Medical Xpress

Genetic causes underlying the disqualification of two elite American Standardbred pacers

October 23 2014

A DNA mutation that can lead to horses being genetically male, but female in appearance, may explain at least two cases of controversial sexual identity, according to research led by professors from the Texas A&M College of Veterinary Medicine & Biomedical Sciences (CVM) and published in *PLOS Genetics*.

This type of genetic abnormality is caused by a mutation called DNA copy number variation (CNV), in which there are deletions and duplications in the genome typically larger than 50 base pairs.

These variations are one way that individuals of the same species are genetically different from one another, and although these mutations contribute to diversity and adaptations, they can sometimes cause diseases and disorders

The international team of researchers studied the genomes of 38 normal horses of 16 diverse breeds and identified 258 regions with CNV. "The resulting dataset of nearly 1500 CNVs is a critical resource for any CNV research in horses in the future," said Dr. Terje Raudsepp, an associate professor at the CVM and principal investigator for the study. Contrary to their expectations, the researchers found only two breed-specific CNVs. "We had to remove the tag 'breed specific' from almost all previously published horse CNVs," said Raudsepp, "but like cattle, dogs, and pigs; horses too might have breed-specific variants. It is just that

their discovery requires analysis of even larger and more diverse populations."

The team also carried out detailed analysis of CNV genes and concluded that the overall pattern observed in horses is similar to that known in humans and other mammals. CNVs tend to involve genes for sensory perception, immunity and reproduction.

In addition to the phenotypically normal horses, the team also analyzed CNVs in a group of horses with disorders of sexual development. Among these were two elite American Standardbred pacers who were disqualified from races in female category due to controversial sexual identity. These two horses are male pseudo-hermaphrodites. In other words, they are female in appearance, but have hidden rudimentary testicles and the male-specific Y chromosome. Both were found to have a large deletion interrupting a cluster of genes that are necessary for sex hormone metabolism and sexual development.

"In order to distinguish between normal and disease-related variants, detailed knowledge about CNVs in the species of interest is needed," said Raudsepp. "Our goal was to both carry out a thorough 'inventory' of previously reported CNVs and to discover new ones, in order to create a whole-genome platform for the study of CNVs in horses." Such an inventory then makes it easier to find variants that distinguish horse breeds from one another, as well as to find which mutations lead to which traits.

"Our findings provide the first hints about likely molecular causes and the involvement of CNVs in equine disorders of sexual development," Raudsepp said. "As similar conditions are also known in humans and other mammals, the findings might have biomedical significance far beyond their importance in horse racing."