



## Multidrug Resistance Gene (MDR1) Test

A number of dog breeds are more prone to have serious side effects from certain drugs than other breeds. The cause of this sensitivity is a DNA sequence change (mutation) in the dog's multi-drug resistance gene, known as the MDR1 gene. The function of this gene is to prevent dangerous drugs from entering the CSF. Dogs with the mutated MDR1 gene have an alteration in the blood brain barrier affecting transport of drugs such as ivermectin. Exposure to these drugs may result in serious neurological symptoms, such as hypersalivation, ataxia, blindness, tremor, respiratory distress and even death. As well as protecting the brain, the MDR1 gene plays a vital role in drug elimination. Dogs that have a mutated MDR1 gene can have reduced drug elimination, resulting in elevated plasma drug levels and an increased tendency to toxicity.

A number of drugs have been shown to cause problems in dogs with a mutated MDR1 gene. These include Acepromazine (tranquilliser), Butorphanol (analgesic), Cyclosporin (immunosuppressant), Digoxin (cardiac inotrope), Doxorubicin (anti-neoplastic), Ivermectin (anti-parasitic), Loperamide (anti-diarrhoeal), Vinblastine (anti-neoplastic) and Vincristine (anti-neoplastic).

Approximately 75% of Collies in Australia have the mutated MDR1 gene. The mutation has also been found in Shetland Sheepdogs, Australian Shepherds, Old English Sheepdogs, German Shepherds, Long-haired Whippets, Silken Windhounds, and a variety of mixed breed dogs.

### Indications for Testing:

Instead of simply avoiding drugs like ivermectin in known susceptible breeds, veterinarians can determine if the dog has a normal MDR1 gene. In unaffected individuals the drug can be safely used. If the MDR1 mutation is present and alternative treatment can be prescribed. Screening may also be appropriate in patients from high risk breeds who are being considered for chemotherapy as the MDR1 gene mutation may carry a risk of increased adverse reactions to many of the commonly used chemotherapeutic drugs. Breeders can also use this information to detect carriers and eliminate this disease through planned breeding programs.

All dogs have two copies of the MDR1 gene: one inherited from the sire and the other inherited from the bitch.



Species:  
Canine



Specimen:  
Buccal swab or whole blood (2-4 ml). Free Sample Collection Kits (with instructions included) for buccal swabbing are available by contacting the Gribbles Molecular Laboratory via the Help Desk.



Container:  
Sterile pot (swab) or EDTA (whole blood)



Collection Protocol:  
Swab inside of cheek with a dry swab. Standard venepuncture.

MDR1 Gene Result	Interpretation
Normal / Normal	These dogs would not be expected to have adverse reactions to normal doses of drugs.
Normal / Abnormal (Carrier)	These dogs may pass on the mutant gene to their offspring. These dogs may experience adverse reactions to normal doses of drugs.
Abnormal / Abnormal (Affected)	These dogs will pass on the mutant gene to their offspring. These dogs are expected to experience drug toxicity to normal doses.

#### References

1. Mealey KL et al. Ivermectin sensitivity in Collies is associated with a deletion mutation of the MDR1 gene. *Pharmacogenetics* 2001 11 (8):727-733.
2. Mealey KL et al. Increased toxicity of p-glycoprotein-substrate chemotherapeutic agents in dogs with the MDR1 deletion mutation associated with Ivermectin sensitivity. *J Am Vet Med Assoc* 2003 223 (10): 1453-1455.
3. Mealey KL et al. Frequency of the mutant MDR1 allele associated with sensitivity in a sample of herding breed dogs living in Australia. *Vet Parasitol* 2005 131 (3-4): 193-196.