

Degenerative Myelopathy tests and Bernese Mountain Dogs



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Degenerative myelopathy : a fatal neurodegenerative disease

age of onset : late, from 8 years old to older
No sex predisposition

What is observed :

Loss of coordination in the rear limbs until paraplegia
Loss of urinary and fecal continence

Disease is progressive, the duration can exceed 3 years but euthanasia is often elected when the dog becomes paraplegic.

Definitive diagnostic is post-mortem by the histopathologic observation of axonal and myelin degeneration

Many canine breeds are affected by DM.

In 2009 : a first mutation for all the breeds

Genome-wide association analysis reveals a *SOD1* mutation in canine degenerative myelopathy that resembles amyotrophic lateral sclerosis

Tomoyuki Awano^a, Gary S. Johnson^{a,1}, Claire M. Wade^{b,c}, Martin L. Katz^{a,d}, Gayle C. Johnson^a, Jeremy F. Taylor^e, Michele Perloski^b, Tara Biagi^b, Izabella Baranowska^f, Sam Long^g, Philip A. March^h, Natasha J. Olbyⁱ, G. Diane Shelton^j, Shahnawaz Khan^a, Dennis P. O'Brien^k, Kerstin Lindblad-Toh^{b,l}, and Joan R. Coates^k

In 2011 : a second mutation for the BMD only

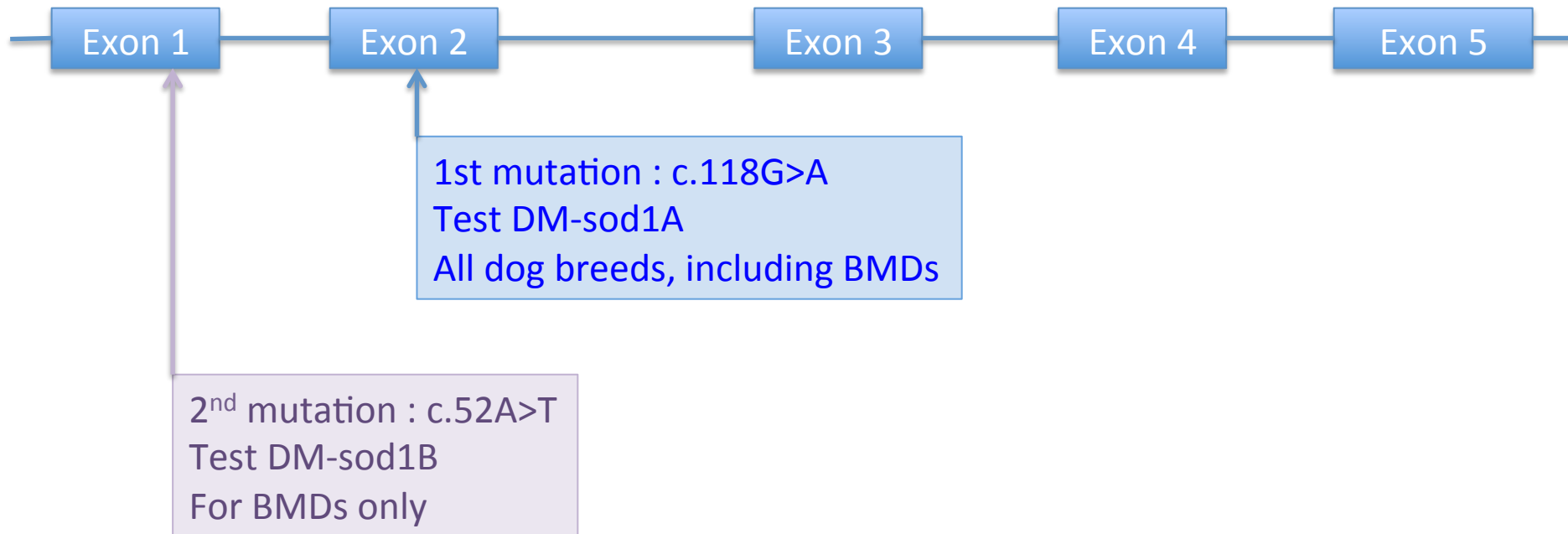
Degenerative Myelopathy in a Bernese Mountain Dog with a Novel *SOD1* Missense Mutation

F.A. Wininger, R. Zeng, G.S. Johnson, M.L. Katz, G.C. Johnson, W.W. Bush, J.M. Jarboe, and J.R. Coates

What we have :






One disease

Two mutations in one same gene : SOD1




Inheritance : autosomal recessive






What are the possibilities for one dog?

	SOD1-A	SOD1-B	Disease status
	Clear	Clear	Healthy
	Heterozygous	Clear	Healthy
	Clear	Heterozygous	Healthy
	Mutated	Clear	Affected
	Clear	Mutated	Affected


What else?

	SOD1-A	SOD1-B	Disease status
	Heterozygous	Heterozygous	


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	SOD1-A	SOD1-B	Disease status
	Heterozygous	Heterozygous	Affected in (almost) all cases

Other possibilities are very very rare

	SOD1-A	SOD1-B	Disease status
	Heterozygous	Heterozygous	Affected in almost all cases

Why?



One individual but two copies of the gene SOD1



























One copy
with the
mutation
SOD1-A















One copy
with the
mutation
SOD1-B

























None of the copies are normal
None of them are functional -> animal =affected













What about matings?

Dog A	Dog B	Puppies
		   
	Either 1st or 2 nd mut 	   
	Either 1st or 2 nd mut 	   
		   

Dog A	Dog B	Puppies
SOD1-A 	SOD1-A 	   
SOD1-B 	SOD1-B 	   

























What about matings?



















Dog A	Dog B	Puppies
		   
	Either 1st or 2 nd mut 	   
	Either 1st or 2 nd mut 	   
		   

Dog A	Dog B	Puppies
SOD1-A 	SOD1-A 	   
SOD1-B 	SOD1-B 	   

What about mating an heterozygote SOD1-A with an heterozygote SOD1-B?
Is this like two independant mutations?

What about matings?

Dog A	Dog B	Puppies
		   
	Either 1st or 2 nd mut 	   
	Either 1st or 2 nd mut 	   
		   

Dog A	Dog B	Puppies
SOD1-A 	SOD1-A 	   
SOD1-B 	SOD1-B 	   
SOD1-A 	SOD1-B 	   

Any other mating produce affected dogs.

Frequencies

SOD1-A (1st mutation) : for the BMDs, over 750 tested dogs – European Countries

47,2% healthy

42,5% heterozygous

10,3% mutated dog

SOD1-B (2nd mutation) : for the BMDs, over 650 tested dogs – European Countries

82,3% healthy

17,1% heterozygous

0,6% mutated dog

Resume

Two mutations:

1st mutation : c.118G>A
Test DM-sod1A
All dog breeds, including BMDs

2nd mutation : c.52A>T
Test DM-sod1B
For BMDs only

High frequency

Moderate frequency BUT be careful!

Breeders have to test both mutations
and be careful with their matings



Double heterozygote dog is affected,
mating two « simple » heterozygotes has
to be avoided



Thanks for your attention

Question?

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