CANINE MDR-1-MUTATION- BREED DISPOSITION AND PREVALENCE IN DOGS IN GERMANY

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MDR-1 (Multi Drug Resistance) is one of the ATP-Binding Cassette-Transporters and its product P-Glycoprotein (P-gp) is a component of the blood–brain barrier and other important tissue borders. P-glycoprotein is encoded by the multiple drug resistance gene, *MDR1* and limits the oral absorption and the entry of the central nervous system of many drugs, like anticancer agents, steroid hormones antimicrobial agents and cardiac drugs. First observed in a fatal case of a Collie in the 1980s after the administration of Ivermectin, a new antiparasiticide, remarkable high concentrations of the drug were found during post-mortem in the central nervous system (CNS). But only after knockout mice lacking Abcb1a, the murine ortholog of *MDR1,* died in a laboratory after the treatment of a mite infection an association with the canine mutation was concluded. MDR1 polymorphism, a 4-bp deletion mutation, in herding breed dogs, including Collies and Australian shepherds, has been demonstrated to be the cause of Ivermectin sensitivity in these breeds.
Between September 2005 and November 2006, 660 dogs were tested in our laboratory by PCR for genotyping MDR-1. Negative for the mutation were 59.8% of all tested dogs, 29.8% were heterozygous carriers and 10.4% were affected (for details see table below).

	MDR-1-Genotyp			
breed	**N/N** +/+	**N/MDR** +/-	**MDR/MDR** -/-	**total**
Collie	18,3%	55%	26,6%	169
Shetland Sheepdog	48,7%	44,7%	6,6%	76
Australian Shepherd	62,6%	31,9%	5,5%	163
Border Collie	100%	0%	0%	63
Bearded Collie	100%	0%	0%	13
Wäller	100%	0%	0%	1
Miscellaneous	84,6%	10,3%	5,1%	175
total	**59,8%**	**29,8%**	**10,4%**	**=660**

Dogs must be homozygous (MDR-/-) for the mutation to show the neurotoxic effect. Heterozygous animals (MDR+/-) rarely show any adverse side effects after the treatment with certain drugs, but as carriers they can pass the affected gene to their offspring. Therefore not only breeding dog should be tested before mating, in pure-bred and mixed dogs of these breeds a test should be performed before the initiation of antiparasitic-, chemo- or any other P-gp-substrate drug.