

Hairy New Findings in Dog Variation A Different Coat Is as Simple as One, Two, Three

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There is astounding variation that exists within dogs. There are different sizes, shapes, and colors. What causes this variety? How can there be so much diversity within a single species?

With the rapid accumulation of genomic data, these questions are beginning to be answered. Several different genes have been associated with variation in coat color of dogs.¹ Now, a new study has found that three genes account for most of the variation in canine fur patterns.²

The researchers of this fascinating study looked at three different coat characteristics: 1) “furnishings,” a moustache and eyebrows commonly seen in wire-haired dogs, 2) hair length, and 3) curl. After performing genome-wide association studies on more than 1000 dogs from 80 breeds, it was found that 95% of the variation in these characteristics was attributable to just three genes: RSPO2, FGF5, and KRT71.

RSPO2 Insertion Furnishing Moustache and Eyebrows

Furnishings found in wire-haired dogs were mapped to the R-spondin-2 (RSPO2) gene on dog (*Canis familiaris*) chromosome 13 (CFA13). The product of this gene is part of a pathway important in developing hair follicles. This pathway is also involved in the development of cystic hair follicle tumors, pilomatricomas, generally a benign neoplasm most commonly seen in breeds with furnishings. Dogs with furnishings carried at least one copy of an allele containing an insertion after the coding region.³

It might seem odd that a change in the nucleotide sequence of the DNA which does not affect the amino acid sequence of the protein could cause this interesting pattern of hair growth. However, this region can influence the stability of mRNA transcripts from which the protein is made. Consistent with this, the researchers found a three-fold increase in mRNA transcripts from this gene in the muzzles of dogs with furnishings. Since only one allele resulted in furnishings and none were found in animals without furnishings, this allele appears to be dominant. It is probably from a mutation, since it has not been found in wild dogs (such as wolves, coyotes, etc.), and it appears to alter the original function of the gene.

The role of RSPO2 is just beginning to be investigated. It is involved in more than just providing furnishings in dogs. It is part of a complex signaling cascade that is important for proper embryonic development. A study in mice where this gene was knocked out (destroyed) resulted in mice that suffered abnormalities in the bones of the midfacial region, loss of the distal limbs, and underdeveloped lungs. In fact, the mice died at birth from respiratory failure.⁴ This is in contrast to the increased expression of this gene in dogs, which provides for interesting variety with minimal negative effects.

FGF5 Mutation and Long-haired Dogs

The fibroblast growth factor 5 (FGF5) gene on CFA 32 was found to be associated with most cases of long hair in dogs. This gene produces a protein that is important in regulating the hair cycle.⁵ Mutation in this gene is associated with long hair in cats, mice, and dogs. In dogs the mutation resulted in an amino acid change (C95F) that apparently impairs the function of the protein. This allele appears to be recessive. There were three long-haired breeds that did not carry this allele, suggesting that other genes can sometimes be involved in long hair.⁶

FGF5 is expressed in the outer root sheath at the base of the hair follicle. With a loss-of-function mutation in this gene, the growth phase of the hair cycle is longer, resulting in longer hair. Although less conspicuous, one study in mice found that some hair shafts were abnormal and the surrounding skin was thickened. Interestingly, when skin from these mutant mice was grafted to normal mice, the long hair trait was maintained.⁷

One might assume that FGF5 is only important in hair growth, but this may not be true. Transcripts from this gene have been detected in various tissues during embryonic development and in adults. What is more likely is that redundancy was built in to the systems where FGF5 is important. In other words, when FGF5 function is impaired through mutation, there are other factors that can compensate so there is a favorable outcome.

Redundancy is an important concept in engineering. Airplanes are designed with redundancy so if one component fails during operation, the plane will continue to function. This should allow the pilot to continue and land safely. This practical and safe design does not arise by accident, but indicates intelligent forethought on the part of the designer.

KRT71 Mutation Sets the Curl

Curly hair in dogs was found to be associated with the keratin 71 (KRT71) gene on CFA 27. Several different mutations in this gene result in curly hair in mice. In dogs, only one mutation was identified; it is associated with an amino acid change (R151W).

