

# Canine Genetics and the MDR 1 Gene Mutation

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## Historical Information

In June of 2004, assisted by a female Boxer named Tasha and funded by the National Institute of Health, the canine genome was completely sequenced at M.I.T.'s Whitehead Institute. This extraordinary project has expanded our understanding of canine evolutionary history as well as provided a model for studying human genetic disease. From this research, we now know that our canine companions are descended exclusively from the gray wolf, not the coyote, the fox or other wild canines as previously speculated.

Other benefits have become apparent from this project as well. As we know, certain breeds of dogs have unique traits; identifying the genes responsible for these traits has resulted in the ability to also identify those genes responsible for certain genetic disorders. More specifically, identification of gene mutations and those carrying that mutation can help provide better and safer medical care for affected individuals. The **multi drug resistance gene mutation** (*MDR1 mutation*) in dogs is a perfect example.

## Multi Drug Resistance Gene

The MDR1 (*also now known as the ABCB1-1 delta triangle polymorphism*) mutation results in a nonfunctional P-glycoprotein. This protein is important for intestinal drug absorption and for drugs crossing the blood /brain barrier. In other words, is important for intestinal drug absorption and for drugs crossing the blood /brain barrier. We now understand why Collies and related breeds experience serious side effects--even death--when administered the drug, ivermectin; they possess the MDR1 gene mutation. Other breeds affected by this mutation include German Shepherds, Shetland Sheepdogs (Shelties), Border Collies, Old English Sheepdogs and even more exotic breeds such as the Longhaired Whippet, Silken Windhounds and a variety of mixed breed dogs.

## Breeds Affected

Approximately 75% of all Collies in the United States carry the mutant MDR1 gene; however, the incidence of the mutation varies within a breed depending on pedigree and origin. For example, Border Collies have approximately a 1% risk if American bred but higher if from imported lines. German Shepherds are at greater risk if they carry the "white factor" but do not need to be white to be affected. To date, the mutation has not been found in the Belgian herding breeds (personal communication, Washington State University lab).

## Drug Sensitivities

In addition to ivermectin, other drugs to which these breeds are sensitive include imodium (an anti-diarrheal), acepromazine (a tranquilizer and pre-anesthetic medication), and butorphanol (a pre-anesthetic agent and a pain control drug; also used as an anti-coughing drug). The implications are obvious for MDR1 affected individuals: these drugs should be avoided or the dosages reduced.

### Effect on USAR Dogs

The importance for Urban Search and Rescue dogs is these three drugs are on the Veterinary Cache list and might be prescribed as part of a treatment plan for an illness while on deployment. There are numerous other medications that affect these individuals as well such as some chemotherapy drugs, cardiac drugs and some antibacterials. (For a more complete list, access the website cited below). Knowledge of the MDR1 status of a member of a susceptible breed and knowledge of the drugs that adversely affect them can be critical for the safety and health of canine patients.

### Testing for the MDR1 Mutation

Washington State University currently offers a genetic test to screen for the MDR1 mutation; test kits are available through their website, <http://www.vetmed.wsu.edu/depts-VCPL/> (email: [VCPL@vetmed.wsu.edu](mailto:VCPL@vetmed.wsu.edu)), cheek swabs are required and the cost is approximately \$70. Test results are reported as follows: normal/normal (no gene mutation), mutant/mutant (carries the mutation) and mutant/normal (carries the gene, will pass it on and MAY show drug sensitivity).

Other labs involved in testing for a variety of inherited diseases include VetGen ([www.vetgen.com](http://www.vetgen.com)), PennGen ([www.upenn.edu/pennngen](http://www.upenn.edu/pennngen)), and Optigen ([www.optigen.com](http://www.optigen.com)). The list of diseases for which there are tests available is rapidly expanding. Currently there are tests for coat color gene variation (Labradors, Springer Spaniels, Flat Coated Retrievers), cystinuria (Newfoundlands, Labradors), narcolepsy (Labradors), progressive retinal atrophy (Labradors, Collies) and, of course, Von Willibrand's disease (Dobermans, Bernese Mountain Dogs, among others). There are also a number of research facilities, which study the inheritability of other diseases such as seizure disorders. Their work has already demonstrated that seizure activity in certain breeds is passed on by an autosomal recessive gene while for other breeds, it is polygenic (multiple genes). The University of Minnesota will soon have a test for exercised induced collapse in Labradors.

Future genetic screening will hopefully be available for many diseases thereby providing an opportunity for breeders to eliminate these diseases by selecting unaffected individuals for their breeding program.

## Sources

1. The Canine genome Project Sheds Light on Mysteries from the Feb 2004 issue of the AKC Gazette
2. The Canine Genome by Elaine A. Ostrander and Robert K. Wayne from Genome Res.15:1706-1716 2005
3. Canine MDR 1 Mutation—Breed Disposition and Prevalence in Dogs in Germany by J. Huebner at the 17<sup>th</sup> ECVIM –CA Congress 2007
4. Genetic Testing for Pet & Breeding Animals ( Vet-43) by Dr. Jerold S. Bell at the Western Veterinary Conference 2004
5. A Complete List of Available Canine and Feline Genetic Tests by Dr. Jerold Bell at the Tufts University Canine and Feline Breeding and Genetics Conference 2003

### Intro for web site

There exists a genetic mutation in certain breeds of dogs that affects how they absorb and metabolize certain drugs. This mutation is called the MRD1 gene mutation or ABCB1-1 ( delta triangle) polymorphism. Affected individuals are sensitive to what would be considered normal doses of certain drugs. The MDR1 status of a search and rescue dog of an at risk breed is important as these drugs may be prescribed as part of a treatment plan for an illness while on deployment.