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Researchers Genetically Link Lou Gehrig's Disease in Humans to Dog Disease

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(PhysOrg.com) -- An incurable, paralyzing disease in humans is now genetically linked to a similar disease in dogs. Researchers from the University of Missouri and the Broad Institute have found that the genetic mutation responsible for degenerative myelopathy (DM) in dogs is the same mutation that causes amyotrophic lateral sclerosis (ALS), the human disease also known as Lou Gehrig's Disease. As a result of the discovery, which will be published in the *Proceedings of the National Academy of Sciences* this week, researchers can now use dogs with DM as animal models to help identify therapeutic interventions for curing the human disease, ALS.

"We uncovered the genetic mutation of degenerative myelopathy, which has been unknown for 30 years, and linked it to ALS, a human disease that has no cure," said Joan Coates, a veterinary neurologist and associate professor of veterinary medicine and surgery in the MU College of Veterinary Medicine. "Dogs with DM are likely to provide scientists with a more reliable animal model for ALS. Also, this discovery will pave the way for DNA tests that will aid dog breeders in avoiding DM in the future."

Previously, ALS research has relied heavily on transgenic rodents that expressed the mutant human gene SOD1, which causes ALS. Researchers found that dogs with DM also had mutations in their SOD1 gene. Many rodent models possess very high levels of the SOD1 protein that can produce pathologic processes distinct from those occurring in ALS patients. Since the SOD1 mutation is spontaneous in dogs, the

clinical spectrum in dogs may represent more accurately that of human ALS.

“Compared with the rodent models for ALS, dogs with DM are more similar to people in size, structure and complexity of their nervous systems, and duration of the disease,” said Gary Johnson, associate professor of veterinary pathobiology in the MU College of Veterinary Medicine. “The results from clinical trials conducted with DM-affected dogs may better predict the efficacies of therapeutic interventions for treating ALS in humans.”

ALS causes progressive neurodegeneration, affecting both the central and peripheral nervous systems. The disease leads to advancing weakness and muscle atrophy, and culminates in paralysis and death. DM has been recognized for more than 35 years as a spontaneously occurring, spinal cord disorder in dogs. DM is reported most commonly in German Shepherds but also exists in other breeds, such as Cardigan and Pembroke Welsh Corgis, Rhodesian Ridgebacks, Chesapeake Bay Retrievers and Boxers. There are no treatments for ALS and DM that clearly have been shown to stop or slow progression of the diseases. Owners of dogs with DM usually elect euthanasia six months to a year after diagnosis when the dogs can no longer support their weight with their pelvic limbs, whereas people with ALS typically progress to the state of complete paralysis and succumb to respiratory failure.

The study, “Genome-wide association analysis reveals a SOD1 mutation in canine degenerative myelopathy which resembles amyotrophic lateral sclerosis,” was published in the Proceedings of the National Academy of Sciences this week. This study was a collaborative project with MU researchers and Kerstin Lindblad-Toh and Claire Wade, who are researchers at the Broad Institute of Harvard and Massachusetts Institute of Technology. The study was funded by the American Kennel Club Canine Health Foundation and participating breed clubs.