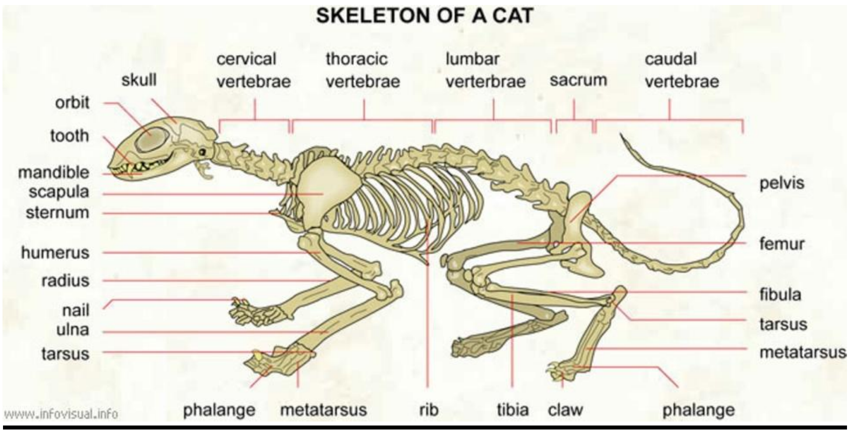
Basic Cat Genetics

Felis sylvestra



All domestic cats are descended from a wild ancestor (probably either Felis silvestris or Felis lybica) a mackerel tabby patterned animal; all domestic cats have an underlying genetic tabby pattern, even if they are solid coloured. Cats have 19 pairs of chromosomes which contain many thousands of genes that govern shape, size, sex, colour, pattern and hair length of the individual animal. During the evolution of domestic cats a number of mutations have occurred leading to a variety of phenotypes and colours. Man has used selective breeding to isolate cats with defined characteristics to produce the various pedigree breeds we see today. Genetic mapping and sequencing of the feline genome has indentified the genes that control coat, colour and pattern along with some of those that control body size, shape and conformation and others which cause diseases and structural abnormalities.

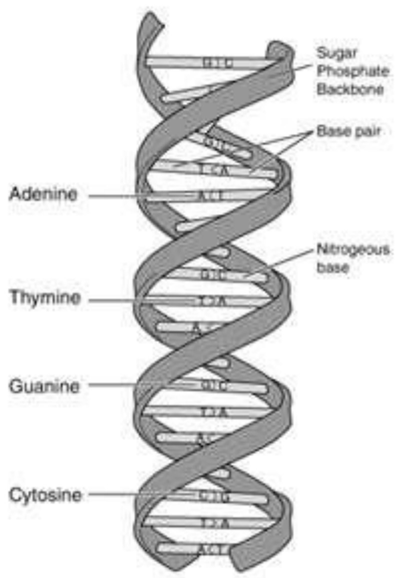
The mapping of the feline genome has indentified the genes that control coat, colour and pattern in cats along with those that control body size, shape and conformation and those which control diseases and structural abnormalities.

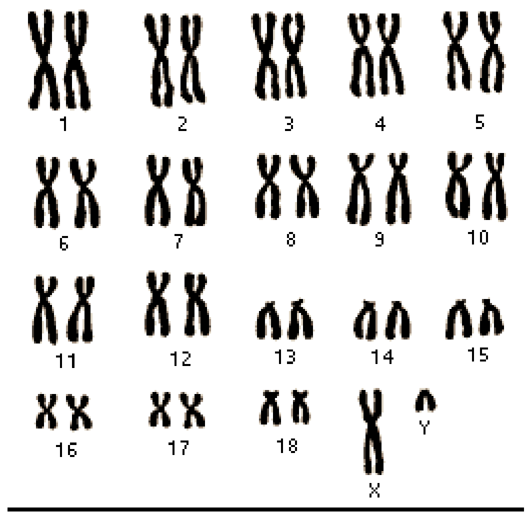
Genetics

Gene: (from the Greek genos) is the hereditary factor transmitted by each parent to offspring which determines hereditary characteristics. **Genetics:** the scientific study of the heredity of individuals, especially of inherited characteristics.

