GENETICS 101

This document is intended to provide a basic understanding of canine genetics to the American Eskimo Dog (AED) owner and breeder. It is simplified from scientific facts and understanding. It is not intended to be a complete discussion of the material, and readers are urged to study on their own through any excellent sources on the Internet, especially the AKC Canine Health Foundation (CHF) which has podcasts of timely health topics. Other links may be found below.

This page will be modified and expanded as time permits and new topics arise. AEDCA members are urged to contact members of the AEDCA Health Committee with subjects about which they are concerned.

GLOSSARY

Allele means one copy of a pair of genes located at the same location (locus) in paired chromosomes. For each gene, one allele is inherited from the sire and one from the dam.

Autosomal means the all of the genes not found on a sex chromosome (the X and Y chromosomes).

Complex inheritance means that several genes are involved in the expression of a trait. A synonymous term is ***polygenetic inheritance***.

Dominance means a relationship between the alleles of a gene in which one allele masks the expression (phenotype) of another allele at the same locus.

Gene means a hereditary unit, ordinarily at a fixed position on a chromosome that influences a particular trait and made up of two alleles.

Genotype means the genetic make-up of an individual, either at a single locus or overall of its genes collectively.

Heterozygous means that the two alleles of a single gene are different. One allele will be dominant (the one that the individual expresses) and one will be recessive (not expressed but can be passed on to offspring).

Homozygous means that the two alleles of a single gene are the same and is the only allele that the individual can pass on to its offspring.

Phenotype means the physical characteristic which is expressed in the individual.

Recessive means that the allele within a gene is not expressed but may be passed on to offspring.

Simple inheritance means that only one gene is responsible for the expression of a trait.

Other terms pertaining to other modes of inheritance and various biochemical reactions and markers are more advanced than this summary will discuss. Readers are urged to go on-line and read more about the facet of genetics that may interest them.

Understanding genetics can be confusing because many breeders commonly use the terms ***gene*** and ***allele*** interchangeably; however, these words have different and precise meanings. Another confusing aspect of genetics is that mutations can occur spontaneously, and no one can predict their occurrence- this is the reason that breeders must be constantly vigilant.

Simple Autosomal Recessive Genetics

Let's quickly review what this term means by looking back at our glossary. ***Simple*** means that we are talking about a trait, which can include a disease, caused one gene. ***Autosomal*** means that we are talking about genes found on any chromosome except the sex chromosomes, X and Y.

Each individual has two alleles for each gene. If the alleles are the same, the individual is ***homozygous*** for that trait and it will be expressed. If the alleles are different, the individual is said to be ***heterozygous***; and the ***dominant*** allele will be expressed, and the ***recessive*** allele will be "hidden".

Most breeders think of simple autosomal recessive traits when they think about canine genetics. To illustrate how this mode of inheritance works, let's use the example of progressive rod-cone dysplasia (prcd) form of Progressive Retinal Atrophy (PRA) in American Eskimo Dogs.

We can write the dominant allele for Normal as a capital N; and the recessive allele (the mutation) as small-case n. A homozygous Normal Eskie will be written as NN and an Affected homozygous Eskie as nn. By definition of a recessive trait, an Affected Eskie is homozygous and has two copies of the mutation; and the term "homozygous Affected" is actually a redundant statement.

However, a heterozygous Carrier Eskie will have one of each of the two alleles and be written as Nn. In simple autosomal recessive diseases like prcd-PRA, Normal is dominant to Affected. The heterozygous Carrier Eskie will never develop prcd-PRA but can pass along the mutant allele to its offspring. Differentiating between the ***phenotypically***-identical Normal and Carrier Eskies (both will never develop the disease) was the historical problem that breeders had in the past. Breeders had no way of looking at the ***genotype*** of the Normal and Carrier to see the difference- this is what modern genetic testing allows us to do.

