

Phenotypic Characterization and Mapping Genes Associated with Canine Degenerative Myelopathy in Boxers

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Participating Breed Clubs: American Boxer Club, Pembroke Welsh Corgi Club of America, Rhodesian Ridgeback Club of the United States

We would like to thank you for participating in this research project. Your involvement with this study is very much appreciated by the project investigators and participating breed clubs. Our ultimate goal for this project is reduce the prevalence of degenerative myelopathy (DM) in the Boxer and other breeds.

Abstract:

Degenerative myelopathy is a disease of the spinal cord causing progressive paraparesis. Though most commonly reported in German Shepherds, high disease prevalence also exists in other breeds, such as Cardigan and Pembroke Welsh Corgis, Rhodesian Ridgebacks, and Boxer dogs. The increased risk in specific breeds suggests a significant genetic predisposition and adds power to mapping any genetic risk factors. The purpose of this proposal is to map genes associated with DM in the Boxer dog and other breeds. We propose characterizing the phenotype in the Boxer dog using sequential antemortem neurodiagnostic testing, and neuropathology. A network of board-certified veterinary neurologists has been established to help diagnose dogs across the country. A small subset of 10 Boxer dogs will be further characterized directly by the principal investigator, to determine if the phenotype and clinical progression is identical to that seen in the Pembroke Welsh Corgi. Genome-wide association mapping will be performed to identify a genomic locus associated with DM in 50-100 affected and 50-100 age-matched boxers using the ~20,000 SNP array. If as expected the same phenotype is seen in Boxers as in the Pembroke Welsh Corgis and Rhodesian Ridgebacks, disease haplotypes are likely to be shared between these breeds. We will thus fine map using Boxers as well as smaller numbers of affected and control Pembroke Welsh Corgis and Rhodesian Ridgebacks. We expect to narrow the region to contain only 1-2 genes. This project will allow for more rapid development of genetic research to identify carrier and affected dogs of DM and thus eliminate the genotype of this late-onset disease from the population. Early, accurate distinction of DM from other neurological disease will facilitate therapeutic trials.

CHECK LIST

Signalment Information: (See Form Below)

History: (See Form Below)

Physical Examination: (See Form Below)

Neurologic Examination: (See Form Below)

Laboratory Results: (if available)

- Complete blood count – attach results
- Serum biochemistry panel – attach results
- Urinalysis – attach results

Radiology Studies: (if available)

- Thoracic Radiographs – attach results
- Myelogram / CT / MRI (if available) – attach results

Blood Samples for Genetic Research:

- Obtain pedigree of DM affected dog
- Collect 5.0 to 10 ml of blood in EDTA tubes from DM affected dog and related dogs (siblings and parents) and ship sample as soon as possible.

Sample submission for Boxers:

- When submitting samples from Boxers, visit www.dogdna.org or contact sample coordinator of the Broad Institute at dog-info@broad.mit.edu.

Sample submission for other breeds (e.g. Rhodesian Ridgeback, Pembroke Welsh Corgi):

- Please email (HansenL@missouri.edu) or call (573-884-3712).
- Complete Individual Dog Information Form (www.caninegeneticdiseases.net)
- Ship blood samples on **ice packs** and pedigree over-night Attn: Dr. Gary Johnson, 320 Connaway Hall, College of Veterinary Medicine, University of Missouri, Columbia, MO 65211

Spinal Cord Sample for Diagnosis:

- Remove section of spinal cord from **T10 to L2** and place in 10% buffered formalin
- Record time of euthanasia _____
- Record time of spinal cord removal _____
- Send tissues to Dr. Joan R. Coates, Department of Veterinary Medicine and Surgery, 379 E. Campus Drive, Clydesdale Hall, University of Missouri, Columbia, MO 65211 or to Dr. Gary Johnson
- Please email: CoatesJ@missouri.edu or call (573-882-7821) prior to shipping

