Canine Coat Colour Test

Summary of Genes and Their Interactions

Introduction

Animal Network's colour testing identifies the hidden colours that are in your dog and allows breeding with the knowledge of expected outcomes.

It is important to understand that there are many genes involved in canine coat colour. The formation of breeds and the introduction of breed standards has restricted the number of recognised coat colour variants in each breed. As a result, undesirable colours and variations have been eliminated from each breed through selective matings over many generations.

Today, most breeds exhibit only a limited number of coat colour variations. One of the reasons for this is that many of the genes involved have become fixed and only a specific allele[2] of the gene remains. Another reason is that many of the colour variations are recessive[3] and require two copies of the allele in order to exhibit the colour. The individual breeds differ in the genes that are fixed and the genes that are polymorphic[4].

Currently, genetic testing can interrogate 6 of the genes involved however, there are many others.

Summary of the loci (genes) involved

Solid colour vs white/colour variations

Canine coat colour originates from a specific type of skin cell called a melanocyte. For hair to be coloured, the cells from which the hair originates, must produce and incorporate melanin into the hair. If these cells are unable to produce melanin, the hair will be white in colour.

Several genes determine melanocyte development, survival and migration. Modifications to any of these genes may result in animals that are either solid, piebald, ticked, roan or a combination of all.

A frequently observed trait is a white chest and/or white paws. This is normally caused by incomplete melanocyte migration to the extremities during embryonic development. The genetics for the development, survival and migration of melanocytes remains unclear, however a limited number of important genes have been identified and tests for these should be available in the future.

Black vs Red/Yellow pigment

There are two forms of melanin; pheomelanin, which is red/yellow and eumelanin, which is black. All other colours are modifications of these two pigments. Three genes determine whether pheomelanin or eumelanin is produced, these are explained below.

Melanocortin 1 Receptor (E Locus: E,e)

The first and most important is the Melanocortin 1 receptor (MC1R) or the E locus. If an individual has at least 1 copy of the wild type (WT) allele (E) then they will be able to produce black eumelanin. If a dog has 2 copies of the non-functional "e" allele, then it will only ever produce the red/yellow pheomelanin.

Agouti Signal Peptide (a^y, a^t, a)

The second is the Agouti Signal Peptide (ASIP) or the A locus. Specific alleles at this locus can interact with a functional MC1R and interfere with its production of black eumelanin. Four alleles have been identified at this locus; these have a dominance hierarchy5 whereby $a^y > a^w > a^t > a$. The ay allele is inherited as the dominant6 allele in this series. It produces the fawn or sable coat, where the majority of the coat is red/yellow hair and some black hairs are intermingled within the coat. The next in the series is the wild type, aw allele. This allele causes some hairs to be banded with eumelanin, phaeomelanin and eumelanin pigments from base to tip. These banded hairs are normally distributed on dorsal (back) surfaces of the dog.

The third allele in the series is the black and tan allele (a^t). This allele results in animals that are primarily black but have areas of pheomelanin, which are normally seen on ventral (legs and belly) regions of the dog, the side of the head and spots above the eyebrows. The amount and distribution of phaeomelanin in black and tan dogs differs between individuals and breeds. The coding sequence of the "a^t" allele is identical to the "a^w" allele, suggesting that undefined differences in the non-coding regions distinguish these alleles. The at allele is responsible for the tricolour pattern in dogs that have white points.

The last allele in the series is the recessive black (a). This allele causes no modification to the production of Eumelanin. The a^y, a^t (same as a^w) and a alleles have been characterised genetically.

Beta-defensin 103 (K Locus: K,k)

The third gene is beta defensin 103 (BDEF103) or the K locus. This locus has been referred to as the "dominant black" locus as the K^B allele overrides the effect of ASIP alleles on MC1R. Three alleles have been described at this locus and have the following dominance hierarchy: $K^B > K^{Br} > k$.

The first is the dominant[6] K^B allele already discussed. The second allele (K^{Br}) results in brindling, which is the expression of eumelanin and phaeomelanin stripes in the regions that are normally fawn (the entire coat in ay animals and the fawn regions in aw and at individuals). The last allele in this series is the wild type k allele and has no effect on the ASIP allele interactions with MC1R. Current genetic tests can distinguish the K^B and the k alleles. At this stage we cannot

K^{Br} and the k alleles and breeders should rely on pedigrees to exclude or include the brindled phenotype.