The KRT71 gene produces a type II keratin expressed in the inner root sheath and is important in linear filament formation. This gene appears to be a hotspot for mutations in mice. Most mutations are similar to the dog in that they result in an amino acid change and mice with curly hair. One mutation in mice results in a severely truncated protein. In this case the mice start with curly hair, but end up losing their hair because of fragility of the hair shaft.⁸

Mix and Match Hair Coats

Various combinations of the alleles from these three genes give rise to at least seven different coat types. Short-haired breeds carry the wild-type alleles for all three genes. The wire-haired dogs always have furnishings and carry the mutant RSPO2 allele. Dogs carrying both RSPO2 and KRT71 mutations have a “curly-wire” hair that is somewhat longer and curled, while similar in texture to wire-haired dogs. Most long-haired breeds carry mutant FGF5 alleles. Dogs that carry both FGF5 and RSPO2 mutations have long hair with furnishings, but their coats are soft rather than wiry. Dogs with FGF5 and KRT71 mutations have long curly hair. No dogs were observed with KRT71 alone. When all three mutations were present, the dogs had long curly hair with furnishings.

Conclusions

These mutations identified in dogs certainly have added interesting variety with minimal negative side effects.⁹ Through artificial selection, many of these mutations have become fixed in various breeds of dogs. Sometimes people will point to these types of changes and claim that this is evidence for evolution. While creationists certainly agree that dogs have changed over time, the changes here do not provide evidence that dogs originated by a process of evolution from some single-celled organism long ago. Instead, it is obvious that these changes required the pre-existing complex pathways necessary for hair formation.

On a molecular basis, all of these changes are degrading the genome, not building it. These genes had to be designed to allow for changes to occur without destroying the animal. The ability of genes to tolerate these types of changes varies from gene to gene.¹⁰ Furthermore, redundancy appears to have been designed in by a Creator with considerable foresight so compensation was possible when certain genes were altered by mutation.

On close examination, these changes are evidence for an awesomely intelligent Designer who created life in a way that allows for some change. Such changes not only add interesting variety as seen here, but may also play a role in animals adapting to new environmental niches or allowing for increased productivity in agriculturally important species.

Footnotes

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2. Cadieu, E. et al., 2009. Coat variation in the domestic dog is governed by variants in three genes. *Science* **326** (5949): 150–153.
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5. Sundberg, J.P., M.H. Rourk, D. Boggess, M.E. Hogan, B.A. Sundberg, and A.P. Bertolino, 1997. Angora mouse mutation: Altered hair cycle, follicular dystrophy, phenotypic maintenance of skin grafts, and changes in keratin expression. *Veterinary Pathology* **34**(3):171–179.
6. Cadieu, Ref. 2.
7. Sundberg et al., Ref. 5.
8. Runkel, F., M. Klafthen, K. Koch, V. Böhnert, H. Büsow, H. Fuchs, T. Franz, and M. Hrabé de Angelis, 2006. Morphological and molecular characterization of two novel Krt71 (Krt2-6g) mutations: Krt71rco12 and Krt71rco13. *Mammalian Genome* **17** (12):1172–1182.

9. Theoretically, God could have created several alleles for different coat characteristics. In these three genes, I think it is more likely that these alleles have arisen through mutation. First, it doesn't look like these alleles exist in other canids (wolves, coyotes, etc.). If they were represented by the pair on the Ark, these alleles should be quite common in all sorts of canids. Second, it appears they alter the gene in a way that may increase risk of disease and/or deteriorate the original gene. Finally, the idea that God created some genes designed to be able to accept changes and allow for future variation is consistent with the characteristics of the biblical God (for example, He is wise, knows the future, and has abilities—including programming and engineering abilities—that greatly exceed ours.)
10. The RSPO2 does not appear to handle loss-of-function mutations as readily as the KRT71 gene. In the dog, the RSPO2 mutation was not a loss-of-function mutation, since more mRNA was detected than normal.

