Color Implications in Health

By Sheila M. Schmutz and Tom G. Berryere, University of Saskatchewan, Saskatoon, Canada; schmutz@ sask.usask.ca. Biographical Sketch: Sheila Schmutz has been a professor at the University of Saskatchewan since 1986, where she teaches animal genetics to agriculture and veterinary students. Most of her research is done using DNA to study traits in cattle, including coat color, which as expanded in the past few years to include dogs (http://skyway.usask.ca/~schmutz/dogcolors.html). Sheila and her husband have had and bred Large Munsterlanders for the past 25 years. Her dogs "volunteer" for her DNA studies regularly but many dog owners participate by sending in cheek brushes for DNA from their litters. (As published in the Pinscher Patter, Dec. 2004)

Coat color has been of considerable interest to dog breeders from many years. In 1957, C.C. Little provided a comprehensive hypolthesis with many genes and alleles to explain most of the colors and patterns in dogs, based on breeding records. For the past few years we have studied genes involved in the pigmentation pathway at the DNA level (http://skyway.usask.ca/~schmutz/dogcolors.html). Many of Little's predictions have held true but some have not.

We found DNA polymorphisms in several genes in the pigmentation pathway. We used these polymorphisms or markers to map genes named EDNRB and DCT to chromosome number 22, KITLG to chromosome number 15, TYR to chromosome number 21 and TYRP1 to chromosome number 11. These markers have also been used in family studies to follow whether the same variant of the marker always was inherited with a particular coat color, pattern, or associated health problem.

We have identified multiple mutations in some genes such as TYRP1 that cause brown color, none of which have ill effects on health. Whereas other coat color genes have multiple effects, including some on health. Whereas other coat color genes have multiple effects, including some on health. For example merle, which when homozygous, usually causes deafness and sometimes also serious eye problems. We have conducted a family study using Australian Shepherds and have excluded several genes as the cause of merle: EDNRB, KITLG, MITF, ASIP, TYR, PAX3. We are currently studying Harlequin and merle in Great Danes using the polymorphisms in these same genes. Family and data collection are still ongoing but results thus far are more optimistic. Harlequin Great Danes are thought to be HhMm, or heterozygous at both the Harl and merle causing genes and so finding which gene causes the Harlequin pattern may also lead us to find the gene that causes merele.

It was suggested that "albino" Dobermans may have a mutation in tyrosinase, since that is the cause of many types of albinism in humans and mice. However, in a recenlty completed study, the entire coding sequence of TYR was normal in such Dobermans (GenBank AY336053) and also in blue and Isabella Doberman Pinschers. These results suggest that the P gene may be the cause of this albinism. We did find that these same Isabella and red Dobermans were both homozygous for the TYRP1 proline deletion mutation indicating both are actually brown in base color.

Black Hair Follicular Dysplasia is a disorder that has occurred in my own kennel in Large Munsterlanders. Areas of the coat that are normally black in color are grey at birth and then these weak hairs break and fall out. The underlying darkly pigmented skin is also wrinkled and sometimes pimply. Using this litter we have shown that neither MCIR, DCT, TYRP1, KITLG, nor TYR are the genes causing this disease. Colleagues at the University of Pennsylvania plan to continue studies of this disease and samples were also sent to other collaborators in Germany.

Currently, we are also studying MITF in microphthalmicied multiple forms of this gene in the dog (GenBank AY2400952). Alternate start codons and some differential splicing of exon 1 and 6 result in different forms in different tissues. There by a mutation in exon 1 may lead to an effect on the eye and not on coat color, whereas a mutation in exon 7 could affect both tissues.

We have recently identified the mutation in MCIR that causes melanistic mask. At amino acid 264 methionine is replaced by valine. Some dogs with melanistic mask have premature greying of the muzzle but his does not seem to be correlated with whether they are homozygous or heterozygous for mask. Some coat patterns such as Harlequin, merle and irish spotting can make it impossible to see the mask. Likewise dogs that are black or brown or blue do not show their mask against their similar body color. This further confirms that dogs in breeds where mask is part of the standard such as Bullmastiffs and Boxers, the reddish coat colors are due to the agouti alleles and not an ee genotype at MCIR.

In the course of this same study we were able to show conclusively that brindle is not caused by an MCIR allele, as Little had predicted. Several dog owners had found that the prediction of an Ebr allele did not fit their breeding data either

We thank the many dog owners who have contributed DNA samples from their dogs or complete litters to our study. In addition we are particularly grateful to C.A. Sharp (Australian Shepherds), J.P. Yousha (Great Danes), and Ione Smith (Doberman Pinschers) who coordinated collection of groups of animals in particular

breeds for family studies.

KEY TO GENE ABBREVIATIONS

Gene Abbreviation	Gene Name	C.C. Little's Locus
ASIP	agouti signalling protein	A Locus
TYRP1	tryosinase related protein 1	B Locus
TYR	tryosinase	C Locus?
MC1R	melanocortin 1 receptor	E locus
DCT	dopachrome tautomerase	
EDNRB	endothelin receptor B	
KITLG	KIT ligand	
MITF	microphthalmia transcription factor	
PAX3	paired box 3 protein	