PURDUE UNIVERSITY
Animal Disease Diagnostic Laboratory

Purdue Canine Genetics Lab

Miniature American Shepherd Non-*HSF4* Hereditary Cataracts (NHHC)

Genetic Test Result Interpretation

We have designated the letter D to indicate the form of the NHHC gene that contains this variant, and N to indicate the reference (normal) form of the gene. A dog's particular combination of N or D forms of the gene is known as its genotype.

Clear (NHHC-N/N): A **clear** dog has no copies of the NHHC variant (this is also referred to as being homozygous normal or free of the variant associated with this form of hereditary cataracts). A clear dog cannot produce NHHC affected (D/D) offspring.

Carrier (NHHC-D/N): A **carrier** dog has one copy of the NHHC variant (this is also referred to as being heterozygous). Based on current data, a **carrier dog is not at risk of developing NHHC**. NHHC carriers will, on average, pass the NHHC variant on to half of their offspring; they can produce **NHHC-D/D** (affected/susceptible) offspring if mated to another carrier (**NHHC-D/N**) or affected (**NHHC-D/D**) dog.

Affected/Susceptible (NHHC-D/D): An **affected/susceptible** dog has two copies of the NHHC variant (this is also referred to as being homozygous affected). Based on current data, **all NHHC-D/D dogs develop clinical signs within the first 3-5 years of life**; clinical signs are characterized by opacity developing in the lens of the eye, which progresses very rapidly (within months) to a severity level that makes the dog blind and requires cataract surgery. **NHHC-D/D** dogs will pass one copy of this variant on to all of their offspring.

Further Information on NAD

Based on current data, NHHC is most likely inherited in a **fully penetrant autosomal recessive** manner. Fully penetrant means that all genetically affected dogs (**NHHC-D/D**) will show obvious clinical signs in their lifetime. Autosomal recessive means that two copies of the mutation are required to show signs of disease; the genotype of NHHC affected / susceptible dogs is D/D. Both clear (NHHC-N/N) and carrier (NHHC-D/N) dogs do not develop the NHHC disease but could still show clinical signs of other cataracts resulting from an unrelated genetic cause or a myriad of non-inherited causes of cataracts (e.g., diabetes mellitus, ocular trauma, advanced age, and more).

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Below are the chances any given puppy in a litter from the indicated mating will have the genotype of N/N, D/N, or D/D. **Matings that produce an affected (NHHC-D/D) dog are not recommended, and are shown in red.**

Matings that will not produce NHHC affected dogs:

- Clear (N/N) x Clear (N/N) = 100% Clear (N/N)
- Clear (N/N) x Carrier (D/N) = 50% Clear (N/N), 50% Carrier (D/N)
  (This is an average, individual litters may see anywhere from 100% Clear to 100% Carrier)
- Clear (N/N) x Affected (D/D) = 100% Carrier (D/N)

Matings that can produce NHHC affected (D/D) dogs and are NOT recommended:

- Carrier (D/N) x Carrier (D/N) = 25% Clear (N/N), 50% Carrier (D/N), **25% Affected (D/D)**
  (This is an average, individual litters may see more or less of any result)
- Carrier (D/N) x Affected (D/D) = 50% Carrier (D/N), **50% Affected (D/D)**
  (This is an average, individual litters may see anywhere from 100% Carrier to 100% Affected)
- Affected (D/D) x Affected (D/D) = **100% Affected (D/D)**

We do not recommend exclusion of NHHC carrier (D/N) dogs from the breeding population. We do recommend avoiding matings that have the potential to produce NHHC affected (D/D) offspring as detailed above. As long as one of the two parents is NHHC clear (N/N), NHHC affected offspring will not be produced.

Immediately eliminating all carrier (NHHC D/N) dogs from breeding may have negative consequences for the genetic diversity of the breed.

Test Limitations

While we have identified this NHHC variant associated with hereditary cataracts in Miniature American Shepherds, other forms of genetic cataracts may exist in the breed. It is therefore important to remember that this NHHC test is diagnostic for only one form of NHHC and will not identify other forms. Thus, it is still possible that offspring could be affected with a different genetic form of NHHC, even if both parents have tested NHHC-N/N (clear). To that end, we recommend that both dogs in a breeding pair be free of any past or present signs of cataracts and have passed their CAER examination, regardless of genotype. Remember that cataracts can also be caused by many non-genetic factors as well. Nonetheless, this NHHC test will help to prevent this form of hereditary cataracts and therefore significantly reduce the frequency of this disorder in the Miniature American Shepherd breed.

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