

## **Rabbit Coat Color Biochemistry**

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### **Melanin**

Melanin is the most basic color pigment. Melanocytes are the cells that produce pigments. There are two different main types of melanin. These are called eumelanin and pheomelanin. They are responsible for producing pigment in rabbits. Eumelanin is the range of dark brown to almost black pigments, and pheomelanin creates the yellow pigment. Both of these pigments are created from the same biochemical pathway that branches. Tyrosine changes via the enzyme Tyrosinase into Dopaquinone. It is from this that the eumelanin and pheomelanin pathways branch out.

### **The Agouti (A) Locus**

On a Chestnut Agouti's hair shaft, there are three bands of color. There is a slate under color, which is a result of eumelanin. The second is an orange band, which is a result of pheomelanin. The top band is black, which is caused by dense eumelanin. The cause of this banding is a peptide called the ASIP, or Agouti Signaling Protein. Melanocytes are cells that produce pigments. The ASIP signals production of pheomelanin in the melanocytes, which causes the orange band in the agouti.

There is a receptor on the melanocytes called "melanocortin receptor 1" or Mc1r. This receptor is also known as the "E" or extension locus. When it binds, it results in producing pheomelanin. This is the "link" between the agouti and extension locus that is clearly seen with the correctly colored Tri's versus the "torted" tri's. When two recessive self genes are present in place of the agouti gene, the Mc1r is not able to produce the pheomelanin for the light orange color.

When the Tan Pattern gene ( $a^t$ ) is present, there is no ASIP expressed on the body of the rabbit which is why it appears self in color. However, in the markings of an otter ASIP is still expressed so pheomelanin can be produced causing the fawn/orange markings.

The Self-Pattern gene (a) causes the ASIP to be absent, which allows the eumelanin production is seen on the entire coat of the animal. Of course, since the Self gene is recessive, two need to be present to cause this effect.

### **The Brown (B) Locus:**

The gene product called Tyrosinase related protein Type I (or, TYRPI) causes the brown intermediate band of eumelanin to turn into eumelanin black. This causes the black coloring. If a rabbit has the brown mutation the TYRPI will be inactive and eumelanin will not be in a mature form. Because of this, the chocolate is displayed because the eumelanin black doesn't cover it up. So, the intermediate band of chocolate brown pigment is carried up the hair shaft. This is what causes the chocolate color.

In cases where the red, orange, fawn, or cream colored rabbit are "smutty", or show excessive dark pigments, the chocolate gene will correct this. It works to hides the dark pigments, without losing intensity. The chocolate gene has no effect on pheomelanin, unlike the dilute gene. The dilute gene will cause the color to lose intensity.

### **The Color Locus:**

The C locus encodes the gene for the enzyme Tyrosinase. Mutations of this enzyme result in altered levels of melanin production, which changes the rabbit's coat color. Total inactivation of Tyrosinase causes albinism, which occurs when the C gene substitutes the A gene in the coding series.

Some mutations cause different levels of activity, such as what happens with the Chinchilla and Himalayan genes. In temperatures below 37 degrees Celsius, the activity decreases in the C Locus. This

affect is most easily seen in the Himalayan. Normal Tyrosinase activity occurs at 37 degrees Celsius. This temperature allows for the melanin production. The change in the melanin production is what causes the chinchilla, shaded (such as Siamese Sable), and Himalayan colors. However, it does not have anything to do with the tort color which is also classified as shaded, but is classified as such based on phenotype.

For the Chinchilla coloring, the effect on eumelanin production is hard to see. Some "black" rabbits may actually be homozygous for the Chinchilla gene. In other words, their genotype for the C locus is  $c^{ch3}c^{ch3}$  or  $c^{ch2}c^{ch2}$ . The color Seal occurs with  $c^{ch1}c^{ch1}$ , as there is very slight shading on a dark sepia animal. When the dark chinchilla gene is homozygous, the rabbit is very black and there may not be a visible difference. Most often, these rabbits are shown as blacks, when in reality they are not. If a rabbit that is supposedly black often throws Chinchillas, it very well may not be a true black. A way to test this would be to breed the "black" to a REW. If all the offspring are Chinchillas of some form, then the "black" is definitely homozygous for the dark chin gene. In Chinchillas, the levels of eumelanin are lower than the levels in a Chestnut.

#### List of the C Locus Genes and Melanin Production

C ~ Complete Tyrosinase activity

$c^{ch3}$  ~ Some temperature sensitivity, reduced eumelanin

$c^{ch2}$  ~ Some temperature sensitivity, reduced eumelanin (less than  $c^{ch3}$ ), no pheomelanin

$c^{chl}$  ~ Temperature sensitive but not to the point of  $c^h$ , pheomelanin production not totally eliminated

$c^h$  ~ Temperature sensitive mutation, where the change in temperature caused by the gene changes the melanin production

c ~ Inactive Tyrosinase

#### Dilute Locus

Contrary to popular belief, the dilute gene does NOT change the coat pigment. For example; the pigments present in a black rabbit are EXACTLY identical to that of a blue; a Chestnut's pigment is the EXACT same as an Opal, and so on and so forth. In a dilute, a protein called myosin 5a (Myo Va) becomes defective. Myo Va is needed for the active transport of the pigment molecules. Because Myo Va is defective when the dilute gene is present, pigment is not packed as densely on the hair shaft and instead is clumped and scattered, creating less intense, i.e. dilute, color.

#### Extension Locus

The "E" gene codes for a G-protein linked cell surface receptor. Activation of the Melanocortin receptor type I (McR1) by alpha-Melanocyte Stimulating Hormone (MSH) leads to a G-protein cascade. This in turn results in eumelanin production. Agouti Signaling Protein, or ASIP, causes a shift from eumelanin to pheomelanin production. So, in English, the E locus is like a switch from eumelanin to pheomelanin production, which is "turned on" by MSH and "turned off" by ASIP. The mutations leading to the inactivation of the E locus have a similar effect of "turning off" the switch, but with a permanent effect. Pheomelanin in this case is continually expressed, because it is turned on. Eumelanin is not expressed, so there is complete or almost complete absence of the dark pigment. This gives rise to the orange phenotype, among others.

#### English Spot Locus

During embryogenesis, the formation of an embryo, melanocytes migrate to where the melanin is found and produced. A lack of the melanocytes in an area will cause no melanin production, as mutations of the En gene inhibit melanocyte migration. This is caused by cell death, called apoptosis, of the pigment cells. Since the melanocytes die, there can be no pigment produced in the area. There are many genes involved in exact migration of melanocytes so no two broken patterned rabbit will have the exact same color spots.