

Swab code: len100100\_swab  
Swab activated on 7/29/2022  
Results completed on 7/29/2022  
Report accessed on 7/29/2022  
Ordered by Lorenz Connelly

vetsupport@embarkvet.com  
1-855-203-8271

## Patient Information

### Lenny

6 yrs 2 mths - NM  
Genetic Age: 55 human years  
Predicted Adult Weight: 90 lbs

## Client Information

### Shan Fry

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555-555-4222

## Breed Information

100.0% Doberman Pinscher



### 1 Increased Risk Result

Dilated Cardiomyopathy, DCM1

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### 219 Clear Results

Lenny is not at increased risk for 219 of the genetic health variants that Embark tests.

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### Glossary

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## 1 Increased Risk Result

### Dilated Cardiomyopathy, DCM1

#### Doberman Pinscher Variant 1

#### How to interpret this result

Lenny has two copies of this dominant variant in the PDK4 gene and is considered at risk for developing Dilated Cardiomyopathy. DCM is characterized by dilation of the ventricles with ventricular wall thinning and can often lead to congestive heart failure. There are two known genetic variants (PDK4 and TTN) that may predispose dogs in certain populations of Doberman Pinschers to DCM. There are likely other genetic variants that increase the risk of DCM in Dobermans and many yet to be determined variants in other breeds. Environment, nutrition, and other factors also likely contribute.

You can learn more about clinical signs, monitoring, and care for Lenny below or email [vetsupport@embarkvet.com](mailto:vetsupport@embarkvet.com) should you desire to speak with a genetic counselor.

#### What is Dilated Cardiomyopathy, DCM1?

Dilated cardiomyopathy (DCM) has been reported to be the most common myocardial disease affecting dogs. DCM is characterized by dilation of the ventricles with ventricular wall thinning. In many cases, dilation of all four chambers of the heart is seen. In general, DCM typically progresses through two distinct stages. An asymptomatic stage, often referred to as the occult stage (dogs with no clinical signs that may have abnormalities detectable by diagnostic testing) and an overt stage, in which clinical signs attributable to congestive heart failure (CHF) become apparent. When caught early, DCM may respond to medical management slowing the progression of the disease but DCM can often lead to congestive heart failure.

#### Age of Onset of Clinical Signs or Symptoms

It is recommended that Dobermans that have the DCM1 and/or DCM2 variants have yearly monitoring echocardiograms and Holter monitors beginning at three years of age.

#### Variant Info

PDK4

Dominant inheritance

2 copies of the variant

## Clinical Signs

As the ability of the heart to serve as a pump is diminished, dogs with DCM may have decreased oxygen in the blood, causing lethargy, weakness, weight loss, and/or collapse. If there is secondary congestive heart failure, dogs may experience pulmonary edema, pleural effusion, or ascites resulting in coughing, increased respiratory rate and/or effort, or abdominal distention. Cardiac dilation, decreased oxygen supply, and increased oxygen demand secondary to elevated heart rate and ventricular wall stress may predispose to the development of cardiac arrhythmias arising from either the atria (atrial fibrillation, supraventricular tachycardia) or from the ventricles (ventricular premature complexes, ventricular tachycardia). Syncope and sudden death are possible sequelae.

## Penetrance and Additional Impact on Phenotype

The vast majority of research exploring the genetics of DCM has been performed on purebred American Dobermans, a high-risk population for DCM. Even in the Doberman, PDK4 (DCM1) and TTN (DCM2) are incompletely penetrant, meaning that while having one or two copies of these variants is thought to confer some increased risk of developing DCM, it is by no means predictive of disease. DCM is a highly complex disease that is modulated by many genetic factors, most unknown.

While the statistics have not been published, Dr. Kate Meurs, at NC State quotes 37% of Dobermans with the DCM1 (PDK4) mutation will develop disease, 50% with the DCM2 (TTN) mutation will develop disease, and 60% with the DCM1 and DCM2 mutations will go on to develop disease. These statistics correlate more to disease in American lines of Dobermans than European lines of Dobermans (European dogs have a lower rate of clinical disease). Additionally, while present in other breeds of dogs, the variants do not seem to be clinically correlated to heart disease in breeds other than Dobermans, and even Doberman mixes appear to have a lower risk from the variant(s).

## Follow-up Diagnostics to Consider

A dilated heart will have an enlarged and/or displaced silhouette on radiographs. DCM is diagnosed by echocardiography, and characteristic findings of DCM include progressive dilation of the left or both ventricles with concurrent systolic dysfunction (reduced fractional shortening). Electrocardiography (EKG) may also be used to characterize heart rhythm and to identify arrhythmias. Because arrhythmias may be transient, a Holter monitor to measure heart rhythm over a 24-hour period is a more sensitive diagnostic test.

## Treatment and Management Options

- Oral or injectable cardiac medications can be given in an effort to improve systolic function of the heart, dilate the peripheral blood vessels to decrease ventricular workload, eliminate pulmonary congestion if present, and control heart rate and cardiac arrhythmias if present.
- Unfortunately, DCM can only be managed; there is no known cure at this time.

## More Information

PDK4 has an important regulatory role in cardiac energy metabolism. Fatty acid oxidation is the preferential form of energy metabolism used by the healthy heart in the non-postprandial state. When glucose levels are high or when fatty acid oxidation is reduced as in an exercising state, circulating fatty acids are suppressed and glucose oxidation, a less efficient source of high energy phosphate generation than fatty acid metabolism, becomes the predominant source of energy. PDK4 plays a pivotal role in regulating energy metabolism by phosphorylating pyruvate dehydrogenase (PDH), and thus decreasing glucose oxidation during periods when fatty acid oxidation can more efficiently generate energy.

