1 (Belgians) stop codon terminating translation of LAMC2 gene. JEB2 (Saddlebreds) deletion in LAMA3 These genes encode subunits of Laminin-5 a structural protein that serves to anchor basal epithelial cells within the dermis.
Testing: Veterinary Genetics Laboratory, University of California, Davis, University of Kentucky

Conflict of interest statement: Drs. Valberg, Mickelson and McCue own the license for PSSM testing and receive sales income from its use. Their financial and business interests have been reviewed and managed by the University in accordance with its conflict of interest policies.