Modifications of the colours defined by E,A and K

Melanistic Mask (E, E^M)

Some breeds of dog can produce a black mask when the rest of their heads are either fawn or brindle. This phenotype[7] is caused by the dominant E^M allele at the E^M locus. The no-mask E allele is the same as the dominant allele at the E locus. The mask phenotype is hidden in solid and spotted black, blue and brown dogs, however it may become obvious for a period of time if they fade to grey as they age. The E^M allele has been characterised genetically.

Brown or Chocolate (B,B^s,B^c,B^d)

The brown or chocolate phenotype is caused by modifications to the Tyrosinase Related Protein 1 (TYRP1) gene or the B locus. There are 4 alleles described at this locus; the wild type "B" allele is dominant over the other three alleles, b^s, b^d and b^c. If an individual has any 2 of b^s, b^d or b^c then all black hairs will, in most instances be modified to brown. There are exceptions where this does not apply. If you receive a result that is b^s,b^c or b^s,b^d your dog may only be a carrier of chocolate. Please contact GTG if you receive this result if you are interested in more information.

Therefore, in brown dogs the individual must first be able to produce eumelanin and thus have at least 1 normal MC1R "E" allele, and second have any 2 of bs, bd or bc alleles. Interestingly, the B locus also affects leather regions, such as the nose, eye rims and pads and this is irrespective of their E locus genotype8. In individuals that are "ee" at the E locus and "bb" at the B locus, their coat will be red/yellow, however their leather regions will be modified from black to liver. Individuals with brown coats will also have brown or chocolate leather regions. Note this modification of the nose leather is different to the fading, seasonal change of the nose from black to cream, observed in some breeds.

Dilution (D,d)

Many genes cause colour dilution in the canine. The D and G loci cause dilution of both black eumelanin and Red/Yellow phaeomelanin, however the effect on eumelanin is much more obvious than phaeomelanin.

The D and G loci produce the dilute black (blue, slate, grey) and the dilute brown (isabella, lilac) phenotype[7] in dogs that are normally black or brown. The difference between the two loci is that D locus, dilute phenotype is present at birth, whereas the G locus dilute phenotype usually occurs with age and is commonly referred to as "progressive greying".

The D locus is a modification of the Melanophillin (MLPH) gene and as mentioned, individuals are born with the dilute phenotype. There are two alleles described at this locus. The wild type allele (D) is dominant to the dilute allele (d). Therefore in order to be dilute, the individual must have 2 copies of the "d" allele. The D locus also dilutes the nose, pads and eye rim leather.

The G locus or "progressive greying" locus is unknown in canines, however a recent study in the horse has demonstrated an association with a specific allele of the Syntaxin 17 gene (STX17). Future studies will hopefully permit testing the G locus for the progressive grey phenotype.

Other loci are believed to dilute only phaeomelanin and some only in "ee" individuals. These loci cause the variation in red/yellow pigment that is observed in breeds such as the Labrador Retriever, Poodle and Afghan Hound where colour can range from white to fox red.

Conclusions

As described, many genes control hair colour in dogs. Currently we can test for 6 of these loci. Colour predictions are unique to each breed and are made through evidence accumulated about the breed and the assumption that some of the loci are fixed for particular variants.

In rare cases, recessive alleles may exist at low frequencies, at the predicted "fixed" loci of a breed. Through chance, these may be inherited from both parents, and the offspring will show a modified phenotype. By requesting tests for all loci available and not just the minimum recommended will limit the possibility of offspring displaying a modified phenotype.

Definitions

1	*Fixed*	*All individuals within the breed have 2 copies of the same allele.*
2	*Allele*	*A variant of a gene.*
3	*Recessive*	*Requires two copies for the phenotype[6] to be expressed.*
4	*Polymorphic*	*More than 1 form of the gene exists.*
5	*Dominance hierarchy*	*Alleles differ in their dominance over other alleles.*
6	*Dominant*	*Requires only 1 copy for the phenotype to be expressed.*
7	*Phenotype*	*The change that can be observed or quantified.*
8	*Genotype*	*The 2 alleles at a particular locus.*

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