One would expect that dogs with this PDK4 defect would then have glucose oxidation as their predominant metabolic pathway, since as glucose oxidation increases, a parallel decrease in fatty acid oxidation has been noted. Ultimately, this change could result in an energy-starved state, since glucose oxidation is a much less efficient source of high energy phosphate production than fatty acid oxidation.

## References

Meurs KM, Lahmers S, Keene BW, et al. A splice site mutation in a gene encoding for PDK4, a mitochondrial protein, is associated with the development of dilated cardiomyopathy in the Doberman pinscher. *Hum Genet.* 2012;131(8):1319-1325. doi:10.1007/s00439-012-1158-2"

Meurs KM, Stern JA, Adin D, Keene BW, De Francesco TC, Tou SP. Assessment of PDK4 and TTN gene variants in 48 Doberman Pinschers with dilated cardiomyopathy. *J Am Vet Med Assoc.* 2020;257(10):1041-1044. doi:10.2460/javma.2020.257.10.1041"

Owczarek-Lipska M, Mausberg TB, Stephenson H, Dukes-McEwan J, Wess G, Leeb T. A 16-bp deletion in the canine PDK4 gene is not associated with dilated cardiomyopathy in a European cohort of Doberman Pinschers. *Anim Genet.* 2013 Apr;44(2):239. doi: 10.1111/j.1365-2052.2012.02396.x. Epub 2012 Jul 27. PMID: 22834541."

Meurs, KM. An Update on Dilated Cardiomyopathy in the Doberman Pinscher. 2016."

# Lenny

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Cornell University College of Veterinary Medicine (n.d.). Canine Dilated Cardiomyopathy (DCM). Retrieved October 21, 2021 from <https://www.vet.cornell.edu/hospitals/companion-animal-hospital/cardiology/canine-dilated-cardiomyopathy-dcm>."

## All Conditions Tested



To view COI and traits information, log into your account.

## Auditory (2)



	Gene	Copies	Results
 Deafness and Vestibular Syndrome of Dobermans, DVDob, DINGS	MYO7A	0	Clear
 Early Onset Adult Deafness, EOAD - Rhodesian Ridgeback Variant	EPS8L2 Deletion Exon 12	0	Clear

## Cardiac (4)

## Dilated Cardiomyopathy




	Gene	Copies	Results
 Dilated Cardiomyopathy, DCM1 - Doberman Pinscher Variant 1	PDK4	2	At risk
 Dilated Cardiomyopathy, DCM2 - Doberman Pinscher Variant 2	TTN	0	Clear

## Other

	Gene	Copies	Results
 Cardiomyopathy and Juvenile Mortality - Belgian Shepherd Variant	YARS2	0	Clear
 Long QT Syndrome - English Springer Spaniel Variant	KCNQ1	0	Clear

## Endocrine (3)

## Hypothyroidism

	Gene	Copies	Results
 Congenital Dyshormonogenic Hypothyroidism with Goiter - Shih Tzu Variant	SLC5A5	0	Clear
 Congenital Hypothyroidism - Rat, Toy Fox, and Hairless Terrier Variant	TPO Exon 3	0	Clear
 Congenital Hypothyroidism - Tenterfield Terrier Variant	TPO Exon 9	0	Clear

## Gastrointestinal (4)

### Gastroenteropathy

	Gene	Copies	Results
✓ Lundehund Syndrome	LEPREL1	0	Clear

### Malabsorptive Disorder

	Gene	Copies	Results
✓ Imerslund-Grasbeck Syndrome, Selective Cobalamin Malabsorption - Beagle Variant	CUBN Exon 8	0	Clear
✓ Imerslund-Grasbeck Syndrome, Selective Cobalamin Malabsorption - Border Collie Variant	CUBN Exon 53	0	Clear
✓ Inherited Selected Cobalamin Malabsorption with Proteinuria - Komondor Variant	CUBN	0	Clear

## Hematologic (32)

### Coagulopathy

	Gene	Copies	Results
✓ Bernard-Soulier Syndrome, BSS - Cocker Spaniel Variant	GP9	0	Clear
✓ Congenital Macrothrombocytopenia - Cairn and Norfolk Terrier Variant	TUBB1 Exon 1	0	Clear
✓ Factor IX Deficiency, Hemophilia B - Rhodesian Ridgeback Variant	F9 Exon 7	0	Clear
✓ Factor IX Deficiency, Hemophilia B - Terrier Variant	F9 Exon 7	0	Clear
✓ Factor VII Deficiency	F7 Exon 5	0	Clear
✓ Factor VIII Deficiency, Hemophilia A - Boxer Variant	F8 Exon 10	0	Clear
✓ Factor VIII Deficiency, Hemophilia A - German Shepherd Variant 1	F8 Exon 11	0	Clear
✓ Factor VIII Deficiency, Hemophilia A - German Shepherd Variant 2	F8 Exon 1	0	Clear
✓ Glanzmann's Thrombasthenia Type I - Great Pyrenees Variant	ITGA2B Exon 13	0	Clear
✓ Glanzmann's Thrombasthenia Type I - Otterhound Variant	ITGA2B Exon 12	0	Clear
✓ May-Hegglin Anomaly - Pug Variant	MYH9	0	Clear