Genes: All animals have 20-25,000 genes; every living being that is reproduced from two parents inherits characteristics equally from both of them. These characteristics are determined by genes, control mechanisms carried rather like beads on strings along two rod-like bodies, called **chromosomes.** For each particular trait or characteristic, there is a gene arranged in a particular order along the chromosome that controls the expression of that trait.

Cells and Chromosomes: Living organisms are composed of cells. A typical cell contains a nucleus within which are DNA and RNA - the building blocks of life. The DNA is organised into chromosomes which in turn carry the genes.





There are two types of cells, body cells and sex cells, and in the cat each cell has 38 chromosomes, which are arranged in pairs-19 pairs in all. Sometimes both halves of a pair carry identical genes, sometimes not. Out of these 38 there are only two chromosomes that determine the sex of the individual-the **X** and the **Y** chromosomes. Only males have the **Y** chromosomes, and **XY** denotes a male, while the female is **XX.** Prior to fertilisation taking place at mating, the gametes (sperm or ova), receive half a set of chromosomes from each parent. During fertilisation, the sperm and ova fuse to produce a new genetic combination in the resulting fertilised cell or **zygote.** The newly formed zygote contains a random selection of those genes the parents have inherited from their parents. These then combine in the new cell to make up the full complement of 19 chromosome pairs. A zygote develops into an embryo/foetus/newborn by cell division called mitosis. In normal cell division, which creates new cells for growth, the full set of genes is replicated for each new cell.

The animal's genetic makeup is called its **genotype.** Some of these characters may be hidden and are not perceived when one looks at the cat. The outward appearance is the **phenotype.** The difference can be caused by **dominant** or **recessive** genes. There are also genes that are not fully penetrant, masking genes, modifier or polygenes, sex-linked genes, and inhibitor genes, as well as disease-causing genes (see later).

Homozygous & Heterozygous: If a kitten receives identical genes from both parents for a particular characteristic, ie the genes on that pair of chromosomes are the same, the animal is said to be **homozygous** for that trait. But if it receives a particular gene from one parent and an alternative from the other, the pair is made up of two different genes, and the animal is said to be **heterozygous** for that characteristic. Genes with a matched partner for a comparable characteristic-hair length for instance-are called **alleles,** and are found in the same spot or **locus** on the chromosome.

Dominant and Recessive Genes: If a cat is homozygous (**BB** or **bb**) the same message is sent and received, both genes on that pair of chromosomes are identical. If it is heterozygous (**Bb**) the dominant gene is in control – the recessive (**b**) is still there, but may have little or no effect over (**B**) its dominant partner. Solid white is a masking gene and is dominant to all other colours; black (or seal) are dominant to chocolate or cinnamon; tabby (**agouti**) is dominant to self or solid (**non-agouti**); shorthair is dominant to longhair, to mention just a few.

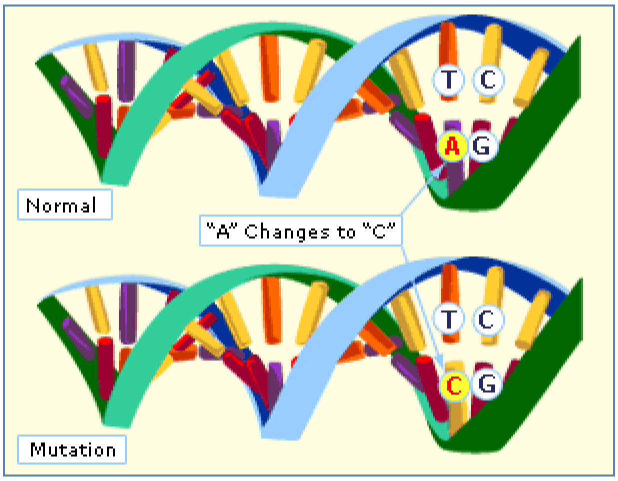
A Seal Point Siamese, for instance, is homozygous for the recessive Himalayan (or Siamese) pattern, but it may also be heterozygous if it carries the recessive gene for chocolate. Recessive genes may be 'carried' undetected for many generations.

