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American Morgan Horse Association PSSM1 Allele Frequency Study Report

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Objective and Background: The American Morgan Horse Association (AMHA) is interested in identifying an accurate estimate of the allele frequency for PSSM1 in horses that were born in the last decade (2012-2021) and registered with their organization. Based on UC Davis Veterinary Genetics Laboratory (VGL) records, prior to this study only 27AMHs were tested for this variant and all were N/N. Previously published research, conducted by others in 2010, suggested the allele frequency was low, with 2 out of 214 horses having the PSSM1 variant. To estimate the current frequency and make recommendations on genetic testing, we randomly selected 300 individuals (YOB 2012-2021) and tested them for the PSSM1 variant.

Methods: A list of all samples from the AMHA tested by the VGL with birth years from 2012-2021 was developed and 15 males and 15 females were randomly selected from each year. DNA was extracted from these samples using our standard methods and then samples were genotyped for PSSM1 using our commercially available test (https://vgl.ucdavis.edu/test/pssm1). Finally, standard analysis for allele and genotype frequencies were performed and confidence intervals were calculated based on a modified Wald test. Samples were also tested for CSNB2 (https://vgl.ucdavis.edu/test/csnb-tennessee-walking-horse) with permission granted by the AMHA. The CSNB2 data are a part of an ongoing VGL research study that is not yet complete and thus the outcome of CSNB2 testing will be shared with the AMHA when that study is submitted for publication.

Results and Conclusions: Nine samples failed our genotyping quality control and thus were not investigated further. For the breakdown of the number of samples with results for each year by gender please see **Table 1**. We did not detect any horses who were homozygous (two copies) for PSSM1 in the samples evaluated. We did identify two out of 291 samples that had one copy of the PSSM1 variant (**Table 2**). One was a female born in 2014 and the other was a male born in 2018. The estimated allele frequency in the population under investigation here was 0.35% (95% CI= 0.01 to 1.33%). This is similar to values given in the McCue et al. study from 2010. Using the estimate from this study, if 1750 horses are registered annually (on average), 12 are expected to be heterozygous for this variant. With the identified low allele frequency only 1 in 100,000 horses in the population would be expected to be homozygous. Homozygotes are thought to be more severely affected as compared to N/PSSM1 horses.

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Samples	n=	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
# of males	143	14	15	15	15	15	13	14	15	13	14
# of females	148	15	14	14	15	15	15	15	15	15	15
Total	291	29	29	29	30	30	28	29	30	28	29

Table 1: Sample distribution by gender and year of birth for those samples with high quality data. After extraction and genotyping 9 samples failed leaving 291 samples for analysis.

Genotypes	total n=	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
N/N	289	29	29	28	30	30	28	28	30	28	29
N/PSSM1	2	0	0	1	0	0	0	1	0	0	0
PSSM1/PSSM1	0	0	0	0	0	0	0	0	0	0	0
Total	291	29	29	29	30	30	28	29	30	28	29

Table 2: Genotype distribution for PSSM1 for total samples and by year of birth

Recommendation on Genetic testing: Given that the PSSM1 allele was detected in the population, genetic testing is recommended for horses that have symptoms of disease to confirm diagnosis. Genetic testing is also recommended to identify horses with PSSM1 to develop a diet and exercise regimen to best manage symptoms. There are several clinical overlapping phenotypes resulting in excessive abnormal glycogen accumulation in the muscle that likely result from different genetic mechanisms. The only scientifically validated variant to cause polysaccharide storage myopathy to date is the one tested in this study. Given the low frequency in the population it is possible to select away from this variant in a single generation by restricting the mating or registration of N/PSSM1 horses. However, in absence of genetic diversity data, and knowledge of surrounding markers that could also be lost in a closed population if mandates were instituted that required selection away from this variant, the decision to restrict registration of such horses (N/PSSM1) should not be made lightly. It is important to note the allele has a relatively high frequency in some draft hose breeds likely resulting from positive selection that allowed for rigorous daily work schedules with limited sugar feed intake. In summary, we recommend genetic testing for the Morgan horse to identify N/PSSM1 horses for proper management. We also recommend continued monitoring of the allele frequency in the population to ensure it remains low.

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