

Defining the Scale of Merle

Chapter taken from the book ~ Merle - SINE Insertion from Mc - Mh the Incredible Story of Merle ~

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The following chart shows the comparison allele lengths from 4 different published papers.
(I have included an older 2015 paper in this comparison.)

#1 - scale includes only 2 alleles, M^c and M, from a paper published in 2015, “Milushova et al”. The length of the two alleles was set using the old testing method and based on phenotype. Dogs 252 bp and below were most likely to express no Merle pattern. Those 253 and above either had a noticeable Merle pattern or were starting to show signs of an unusual coat shading or faint pattern.

#2 - scale as set by Paw Print Genetics “Ballif et al” including 4 alleles, M^c, M^a, M and M^h based on phenotype, with M^a starting at 247 bp which was a number already set by Biofocus with the help of Dr. Helena Synková in 2011. This leaves the M^c extending as far as 246 bp.

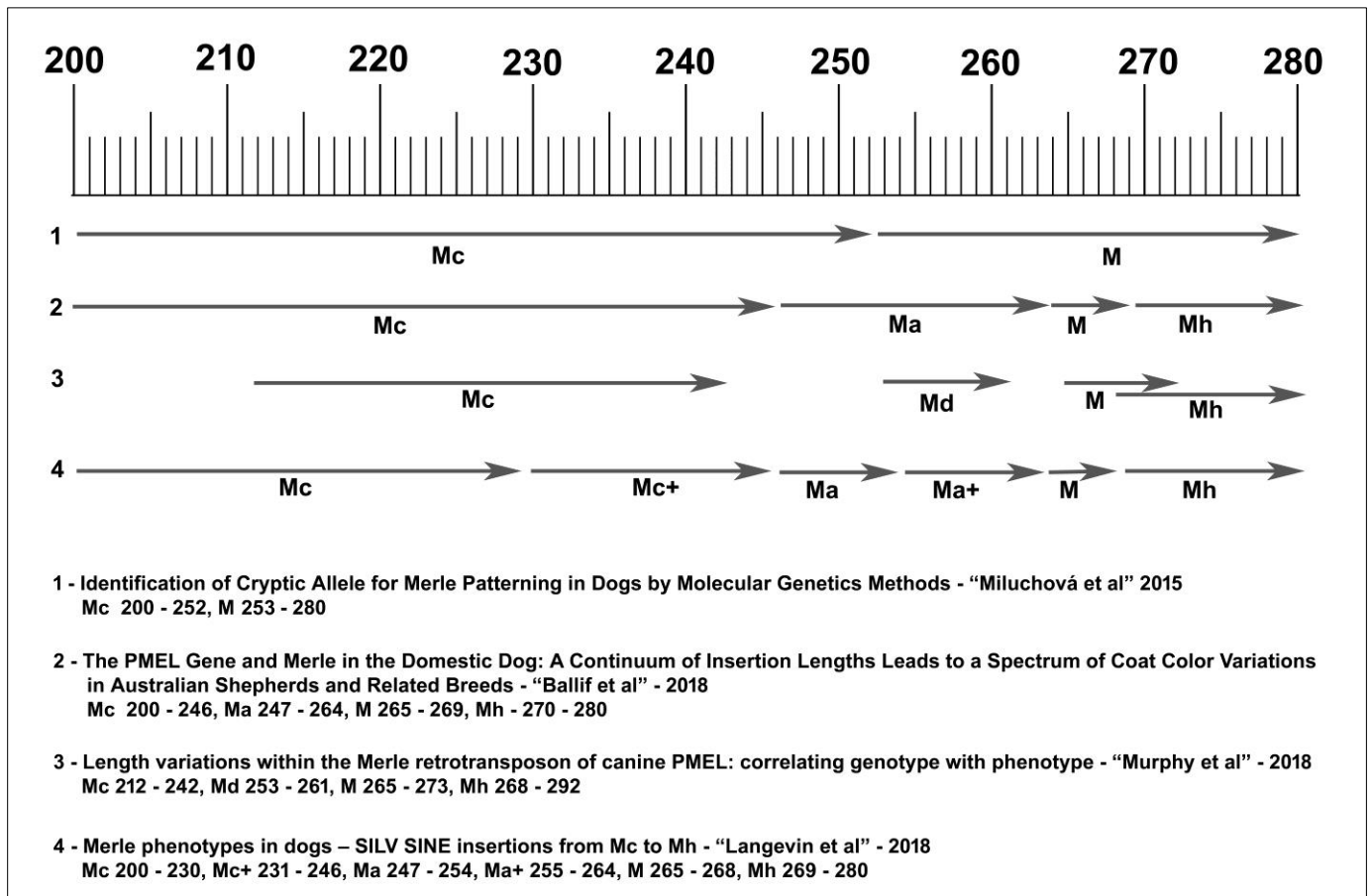
#3 - scale from the “Murphy et al” (Dr Clark) paper including 4 alleles with M^d (equivalent to M^a) starting at the same number as scale #1’s M allele of 253 bp based on phenotype. This leaves a gap between M^c and M^a with M^c possibly extending to 252 bp. M and M^h overlap.

