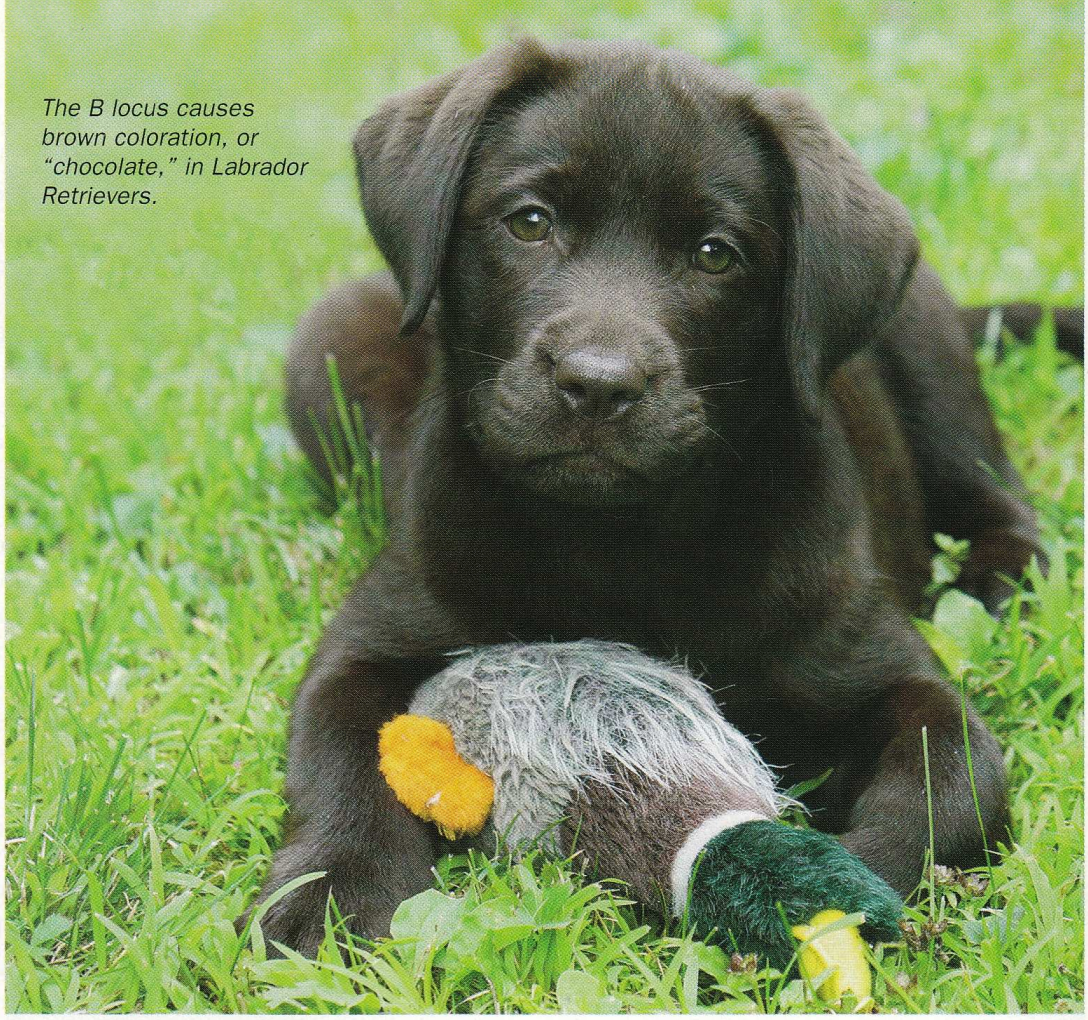

The B locus causes brown coloration, or "chocolate," in Labrador Retrievers.

Decoding coat color

Basic genetics of the canine color palette

By Leslie Crane Rugg and Eva Saks

In the 1950s, Clarence Little and Ojvind Winge wrote seminal works postulating genes that explain canine coat color and pattern inheritance. Since the mapping of the canine genome in 2005, veterinary geneticists have begun to confirm—or deny—the accuracy of Little and Winge's hypotheses.

Sheila Schmutz, Ph.D., at the University of Saskatchewan, is a leading researcher in coat-color genetics. She says, "We may be about halfway in discovering the key genes involved." These DNA discoveries give breeders powerful new tools to improve their breeding programs.

What Color Is Your Dog?

Breeders have been creative in naming canine coat colors and patterns: chocolate Labradors, apricot Poodles, belton English Setters, mantle Great Danes. But for all the variation in terminology and appearance, science has revealed only two basic pigments in dogs: eumelanin (black/brown) and pheomelanin (red/yellow). All coat-color variants result from these two pigments. The interaction and combination of color and pattern genes—called genotype—determine the phenotype, or visible shade of the pigment and its distribution throughout the coat.

