Drug Therapy May Bridge DM and ALS

Dr. Joan Coates, a veterinary neurologist and professor at the University of Missouri College of Veterinary Medicine, was recently awarded a grant from the National Institute of Neurological Disorders and Stroke, part of the National Institutes of Health, to explore a potential therapy for canine degenerative myelopathy. The study involves treating dogs diagnosed with degenerative myelopathy (DM) with a drug therapy that is also being tested in people with amyotrophic lateral sclerosis (ALS), or Lou Gehrig's disease.

"What we hope to do is slow the disease progression, and ultimately, halt the disease progression," Coates said.

Coates was part of a team that also includes Dr. Gary Johnson, an associate professor in the MU CVM Department of Veterinary Pathobiology who is involved in genomics research, and investigators at the Broad Institute and Massachusetts Institute of Technology, who established that the same genetic mutation that causes DM in dog also causes some forms of ALS in people. The mutation is wide-spread in the dog population and DM exists in many breeds, such as Pembroke Welsh corgis, Rhodesian ridgebacks, German shepherd dogs, Chesapeake Bay retrievers and boxers.

Both DM and ALS are incurable neurological diseases that cause progressive neurodegeneration in both the central and peripheral nervous systems. The diseases lead to weakness and muscle atrophy, and culminate in paralysis and death. In DM, the onset of clinical signs starts at around 9 years of age with weakness beginning in the hind limbs and affected dogs are usually paralyzed within 11 months. Many pet owners choose euthanasia when their dogs can no longer use their hind limbs. However, if the dogs live longer with DM, the disease would continue to spread through the central nervous system eventually affecting the rest of the spinal cord, muscles, nerves and the brain. In end-stage DM, dogs can develop swallowing dysfunction and lose their bark.

Coates' focus now is the search for a treatment that will benefit DM and ALS patients.

She is collaborating on a drug therapy project with Dr. Timothy Miller at Washington University in St. Louis. Miller is leading a clinical trial in ALS patients. Coates said beneficial effects of the drug have been observed in rodent studies giving hope that those benefits will carry over to treating DM and ALS.

"Possibly more can be learned in treating DM so that we can then go back and expedite

therapeutic approaches in treating ALS," Coates explained. "We hope to have pharmacologic studies completed in a year and from there we can take it to a clinical trial in DM-affected dogs."

Similarities between the canine and human nervous systems, and the homogeneity in onset and clinical progression of canine DM, will facilitate translation of therapies into human applications. Furthermore, dogs with DM offer a ready clinical population in which therapies can be evaluated in an environment closely mimicking human clinical trials.

ALS is caused by many different genetic mutations or is sporadic. Moreover, the disease progression and the type of onset are variable. These heterogeneities pose challenges in management of clinical trials for the ALS community.

"The challenge in any therapy involving the nervous system is getting the therapy where the pathology resides — you have to get the treatment into the spinal fluid and the nervous tissue."

To that end, Coates is collaborating on other translational and comparative medicine projects. With her fellow researchers within the College's Comparative Neurology Program, she is working to establish biomarkers — the biochemical signatures of diseases — in spinal fluid and blood in an effort to further characterize DM. She is also partnering with Dr. Teresa Lever, an assistant professor in the MU School of Health Professions, to study swallowing dysfunction in dogs.

As the links between ALS and DM becomes clearer, Coates hopes that she, together with fellow veterinary neurologists, will foster collaborations with other ALS researchers to expand on different treatment approaches for DM and ALS and eventually a cure.

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