A Discussion of

Coat Colour

Genetics in the

Lakeland Terrier

Chapter 3— DNA

By

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Dominance and Recessiveness - Pathways

When Gregor Mendel coined the terms *Dominant* and *Recessive* in 1866 he had no idea what genes actually were, it was mathematical analysis of assortment of traits in peas that led to the conclusion that genes must exist. Alleles in original form would always be the same and produce a standard characteristic (wild type) but where mutations have taken place over time the Mendelian genetics assumption is that a gene is dominant when just one allele of that gene is required to express a feature (trait) and it doesn't matter what the other one is doing (one recessive gene is just carried.) Obviously it follows that both alleles have to be the recessive gene for that type to be expressed.

Most traits do follow the recessive / dominant pattern. But there are more complex interactions between alleles, sometimes we see co- dominance such as mating Red cattle to White ones producing Roan. Partial dominance is really quite rare but does occur in snapdragon flowers where crossing a white flower with a red one produces pink. If Mendel's peas had one dominant *T* gene they were tall, they were not any taller for having two (*TT*) but Breeders sometimes think they can detect carriers of a recessive gene visually such as liver carriers having a bit of a liver cast to them and mating Red to Saddle Pattern producing pups with a lesser saddle, if this was correct it goes against basic Mendelian genetics and indicates partial dominance so such observations would have to be quantified in some way and recorded consistently to be convincing.

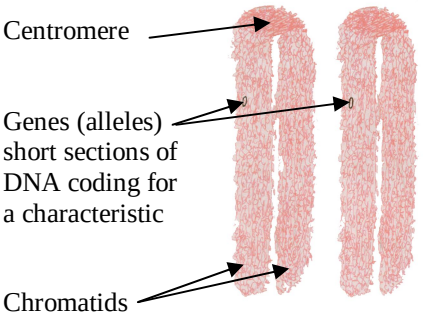
Most attempts to explain epistasis, in layman's terms, where one gene series affects another in terms of dominance and recessiveness are not fully convincing - the best way that I have found to think of this is in terms of pathways, for example:

The recessive red is controlled by the MC1R gene which initiates a complex signaling cascade that leads to the production of the brown or black pigment eumelanin in hair cells. The gene is about 1100 base pairs long but the *e* mutation is a change of just one base pair and that's enough to cause a stop to the cascade but with just one *e* there is still a pathway provided by the normal gene from the other chromosome so *E* is dominant and a single *e* can have no effect to stop black pigment being produced. Recessive genes such as *e* are generally acting negatively.
The complication is that the process can be "antagonized" locally by the agouti gene that can produce proteins in the dermal papilla cells at the base of a hair follicle, that binds to and inhibits signalling by the Mc1r. This is how the dominant red works when the *E* locus is allowing a pathway for the hair to produce black but the A^y allele of the agouti series overrides it and stops black being produced in the hair. Just one Ay allele will provide a pathway for the inhibiting protein to be produced so Ay is dominant to saddle pattern and the dog will be the dominant red type. Dominant genes are generally acting positively.
When the dog is homozygous for *ee* no pathway is provided for production of eumelanin in the coat, so by default melanocytes make pheomelanin in hair cells which gives no opportunity for the agouti saddle pattern and K genes to have any influence and the hair will be pigmented only with yellow. Of course the yellow shade is very variable but that's another matter.

The dilution genes *bb* and *dd* stop some function in formation of a proper black eumelanin where a single normal gene will provide a pathway but two mutants do not and the eumelanin is not fully developed or normally distributed in some way.

DNA and the genome (genome is a complete nuclear DNA sequence)

The dog genome isn't much different to the human one but it's divided into more chromosomes which are mostly not X shaped (as is typical for human ones) but with the centromeres more towards the end. In fact all mammals have much the same basic genome and most research on how genes operate has been done with Mice. The total length of the DNA double strands on each sides of the chromosomes is said to be about a meter, it has 3 billion base pairs which define about 20,000 genes in humans (a lot fewer than previously estimated.) and rather fewer in dogs All this has to be fitted into the cell nucleus just 0.01 mm diameter. If it was wound up like a ball of wool the genes would not be able to express themselves, in fact it is wound onto lots of little bobbins known as histones which compact and organize DNA. These compact structures guide the interactions between DNA and other proteins, helping control which parts of the DNA are transcribed. Although the chemistry might be complex the genetic code is simply a binary code like computer code, four different acids (guanine, adenine, thymine, and cytosine) link to form base pairs and it's the sequence of these bases that provide the genetic code. As *t* always pairs with *a* and *c* with *g* only one half of the double strand is required to obtain a sequence .Vast stretches of the DNA contain no genetic information at all and only about 2% of it actually codes for proteins by transcribing into RNA which produces proteins and folds them into structures that form the cell. Although the entire genetic code is contained in every cell only certain parts are active in any particular type of cell.



