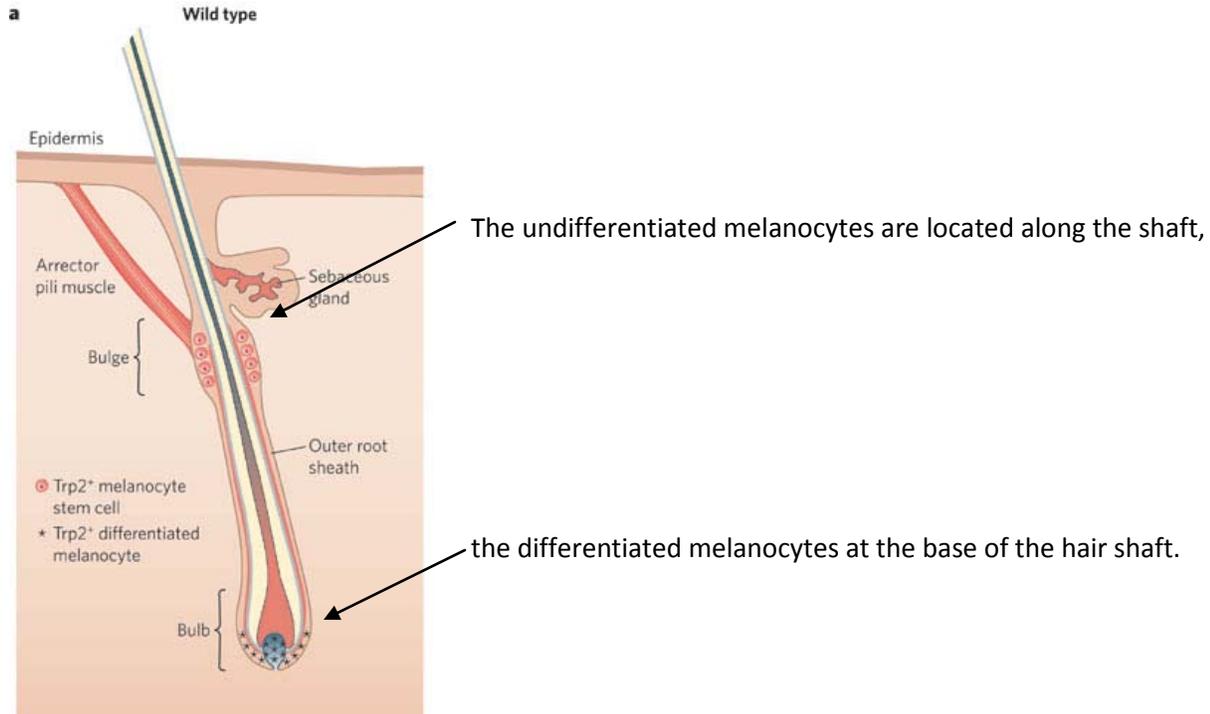


The Agouti Locus – more than 2 alleles of a gene at one locus

The study of the color genes in the dogs is a good way to understand how many different genes can affect one specific aspect of a dog – in this instance the color. Color in a dog is dependent on the function one cell located in the epidermis of the dog. In the case of hair color these cells are located along and at the base of the hair shaft.



Melanocytes make two types of melanin - eumelanin and pheomelanin. This is the molecule that produces the color of the coat. Eumelanin is black, or if altered by other genes blue gray or chocolate brown (liver). Pheomelanin generally is reddish brown or yellowish tan. Every melanocyte is capable of producing either melanin. The agouti locus produces a peptide that signals the cell to tell it what type of melanin, and which cells (or areas) should produce it. This determines where the black is produced in the coat.

There are 4 accepted alleles at the agouti locus in dogs. The locus producing dominant black used to be thought one of the Agouti alleles. However research has shown that dominant black is due to a different locus called the K locus. A^w is the "wild type" allele – this produces hairs that are banded with eumelanin and melanin. You don't see this in Lhasas – but this is the allele that you find mostly in the wolf and coyote. A^v is the sable allele. This is the dominant allele in the Lhasa. This allele determines not only where in hair the eumelanin (black) pigment is found but where on the body it is found. This allele causes black hairs to be interspersed throughout the coat to varying degree and the black "mask". There are some researchers that propose a separate locus determines the presence or absence of a mask. A^t is the allele that produces black and tan. The tan hairs have pheomelanin, and are located at the base of the tail, stomach, lower legs and around the eyes. The remainder of the coat is eumelanin and is therefore black. The aa locus is recessive black – unless modified by another locus, such as the E locus, the dog will be solid black. The dominance of the different alleles are thought to be as follows:

$A^w > A^y > A^t > a$

It would be nice if things were this simple however they are not. It is thought that there may be another allele – A^s or the saddle allele causing the black pigment to be located mainly in a saddle over the back. There also may be some incomplete dominance of the A^y over A^t , but this has not yet been proven. What affects the density of the black hairs – ie some sables are very dark and some very light, is not yet known. A^y may have only partial dominance over A^t . Some authors feel that heterozygotes (one of each allele) for A^yA^t may be darker than a homozygous sable (A^yA^y)

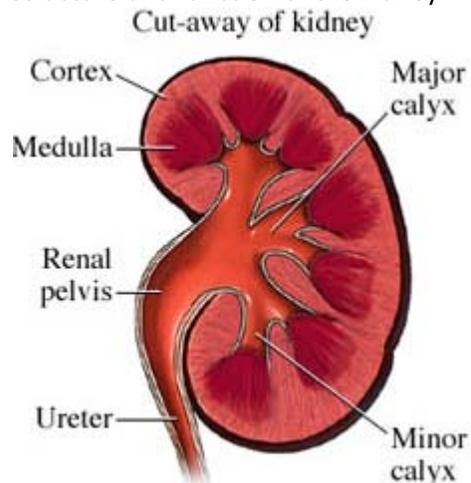
Now if that does not complicate things enough:

One locus affecting the expression of another.