	Gene	Copies	Results
✔ P2Y12 Receptor Platelet Disorder - Greater Swiss Mountain Dog Variant	P2Y12	0	Clear
✔ Platelet Factor X Receptor Deficiency, Scott Syndrome - German Shepherd Dog Variant	TMEM16F	0	Clear
✔ Prekallikrein Deficiency - Shih Tzu Variant	KLKB1 Exon 8	0	Clear
✔ Thrombopathia - American Eskimo Dog Variant	RASGRP1 Exon 5	0	Clear
✔ Thrombopathia - Basset Hound Variant	RASGRP1 Exon 5	0	Clear
✔ Thrombopathia - Landseer Variant	RASGRP1 Exon 8	0	Clear
✔ Von Willebrand Disease Type I, Type I vWD	VWF	0	Clear
✔ Von Willebrand Disease Type II, Type II vWD - Pointer Variant	VWF	0	Clear
✔ Von Willebrand Disease Type III, Type III vWD - Shetland Sheepdog Variant	VWF Exon 7	0	Clear
✔ Von Willebrand Disease Type III, Type III vWD - Terrier Variant	VWF Exon 4	0	Clear

### Red Blood Cell Abnormality

	Gene	Copies	Results
✔ Canine Elliptocytosis - Labrador Retriever Variant	SPTB Exon 30	0	Clear
✔ Methemoglobinemia - Pomeranian Variant	CYB5R3	0	Clear
✔ Pyruvate Kinase Deficiency - Basenji Variant	PKLR Exon 5	0	Clear
✔ Pyruvate Kinase Deficiency - Beagle Variant	PKLR Exon 7	0	Clear
✔ Pyruvate Kinase Deficiency - Labrador Retriever Variant	PKLR Exon 7	0	Clear
✔ Pyruvate Kinase Deficiency - Pug Variant	PKLR Exon 7	0	Clear
✔ Pyruvate Kinase Deficiency - Terrier Variant	PKLR Exon 10	0	Clear



**White Blood Cell Abnormality**

	Gene	Copies	Results
✔ Canine Leukocyte Adhesion Deficiency Type I, CLAD I - Setter Variant	ITGB2 Exon 3	0	Clear
✔ Canine Leukocyte Adhesion Deficiency Type III, CLAD III - German Shepherd Variant	FERMT3	0	Clear
✔ Trapped Neutrophil Syndrome, TNS	VPS13B Exon 19	0	Clear

**Other**

	Gene	Copies	Results
✔ Ligneous Membranitis, LM - Scottish Terrier Variant	PLG	0	Clear

**Immunologic (6)**

	Gene	Copies	Results
✔ Complement 3 Deficiency, C3 Deficiency - Brittany Variant	C3	0	Clear
✔ Severe Combined Immunodeficiency, SCID - Terrier Variant	PRKDC	0	Clear
✔ Severe Combined Immunodeficiency, SCID - Wetterhoun Variant	RAG1	0	Clear
✔ Shar-Pei Autoinflammatory Disease, SPAID, Shar-Pei Fever	MTBP	0	Clear
✔ X-linked Severe Combined Immunodeficiency, X-SCID - Basset Hound Variant	IL2RG Exon 1	0	Clear
✔ X-linked Severe Combined Immunodeficiency, X-SCID - Corgi Variant	IL2RG	0	Clear

**Integument (18)****Collagen Abnormality**

	Gene	Copies	Results
✔ Dystrophic Epidermolysis Bullosa - Central Asian Shepherd Dog Variant	COL7A1	0	Clear
✔ Dystrophic Epidermolysis Bullosa - Golden Retriever Variant	COL7A1 Exon 68	0	Clear

	Gene	Copies	Results
✓ Ehlers Danlos - Doberman Pinscher Variant	ADAMTS2	0	Clear
✓ Musladin-Lueke Syndrome, MLS - Beagle Variant	ADAMTSL2 Exon 7	0	Clear

**Keratin Abnormality**

	Gene	Copies	Results
✓ Congenital Keratoconjunctivitis Sicca and Ichthyosiform Dermatitis, Dry Eye Curly Coat Syndrome, CKCSID - Cavalier King Charles Spaniel Variant	FAM83H	0	Clear
✓ Focal Non-Epidermolytic Palmoplantar Keratoderma, Pachyonychia Congenita - Dogue de Bordeaux Variant	KRT16 Exon 6	0	Clear
✓ Hereditary Footpad Hyperkeratosis - Rottweiler Variant	DSG1	0	Clear
✓ Hereditary Footpad Hyperkeratosis - Terrier and Kromfohrlander Variant	FAM83G	0	Clear
✓ Hereditary Nasal Parakeratosis, HNPk - Labrador Retriever Variant	SUV39H2	0	Clear
✓ Ichthyosis, Epidermolytic Hyperkeratosis - Terrier Variant	KRT10 Intron 5	0	Clear
✓ Ichthyosis, ICH1 - Golden Retriever Variant	PNPLA1 Exon 8	0	Clear
✓ Ichthyosis - American Bulldog Variant	NIPAL4 Exon 6	0	Clear
✓ Ichthyosis - Great Dane Variant	SLC27A4	0	Clear

**Other**

	Gene	Copies	Results
✓ Bald Thigh Syndrome - Greyhound Variant	IGFBP5	0	Clear
✓ Ectodermal Dysplasia, Skin Fragility Syndrome - Chesapeake Bay Retriever Variant	PKP1 Intron 1	0	Clear
✓ Lethal Acrodermatitis, LAD - Bull Terrier Variant	MKLN1	0	Clear

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	Gene	Copies	Results
✔ Oculocutaneous Albinism, OCA - Small Breed Variant	SLC45A2	0	Clear
✔ X-linked Ectodermal Dysplasia, Anhidrotic Ectodermal Dysplasia, XHED - German Shepherd Dog Variant	EDA	0	Clear