NOTE – this paper uses T length numbers, I have converted them to base pairs for easier comparison.

#4 - scale as defined by “langevin et al” with 6 alleles – M^c, M^{c+}, M^a, M^{a+}, M and M^h

The two distinct differences between scale 1, 2 and 3 when compared with the “langevin et al” scale is that 4 is based on phenotype AND breeding results. These breeding results include HOMOZYGOUS results.

Scale 1, 2 and 3 have only included heterozygous dogs in their research. Given that Merle is an incomplete dominant this is a very important distinction which is explained and demonstrated in more detail on the follow pages.



Murphy et al

“Length variations within the Merle retrotransposon of canine PMEL: correlating genotype with phenotype.”

Sarah C. Murphy, Jacquelyn M. Evans, Kate L. Tsai and Leigh Anne Clark

Received - June, 5, 2018; Accepted - July, 27, 2018; Published - Aug, 3, 2018

Murphy et al. Mobile DNA (2018) 9:26 <https://doi.org/10.1186/s13100-018-0131-6>

#1 - Base Pair Ranges

“Base pair ranges that correspond to the four varieties of the merle phenotype: cryptic (212 - 242 bp), dilute (253 - 261 bp), standard (265 - 273 bp), and harlequin (268 - 292 bp).”

Note the lengths are not a continuum - there are gaps between cryptic/dilute and dilute/standard.

Their “harlequin” phenotype overlaps their “standard” phenotype. We did find a clear border between M and M^h.

Their “dilute” phenotype starts at 253 bp which compares to the lower end of our M^{a+} allele.

No difference in phenotype was noted under 253 bp which encompasses our M^c, M^{c+} and M^a alleles which are all “non-expressing”.

The expression of these 3 shorter alleles can appear very similar as heterozygous however as homozygous combinations they can create clear phenotypical differences. Since all 259 dogs in the Murphy et al paper were heterozygous for Merle there was no ability to compare base pair ranges as homozygous combinations or any combination with other length alleles.

Being that Merle is an incomplete dominant this is a very important distinction.



ASD - Rory - m/M^c - m/220



AK - Bullet - m/M^{c+} - m/235



LC - Monkey - m/M^a - m/248



ASD - Jax - M^c/M^c - 216/223



ASD - Sky - M^{c+}/M^{c+} - 234/246



LC - Lennox - M^a/M^a - 249/249

Paw Print Genetics

“The PMEL Gene and Merle in the Domestic Dog: A Continuum of Insertion Lengths Leads to a Spectrum of Coat Color Variations in Australian Shepherds and Related Breeds”

Ballif BC, Ramirez CJ, Carl CR, Sundin K, Krug M, Zahand A, Shaffer LG, Flores-Smith H.

Paw Print Genetics, Genetic Veterinary Sciences, Inc., Spokane, WA, USA

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Paw Print Genetics <https://www.ncbi.nlm.nih.gov/pubmed/30071510> PMID: 30071510 DOI: 10.1159/000491408

There are two main issues I would like to address when comparing the “Paw Print Genetics” paper to “Langevin et al”.

