

UNDERSTANDING MDR1 GENE MUTATION

TIBETANMASTIFFS.AU | tibetanmastiffau@gmail.com

Anaesthetics, Medications, and the MDR1 Gene in Tibetan Mastiffs



Understanding the MDR1 Gene Mutation

The MDR1 gene (Multidrug Resistance 1) plays a critical role in protecting the brain by preventing harmful substances from crossing the blood-brain barrier and entering the cerebrospinal fluid (CSF). In some Tibetan Mastiffs, a mutation in this gene can cause severe sensitivity to certain medications, leading to life-threatening side effects.

This genetic mutation affects drug transport proteins, which are essential for eliminating toxins and medications from the brain and body. When this process is impaired, certain drugs accumulate to toxic levels, causing adverse reactions.

Why is the MDR1 Gene Important?

When the MDR1 gene is mutated, the dog's blood-brain barrier becomes compromised, allowing specific drugs to reach the brain. This can result in neurological symptoms such as:

- Hypersalivation (excessive drooling)
- Ataxia (loss of coordination and unsteady movements)
- Blindness (temporary or permanent)
- Tremors (uncontrolled muscle movements)
- Respiratory distress (difficulty breathing)
- Potential death within 24 hours of drug exposure

How Does the MDR1 Gene Affect Drug Metabolism?

The MDR1 gene is responsible for producing P-glycoprotein, a transporter protein that expels harmful substances from the brain and regulates drug absorption and elimination in organs like the liver, kidneys, and intestines. A mutation in this gene disrupts these processes, resulting in drug toxicity due to higher-than-normal drug concentrations in the body.

Medications to Avoid – Always be informed and take caution with any Medication!

Tibetan Mastiffs with an MDR1 mutation are particularly sensitive to several commonly used drugs. The following medications have been identified as high-risk:

- **Anesthetics:** Ketamine (known to cause fatalities in Tibetan Mastiffs), Thiopental
- **Tranquilizers:** Acepromazine (causes prolonged sedation)
- **Analgesics:** Butorphanol, Morphine
- **Immunosuppressants:** Cyclosporin
- **Cardiac Medications:** Digoxin, Quinidine
- **Anti-Neoplastic Drugs:** Doxorubicin, Vinblastine, Vincristine, Paclitaxel
- **Anti-Parasitics:** Ivermectin, Milbemycin, Selamectin (commonly found in heartworm preventatives)
- **Anti-Diarrheal:** Loperamide (over-the-counter Imodium)

Pre-Operative Considerations

Before administering anesthesia or any medications, it is essential to:

1. **Inform your veterinarian** about the breed's sensitivity and provide details of any past reactions.
2. **Avoid high-risk drugs** when possible and choose safer alternatives.
3. **Use appropriate drug dosages;** Tibetan Mastiffs may require adjusted doses even with safe medications.
4. **Monitor closely** during and after any medical procedure to detect early signs of adverse reactions.
5. **Maintain comprehensive records** of medications administered for future reference.

Testing for the MDR1 Mutation

Testing for the MDR1 gene mutation is a simple and effective way to ensure your dog's safety. This test MDR1 (Multi Drug Resistance) determines whether your Tibetan Mastiff has a normal or mutated MDR1 gene, providing crucial information for safe medication use.

- **Who Should Test?**
 - Tibetan Mastiffs and other high-risk breeds
 - Dogs being considered for chemotherapy or long-term medication
 - Breeding dogs to help reduce the occurrence of the mutation

Where to Get Tested: Orivet, a leader in genetic testing for dogs, offers the MDR1 mutation test along with over 260 other health and phenotype tests. Testing helps veterinarians make informed decisions and breeders implement responsible breeding practices.

<https://www.orivet.com/store/ivermectin-sensitivity-mdr1-multi-drug-resistance/p/160>

Breeds Commonly Affected

While Tibetan Mastiffs are susceptible, other breeds known to carry the MDR1 mutation include:

- Collies (up to 75% in Australia)
- Shetland Sheepdogs
- Australian Shepherds
- Old English Sheepdogs
- German Shepherds
- Long-Haired Whippets
- Silken Windhounds
- Border Collies (less commonly)
- Mixed-breed dogs with herding ancestry

How to Interpret MDR1 Test Results

- **Normal/Normal:** Both gene copies are normal; no drug sensitivity.
- **Mutant/Normal (Carrier):** One normal and one mutant copy; increased drug sensitivity possible.
- **Mutant/Mutant (Affected):** Two mutant copies; high sensitivity to listed medications.

Safe Practices for Owners of Affected Dogs

- Inform all veterinarians and specialists about your dog's MDR1 status.
- Avoid listed high-risk medications unless absolutely necessary.
- Use heartworm preventatives with non-ivermectin ingredients.
- Monitor your dog closely when introducing new medications.

Conclusion

Ensuring your Tibetan Mastiff's safety during medical treatments requires awareness of the MDR1 gene mutation. Speak with your veterinarian about appropriate medication choices, and consider genetic testing to protect your dog from potentially life-threatening drug reactions.

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For more information on genetic testing, visit Orivet or consult your veterinarian.