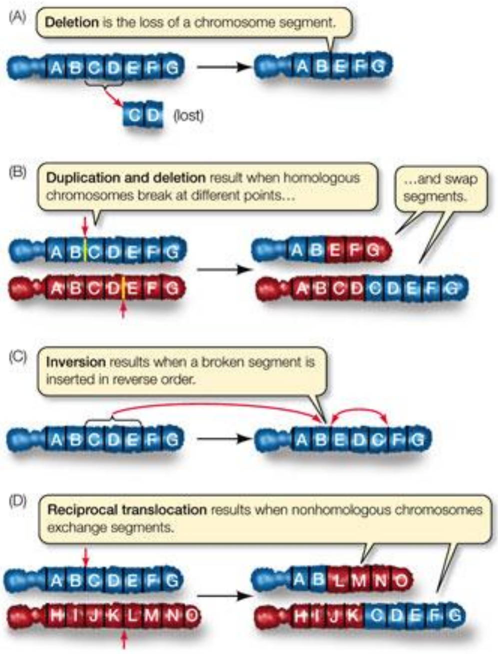
Undesirable Recessive Genes are very difficult to eliminate because they are not expressed or seen until they meet up with an identical partner in a particular mating (hence the desire for DNA tests to locate these genes). Some of the undesirable recessive genes which concern cat breeders are: kinked tails, squints, malocclusions, haemophilia, flat-chested kitten syndrome, cryptorchidism (no testes descended) and monorchidism (only one testicle in the scrotum).

Dominant genes include split foot, and polydactily (abnormal number of toes). Other abnormalities which are thought to be genetic but the exact method of transmission is as yet unclear are: luxating patella (footballers knee), amyloidosis, umbilical hernia, and protruding sternum. Genes for dwarfism, cleft palate, deafness, cardiomyopathy (heart disease) have also been identified in other mammals, eg humans and/or mice.

Once the basic rules of inheritance are understood, and the dominance or recessivity of any specific characteristics have been determined, it is possible to work out the characteristics to be expected from virtually any crosses between cats whose ancestry and genetic makeup is known.

Mutations: A rare mistake in the process of cell division or, for instance, the effects of radiation, can bring about minute chemical changes which produce a variation in the DNA, or mutation. Several mutations have given rise to the various coat colours and patterns we see in our cats today.





***LIFE 8e*, Figure 12.19**

In cats, the chocolate gene (**b**) is known to be a mutation of the black gene (**B**). It was a natural spontaneous mutation which changed black to chocolate by changing the eumelanin granules to a spheroid shape which refracts the light in a different way, making them appear chocolate. So the Chocolate Point Siamese was a spontaneous mutation and no outcross was used to produce the chocolate colour.

Many other feline mutations are obvious, such as the Rex coat, the hairless Sphynx, the ears of the Scottish Fold and the American Curl, the Manx, Japanese Bobtail, and so on.

Pigmentation: Melanin is the substance which causes colouration of the hair shaft. The size and shape of these melanin granules is what determines the colour of the cat, and these in turn are controlled by its pigment production genes. Melanin production is a metabolic pathway that starts with the amino acid, tyrosine.

The pigment granules in each hair of the cat's coat contain either **Eumelanin** which is black, or **Phaeomelanin** which is yellow. Black melanin or eumelanin granules are thought to be oval in shape and absorb almost all light. Red melanin or phaeomelanin granules are thought to be like elongated footballs in shape and refract light in the red-orange-yellow range. The true red gene, called orange by some geneticists and symbolised by O, converts eumelanin to phaeomelanin, and results in a rich orange-red coat. When the dilution gene is present, the colour appears cream or buff. The red and cream colour in the cat is called a sex-linked gene because it is carried on the X chromosome. To understand its mode of inheritance, we need to know sex and colour of parents. The mating of a red and a black parent can result in the spectacular mixture of shades of red and black seen in the tortoiseshell pattern that generally occurs in female cats. The possible kitten colours from the various combinations of red, tortoiseshell and non-red parents are better understood by the checkerboard colour diagrams,

Most reds and creams will show tabby markings to a greater or lesser degree, as the non-agouti gene does not affect phaeomelanin. To achieve a clear-coated red the cat needs to be an agouti (ticked) tabby and highly rufoused. Rufousing (or ruddyness) is an enhancement of ground colour caused by the rufousing polygene(s), as in selectively bred Abyssinans, and some brown tabbies, which show a rich warm apricot ground colour. A lighter brown($\mathbf{b^1}$), which is more reddish than chocolate (**b**), known as **Cinnamon,** is a different recessive of the **B** gene than the one that causes chocolate. It is not to be confused with the sex-linked red/orange gene (**O**).