#1 - Base Pair Ranges

200 – 246 Cryptic - Most cases are non-merle but in rare cases may have very small merle patch(es) or subtle color anomalies.

247 – 264 Atypical - Most cases show a significant shift from normal coat color often giving a diluted color, show reddish undertones, or have an otherwise atypical merle appearance.

265 – 269 Classic - Most cases show classic merle with a significant amount of merle color and patterning, although some cases may only show a minimal amount of merle.

270 – 280 Harlequin Most cases display patches of multiple shades of the same or different colors without white (tweed) or with white (harlequin) and are often referred to as patchwork.

Their “Cryptic” bin of 200 - 246 bp includes both our M^c and M^{c+} alleles, which can express different phenotypes when homozygous and also when inherited with different length alleles.



The M^c allele as set with Vemodia at 230 bp will not delete pigment to white when combined with M.

However when M^{c+} is combined with M there is the possibility of pigment being deleted to white in the Merle pattern which some breed standards do not allow and could be a concern for impairments.

Cola is M^{c+}/M - 242/266 and has quite a bit of pigment deleted to white.

You will note that her M^{c+} allele is 242 bp which falls into PPG’s Cryptic bin.

Their “Atypical” bin of 247 - 264 bp includes both our M^a and M^{a+} alleles, which can express very different phenotypes either as heterozygous or homozygous and also when combined with the M allele.



Lassie m/M^a - m/251



Rodeo M^a/M^a - 249/249



Cougar m/M^{a+} - m/260



Bulleit M^{a+}/M^{a+} - 258/258

Two important distinction are -

m/M^a does not create a Merle pattern whereas m/M^{a+} can.

M^a/M^a will not create white in the Merle pattern whereas M^{a+}/M^{a+} can delete pigment to white.

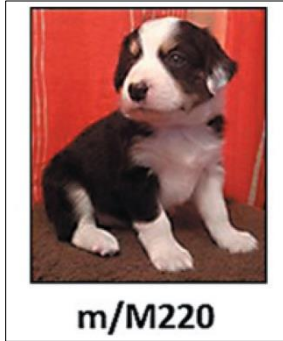
#2 - Cryptic and "small merle patch(es)" or subtle color anomalies.

m/M^c does not create any Merle pattern what-so-ever, nor any change to the coat color or shading.

The expression of Minimal Merle "small merle patches" is well documented to be caused by two distinct Merle genotypes -

#1 - M^h - Harlequin Merle

#2 - mosaicism where the longer M allele has become the minor allele.



PPG tested this pup as m/M^c and unfortunately came to the incorrect assumption that the M^c allele could cause "small merle patch(es)".

In this case correlation does not imply causation as any researcher should understand. This pattern on the pup's ear is NOT minimal merle caused by the M^c allele. This phenotype is commonly seen in breeds where "Whitehead" is common and there is pigment deletion on the ear area.

We have many examples of dogs tested as m/m Non-Merle with this same expression.



All these Australian Shepherds have tested as m/m - Non-Merle.

The pattern on the ear is NOT "Minimal Merle" but a pattern caused by the pigment deletion of Whitehead leaving a mix of white and pigmented areas. I would hope that 4 years after the publication of their paper Paw Print Genetics understands their error but they have not yet issued a revision on their paper nor changed the information they offer to their clients.

It is very unfortunate that their paper gives such incorrect information regarding the M^c allele.



This is Not a Minimal Merle Pattern

This type of residual black pigment interlaced with white is a common phenotype for "Whitehead" especially notable on the ear area.

Paw Print Genetics tested one pup with this phenotype as m/M^c in their research paper. They then made the unfortunate claim that M^c could cause "very small merle patches" (minimal merle). As a lab they should have realized that "correlation does not imply causation". This is not a "merle patch". After 4 years they must realize their error but have not yet revised their paper nor updated merle information offered on their website or test results they send to customers.

The M^c allele 200 - 230 bp will always express (and breed) the same as non-merle.

The following dogs express this same type of black and white pattern on the ear and are tested as m/m - non-merle



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