DIAGNOSTIC news

Genetic Screening for Inherited Conditions

By: Tuddow Thaiwong, DVM, PhD, Diplo. ACVP

Why is genetic testing important?

Genetic information obtained from DNA works as a "blueprint" dictating physical and biological characteristics. As half of the information comes from each parent, inherited conditions can be passed on to offspring. The Michigan State University Veterinary Diagnostic Laboratory (MSU VDL) offers a series of diagnostic genetic tests for the purpose of detecting disease-associated genetic alterations and identifying an animal's risk of developing inherited conditions. Moreover, it can help determine a breeding plan leading to the reduction and eventual elimination of inherited conditions in a particular breed. A small blood sample (1 ml) is all that is needed, and the results are ready in two weeks on average.

When should one consider submitting genetic testing?

Genetic testing for inherited conditions should be strongly considered when:

- The animal has a clinical presentation or family history that suggests an inherited condition
- A parent of the animal is a carrier for an inherited condition
- There is a presence of birth defects, such as neurologic or skeletal abnormalities, that are known to be associated with inherited disease
- Purebred or mixed breed animals are known to have an increased chance of having a certain hereditary condition

How does it work?

Genetic testing is performed in different ways, including:

- Diagnostic testing is performed in order to identify or rule out the symptom causing mutation and, in many cases, to confirm the diagnosis.
- Predictive testing is used when there is a probability of carrying the mutation and developing symptoms later in life yet no symptoms are detected.
- Carrier testing is relevant for animals that may carry a mutation (but are not themselves affected) as there is risk for their offspring to be affected.
- Pharmacogenomic testing gives information about how certain medicines are processed by an animal's body. This type of testing can help veterinarians choose the medicines that work best with the animal's genetic makeup.

Conditions

This genetic testing assesses an animal's mutation status for inherited conditions, including:

- Conditions that shorten lifespan or affect quality of life
- Conditions where early treatment can make a difference
- Conditions where specific treatments/managements are required
- Conditions where there are limited or no treatment options available

A full list of inherited conditions/mutations that are currently available at the MSU VDL is included here.

Conditions	Species	Affected breeds	Clinical signs
Centronuclear Myopathy	Canine	Labrador Retrievers	Weight loss, a loss of muscle tone and control, an awkward gait, and extreme exercise intolerance
Degenerative Myelopathy	Canine	Bernese Mountain Dog and multiple breeds	Progressive weakness and incoordination of limbs
Dystrophic Epidermolysis Bullosa	Canine	Golden Retriever	Fragile skin that is easily damaged from rubbing or trauma resulting in blisters and ulcers of the oral and esophageal mucosal, scarring of the skin, nails dystrophy, and growth retardation
Exercise-induced Collapse	Canine	Labrador Retrievers	Wobbly gait after exercise, which soon progresses to nonpainful, flaccid paraparesis and a loss of control of the rear limbs
F7 deficiency	Canine	Airedale Terrier, Beagle, Deerhound, Finnish Hound, Giant Schnauzer, Welsh Springer Spaniel, and Alaskan Klee Kai	Mild bleeding disorder
Hereditary Cataracts	Canine	Australian Shepherd	Bilateral progressive posterior cataract
Hyperuricosuria	Canine	Multiple breeds	Urate urolithiasis, Urinary tract obstruction
Ichthyosis	Canine	Labrador Retriever, Flat-Coated Retriever, Curly Coated Retriever, and Chesapeake Bay Retriever	Excessive production of dandruff, thickened and hyperpigmented skin, generalized scaling
Junctional Epidermolysis Bullosa	Canine	German Pointer	Fragile skin and blistering disorder of the skin and mucous membranes
Late Onset Ataxia	Canine	Parson Russell Terrier and Jack Russell Terrier	Incoordination of gait and lack of balance
Multidrug Sensitivity	Canine	Multiple breeds	Accumulation and toxicity of some drugs
Neonatal Encephalopathy with Seizures	Canine	Poodle	Severe generalized clonic-tonic seizures
Neuronal Ceroid Lipofuscinosis	Canine	Golden Retriever	Progressive neurodegeneration resulting in progressive motor decline with seizures and loss of coordinated muscle movements, cognitive decline and abnormal behavior, and early death
Obesity	Canine	Labrador Retriever, Flat-Coated Retriever	Obesity
Persistent Mullerian Duct Syndrome	Canine	Miniature Schnauzer	Developmental abnormalities of the male reproductive tract
Pituitary Dwarfism	Canine	German Shepherd, White Shepherd, Karelian Bear Dog, Saarloos Wolfdog and the Czechoslovakian Wolfdog	Growth retardation and poor body condition due to inadequate production of the Growth Hormone
Primary Lens Luxation	Canine	Multiple breeds	Dislocation or displacement of the lens in the eye due to weakened zonular fibers
Progressive Retinal Atrophy	Canine	Golden Retrievers and Golden-doodles	Progressive vision loss leading to total blindness due to bilateral degeneration of the retina.

