MDR1-based Multiple Drug Sensitivity

What is MDR1?

MDR1 is a gene that encodes a protein involved in transporting drugs and other toxins out of brain tissue. The canine version of the MDR1 gene resides on chromosome 14.

What is *mdr1-1Δ*?

***Mdr1-1Δ* is a mutant (non-functional) form of the canine *MDR1* gene (Mealey et al. 2001; Roulet et al. 2003).**

What is the connection between *mdr1-1Δ* and drug sensitivity?

***Mdr1-1Δ* was first discovered in collies that have ivermectin sensitivity (Mealey et al. 2001). Ivermectin is the main ingredient in popular heartworm medications. Dogs with two mutant copies of the *MDR1* gene (M/M) have sensitivity to a number of drugs. These drugs include certain antibiotics, antidiarrheal agents, analgesics, antiparasitics and chemotherapeutic agents. For a relatively current list of problem drugs, see http://www.vetmed.wsu.edu/depts-VCPL/drugs.aspx and http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1636591/table/t1-cvj47pg1165/.**

Dogs with MDR1 hypersensitivity typically exhibit adverse neurological reactions such as hypersalivation, ataxia, blindness, tremor, depression, coma, respiratory compromise, and death after exposure to one of these drugs.

Dogs with one copy of the mutant gene (M/N) also are at risk for increased drug sensitivity. The above site at Washington State University contains recommendations for reduced drug dosing in both M/M and M/N dogs. It is worth noting the statement by the College of Veterinary Medicine at Washington State University (see above site) regarding the safety of common monthly LOW DOSE monthly heartworm preventatives (ivermectin (Heartguard), selamectin (Revolution), milbemycin (Interceptor and Sentinel), and moxidectin (Proheart)) in these dogs. They state "these drugs are safe in dogs with the mutation if used for heartworm prevention at the manufacturer's recommended dose".

What is the relevance of all this to Longhaired Whippets?

All present-day breeds carrying the *mdr1-1Δ* mutation obtained it from this single pre-1873 ancestor in their common past (Neff et al. 2004). These breeds include the following contemporary herding breeds: Old English Sheepdogs, Collies, Shetland Sheepdogs, McNabs, English Shepherds and Australian Shepherds. In addition, both Longhaired Whippets and Silken Windhounds carry this mutation. Unfortunately, the *mdr1-1Δ* mutation is quite common in our breed. In this 2004 study, 89 Longhaired Whippets were genetically tested and ~16% were M/M, and ~52% were M/N. Among 84 tested Silken Windhounds, 1.2% were M/M and 33.3% were carriers M/N.

How can I have my Longhaired Whippet tested for the *MDR1* mutation?

The Veterinary Clinical Pharmacology Laboratory at the College of Veterinary Medicine at Washington State University offers a *MDR1* genetic test.

If you would like more information on MDR1 drug sensitivity in dogs, please visit

Understanding Genetic Variability in Dogs and Its Potential Role in Drug Development.
Pharmacogenetics: It's not just about ivermectin in collies
The American Working Collie Association
The Australian Shepherd Health and Genetics Institute

References

Mealey, K.L. et al. (2001) Ivermectin sensitivity in collies is associated with a deletion mutation of the mdr1 gene. *Pharmacogenetics*, 11:727-733.

Neff, M.W. et al. (2004) Breed distribution and history of canine mdr1-1Δ, a pharmacogenetic mutation that marks the emergence of breeds from the collie lineage. *Proc. Nat. Acad. Sci. USA*, 101(32):11725-11730.

Roulet, A. et al. (2003) MDR1-deficient genotype in Collie dogs hypersensitive to the P-glycoprotein substrate ivermectin. *Eur. J. Pharmacol*. 460: 85-91.