The E or extension locus and the proposed K locus

The E locus determines whether or not the black at the Agouti or A locus will be expressed. The dominant allele is the E^+ or wild type. When this allele is present, and the dog has the A^y or sable allele the dog will be sable. Some authors feel that there is a E^M allele which produces the black mask, and some feel that the mask is produced by a totally separate gene or locus. A dog that has the recessive E^e allele of the E gene will have no black, there is only phaeomelanin produced. The shades fawn/red are affected by other genes. There is also postulated a K locus - or dominant black. It is thought that this locus along with the E locus affects the expression of color at the A locus. There are several other loci that determine progressive graying, dilution of color - for example black to blue (more like the blue/gray Weimaraners), etc. All in all there are 14-17 different genes that determine the color of the dog. These genes affect only one cell type - the melanocyte (Table 1).

Moving on to genetic disorders - I will use juvenile renal dysplasia as an example. The kidney has several different cell types - each important for kidney function. If there are 14-17 different genes governing coat color expression, then you can imagine how many different genes are involved in the development, structure and function of the kidney.



http://www.lifescript.com/Health/A-Z/Conditions_A-Z/Conditions/K/Kidney_cancer.aspx

The fact that renal dysplasia can be very mild to very severe leads to the conclusion that there must be more than one gene involved. This is why excluding any dog or bitch that has produced a puppy with renal dysplasia doesn't make sense. We have no idea how close these genes are on the chromosomes, they may perhaps be on totally different chromosomes. In the Fell Pony there is a disorder called Fell Pony Syndrome - the foal lacks an immune system and dies usually by the age of 3 months of severe infection. The exact genetics is unknown, however the breeders in the US and UK agreed (yes this is possible!) to never breed one carrier to another. The gene can eventually be bred out of the population, but the genetic diversity still remains. There are only about 3000 breeding mares in the world - so the gene pool is very small. Using this approach to control renal dysplasia only makes sense.

Next - hybrid vigor - how inbreeding and outcrossing can improve genetic diversity.

References:

<http://www.lhasa-apso.org>

Ruvinsky, A and Sampson, J (2001) **The Genetics of the Dog**, CAB International, 2001

Schmutz, SM and Berryere, TG (2007) *Animal Genetics* 38, 539-549

Table 1

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Table 1 Genes and loci discovered and predicted to be involved in dog pigmentation.

BASIC COLOURS	
A (agouti) = <i>agouti signalling protein (ASIP)</i> CFA24	
a^y	Fawn/sable (cream to yellow to red with darker tips) (some solid black hairs intermingled amongst reddish hairs in some breeds)
a^w	Wolf sable – wild type colour (many banded hairs – black-reddish-black)
a^t	Black-and-tan or brown-and-tan
a	Recessive black
B (brown) = <i>tyrosinase related protein 1 (TYRP1)</i> CFA11	
B	Black eumelanin
b (b^s, b^d, b^r)	Brown eumelanin
E (extension) = <i>melanocortin receptor 1 (MC1R)</i> CFA5	
E^M	Melanistic mask
E	Eumelanin (black, brown, blue) can be produced
e	Only phaeomelanin (red, yellow, cream) produced
K (from 'dominant black') = <i>(CBD103)</i> CFA16	
K^B	Black, brown or blue (eumelanin pigmentation only)
K^{br}	Brindle (on body region that would be phaeomelanin pigmented otherwise)
K^r	Expression of agouti alleles that express phaeomelanin possible
DILUTED COLOURS	
D (dilutes eumelanin) = <i>melanophilin (MLPH)</i> CFA25	
D	Not diluted
d	Diluted pigmentation
d2?	Diluted pigmentation with skin problems
C (coloured) = ? gene	
C	Full pigmentation
c^h	'Chinchilla' which causes paler eumelanin and phaeomelanin
c^a	Complete albinism
P (dilutes both melanins) = P gene? (dominant/recessive)	
P	Not diluted
p	Diluted but not to completely white
I (dilutes only phaeomelanin) = ? gene (co-dominant)	
I	Intense, not diluted
i	Co-dominant decrease in intensity
G (progressive grey) = ? gene (dominant/recessive)	
G	Greying at early age, progressive greying
G	Not greying
WHITE MARKINGS	
M (merle) = <i>(SILV)</i> (M/m is the merle genotype) (co-dominant) CFA10	
M	Not coloured
m	Coloured
S (spotting) = <i>(MITF)</i> CFA20	
S	Solid coloured
sⁱ	Irish spotting
s^P	Piebald
s^w	Extreme white
T (ticking) = ? gene (dominant/recessive)	
T	Ticked
t	Not ticked
R (roan) = ? gene	
R	White in homozygote
r	Coloured in homozygote
H (Harlequin) = ? gene (dominant/recessive if M allele causing merle is present)	
H	Harlequin if also M/m or M/M
h	Not Harlequin

The alleles are listed in their 'predicted' dominance hierarchy. Those in bold have been confirmed at the DNA level.