## Metabolic (33)

### Enzyme Deficiency

	Gene	Copies	Results
✔ Hypocatalasia, Acatlasemia - Beagle Variant	CAT	0	Clear
✔ L-2-Hydroxyglutaricaciduria, L2HGA - Staffordshire Bull Terrier Variant	L2HGDH	0	Clear
✔ Pyruvate Dehydrogenase Deficiency - Spaniel Variant	PDP1	0	Clear

### Storage Disease

	Gene	Copies	Results
✔ Canine Fucosidosis - English Springer Spaniel Variant	FUCA1	0	Clear
✔ GM1 Gangliosidosis - Alaskan Husky Variant	GLB1 Exon 15	0	Clear
✔ GM1 Gangliosidosis - Portuguese Water Dog Variant	GLB1 Exon 2	0	Clear
✔ GM1 Gangliosidosis - Shiba Inu Variant	GLB1 Exon 15	0	Clear
✔ GM2 Gangliosidosis - Japanese Chin Variant	HEXA	0	Clear
✔ GM2 Gangliosidosis - Poodle Variant	HEXB Exon 3	0	Clear
✔ Globoid Cell Leukodystrophy, Krabbe Disease - Terrier Variant	GALC Exon 5	0	Clear
✔ Glycogen Storage Disease Type IA, Von Gierke Disease, GSD IA - Maltese Variant	G6PC	0	Clear
✔ Glycogen Storage Disease Type II, Pompe's Disease, GSD II - Finnish and Swedish Lapphund, Lapponian Herder Variant	GAA Exon 15	0	Clear
✔ Glycogen Storage Disease Type IIIA, GSD IIIA - Curly Coated Retriever Variant	AGL GDE	0	Clear

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	Gene	Copies	Results
✓ Glycogen storage disease Type VII, Phosphofructokinase Deficiency, PFK Deficiency - Wachtelhund Variant	PFKM Exon 8	0	Clear
✓ Glycogen storage disease Type VII, Phosphofructokinase Deficiency, PFK Deficiency - Whippet and English Springer Spaniel Variant	PFKM Exon 21	0	Clear
✓ Lagotto Storage Disease	ATG4D Exon 10	0	Clear
✓ Late-Onset Neuronal Ceroid Lipofuscinosis, NCL12 - Australian Cattle Dog Variant	ATP13A2	0	Clear
✓ Mucopolysaccharidosis IIIB, Sanfilippo Syndrome Type B, MPS IIIB - Schipperke Variant	NAGLU	0	Clear
✓ Mucopolysaccharidosis Type IIIA, Sanfilippo Syndrome Type A, MPS IIIA - Dachshund Variant	SGSH	0	Clear
✓ Mucopolysaccharidosis Type IIIA, Sanfilippo Syndrome Type A, MPS IIIA - New Zealand Huntaway Variant	SGSH	0	Clear
✓ Mucopolysaccharidosis Type VII, Sly Syndrome, MPS VII - German Shepherd Variant	GUSB	0	Clear
✓ Mucopolysaccharidosis Type VII, Sly Syndrome, MPS VII - Terrier Brasileiro Variant	GUSB	0	Clear
✓ Neuronal Ceroid Lipofuscinosis 1, NCL1 - Dachshund Variant	PPT1 Exon 8	0	Clear
✓ Neuronal Ceroid Lipofuscinosis 10, NCL10 - American Bulldog Variant	CTSD Exon 5	0	Clear
✓ Neuronal Ceroid Lipofuscinosis 2, NCL2 - Dachshund Variant	TPP1 Exon 4	0	Clear
✓ Neuronal Ceroid Lipofuscinosis 5, NCL5 - Border Collie and Australian Cattle Dog Variant	CLN5 Exon 4	0	Clear
✓ Neuronal Ceroid Lipofuscinosis 5, NCL5 - Golden Retriever Variant	CLN5 Exon 4	0	Clear
✓ Neuronal Ceroid Lipofuscinosis 6, NCL6 - Australian Shepherd Variant	CLN6 Exon 7	0	Clear
✓ Neuronal Ceroid Lipofuscinosis 7, NCL7 - Chihuahua and Chinese Crested Variant	MFSD8	0	Clear
✓ Neuronal Ceroid Lipofuscinosis 8, NCL8 - Australian Shepherd and German Shorthaired Pointer Variant	CLN8	0	Clear

	Gene	Copies	Results
✓ Neuronal Ceroid Lipofuscinosis 8, NCL8 - English Setter Variant	CLN8 Exon 2	0	Clear
✓ Neuronal Ceroid Lipofuscinosis 8, NCL8 - Saluki Variant	CLN8	0	Clear
✓ Neuronal Ceroid Lipofuscinosis, Cerebellar Ataxia, NCL4A - American Staffordshire Terrier Variant	ARSG Exon 2	0	Clear

## Muscular (13)

### Movement Disorder

	Gene	Copies	Results
✓ Myotonia Congenita - Australian Cattle Dog Variant	CLCN1 Exon 23	0	Clear
✓ Myotonia Congenita - Miniature Schnauzer Variant	CLCN1 Exon 7	0	Clear

### Muscular Dystrophy

	Gene	Copies	Results
✓ Limb Girdle Muscular Dystrophy - Boston Terrier Variant	SGCD	0	Clear
✓ Muscular Dystrophy - Cavalier King Charles Spaniel Variant 1	DMD	0	Clear
✓ Muscular Dystrophy - Golden Retriever Variant	DMD	0	Clear
✓ Ullrich-like Congenital Muscular Dystrophy - Labrador Retriever Variant 1	COL6A3 Exon 10	0	Clear