Masking genes: Phaeomelanin masks eumelanin, so a red cat masks the black. **White** is not really a colour, but an absence of colour. The white gene is dominant and masks all other colours completely. The Foreign White is really a cat of quite another colour (usually a Siamese) wearing a white overcoat! Sometimes Nature gives us a clue by showing a few hairs of the underlying colour on top of a white kitten's head.

The genetics of coat colour in cats and other mammals is complex. During the development of the embryo, melanoblasts (precursors to melanocytes, the melanin-producing cells) migrate in a dorsal-to-ventral direction from the neural crest, and end up in the skin. This migration is controlled by at least two genes (w and S). Once at their target location the melanoblasts differentiate into the melanocytes and can start pigment production. The production of, pattern and location of pigmentation depends on additional genes some major and others minor or polygenetic in their effect; the major genes are discussed below.

Agouti (A) - the natural "wild" gene that is the basis of the tabby cat. The base agouti pattern is bands of black on a yellow background in wild mice, rabbits and cats; in the cat this is overlaid with one of the tabby patterns. The Agouti gene (**A**) is dominant over the non-agouti (**a**) gene, ie, the gene for solid colour,

Non- agouti or "hypermelanistic" (a) - a recessive gene mutation that turns the original "wild" tabby cat into a self black by overlaying the agouti base colour with melanic pigment, making the whole animal appear black, although often in certain light the underlying tabby pattern may still just be discernible. Other genes work to change this black pigment to other colours (see below).

Full Colour (C); reduced colour (c_b, c_s** or **c) - The **C,** or colour gene product is tyrosinase, an enzyme responsible for the first step in the synthesis of melanin from the amino acid tyrosine. The **C** allele is fully dominant and gives full coat colour. Alleles $\mathbf{c_b}$ (Burmese) and $\mathbf{c_s}$ (Siamese) produce thermo-sensitive (*temperature-sensitive)* versions of the enzyme – the enzyme works at lower temperatures but not at the normal core body temperature of the cat. Consequently, pigment production is restricted to the cooler extremities. $\mathbf{c_b}$ is less temperature sensitive than $\mathbf{c_s}$, so there is more pigmentation with $\mathbf{c_b c_b}$ cats than with $\mathbf{c_s c_s}$ cats. Even at the extremities, however, these temperature sensitive enzymes are not working to full capacity; the colour at the extremity tips of a Siamese cat is usually not as intense as the colour in a cat with the dominant allele, **C**. Allele **c** does not produce any active enzyme; **cc** animals are albino (white). $\mathbf{c_b c_s}$ cats are Tonkinese, a non-pure breeding hybrid of the Burmese and Siamese. (A litter of kittens whose father and mother are both Tonkinese may have up to 12 different coat patterns ranging from that of the typical Burmese and Siamese as well as intermediates.) The dominance series for coat colour alleles is $\mathbf{C} > \mathbf{c_b} = \mathbf{c_s} > \mathbf{c}$. (**C** is fully dominant over the other alleles; $\mathbf{c_b}$ and $\mathbf{c_s}$ are incompletely dominant with respect to each other, and **c** is fully recessive to the other alleles.) *Note: **cc** is the only genotype that is epistatic to the **W** allele; an albino cat cannot produce any pigment at all, no matter whether the melanocytes are present in the skin or not. Albino cats also lack eye pigmentation.*

Chocolate (b) and Cinnamon (b1) – two mutations of the basic black non-agouti gene which modifies black into dark brown or medium brown respectively

Orange (O) – this is a mutation on the X chromosome and is thus sex-linked. The gene eliminates all melanin pigment (black and brown) from the hair fibres, replacing it with phaenomelanin, a lighter compound appearing yellow or orange depending on the density of pigment granules. The O allele is also epistatic over the non agouti genotype; that is, the agouti to non-agouti mutation does not have a discernible effect on red or cream coloured cats, resulting in these self-coloured cats displaying tabby striping independent of their genotype at this locus. This explains why you can usually see some tabby pattern on red, cream and apricot coloured non-agouti cats, even if only on the head/face. Rufus polygenes, as yet unidentified, affect the richness of the orange gene's expression.

