



PROTOCOL

Detecting Multi-drug Sensitivities in Dogs (MDR1 Gene Test)

Introduction

A number of dog breeds are more prone to serious side effects from certain drugs than other breeds. For example, Collies can have severe adverse reactions to the antiparasitic drug, ivermectin.

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 signs, 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 compared to others, resulting in elevated plasma drug levels and an increased tendency for 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 (antineoplastic)
- Ivermectin (antiparasitic)
- Loperamide (antidiarrhoeal)
- Vinblastine (antineoplastic)
- Vincristine (antineoplastic)

(Please note that this is not a complete list of drugs that may affect dogs with the MDR1 gene mutation)

Affected Breeds:

Approximately 75% of Collies in Australia have the mutated MDR1 gene. The mutation has also been found in Shetland Sheepdogs (Shelties), Old English Sheepdogs, German Shepherd Dogs, Long-haired Whippets and a variety of mixed breed dogs.

DNA Test

Gribbles Molecular Science and Gribbles Veterinary Pathology have an exclusive licence from Washington State University to provide the MDR1 DNA test in Australia.

The test is easy to undertake, requiring only a cheek swab to determine whether a dog has the MDR1 gene mutation. Alternatively the test can be conducted using a blood sample.

Because this test targets the gene, it is 100% accurate and provides definitive information on the genetic status of the dog tested.

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 an 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 condition through planned breeding programs.

Sample:

Please send either a buccal swab or 2-4 mL of EDTA blood, along with a standard submission form stating: "MDR1 gene testing required" to Gribbles Veterinary Pathology.

Collection Method:

Free sample collection kits (with instructions included) for buccal swabbing are available via one of the following methods:

Phone: (03) 9538 2259

Email: GMS@gribbles.com.au

Write to: Molecular Science, Gribbles.

1868 Dandenong Road

Clayton, Victoria 3168.

Interpretation:

Please note that all dogs have two copies of the MDR1 gene: one inherited from the sire and the other inherited from the bitch.

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.