

## Recent Advances for Diagnosis of Polysaccharide Storage Myopathy

Polysaccharide Storage Myopathy (PSSM) is a common form of tying-up in many horse breeds and is characterized by excessive and abnormal storage of sugar (polysaccharide) in muscle cells. We have recently found a mutation in a gene that is highly associated with the presence of abnormal polysaccharide in muscle biopsies in several horse breeds. The genetic test for this mutation is now commercially available to horse owners and veterinarians through the University of Minnesota Veterinary Diagnostic Laboratory. We are calling this the classic or type 1 form of PSSM. This mutation accounts for greater than 90% of PSSM cases in some horse breeds. For specifics about breeds see the flow chart below. This mutation appears to have its origins prior to the foundation of modern horse breeds, which is why it occurs in several horse breeds.

McCue ME, Valberg SJ, Miller MB, Wade C, DiMauro S, Akmand HO, Mickelson JR. Glycogen synthase (GYS1) mutation causes a novel skeletal muscle glycogenesis. Genomics (in press)

There appears to be a second genetic mutation (MH) that makes signs of PSSM more severe in Quarter Horses and related breeds. The PSSM and MH genetic tests are recommended in Quarter Horse-related breeds so we can make the best management and treatment recommendations.

Not all cases of tying up are caused by the PSSM mutation. If a horse is N/N but is showing signs of tying-up or muscle pain, it is possible that the horse has another muscle disorder which must be diagnosed by muscle biopsy.

**Inheritance of PSSM:** Each horse has two copies of every gene (genotype), one inherited from the dam and one from the sire. Every horse inherits either a normal or a mutant gene from each parent. We have designated the letter P to indicate the mutant PSSM gene and MH to indicate the mutant MH gene. A normal horse is designated as N/N. A horse with PSSM may be heterozygous P/N or rarely homozygous P/P for the mutation. Those horses that are P/P are often more severely affected and harder to manage.

The PSSM mutation we have discovered is inherited in a dominant fashion, meaning that one copy of the mutation can cause PSSM. This is different from diseases such as HERDA and GBED, which are inherited in a recessive fashion, where 2 copies of the mutant gene are required for disease. Because PSSM is inherited in a dominant fashion the chances of an affected foal being born are dependant on the genotype of the parents as follows:

		Sire's genotype		
		N/N	P/N	P/P
Dam's genotype	N/N	0 %	50%	100%
	P/N	50%	75%	100%
	P/P	100%	100%	100%

- **For example, breeding a P/N horse to an N/N horse gives a 50% chance that the offspring will have PSSM.**

Thus any time a horse with PSSM is bred there is a minimum chance of 50% of an affected foal being born even if the selected mate is completely normal. The risk of producing an affected offspring when breeding a horse with PSSM is much higher because it is a dominant disease. Unlike the recessive diseases, where a horse with one copy of the gene is a “carrier” a horse with one copy of the PSSM mutation has PSSM.

We are currently in the process of publishing this information in scientific journals and more detailed information regarding the names of the abnormal genes and the specific breeds affected will be available after publication of these findings.

## CURRENT RECOMMENDATIONS FOR SUBMITTING FOR GENETIC TESTING, MUSCLE BIOPSY OR BOTH

\*Disclosure of financial interest: Drs. McCue, Mickelson and Valberg are the patent owners for the genetic testing for *GYST*. A portion of the proceeds from this test will go towards their continued research as well as patent royalties.

Based on our current understanding of the two forms of PSSM and the genetic mutations we have identified, we are currently recommending the following approach in the diagnostic process for PSSM:

**Signs of exertional rhabdomyolysis:** Muscle stiffness, cramping, pain, muscle fasciculation exercise intolerance, firm muscles, lameness, discolored brown urine (myoglobinuria), or progressive weakness, **and suspect PSSM**