Dilute (d) – a recessive gene which reduces and spreads out the pigment granules along the hair-shaft and turns a black to blue, chocolate to lilac, cinnamon to fawn and red to cream.

Dilute modifier (Dm) – a dominant gene which serves to modify the action of the dilute gene (it has no effect on undiluted colours), it lightens and "caramelizes" the colour turning blue into brownish-grey, lilac and fawn into pale taupe (in all three cases known as Caramel) and cream into a warmer pinkish-cream tone (Apricot)

Inhibitor (I) – a dominant gene that suppresses the development of pigment in the hair of the coat, typically producing hairs that are fully coloured only at the tip and have a silvery white base. It has greater effect on the lighter pigment in an agouti cat, removing the yellow colour and turning the base colour white or "silver". In the case of a non-agouti cat the inhibitor removes colour from the base of the hair-shaft to produce a silvery white hair with a coloured tip, i.e a Smoke. This allele appears to interact with other genes to produce various degrees of tipping, ranging from deeply tipped silver tabby to lightly tipped silver shaded tabby.

Tabby patterning genes – Traditionally it had been believed that the three forms of tabby pattern were inherited as an allelic series; however it now appears as if at least two, and probably three, different loci are responsible for the various tabby patterns (Lorimer, 1995). At one locus are the alleles for mackerel and blotched (classic) tabby patterns with mackerel dominant to classic; at another locus is the Abyssinian or ticked pattern, which is epistatic (masking) to both mackerel and blotched; and at the third locus there appears to be a modifying gene for either the classic or mackerel patterns resulting in the spotted tabby pattern. The patterns can be summarised as follows:

Mackerel (Mc) – the basic striped tabby pattern that overlays the agouti base (ie "wild" form)

Ticked (T) – an incompletely dominant gene which removes most of the stripe pattern leaving the ticked agouti base pattern on the body with minimal overlaying stripes on legs, chest (necklace) and face.

Spotted (Sp) – current thinking is that it is likely that a specific single gene causes the spotted tabby pattern, breaking up the mackerel or classic pattern into elongated or rounder spots respectively.

Classic (mc) – a mutation of the mackerel allele recessive to all other tabby patterns which gives a blotched pattern with the characteristic "butterfly" motif across the shoulders and "oysters" on flanks.