In the "old days", whenever an Affected Eskie was produced, breeders knew that *both* parents were Carriers. However, with a late-onset disease such as prcd-PRA in the Eskie, the offspring were likely six years of age or older before they developed the disease and breeders knew the parents' status; and those parents were often dead or at least retired from breeding. That left the problem of determining the genetic status of the Affected Eskie's offspring and what mates would be appropriate for them. Many breeders solved that question be deciding to terminate breeding any of the descendants of the Affected Eskies, thus removing their diversity from the breed's gene pool.

Modern genetic testing allows breeders to retain Carriers and Affecteds in a responsible breeding program. Let us consider the six possible mating combinations for a simple autosomal recessive disease such as prcd-PRA in American Eskimo Dogs:

1. **Homozygous Normal to homozygous Normal**- This mating can be written as NN x NN and all offspring will all be homozygous Normal (NN). Optigen refers to this mating as Pattern A x Pattern A.

2. **Homozygous Affected to homozygous Affected**- This mating can be written nn x nn and all offspring will all be homozygous Affected (nn). OptiGen refers to this mating as Pattern C x Pattern C.

3. **Homozygous Normal to homozygous Affected**- This mating can be written as NN x nn and all offspring will be heterozygous Carrier (Nn). Optigen refers to this mating as Pattern A x Pattern C.

We can draw a table showing one parent's alleles down the shaded left side (NN) and the other parent's alleles along the shaded top (nn). Each parent contributes one allele to each offspring, so the resulting gene combinations can be written in the remainder of the table.

	n	n
N	Nn	Nn
N	Nn	Nn

4. **Homozygous Normal to a heterozygous Carrier**- This mating can be written as NN x Nn. Half (50%) of the offspring will be homozygous Normal (NN) and 50% will be heterozygous Carrier (Nn). OptiGen refers to this mating as Pattern A x Pattern B.

	N	n
N	NN	Nn
N	NN	Nn

5. **Homozygous Affected to a heterozygous Carrier**- This mating can be written as nn x Nn. Half (50%) of the offspring will be heterozygous Carrier (Nn) and 50% will be homozygous Affected (nn). OpitGen refers to this mating as Pattern C x Pattern B.

	N	n
n	Nn	nn
n	Nn	nn

6. **Heterozygous Carrier to a heterozygous Carrier**- This mating can be written as Nn x Nn and results in the greatest diversity of offspring- 25% will be homozygous Normal (NN), 50% will be heterozygous Carrier (Nn), and 25% will be homozygous Affected (nn). OpitGen refers to this mating as Pattern B x Pattern B.

	N	n
N	NN	Nn
n	Nn	nn

The "odds" provided for the prcd-PRA Eskies in the scenarios from the matings shown in 3 through 6 above are for large populations; however, any litter could be all of any one of the possibilities for that mating. The odds of producing Normal, Carrier, and/or Affected Eskies from the scenarios shown in 3 through 6 are *independent variables*. This means that each puppy in the litter is unique, and each puppy has an equal chance of being one of the possible combinations without any influence from the other puppies in the litter. It is the same as the "odds" for the sex of a puppy- it can be either male or female, and each puppy has a 50% chance of being male or female. The sex of one puppy has nothing to do with the sex of another puppy in the same litter. Overall in a large population of puppies, we see approximately the same number of males as females; but within one litter we could have all of one sex or the other.

The goal of any breeding program is to never produce Affected animals. For autosomal recessive diseases, if we can identify the heterozygous Carriers (Pattern B or Nn) and homozygous Affecteds (Pattern C or nn) and never breed them to any Eskie except a homozygous Normal (Pattern A or NN), then we can still use Carrier and Affected Eskies in a responsible breeding program. Maintaining genetic diversity in the breed while producing Eskies of strong mental and physical health should be our goal.

When breeders select only homozygous Normal (Pattern A or NN) Eskies, they are effectively removing all Affecteds and Carriers from the gene pool today. Our goal should be to keep as many Eskies as possible in our breeding programs for the genetic diversity they provide, so that we increase the numbers of individuals to maintain genetic diversity.

Breeders should plan to replace each Affected or Carrier Eskie with a Normal offspring sometime during the life of the Affected or Carrier. The time period could be in two years or ten years because each breeder and situation is unique. AED breeders should not be in a rush to remove all Carriers and Affecteds as they have a necessary place in a managed breeding program.