Signalment

Date of Sample Submission: _____

Owner's Name: _____

Address: _____

Phone: Home: _____

Work: _____

Email: _____

Dog's Name: _____

D.O.B. _____ Age _____

Sex Female Male Neutered

Breed: _____

Colors: _____

Referring DVM:

Name: _____

Address: _____

Phone: _____

History

Chief Complaint		
History of Present illness (describe signs, start and rapidity of disease progression)		
Past History		
	Vaccination	
	Deworming	
	Prior illness	
	Surgery	
	Trauma	
	Toxicity	
Medications (include insecticides)		
Environment		
	Family History (other related dogs affected)	
Diet		
	Dog food	
	Supplements	

Physical Examination

T _____ P _____ R _____ Wt _____ lbs

Outline	NAF	Description of Abnormal Findings
General		
Eyes, Ears, Nose		
Skin		
Musculoskeletal		
Cardiovascular		
Respiratory		
Digestive		
Urinary		
Reproductive		
Lymphatic		
Neurologic		
Other		

NAF = No Abnormal Findings

Neurologic Examination Findings (At time of Euthanasia)

MENTATION: Alert Obtunded Disoriented
 Stupor Coma

MUSCLE MASS/TONE:

 Increased tone in pelvic limbs Decreased tone in pelvic limbs
 Muscle atrophy in pelvic limbs Muscle atrophy in all limbs

TREMORS: yes (Location) _____ no

POSTURE: Normal Head Tilt Falling Wide base stance

GAIT:

Date gait abnormalities first noticed: _____

Gait at time of euthanasia: (Circle all that apply)

 Normal Ataxia Pelvic limbs only Ataxia all limbs
 Paraparesis Right asymmetric paraparesis Left asymmetric paraparesis
 Intermittently falls in pelvic limbs Frequently falls in pelvic limbs
 Unable to support weight but still can move pelvic limbs
 Paraplegia
 Thoracic limb weakness
 Tetraplegia

FECAL INCONTINENCE: yes no Date of onset: _____

URINARY INCONTINENCE: yes no Date of onset: _____

POSTURAL REACTIONS: N=Normal; ↑= Exaggerated; ↓=Decreased; A=Absent

Left	Reaction	Right
	Proprioception	
	Fore	
	Rear	
	Hopping	
	Fore	
	Rear	
	Extensor Postural Thrust	
	Fore	
	Rear	
	Wheelbarrowing	
	Fore	
	Rear	

CRANIAL NERVES: N=Normal; ↑= Exaggerated; ↓=Decreased; A=Absent

Left	Nerve + Function	Right
	II Vision + Menace	
	II/III Pupil Size	
	V/VI/VII Corneal	
	V/VII Palpebral	
	II/III PLR	
	VIII Strabismus	
	Spontaneous Nystagmus (direction)	
	Positional Nystagmus	
	Physiologic Nystagmus	
	V Sensation Face	
	VII Sensation Pinnae	
	V Mastication	
	VII Facial Muscles, Symmetry	
	IX/X Swallowing	
	XII Tongue	

SPINAL REFLEXES: N=Normal; ↑= Exaggerated; ↓=Decreased; A=Absent

	Left	Reflex	Right
Myotactic		Triceps	
		Biceps	
		Patellar	
		Gastrocnemius	
		Cranial Tibial	
Flexor		Flexor Fore	
		Flexor Hind	
		Cutaneous Trunci	

Crossed Extensor: L fore _____ R fore _____ L hind _____ R hind _____

Perineal Reflex: **exaggerated** **normal** **decreased** **absent**

TAIL TONE: **normal** **decreased** **absent**

PAIN ON SPINAL MUSCLE PALPATION:

Cervical: **yes** **no** **Thoracic:** **yes** **no**

Lumbar: **yes** **no** **Sacral:** **yes** **no**

SENSATION: N=Normal; ↑= Exaggerated; ↓=Decreased; A=Absent

Superficial Pain		Deep Pain
	L fore	
	R fore	
	L hind	
	R hind	