### Myopathy

	Gene	Copies	Results
✓ Centronuclear Myopathy, CNM - Labrador Retriever Variant	PTPLA	0	Clear
✓ Exercise-Induced Collapse, EIC	DNM1	0	Clear
✓ Inflammatory Myopathy - Dutch Shepherd Variant	SLC25A12	0	Clear
✓ Inherited Myopathy of Great Danes	BIN1	0	Clear

	Gene	Copies	Results
✔ Myotubular Myopathy 1, X-linked Myotubular Myopathy, XL-MTM - Labrador Retriever Variant	MTM1 Exon 7	0	Clear
✔ Nemaline Myopathy - American Bulldog Variant	NEB	0	Clear
<b>Other</b>			
✔ Myostatin Deficiency, Bully Whippet Syndrome	MSTN	0	Clear

## Neurologic (32)

### Brain or Seizure Disorder

	Gene	Copies	Results
✔ Alaskan Husky Encephalopathy, Subacute Necrotizing Encephalomyelopathy	SLC19A3 Exon 2	0	Clear
✔ Alexander Disease - Labrador Retriever Variant	GFAP Exon 4	0	Clear
✔ Benign Familial Juvenile Epilepsy, Remitting Focal Epilepsy - Lagotto Romagnolo Variant	LG12 Exon 8	0	Clear
✔ Cerebellar Abiotrophy, Neonatal Cerebellar Cortical Degeneration, NCCD - Beagle Variant	SPTBN2	0	Clear
✔ Cerebellar Hypoplasia - Eurasier Variant	VLDLR	0	Clear
✔ Hereditary Ataxia, Cerebellar Degeneration - Old English Sheepdog and Gordon Setter Variant	RAB24 Exon 1	0	Clear
✔ Neonatal Encephalopathy with Seizures, NEWS - Poodle Variant	ATF2	0	Clear
✔ Progressive Early-Onset Cerebellar Ataxia - Finnish Hound Variant	SEL1L	0	Clear
✔ Spinocerebellar Ataxia with Myokymia and/or Seizures - Terrier Variant 2	KCNJ10	0	Clear
✔ Spinocerebellar Ataxia, Late-Onset Ataxia, LoSCA - Terrier Variant 1	CAPN1	0	Clear

	Gene	Copies	Results
✓ Spongy Degeneration with Cerebellar Ataxia 1, SDCA1, SeSAME/EAST Syndrome - Shepherd Variant 1	KCNJ10	0	Clear
✓ Spongy Degeneration with Cerebellar Ataxia 2, SDCA2 - Shepherd Variant 2	ATP1B2	0	Clear

**Movement Disorder**

	Gene	Copies	Results
✓ Degenerative Myelopathy, DM	SOD1A	0	Clear
✓ Hypomyelination and Tremors - Weimaraner Variant	FNIP2	0	Clear
✓ Juvenile Myoclonic Epilepsy - Rhodesian Ridgeback Variant	DIRAS1	0	Clear
✓ Progressive Neuronal Abiotrophy, Canine Multiple System Degeneration, CMSD - Chinese Crested Variant	SERAC1	0	Clear
✓ Progressive Neuronal Abiotrophy, Canine Multiple System Degeneration, CMSD - Kerry Blue Terrier Variant	SERAC1	0	Clear
✓ Shaking Puppy Syndrome, X-linked Generalized Tremor Syndrome - English Springer Spaniel Variant	PLP1	0	Clear

**Narcolepsy**

	Gene	Copies	Results
✓ Narcolepsy - Dachshund Variant	HCRT2	0	Clear
✓ Narcolepsy - Doberman Pinscher Variant	HCRT2	0	Clear
✓ Narcolepsy - Labrador Retriever Variant	HCRT2	0	Clear

**Neurodegenerative Disorder**

	Gene	Copies	Results
✓ Fetal-Onset Neonatal Neuroaxonal Dystrophy - Giant Schnauzer Variant	MFN2	0	Clear
✓ Neuroaxonal Dystrophy, NAD - Rottweiler Variant	VPS11	0	Clear
✓ Neuroaxonal Dystrophy, NAD - Spanish Water Dog Variant	TECPR2	0	Clear

**Neuropathy**

	Gene	Copies	Results
✓ Alaskan Malamute Polyneuropathy, AMPN	NDRG1	0	Clear
✓ Demyelinating Polyneuropathy - Miniature Schnauzer Variant	SBF2/MTRM13	0	Clear
✓ Juvenile Laryngeal Paralysis and Polyneuropathy, Polyneuropathy with Ocular Abnormalities and Neuronal Vacuolation, POANV - Rottweiler Variant	RAB3GAP1	0	Clear
✓ Juvenile-Onset Polyneuropathy, Leonberger Polyneuropathy 1, LPN1	ARHGEF10 Exon 17	0	Clear
✓ Juvenile-Onset Polyneuropathy, Leonberger Polyneuropathy 2, LPN2	GJA9	0	Clear
✓ Laryngeal Paralysis - Miniature Bull Terrier Variant	RAPGEF6	0	Clear

**Sensory Neuropathy**

	Gene	Copies	Results
✓ Hereditary Sensory Autonomic Neuropathy, Acral Mutilation Syndrome, AMS - Spaniel and Pointer Variant	GDNF-AS	0	Clear
✓ Sensory Neuropathy - Border Collie Variant	FAM134B	0	Clear

