Inheritance of Uric Acid Production

By Mary-Lynn Jensen, Ph.D.

Genetics and inheritance can be a very complicated subject. Because the gene that creates the high levels of uric acid produced in Dalmatians is what is referred to as a simple dominant, it is fairly easy to explain. This means that this trait is controlled by one pair of genes and is relatively easy to breed away from or towards should it be so desired. This is very much like the relationship between the genes that determine whether a Dalmatian is black or liver spotted, which is something that most Dalmatian breeders are quite familiar with.

Let's start with a few definitions of basic genetic terms.

Phenotype is what you see outwardly in an animal. It is the physical appearance that is caused by an animal's genetic makeup. However, it is not always a clear indicator of an animal's genetic makeup.

Genotype is the actual genes that are present in an animal's DNA. While not always outwardly visible, an animal's genotype controls what traits that animal can pass on through the breeding process.

A **Dominant** gene is one that is more likely to be expressed. Generally, only a single copy of a dominant gene is necessary for it to be present as a physical quality.

A **Recessive** gene is one that is less likely to be expressed. If there is a dominant gene for the same trait present, the recessive trait will not be present as a physical quality; however it will be present in the animal's genotype and can be passed on through breeding. If an animal has two copies of a recessive gene, then that particular trait will be present.

Homozygous means that an animal has two copies of the gene for a particular trait. Heterozygous means that an animal has two different copies of the gene for a particular trait.

The high levels of uric acid produced by Dalmatians (along with humans and great apes) make them unique among mammals. Because the canine kidney is more efficient in removing uric acid from the bloodstream, it is removed in the kidneys and may create urate stones in the bladder. In humans and primates, excess uric acid builds up in the joints, often the ankles and joints of the feet. *(Benjamin Franklin is probably one of the best know sufferers of gout.)*

As mentioned previously, the gene that controls the level of uric acid production is a simple dominant gene. The dominance is for production of low levels of uric acid (10-60 mg/day). With the exception of some of the backcross Dalmatians, all Dalmatians tested to date have high levels of uric acid excretion (400-600 mg/day) compared to other breeds of dogs (10-60 mg/day). This means that Dalmatians are homozygous for the recessive version of the gene that controls uric acid production, or uu in genotype, which makes them high uric acid producing (HUA) in phenotype. Other breeds of dogs (like the Pointer used in the original backcross breeding) are UU in genotype and low uric acid (LUA) in phenotype.

Much like the breeding predictions that we can do related to liver vs. black spotting (another simple recessive trait), we can predict with accuracy the approximate percentages of genotypes and phenotypes that will be produced from breeding a backcross Dalmatian to an AKC Dalmatian. While these percentages may not be 100% accurate for an individual litter, they are quite accurate over time for these breeding combinations.

How Does This Relate To The Backcross Project?

Figure 1 represents the genotypes of the dogs in the initial Dalmatian x Pointer backcross breeding. Figure 2 represents most of the subsequent breedings done as part of the backcross project. There was one experimental breeding like Figure 3 done by Holly Nelson DVM in the 1980's. But, following Holly's untimely demise, any homozygous dominant dogs were lost to the backcross project. Figure 3 represents breedings that will be planned for the future at such time that there is enough genetic diversity within the heterozygous dominant population to avoid excessive inbreeding and a genetic bottleneck among the Dalmatians carrying the dominant gene for low levels of uric acid production (10-60 mg/day). Figure 4 represents a long term goal of the backcross project – the ability to breed a litter of Dalmatians where all of the offspring will produce low levels (10-60 mg/day) of uric acid.

It is important to remember when looking at Punnett Square explanations of breeding probabilities is that these percentages will not always be true *within every litter* (as in the case of the recent litter born in Northern California to Rambler O'Brogan Indelible – out of six pups, the results of the DNA show only two pups to be heterozygous for the LUA gene). The probability of these percentages expressed in the Punnett Squares in figures 1-4 occurs over time with many litters.

Within an individual litter, the percentages may or may not agree with the ratios expressed above, but the Punnett Squares do accurately portray the genetic combinations that are ***possible***. For example in Figure 3, just because the first pup inherits a dominant LUA gene from both parents, does not mean that the next pup must/will inherit the recessive HUA gene. Each and every pup has an equal chance of inheriting either of the genes possessed by each parent. It would be possible for all of the offspring produced in the breeding illustrated in Figure 3 to be *all HUA* or *all LUA*.

Pointer

AKC Dalmatian		U	U
	u	Uu	Uu
	u	Uu	Uu

Figure 1
Pointer x Dalmatian Breeding

All offspring from this breeding will produce uric acid levels between 10 and 60 mg/day and are considered "normal" uric acid producers. The term "low" is also sometimes used since this amount is much lower than that produced by all non-backcross Dalmatians that have been tested.

Heterozygous Normal Dalmatian

Homozygous High Dalmatian		U	u
	u	Uu	uu
	u	Uu	uu

Figure 2
Backcross Breeding

50% of the offspring from this breeding (Uu) will produce uric acid levels between 10 and 60 mg/day and are considered "low" uric acid producers. The other 50% (uu) will produce uric acid levels between 400 and 600 mg/day (like all previously tested Dalmatians outside the backcross project) and are considered "high" uric acid producers.

Heterozygous Normal Dalmatian

Heterozygous Normal Dalmatian		U	u
	U	UU	Uu
	u	Uu	uu

Figure 3
Heterozygous to Heterozygous Breeding

75% of the offspring from this breeding (UU or Uu) will produce uric acid levels between 10 and 60 mg/day and are considered "low" uric acid producers. The other 25% (uu) will produce uric acid levels between 400 and 600 mg/day (like all other known Dalmatians outside the backcross project) and are considered "high" uric acid producers. However, roughly 25% of the offspring from this breeding will be homozygous (UU) for the dominant gene for Normal Uric Acid. This means that any offspring produced by this Dalmatian will inherit the dominant gene for normal levels of uric acid production.

Homozygous Normal Dalmatian

Homozygous High Dalmatian		U	U
	u	Uu	Uu
	u	Uu	Uu

Figure 4
Homozygous to Homozygous Breeding

All of the offspring from this breeding will inherit at least one copy of the dominant gene for normal uric acid production (10-60 mg/day) and can be considered "low" uric acid producers.

However, it would not be possible for any of the pups produced in the breedings illustrated in Figure 1 or Figure 4 to be HUA in phenotype. Some may be HUA carriers (Uu) while others may be homozygous for the LUA trait (UU), but because the parent represented on the upper side of the Punnett Square is homozygous for the LUA trait, that is the only gene for this trait that this parent can pass on and all of the offspring will be LUA in phenotype.

As the famous scientist, Stephen Wright once said, "The most incomprehensible thing about the universe is that we can comprehend it at all." With respect to the complexity of inheritance of many genetic traits, we are very fortunate that this potentially life-threatening trait is a simple gene to understand.

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