Representation of tightly organised DNA forming chromosomes

Of course there are two strands of double helix DNA –one inherited from each parent forming the chromosome pair and both can be coding for proteins. Pairs of genes on corresponding location (locus) on chromosome pairs are called alleles. Chromatids are not inherited complete, they break into pieces and recombine with pieces from each pair of chromosomes to form a new arrangement for reproductive cells, that is why it's almost certain that every individuals DNA is different.

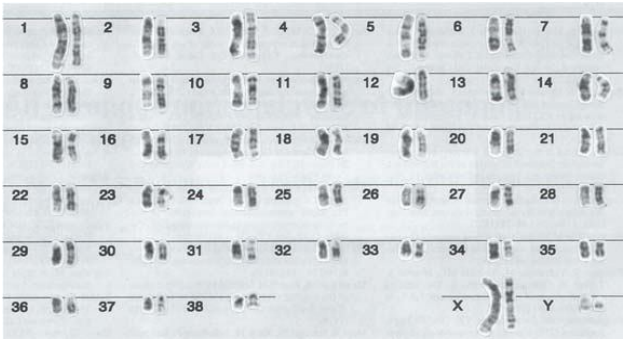
When cells are dividing it's possible to see the chromosomes with a microscope but we can't see into the DNA. Gene sequencing (DNA testing) to record the binary code is more complex but machines to do it, using a combination of chemistry and computing are now readily available, and by comparing sequences from different dogs it has been possible to identify exactly where on the DNA some of the colour coat genes are located and develop commercially available tests. "Pictures" of DNA structure and videos of DNA in action are computer models and simulations based on research using chemical and x -ray probes. A great deal of information is available on the internet at many levels of explanation but some of it can be misleading and in fact very confusing as there is little consistency with how the information is presented. For example DNA is sometimes show as a ladder with straight rungs –in fact the bases are angled across the two sides and when wound into the double helix from two unequal grooves. The base pairs are often shown as if welded together when in fact they do not actually touch but are attracted to each other by weak hydrogen bonds –slight differences in electrical charge. The hydrogen bonds are easily "unzipped" to allow the DNA to replicate. Many simplified drawings make no attempt to represent the alternating phosphate and sugar "backbone" strands on the outside of DNA structure. When studding into the biology the simplified explanations become less and less relevant but fortunately for dog breeders we don't need to understand much of the biology -just think in a abstract way what genes produce in the dog.

mtDNA

It should just be mentioned that the nucleus is not the only DNA containing organelle in the cell –**mitrochondria** contain a type of DNA that, as well as some other functions, produce by respiration, ATP (adenosine triphosphate) the energy for the cell. The mitochondrion has its own independent genome inherited solely from the mother with only mutation making small changes over time. However, many breeds contain several mtDNA types, suggesting that multiple bitch lines were involved in the founding of a dog breed.

The canine genome:
http://genome.cshlp.org/content/15/12/1706.long#sec-5

chromosomes



Dog chromatids stained

The term chromosome comes from the Greek words for colour (chroma) and body (soma) -bodies that are strongly stained by some colourful dyes used in research. It was once thought that the distinctive coloured bands could be the actual genes.

Centogenetic location

Some confusion is still created today when a band is identified as the location of a gene but this is just narrowing down it's location to within that area –each autosome chromosome has been ascribed a standard number and the sex chromosomes are designated X or Y. The bands also have numbers or if a gene is very near the centromere that's abriviated to "cen" and if its near the end "tel" or "ter" (telomeres define the end of a chmosome.)

Molecular location

Is the precise location counting along the base pairs of the chromosome
For example: 89,987,384 to 89.986,286

In standard notation a dominant gene is uppercase and a recessive lowercase the suffix for a variant is put as a superscript.
For clarification gene notation in the text has mostly been italicised.

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