To date, DNA mapping has identified several relevant coat-color and -pattern genes, each with its own set of alleles (variants of the same gene). Schmutz identifies the following eight:

- *Melanocortin 1 receptor* (MC1R), referred to as the E locus, establishes which basic pigment will be produced. It also produces masking.
- *Tyrosinase-related protein 1* (TYRP1), the B locus, causes brown, modified from black. TYRP1 allele interaction with color genes also accounts for non-black dogs presenting brown or black noses, eye rims, and pads.
- *Agouti signal peptide* (ASIP), the A locus, contains four alleles that interact with MC1R and prevent eumelanin dominance; instead, coats feature fawn/sable, a banded area of mixed pigment, black and tan configuration, or recessive black.
- *Beta-defensin 103* (BDEF 103), the K locus,

LABRADOR RETRIEVER PUPPY/MARY BLOOM

primarily reestablishes eumelanin dominance by undermining agouti alleles; alternately, other K alleles create brindling or remain neutral, not influencing agouti and melanocortin interaction.

• *Melanophilin* (MLPH), the D (dilution) locus, modifies both eumelanin and pheomelanin, diluting body or mask color, often including nose and foot-pad color. Schmutz cites diluted brown as in the lilac Shar-Pei and the Isabella Doberman Pinscher. Dogs with a clear red phenotype may also be affected by this gene, but the dilution is not easily seen.

• *Microphthalmia-associated transcription factor* (MITF), the S (spotting) locus, has emerged as a consistent cause of extreme white markings, random white spotting, and other variations of piebald coats.

• *SILV,* at the M (Merle) locus, causes merling. Leigh Anne Clark, Ph.D., a prominent researcher of the merle gene at Clemson University, says merling dilutes the base color to create a marbled look. It may also lighten eye, nose, and pad color.

• *Harlequin* (H), though the gene is not yet identified, is known to be a dominant modifier of merle. Unlike double merling, harlequin strips away only diluted pigment, leaving behind articulated white and black. This pattern is unique to Great Danes, and each dog is uniquely patterned.

But many color mysteries persist. One example is the gene and mutation creating progressive graying, which is not apparent at birth, Schmutz says. This type of graying is desirable in Yorkshire Terriers but dreaded in black Poodles.

Another example is the gene that creates ticking, described as "a dominant mutation that adds spots onto a white coat" by Danika Bannasch, DVM, at the University of California, Davis.

Nor have geneticists discovered the source of tweed, which causes dilution spots within the merle pattern, as seen in Australian Shepherds, according to C.A. Sharp, president of the Australian Shepherd Health and Genetics Institute.

Breeding for Coat Color and Health

Generally, "color is just color," Schmutz says. But four exceptions that link pigmentation to disease are canine cyclic neutropenia, white spotting and deafness, double merle deafness/blindness, and color-dilution alopecia.

Also known as "gray collie syndrome," canine cyclic neutropenia has been documented in rough and smooth Collies in the United States and in Border Collies in the United Kingdom. This disease produces a distinctive grayish coat color with a yellow or beige tinge, and loss of pigment on the nose (gray or pale tan). Internally, puppies suffer from low blood-cell production, resulting in life-threatening infections. Affected puppies rarely live to maturity. Healthgene Corporation (Canada) offers a simple DNA test enabling breeders to distinguish cleared dogs from carriers.

Deafness associated with certain forms of white spotting can be seen in any breed. White spotting is caused by a variety of different genes, affects breeds differently, and is not always linked to deafness. George M. Strain, professor of neuroscience at the Louisiana State University School of Veterinary Medicine, found an association between deafness and lack of pigment cells in the inner ear. More research is needed to clarify this link.

Double-merle dogs have a significantly higher incidence of deafness and blindness than single- or non-merle dogs. Double merles are produced when a dog inherits two merle alleles, one from each parent. The double merle is usually predominantly white with a few areas of extremely diluted color. "Breeders need to understand that while heterozygous [single] merles are desirable, homozygous [double] merles can suffer from auditory and ocular anomalies," Clark says. The percentage of double merles born deaf or blind is controversial, as is the question of whether these dogs commonly have physical problems beyond their eyes and ears.

The merle gene randomly dilutes base color for a mottled appearance.

CARDIGAN WELSH CORGI/CAROL BEUCHAT

Breeding merle to merle should be avoided. As Collie and Sheltie breeders have long known, a merle may safely be bred to a solid (non-merle) dog to produce merles. Testing for the merle gene is now available in North America through IDEXX Reference Laboratories, according to IDEXX's Janice Greenwood, Ph.D. With this test, breeders can confirm that their sable or tricolored dog is not a cryptic (or phantom) merle—that is, a dog whose merling is not easily visible but is nonetheless a merle genetically.

Color-dilution alopecia (CDA) is a disease of hair loss, sometimes with bacterial infection of hair follicles. It occurs in some but not all breeds with diluted coat color, and can affect dogs who are blue (genetically, diluted eumelanin) and what Schmutz calls "peachy red" (diluted pheomelanin). CDA afflicts breeds ranging from Doberman Pinschers ("blue Doberman syndrome") to Italian Greyhounds to Chows to Chihuahuas. The cause for CDA remains unknown.

Despite the current lack of data correlating color and pattern genes with additional health concerns, underlying factors do influence both color and physical characteristics. Schmutz says on her dog coat-color genetics website that "the pigmentation pathway shares many genes with other biochemical pathways. Therefore mutations in some of these genes which affect coat color, might also affect neurological function, immunological function, fertility, etc." GZ

Leslie Crane Rugg and Eva Saks collaborate on print and media projects related to dogs and culture, including articles for Animal Wellness, Fido Friendly, The Bark, *and no-kill PSAs.*