Gene test reveals severe skeletal disease in Shetland ponies

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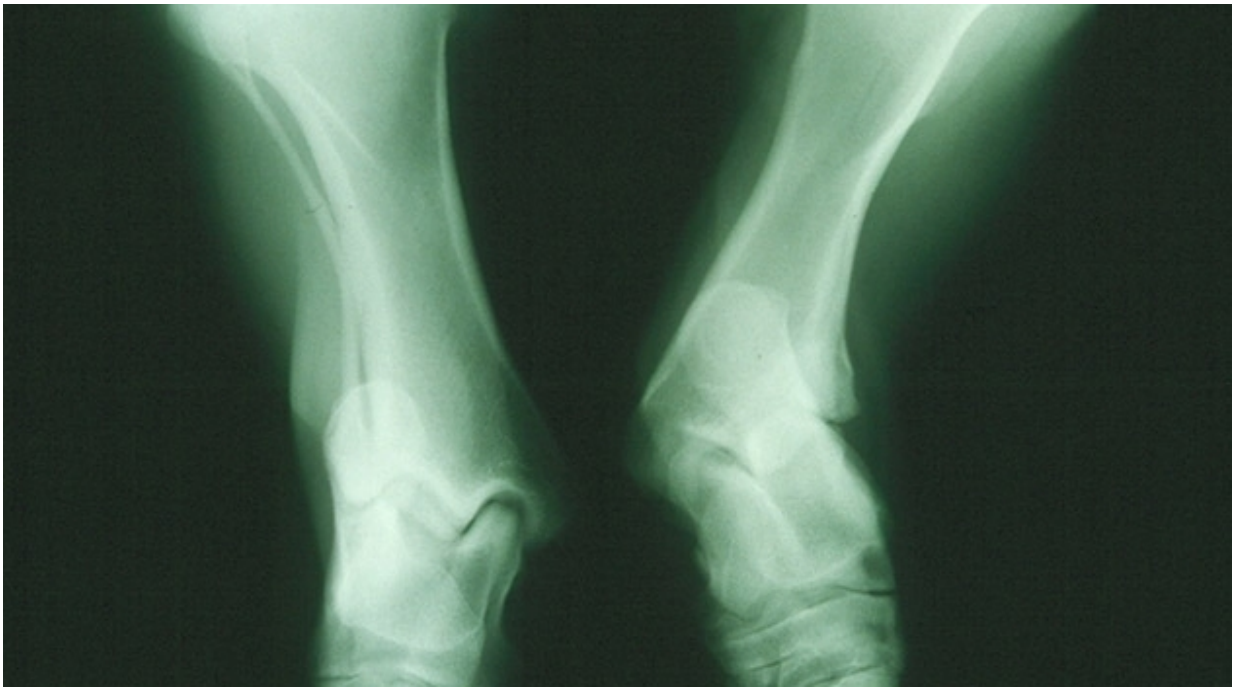

X-ray image of an affected foal's hind legs. Credit: Göran Dalin

A genetic defect that can cause skeletal deformities in Shetland ponies (skeletal atavism) has been identified by researchers at Uppsala University and the Swedish University of Agricultural Sciences, in cooperation with colleagues in the USA. The discovery means that healthy carriers now can be tracked using a gene test.

In Shetland ponies, a serious malformation of the legs represents a significant problem. Affected foals get progressively more curved legs, which in turn leads to incorrect conformation, lameness, and foals must often be euthanized at a young age.

The disease, called skeletal atavism, is known since the 1950s, and has since been reported across Europe. In the mid-1990s the disease was highlighted in Sweden, and several breeding stallions were found to be carriers. To reduce the risk of having affected foals, carrier stallions were prohibited from further breeding. Skeletal atavism follows a so-called recessive inheritance in which both parents must contribute a disease variant of the gene to get affected offspring.

The genetic study, recently published in the journal G3: *Genes, Genomes, Genetics* is the result of a collaboration between researchers at Uppsala University (UU), the Swedish University of Agricultural Sciences (SLU) and several American universities. By sequencing the entire genomes of affected and healthy individuals, the researchers found that genetic deletions within and around the SHOX gene causes skeletal atavism. Mutations in this gene cause dwarfism and skeletal deformities also in humans.

'Since most disease gene carriers are healthy, it's almost impossible to eliminate the disease from the population by traditional breeding', says Carl-Johan Rubin, researcher at Uppsala University and responsible for the study.

'Our discovery will now help breeders to conduct liable breeding as they can use a genetic test to screen for carriers in their breeding stock', adds Sofia Mikko, researcher at SLU and Director of the Animal Genetics Laboratory.

The SHOX gene is located in a region shared between the two sex

chromosomes X and Y, known to be difficult to study by traditional methods because of its complex structure. To reveal the sequence of this chromosomal region the researchers used a newly developed method, Single Molecule Real Time (SMRT) sequencing, available at SciLifeLab in Uppsala. This method is used to sequence very long stretches of DNA.

'We are now very pleased to describe some characteristics of one of the most problematic regions in the genome of mammals. That we also contribute to improved animal welfare, as fewer affected foals will be born, feels great', says Nima Rafati, PhD student at UU.

More information: Rafati N et al. Large Deletions at the SHOX Locus in the Pseudoautosomal Region Are Associated with Skeletal Atavism in Shetland Ponies. *Genes, Genomes, Genetics*. 2016 May 20. pii: g3.116.029645. DOI: 10.1534/g3.116.029645.

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