Another interesting note is that OptiGen states on their website that any American Eskimo Dog which tests as a Affected (nn or Pattern C) *will* develop the disease. The prcd form of PRA in the Eskie is late-onset and may not start to affect the Eskie until 10 or 12 years of age; or it may not result in total blindness before the AED dies. If you have or know of Eskies which test as Pattern C, or Affected, and are at least 10 years old and have not developed prcd-PRA, you should arrange for your Eskies to be examined by OptiGen or one of their ophthalmologists. If you cannot get your dogs to them, you should at least make contact them to let them know of your situation.

Breeders and owners have several options to assist research scientists, including donating tissue to the scientists upon an Eskie's death. While this is a difficult emotional decision, owners should consider this possibility before your Eskie passes and make arrangements with your vet before your beloved Eskie passes. This donation is truly a gift to the breed's future.

Simple Autosomal Dominant Genetics

Dominant diseases should concern all breeders because they pose an even greater threat than recessive diseases. Let's quickly review our glossary. ***Simple*** means that we are talking about a trait, which can include disease, caused one gene. ***Autosomal*** means that we are talking about genes found on any chromosome except the sex chromosomes, X and Y.

Each individual has two alleles for each gene. If the alleles are the same, the individual is ***homozygous*** for that trait and it will be expressed. If the alleles are different, the individual is said to be ***heterozygous***; and the ***dominant*** allele will be expressed, and the ***recessive*** allele will be "hidden".

Most Eskie breeders think of simple autosomal recessive traits when they think about canine genetics. Our breed is not believed to have not been affected by a simple dominant disease, but all it would take is a single mutation in the right place. If the disease is late-onset like prcd-PRA, we wouldn't even know of the problem for several years; and by then we could have real problems on our hands.

Why the gloom and doom? Let's look at how a simple dominant disease could hurt our breed.

Three possibilities exist for the genotype of any individual in a simple trait- two are homozygous and one is heterozygous. Geneticists prefer to write a dominant trait as capital letters and recessive traits as small letters. We can write homozygous Affected as AA and homozygous Normal as nn. The heterozygous Eskie is written as An and *will* develop the disease because in the dominant disease only one copy of the mutant allele needs to be present. We would no longer refer to heterozygous Eskies as "heterozygous Carriers" but as "heterozygous Affecteds". Out of the three possible genotypes, two will have disease- far different than the one-in-three possibilities of the recessive disease.

Let's look at some possible matings and their outcomes when dealing with simple dominant traits:

1. **Homozygous Affected (AA) mated to a homozygous Normal (nn)**- All offspring are heterozygous Affected (An) and will have the disease.

	n	n
A	An	An
A	An	An

Obviously a homozygous Affected Eskie (AA) would be devastating to the breed because even when bred to a genetic Normal (nn), all of its offspring will be heterozygous Affected and will have the disease.

2. **Heterozygous Affected (An) mated to a homozygous Normal (nn)**- Half of the offspring (50%) will be heterozygous Affected (An) and will have the disease; and 50% will be homozygous Normal (nn).

	n	n
A	An	An
n	nn	nn

The would be the best-case breeding scenario using a heterozygous Affected Eskie (An) and would result in 50% heterozygous Affected Eskies which will develop the disease.

3. **Heterozygous Affected (An) mated to a heterozygous Affected (An)**- Matings of heterozygous animals produce the greatest variation in offspring. One-fourth (25%) of the offspring will be homozygous Affected (AA); half (50%) will be heterozygous Affected (An); and one-fourth (25%) will be homozygous Normal (nn). The end result is that 75% of the offspring (25% as AA plus 50% as An) will have the disease.

	A	n
A	AA	An
n	An	nn

Obviously, an autosomal dominant disease would be much more devastating than a simple autosomal recessive disease such as prcd-PRA in the American Eskimo Dog. Other breeds of dogs and animals have genetic disease issues which are caused by simple dominant genes, and the solutions are not so simple.