Development of genetic testing to eliminate Caroli liver fibrosis (CLF) in the Franches-Montagnes horse

Tosso Leeb[1]
[1]*Institute of Genetics, Vetsuisse Faculty, University of Bern, CH-3001 Bern*

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Horse, Animal welfare, Animal breeding, hereditary disease, liver fibrosis, genetic testing

Aim of the study
A lethal hereditary disease termed Caroli liver fibrosis (CLF) is known to occur in Franches-Montagnes Horses. The aim of this study was to identify the mutation and to develop genetic testing, so that the deleterious mutation can be eradicated from the Franches-Montagnes breeding population.

Material and methods
DNA was isolated from blood or tissue samples of 21 CLF affected Franches-Montagnes foals, 402 non-affected Franches-Montagnes horses, and 48 health control horses from other breeds. DNA from 3 affected foals was genotyped on the illumina equine SNP50 bead chip containing 54'602 SNP markers. Homozygosity mapping using the software plink was performed to assigned the CLF mutation to a defined chromosomal region. Microsatellite markers were genotyped using fluorescently labeled primers and an ABI3730 capillary sequencer. Sequence analyses were also performed on an ABI 3730 capillary sequencer.

Results and significance
Caroli liver fibrosis (CLF) is inherited as a monogenic autosomal recessive trait. Pedigree analyses confirmed that the important Franches-Montagnes stallion Elu (02119640001 FM A/F 1964 SBC) was a carrier for CLF. The most likely founder animal for the pathogenic mutation is the stallion Wigar, born in 1929. The molecular genetic analyses showed that the CLF mutation maps to a ~4.8 Mb interval on horse chromosome 20. In this interval, an excellent functional candidate gene called polycystic kidney and hepatic disease 1 (PKHD1) for CLF is located. Mutations in this gene cause a very similar disease in humans. Therefore, we assume that a mutation of the equine PKHD1 gene is responsible for CLF in Franches-Montagnes Horses. Mutations in the PKHD1 gene are perfectly associated with the CLF phenotype in Frances-Montagnes horses. We established genetic testing for Franches-Montagnes horses using one of these associated mutations. The genetic test is a marker test, which means that it does not interrogate the still unknown causative mutation but rather a polymorphism in tight linkage disequilibrium with the causative mutation. Nonetheless, together with pedigree information this marker test will allow the efficient eradication of the CLF mutation from the Franches-Montagnes breeding population.

Publications, posters and presentations
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Genetic testing website: http://www.genetics.unibe.ch/content/dienstleistung/pferd/index_ger.html (German) http://www.genetics.unibe.ch/content/service/horse/index_eng.html (English).

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