**Neuromuscular (7)****Junctionopathy**

	Gene	Copies	Results
✓ Congenital Myasthenic Syndrome, CMS - Golden Retriever Variant	COLQ Exon 13	0	Clear
✓ Congenital Myasthenic Syndrome, CMS - Heideterrier Variant	CHRNE	0	Clear
✓ Congenital Myasthenic Syndrome, CMS - Jack Russell Terrier Variant	CHRNE Exon 7	0	Clear
✓ Congenital Myasthenic Syndrome, CMS - Labrador Retriever Variant	COLQ Exon 14	0	Clear
✓ Congenital Myasthenic Syndrome, CMS - Old Danish Pointing Dog Variant	CHAT Exon 6	0	Clear



**Movement Disorder**

	Gene	Copies	Results
✓ Episodic Falling Syndrome - Cavalier King Charles Spaniel Variant	BCAN Exons 1-4	0	Clear
✓ Paroxysmal Dyskinesia, PxD - Soft Coated Wheaten Terrier Variant	PIGN	0	Clear

**Ophthalmologic (31)****Glaucoma**

	Gene	Copies	Results
✓ Goniodysgenesis and Glaucoma, Pectinate Ligament Dysplasia, PLD - Border Collie Variant	OLFML3	0	Clear
✓ Primary Open Angle Glaucoma and Primary Lens Luxation - Chinese Shar-Pei Variant	ADAMTS17	0	Clear
✓ Primary Open Angle Glaucoma - Basset Fauve de Bretagne Variant	ADAMTS17	0	Clear
✓ Primary Open Angle Glaucoma - Beagle Variant	ADAMTS10	0	Clear
✓ Primary Open Angle Glaucoma - Norwegian Elkhound Variant	ADAMTS10	0	Clear

**Iris or Lens**

	Gene	Copies	Results
✓ Hereditary Cataracts, Early-Onset Cataracts, Juvenile Cataracts - Australian Shepherd Variant	HSF4	0	Clear
✓ Primary Lens Luxation	ADAMTS17	0	Clear

**Retinopathy**

	Gene	Copies	Results
✓ Achromatopsia - German Shepherd Variant	CNGA3 Exon 7	0	Clear
✓ Achromatopsia - Labrador Retriever Variant	CNGA3 Exon 7	0	Clear
✓ Autosomal Dominant Progressive Retinal Atrophy - English Mastiff and Bullmastiff Variant	RHO Exon 1	0	Clear
✓ Canine Multifocal Retinopathy, cmr1	BEST1/VMD2 Exon 2	0	Clear

	Gene	Copies	Results
✓ Canine Multifocal Retinopathy, cmr2 - Coton de Tulear Variant	BEST1/VMD2 Exon 5	0	Clear
✓ Canine Multifocal Retinopathy, cmr3 - Finnish and Swedish Lapphund, Lapponian Herder Variant	BEST1/VMD2 Exon 10	0	Clear
✓ Collie Eye Anomaly, Choroidal Hypoplasia, CEA	NHEJ1 Intron 4	0	Clear
✓ Congenital Stationary Night Blindness - Beagle Variant	LRIT3	0	Clear
✓ Congenital Stationary Night Blindness - Briard Variant	RPE65	0	Clear
✓ Day Blindness, Cone Degeneration, Achromatopsia - Alaskan Malamute Variant	CNGB3 Deletion	0	Clear
✓ Day Blindness, Cone Degeneration, Achromatopsia - German Shorthaired Pointer Variant	CNGB3 Exon 6	0	Clear
✓ Golden Retriever Progressive Retinal Atrophy 1, GR-PRA1	SLC4A3 Exon 16	0	Clear
✓ Golden Retriever Progressive Retinal Atrophy 2, GR-PRA2	TTC8 Exon 8	0	Clear
✓ Macular Corneal Dystrophy, MCD - Labrador Retriever Variant	CHST6	0	Clear
✓ Progressive Retinal Atrophy, CNGA - Shetland Sheepdog Variant	CNGA1 Exon 9	0	Clear
✓ Progressive Retinal Atrophy, Cone-Rod Dystrophy 1, crd1 - American Staffordshire Terrier Variant	PDE6B	0	Clear
✓ Progressive Retinal Atrophy, Cone-Rod Dystrophy 4, crd4/crd1	RPGRIP1 Exon 2	0	Clear
✓ Progressive Retinal Atrophy, PRA1 - Papillon Variant	CNGB1	0	Clear
✓ Progressive Retinal Atrophy, PRA3 - Tibetan Spaniel and Terrier Variant	FAM161A	0	Clear
✓ Progressive Retinal Atrophy, Progressive Rod-Cone Degeneration, prcd	PRCD Exon 1	0	Clear
✓ Progressive Retinal Atrophy, Rod-Cone Dysplasia 1, rcd1 - Irish Setter Variant	PDE6B Exon 21	0	Clear
✓ Progressive Retinal Atrophy, Rod-Cone Dysplasia 3, rcd3 - Corgi Variant	PDE6A	0	Clear

	Gene	Copies	Results
✓ Progressive Retinal Atrophy - Basenji Variant	SAG	0	Clear
✓ X-Linked Progressive Retinal Atrophy 1, XL-PRA1 - Samoyed and Husky Variant	RPGR Exon 15	0	Clear

## Oral Cavity (4)

### Developmental Disorder

	Gene	Copies	Results
✓ Cleft Lip and/or Cleft Palate - Nova Scotia Duck Tolling Retriever Variant	ADAMTS20	0	Clear

### Tooth Structure Defect

	Gene	Copies	Results
✓ Autosomal Recessive Amelogenesis Imperfecta, Familial Enamel Hypoplasia - Italian Greyhound Variant	ENAM	0	Clear
✓ Autosomal Recessive Amelogenesis Imperfecta, Familial Enamel Hypoplasia - Parson Russell Terrier Variant	ENAM	0	Clear
✓ Raine Syndrome, Canine Dental Hypomineralization Syndrome - Border Collie Variant	FAM20C	0	Clear

