Statement to AMSC on Type B PRA in the Miniature Schnauzer

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Optigen has announced their findings on the discovery of a genetic variant related to progressive retinal atrophy (PRA) in the Miniature Schnauzer. PRA refers to a collection of inherited disorders that cause the retina to "die off" (atrophy) causing progressive blindness. Different forms of PRA have different average ages of onset and progression, and are caused by different genetic mutations. Some PRAs are caused by a single gene pair, and some by the combined effect of several different genes (complex inheritance). Most PRAs are specific to one or a handful of related breeds. Many breeds have more than one type of PRA occurring in the breed. In many forms of PRA the causative mutation(s) have not been identified.

OFA Eye examination statistics (based on Boarded ophthalmologist direct retinal examination) show less than 0.5% of Miniature Schnauzers affected with PRA (less than one in 200 dogs examined). As many dogs are examined at a young age (for pre-breeding screening) they may be examined earlier than the age of onset of PRA. However, it is accepted that PRA is a rare but present disorder in the breed.

The researchers associated with Optigen (including Dr. Aguirre's group at UPenn) had in 2000 identified a mutation causing PRA in the breed called Type A PRA. Through subsequent testing of a general population of Miniature Schnauzers none were found to carry this mutation. It is likely that Type A PRA represents a mutation that occurred in only a small family of Miniature Schnauzers, or is a very rare mutation in the breed.

Optigen has a DNA sample set of 76 Miniature Schnauzers diagnosed with PRA. All of the affected PRA cases have retinal exam changes consistent with PRA by 7 years of age. Some of these PRA affected Miniature Schnauzers may not show clinical signs of diminished vision until later in life.

The researchers at Optigen have recently identified a genetic variant (Type B PRA) that explains 55% of the Miniature Schnauzer PRA cases in their sample set. This indicates that the variant is a major factor in the development of PRA in the breed. In several other Miniature Schnauzer PRA cases, genetic analysis indicates a different chromosomal location for a causative gene confirming that more than one form of PRA exists in the breed.

On the Optigen website (http://www.optigen.com/opt9_typeb_test.html) it states, "The Type B PRA test results are reported as **Risk Variants** because, although dogs carrying two copies of the variant are very likely to develop PRA, a subset (14%) of the research sample set that were homozygous for the variant did not develop PRA by 7 years of age. It is not clear at this time whether the variant represents a causal mutation –and that other factors influence the "penetrance" of the mutation—i.e. its ability to cause disease-- or if the variant is a genetic marker that resides near the causal mutation. OptiGen and the University of Pennsylvania scientists will continue research aimed at better understanding this question."

What the PRA B test does tell us is that presently 84% of Miniature Schnauzers homozygous (with two copies) of the risk variant will develop PRA.

Limited testing of the population of Miniature Schnauzers with DNA stored at Optigen show 73% testing homozygous (2 copies) normal, 25% heterozygous carrier, and 2% homozygous "at risk" for the Type B PRA risk variant. The percentage of carriers in the stored samples is high, and probably relates to a biased sample where breeders with PRA affected dogs have sent in DNA samples from close relatives that are more likely to be carriers. The only way to determine the true frequency of the Type B PRA risk variant in the Miniature Schnauzer gene pool will be after widespread testing of the general population.

The Type B PRA risk variant testing is a useful tool for the prevention of PRA in the Miniature Schnauzer breed. No quality dogs need to be discarded from breeding due to their risk variant results. I recommend testing prospective breeding stock and not breeding carrier or affected dogs together. Quality carriers can be bred to normal testing mates and replaced for breeding with quality normal testing offspring. In this way quality lines are not abandoned and the genetic diversity of the breed is maintained.