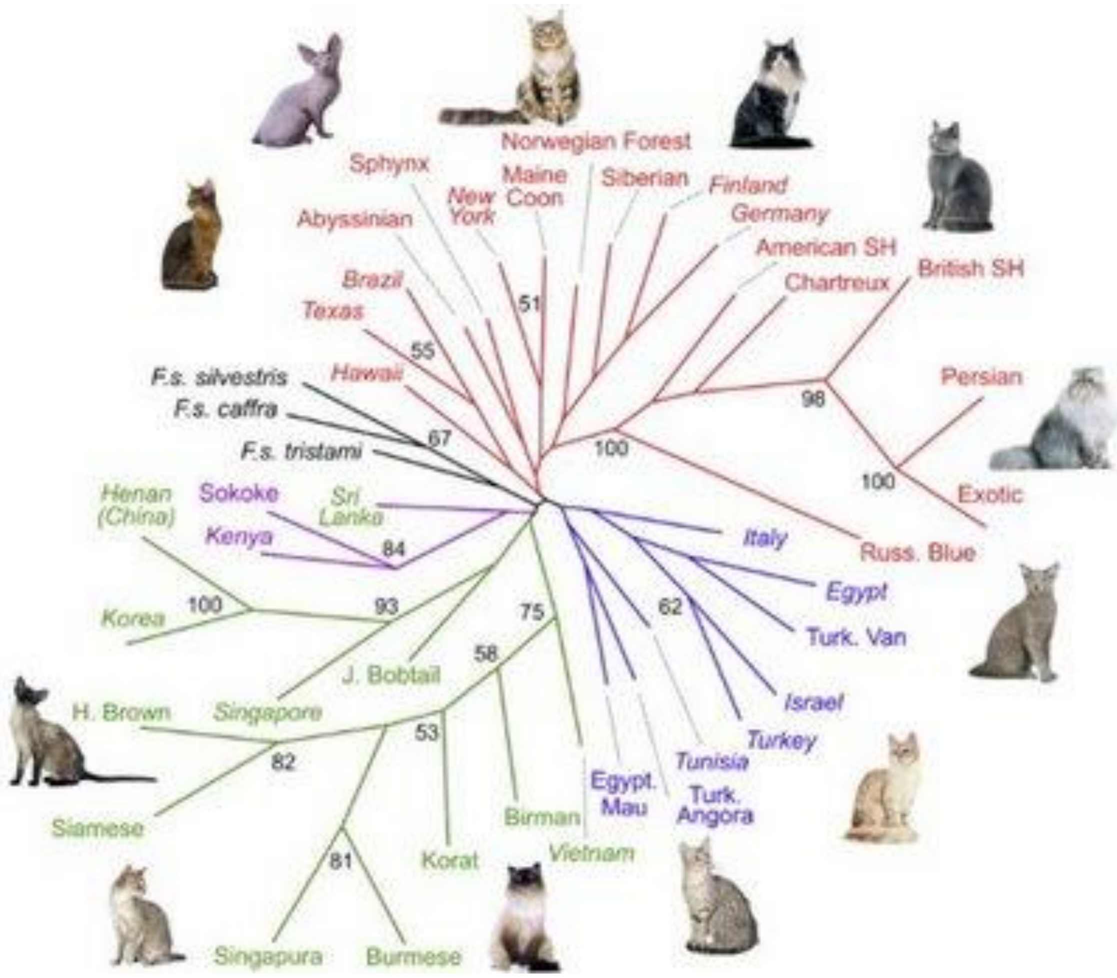
Wide-banding (Wb) – this has been hypothesized either as a gene (Robinson) or more probably a group of genes (Joan Wasselhuber, who coined the term "wide-banding genes"): increasing evidence for their existence has led to wide acceptance. Undercoat width genes determine the width of the undercoat whether or not the cat has a silver inhibitor gene. The term "undercoat" used here refers to part of the hair shaft closest to the body, and includes both guard hairs and the shorter hairs often referred to as "undercoat" hairs. The variability seen in the undercoat widths in cats points to the polygenetic nature of wide-banding genes. If a single gene it is likely an incompletely dominant gene mutation, the effect serving to push the darker, pattern colour in the cat up away from the hair base towards the tip, turning the normal tabby patterns into a Shaded or Tipped cat. Precisely how the agouti, inhibitor and wide-banding genes interact on a molecular level is not clear - one possibility is that the wide-banding genes influence the agouti protein production to remain high so that eumelanin pigment remains inhibited or down-regulated; another possibility is that the wide-banding gene encodes for a second inhibitory protein that also down-regulates eumelanin.

Long-hair (l) – a recessive gene mutation which produces a semi-long haired cat. **LL** or **Ll** cats have short hair; **ll** cats have long hair. Every kitten is born with all the hair follicles it will ever have. Each hair follicle can produce hair in several rounds. The hair has a distinct growth period followed by a resting period. Eventually, the hair is shed and the follicle will produce another hair. A popular hypothesis to explain long-haired cats is that in **ll** cats, the growth phase is extended beyond the normal range.

Dominant White (*W*) - is called the “dominant-white” gene because it is an **epistatic** gene. Before melanocytes can start making fur pigment, the melanoblasts must migrate to the skin. Melanoblasts make it to the skin only in **ww** (homozygous recessive) animals. In **WW** or **Ww** animals, the skin lacks melanocytes and the cat is a solid white color (**W** is a completely dominant allele). The epistatic dominant white phenotype masks other pigment traits. A cat that has any colour in its fur will be **ww**.