## Personalized Medicine (3)

	Gene	Copies	Results
✓ Alanine Aminotransferase Activity	GPT	0	Clear
✓ MDR1 Drug Sensitivity	ABCB1	0	Clear
✓ Malignant Hyperthermia	RYR1	0	Clear

## Pulmonary (4)

	Gene	Copies	Results
✓ Neonatal Interstitial Lung Disease - Airedale Terrier Variant	LAMP3	0	Clear

	Gene	Copies	Results
✓ Primary Ciliary Dyskinesia, PCD - Alaskan Malamute Variant	NME5	0	Clear
✓ Primary Ciliary Dyskinesia, PCD - Old English Sheepdog Variant	CCDC39	0	Clear
✓ Recurrent Inflammatory Pulmonary Disease, RIPD - Rough Collie Variant	AKNA	0	Clear

## Skeletal (10)

### Chondrodystrophy

	Gene	Copies	Results
✓ Chondrodystrophy and Intervertebral Disc Disease, CDDY/IVDD, Type I IVDD - Retrogene	FGF4 - chr12	0	Clear
✓ Chondrodystrophy - Norwegian Elkhound and Karelian Bear Dog Variant	ITGA10	0	Clear
✓ Oculoskeletal Dysplasia 2, Dwarfism-Retinal Dysplasia 2, drd2, OSD2 - Samoyed Variant	COL9A2 5' UTR	0	Clear
✓ Osteochondrodysplasia, Skeletal Dwarfism - Miniature Poodle Variant	SLC13A1	0	Clear
✓ Skeletal Dysplasia 2, SD2 - Labrador Retriever Variant	COL11A2	0	Clear

### Decreased Bone Strength

	Gene	Copies	Results
✓ Hereditary Vitamin D-Resistant Rickets - Pomeranian Variant	VDR Exon 4	0	Clear
✓ Osteogenesis Imperfecta, Brittle Bone Disease - Beagle Variant	COL1A2	0	Clear
✓ Osteogenesis Imperfecta, Brittle Bone Disease - Dachshund Variant	SERPINH1 Exon 5	0	Clear
✓ Osteogenesis Imperfecta, Brittle Bone Disease - Golden Retriever Variant	COL1A1 Exon 18	0	Clear

### Other

	Gene	Copies	Results
✓ Craniomandibular Osteopathy, CMO - Terrier and Australian Shepherd Variant	SLC37A2 Exon 15	0	Clear

## Urogenital (14)

## Nephropathy

	Gene	Copies	Results
✓ Autosomal Recessive Hereditary Nephropathy, Familial Nephropathy, ARHN - Cocker Spaniel Variant	COL4A4 Exon 3	0	Clear
✓ Autosomal Recessive Hereditary Nephropathy, Familial Nephropathy, ARHN - English Springer Spaniel Variant	COL4A4 Exon 30	0	Clear
✓ Fanconi Syndrome - Basenji Variant	FAN1	0	Clear
✓ Polycystic Kidney Disease, PKD - Bull Terrier Variant	PKD1 Exon 29	0	Clear
✓ Protein Losing Nephropathy, PLN - Soft Coated Wheaten and Airedale Terrier Variant	NPHS1	0	Clear
✓ X-Linked Hereditary Nephropathy, XLHN - Samoyed Variant 2	COL4A5 Exon 35	0	Clear

## Urolithiasis

	Gene	Copies	Results
✓ 2,8-Dihydroxyadenine Urolithiasis, 2,8-DHA Urolithiasis - American Indian Dog Variant	APRT Exon 3	0	Clear
✓ Cystinuria Type I-A - Newfoundland Variant	SLC3A1 Exon 2	0	Clear
✓ Cystinuria Type II-A - Australian Cattle Dog Variant	SLC3A1 Exon 6	0	Clear
✓ Cystinuria Type II-B - Miniature Pinscher Variant	SLC7A9 Exon 9	0	Clear
✓ Hyperuricosuria and Hyperuricemia or Urolithiasis, HUU	SLC2A9 Exon 5	0	Clear
✓ Primary Hyperoxaluria - Coton de Tulear Variant	AGXT Exon 2	0	Clear

## Other

	Gene	Copies	Results
✓ Persistent Mullerian Duct Syndrome, PMDS - Miniature and Standard Schnauzer Variant	AMHR2	0	Clear
✓ Renal Cystadenocarcinoma and Nodular Dermatofibrosis, RCND - German Shepherd Dog Variant	FLCN	0	Clear

## Glossary

### Key Terms

#### Increased Risk Result

The dog is at risk for showing clinical signs (phenotype) of a given condition. For recessive conditions, this means a dog has inherited two copies of an associated variant. For dominant, codominant, and additive conditions, this means a dog has inherited at least one copy of the variant. X-linked conditions will vary based on sex of the dog.

A dog's breed(s) and genetic background are also considered in this assessment. Genetic testing is an assessment of risk and not a clinical diagnosis, and not all dogs in this category will develop clinical signs.

#### Notable Result

A result may be notable for several reasons. The variant may not induce a disease state but rather inform patient care (this may include the tests listed under Personalized Medicine). The dog may have only one copy of a variant with a recessive mode of inheritance (meaning the dog is a carrier and is not expected to show the phenotype associated with the variant). The impact of the variant may also be influenced by a dog's breed(s). Based on the available research within the breed or related breeds, you will see more specific text within the results.

