# Understanding the dog model of Duchenne muscular dystrophy

Animal models are indispensible in the development of novel therapies. A clear understanding of the model itself is essential before the model is used in research. This means we need to know every aspect of the model including its strengths and weaknesses. Without such information, it will be impossible to make precise and correct interpretations of the animal study results. The commentary "*Early loss of ambulation is not a representative clinical feature in Duchenne muscular dystrophy dogs*: remarks on the article of Barthelemy et. al." provides an example on why accurate characterization of Duchenne muscular dystrophy (DMD) dogs is important.

DMD is a severe childhood lethal muscle disease that mainly affects boys. The disease is caused by genetic mutations in a gene called dystrophin. Patients show problems with walking and stair climbing around 2 to 5 years of age and are bound to a wheelchair in their teenage years. DMD is a worldwide disease and patients can come from any race and any country. Much like humans, dogs can also be affected by DMD. Mutations in the dystrophin gene have been found in various breeds. Since the first DMD dog was found in the golden retriever breed, most researchers around the world have been using the progeny from this dog in their studies. This brings two problems. First, DMD can be caused by thousands of different types of mutations, but the golden retriever muscular dystrophy dog (GRMD) only has one type of mutation. So studies based on GRMD cannot reflect other types of mutations. Second, to generate more DMD dogs for research purposes, scientists have used a method called inbreeding. Which means all DMD dogs generated by this method will be close relatives. These dogs will carry genetic traits unique to the family but may be uncommon in the entire dog population. Sometimes, the traits unique to the family can alter disease manifestations. Studies performed in this family will thus not be representative of the general population.

Like in humans, DMD will eventually cause the dogs to lose their ability to walk. If DMD boys lose their ability to walk at teenage, when should DMD dogs loss their walk ability? If we take 80 years as the average life span of a man and 10 years as the average life span of a dog, we may guess DMD dogs will likely loss their ability to walk around 1.25 years of age. To determine when DMD dogs lose their walk ability, Barthelemy et al studied an inbred GRMD dog colony. Interestingly, they found that about a quarter of the DMD dogs in their colony lose their walk ability at about 6 months of age, much earlier than expected. To determine whether this is the case for the entire DMD dog population, Duan et al examined several different breeds of DMD dogs, including GRMD dogs that were housed in other locations. In contrast to the results of Barthelemy et al, the study by Duan et al did not find early loss of walking ability as a general feature of DMD dogs. It is currently unclear why the colony studied by Barthelemy et al showed this unique feature. It could be caused by inbreeding and/or different environment these dogs were raised. Nevertheless, it is important to know the difference. For example, if all the dogs studied by Barthelemy et al remain ambulant at 8 months of age after receiving an experimental drug, it may suggest this drug is

effective. But we cannot draw this conclusion if we get the same results on DMD dogs from other colonies.

***Joe W. McGreevy, Dongsheng Duan***
*Department of Molecular Microbiology and Immunology, School of Medicine, University of Missouri, USA*

## Publication

Early loss of ambulation is not a representative clinical feature in Duchenne muscular dystrophy dogs: remarks on the article of Barthélémy et al.
Duan D, Hakim CH, Ambrosio CE, Smith BF, Sweeney HL
*Dis Model Mech. 2015 Mar*