White Spotting or “piebald-spotting” (S) - is the "piebald-spotting" gene – a second gene that affects melanocyte migration. **S** and **s** are incompletely dominant alleles. In **ss** animals, melanocytes migrate evenly to the ventral surface of the animal, so the cat is completely pigmented. **Ss** animals have less than 50% white fur and **SS** animals have white patches on more than 50% of the body.

Polygenes – these are collections of genes which modify the effect of the main dominant and recessive genes above. A build up of polygenes creates a bigger effect, for example a collection of certain polygenes increases the length and density of the long-hair gene to create the Persian, and a build-up of polygenes serves to enhance the effect of the main colour genes, turning the effect of the orange gene from the sandy colour of the ginger domestic tom to the rich vibrant red of the Red Persian, British or Asian Self. It is likely that a group of polygenes is the reason for variation in the degree of tipping in the Shaded Tabby/Burmilla, the polygenes working to create the band-width in interaction with the inhibitor gene (when present) resulting in the range of pattern from tipped to heavily shaded. Also responsible for the depth of colour in fur or eyes



Applying Genetics to Breeding There are three recognised types of breeding: outcrossing, inbreeding, and line breeding.

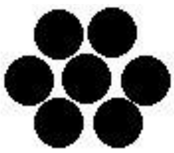
Outcrossing means breeding to unrelated stock in order to strengthen one's one lines; the term **hybrid vigour** is a key benefit of outcrossing. The problem with outcrossing is that along with all that vigour can come too many undesirable or unpredictable genes because with increased vigour comes an increase in the number of variable genes.

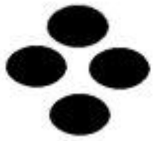
Inbreeding means back crosses to parents, and crosses to litter mates. It is important to know what is in one's breeding stock, and inbreeding is the easiest and quickest way of learning what is bad, but even more significantly, what is good becomes apparent as well.

Line breeding means breeding to a family of cousins of similar lines that have produced your own stock. Upgrade stock to the best points in each related line, and only line breed to an outstanding individual. The big deal is to get the genes we really want. To do this requires knowledge, patience and goals.

Pure breeding means cats that have registered ancestry, generation after generation standing behind them, and that means they should produce predictable kittens.

Glossary of Genetic Symbols

symbol	image	name	description
A		**agouti gene**	**native, wild, controls the production of pigment in the hair shaft, turning it on and off to produce a striped pattern on each hair**
a		**agouti off**	**mutation that blocks the normal on-off colour production and produces hair that is one solid colour tip to root.**
B		**black**	**native, wild, produces black (eumelanin) pigment granules that are round in shape**

b		**chocolate**	**mutation of B which changes the shape of the pigment granules to oval giving the impression of brown**
b1		**cinnamon**	**mutation of B which changes the shape of the pigment granules to cigar shaped to give the impression of the colour of cinnamon**
C		**Full Colour**	**native wild type gene, allows the production of full colour**
c		**no colour**	**two copies of this recessive gene will produce pink eyed white with no colour pigment**
ca		**albino**	**two copies of this recessive gene will produce blue eyed white cats with china blue eyes**
cb	.	**Burmese**	**a sight restriction of the colour production that is temperature sensitive. More pigment is produced in the areas of the skin that are cooler temperature.**
cs	.	**Siamese**	**a distinctive restriction of colour production with cooler areas being very dense pigment and warmer areas being little colour at all.**

D		**Dense**	**Dense production of pigment produced in the hair shaft**
d		**dilute**	**pigment granules are produced in clumps with spaces of no pigment between the clumps giving the impression of a lighter colour.**
I		**Inhibitor**	**a mutation that stops the production of colour in the base of each hair shaft**
i		**non-inhibited**	**native, wild, allows pigment to be produced normally**
O		**red**	**changes the pigment production from native eumelanin to phaomelanin**

o		**non-red**	**native, wild, allows normal production of Eumelanin**
S	..	**spotting**	**slows down the migration of pigment cells in the forming foetus leaving parts of the animal with no pigment (white)**
s	..	**no-spotting**	**native, wild, allows normal migration of pigment cells to cover the entire body.**
W		**white**	**blocks the production of pigment in the hair shaft leaving a coat with no pigment**

SC & DrKK – GCCFGenetics – January 2022