#### Clear Result

A dog with two healthy copies of a gene sequence is not at risk for developing the associated disease due to that variant. Many diseases can manifest as a result of other unknown genetic variants and/or environmental factors.

#### Variant

An alteration in the DNA with the potential to cause a change in phenotype (i.e. disease). A report may state that the dog has zero, one, or two copies of the variant for which we test. The term "variant" may be used interchangeably with "mutation."

#### Genotype

The genetic code related to the variant being present or absent in the dog's DNA.

#### Phenotype

The physical impact or appearance directed by the genotype. The phenotype is often described as an expression of the genotype.

#### Complex Phenotype

The condition, appearance, or other physical expression of the genotype controlled by both genetic and environmental factors.

#### Penetrance

Proportion of dogs with a particular genotype that expresses the associated phenotype. There are two types of penetrance.

1. Incomplete penetrance means that not all dogs with the genotype will develop the clinical signs of the phenotype.
2. Complete penetrance means that all dogs with the genotype will develop the clinical signs of the phenotype.

#### Carrier

This term has traditionally been used to describe a dog that has one copy of the variant but is not expected to show the phenotype associated with the variant (this is applicable to variants with a recessive mode of inheritance (MOI) as described below). If used in a breeding pair, a carrier may pass the variant to its litter.

#### At-risk

This indicates that the dog may manifest the disease and generally is used when a dog has two copies of the variant (but this depends on the MOI).

Embark uses the term "at-risk" and not "affected" because genetic testing is an assessment of risk and not a clinical diagnosis.

## Linkage Disequilibrium Test

When a causal variant cannot be identified or when the variant is incompatible with the genotyping platform constraints, allelic association or linkage disequilibrium (LD) tests can be utilized. This is typically done to assist dog breeders in selectively breeding out a deleterious condition. LD tests are based on a statistical association between two loci that are physically very close in the DNA. The coupling of the chosen proxy marker to the causal variant is known mathematically for the most relevant populations.

LD-based tests have a slightly increased incidence of false positives and false negatives, which are test-specific and known. Embark offers limited numbers of these tests. Embark continuously works to refine LD-based tests by assaying the direct variant in a subset of dogs using alternative methods. These inputs help to refine the tests over time.

## Provisional Result

Embark combines random sampling and sequencing with the use of blinded controls to confirm that each test is performing to standard at >99% genotyping accuracy and reproducibility. Our standard health tests have been validated using known heterozygous and homozygous samples to ensure design accuracy and use multiple probes per condition to ensure reproducibility. Provisional tests are for rare disorders for which DNA samples from carrier and/or at-risk individuals are not available for calculating test reliability, or for structural variants where more testing is needed to ensure the same level of accuracy.

If you have access to DNA from carrier or at-risk individuals and are interested in helping us validate a test, please contact us at [vetsupport@embarkvet.com](mailto:vetsupport@embarkvet.com)

## Modes of Inheritance

### Recessive

A dog is thought to need two copies of a variant to be considered at-risk for the clinical disease or to have the visible phenotype for traits. This may apply to autosomal or X-linked variants, however. Read below for additional details regarding X-linked variants.

### Dominant

A dog is thought to need only one copy of the variant to be considered at-risk for the clinical disease or to have the visible phenotype for traits.

### Codominant/Additive

In general, these terms are used to describe variants in which dogs with one copy of the variant have a different phenotype compared to dogs with zero or two copies of the variant (although there is a slight difference between the two terms).

### X-linked

The variant resides on the X chromosome, and male dogs need just one copy of the variant to be considered at-risk. For recessively inherited X-linked conditions, female dogs typically require two copies of the variant to be considered at-risk. Female dogs who have one copy of a recessively inherited X-linked variant are often referred to as carriers, but they can exhibit signs of disease that range from clinically asymptomatic to fully affected. This is due to a normal phenomenon known as X-chromosome inactivation, where one X chromosome is silenced in each cell.

## Weight

The Embark DNA test provides a genetic size based not just on breed ancestry but on over a dozen genes known to influence a dog's weight, as well as sex and breed-specific modifiers.

Our algorithm explains over 85% of the variance in healthy adult weight. However, due to a few as-yet-undiscovered genes and genetic interactions that affect size, this algorithm sometimes under or over-predicts weight.

## Genetic Age

Dogs age at very different rates due to a number of genetic and environmental factors. Embark's genetic age calculates how old a dog would be if he or she were aging at an average human rate (using humans in the USA as the baseline). This measure is more personalized than "one dog year = seven human years".

[View the patient's profile see the personalized genetic age table for this dog.](#)

We start by asking the dog's approximate calendar age. We then calculate genetic age by factoring a dog's breed composition along with information from genes that affect size, sex, and the dog's inbreeding coefficient (COI).

## Impact of Breed

When determining whether or not a variant is expected to have a clinical impact for a breed, we have taken into account research either published, internal, or otherwise presented by a subject matter authority as our primary criteria. So, while a dog may have the variant associated with a disease (one or two copies for dominant variants and two copies for autosomal recessive variants), he or she may not be known to be at significant clinical risk from that variant.

Based on the available research within the breed or highly related breeds, you may see text similar to the following options:

1. This genetic variant is not likely to significantly increase the risk that this dog will develop the clinical disease.
2. This genetic variant is associated with an increased risk that this dog will develop the clinical disease.
3. We do not know whether this variant increases the risk that this dog will develop the clinical disease.

Embark is continuing to explore the relationship of genotype to phenotype, and risk assessment may be updated as more data is reviewed. You can contact [vetsupport@embarkvet.com](mailto:vetsupport@embarkvet.com) or call 1-855-203-8271 to report any clinical diagnoses.