Conditions	Species	Affected breeds	Clinical signs
Progressive Retinal Atrophy	Canine	Multiple breeds	Night blindness and loss of peripheral vision leading to total blindness due to degeneration of both rod and cone photoreceptor cells of the retina
PTPN11 Mutation	Canine	Bernese Mountain Dog and multiple breeds	Histiocytic sarcoma
Renal Cystadenocarcinoma and Nodular Dermatofibrosis	Canine	German Shepherd	Bilateral multifocal tumors in the kidneys, uterine leiomyomas and dermatofibrosis in the skin
Skeletal Dysplasia	Canine	Labrador Retrievers	Short legs with normal length and width of the body
Spinocerebellar Ataxia	Canine	Jack Russell Terrier, Smooth-haired Fox Terrier and Toy Fox Terrier	Prominent hypermetria along with a bouncing gait and falling with difficulty returning to standing position
Von Willebrand's Disease Type 1	Canine	Multiple breeds	Excessive bleeding
Von Willebrand's Disease Type 2	Canine	Chinese Crested, Collie, Deutsch Drahthaar, German Longhaired Pointer, German Shorthaired Point, German Wirehaired Pointer, and Pointer	Bleeding disorder
Von Willebrand's Disease Type 3	Canine	Scottish Terriers, Dutch Kooiker	Severe bleeding disorder
Hypertrophic Cardiomyopathy	Feline	Maine Coon, Ragdoll	Cardiac disease, heart failure
Polycystic Kidney Disease	Feline	Multiple breeds	Renal failure, multiple cysts forming in the kidneys as well as hepatic and pancreatic cysts
Pyruvate Kinase Deficiency	Feline	Multiple breeds	Hemolytic anemia
Spinal Muscular Atrophy	Feline	Maine Coon	Abnormal gaits due to muscle weakness

What happens next?

Results from genetic testing can predict with a high level of confidence that an animal will fall into one of three categories:

An **"Affected"** test result means that the animal has a specific genetic alteration (or mutation) that is associated with a hereditary disease. If the animal has a clinical abnormality, it confirms the diagnosis of a hereditary condition. If the animal is clinically normal, an affected result may indicate an increased risk of developing certain conditions in the future. *However, it does not guarantee the animal will get the disease.* It does mean the mutation will be passed on to offspring.

A **"Carrier"** test result means that the animal has both a normal and mutated copy of the gene (autosomal recessive diseases). Active disease is unlikely to occur. This mutation can, however, be passed to offspring. If both parents have a mutation, there is a 1 in 4 (25%) chance for every pregnancy that the offspring will inherit the mutation from both parents and develop disease.

A **"Clear"** test result means that the animal does not have the gene change. This may mean the disease does not run in their family or was not passed on to them. *A "Clear" result means that the animal is extremely unlikely to develop the genetic condition.* The risk of developing the disease is the same as it is for other animals.

Why MSU VDL?

Our genetic testing has been designed to be highly accurate and comprehensive. We are dedicated to helping veterinarians and pet owners make informed decisions about their animal's health.

Later this year, individual tests will be bundled into breed-specific panels to make it easier to order genetic screening for a particular breed.

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The Michigan State University Veterinary Diagnostic Laboratory client newsletter is here!

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Therapeutic Drug Monitoring for Antiepileptic Drugs in Dogs and Cats

By John Buchweitz, PhD, DABT

To better serve our veterinary clients treating animals with anticonvulsant therapy, the MSU VDL has recently added tests for therapeutic monitoring of Levetiracetam (Keppra) and Zonisamide. These drugs are human medications that have been adopted for veterinary use in situations where the animal becomes refractory to both phenobarbital and potassium bromide. As with phenobarbital or potassium bromide therapy, therapeutic monitoring is important. Therapeutic and toxic effects of drug therapy are related to serum concentrations.

Levetiracetam (Keppra, test code 70057)

Keppra is a new generation antiepileptic drug that is advantageous in that it is nearly 100% bioavailable, has a large margin of safety and, unlike phenobarbital, it is not metabolized by the hepatic cytochrome P450 system. Although a therapeutic range has not been established for either dogs or cats, the therapeutic range for humans (5 – 45 µg/mL) can be adopted and the animal should be monitored to establish baseline and then be repeated if the patient becomes uncontrolled or the owner is noncompliant.

Zonisamide (test code 70056)

Zonisamide is another human anticonvulsant drug adopted for veterinary use with a high margin of safety. Unlike levetiracetam, zonisamide is metabolized by hepatic cytochrome P450 and serum concentrations may be influenced by phenobarbital and related drugs. Similar to levetiracetam, a species-specific therapeutic range is not available for dogs and cats. Therefore, adoption of the therapeutic range for humans (10-40 µg/mL) is acceptable and drug monitoring is important.

It is important to remember that therapeutic drug monitoring parameters are simply guidelines and are not intended to replace clinical assessment and professional judgment. For both tests, a minimum of 0.5 mL of serum collected just prior to the next dose (trough) is appropriate. Analysis is performed by liquid chromatography.

Reference

Dewey, C. W. (2006). Anticonvulsant therapy in dogs and cats. *Veterinary Clinics: Small Animal Practice*, 36(5), 1107-1127.

New MSU VDL Website Coming Soon!

The MSU VDL has been working on a redesigned website that should launch before you receive our spring newsletter. The functions that clients rely on such as online access to test results via WebView are not going away but the site will look VERY different. Content will be reorganized but should be easier to access. We hope you quickly locate what you are looking for, and find the changes refreshing. Even our website is getting a new year makeover!