

Scientists identify genetic basis for the black sheep of the family

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Coat color of wild and domestic animals is a critical trait that has significant biological and economic impact. In a study published online in *Genome Research*, researchers have identified the genetic basis for black coat color, and white, in a breed of domestic sheep.

In the wild, mammalian coat color is essential for camouflage and plays a role in social behavior. Coat color also strongly influences the animals we choose to breed both as livestock and as pets. Understanding the genetic determinants of coat color in livestock species such as sheep, specifically bred for their coat color, is critical for improving efficient selection of the desired trait.

Classical genetics has associated alternative forms, or alleles, of the agouti signaling protein gene (*ASIP*) with coat color variation in a number of mammals including mice, rats, dogs, cats, pigs, and sheep. However, most research has been focused on the mouse, with little understood about the genetic basis for coat color in economically important livestock species such as sheep.

The wild-type coat color of sheep is typically dark-bodied with a pale belly, however sheep raisers have strongly selected for a uniformly white coat domestic sheep. A problem for the sheep industry is a recessive black "non-agouti" allele of the *ASIP* gene carried by white sheep that cannot be distinguished within the flock, resulting in black coat color at a low, but persistent frequency. Determining the exact genetic differences at the *ASIP* locus could assist in efficient selection for white

coat color.

Scientists at the CSIRO Queensland Bioscience Precinct in Australia have now taken this step and identified the molecular mechanisms underlying white and black coat color in domestic sheep. The researchers investigated the genetic architecture of the *ASIP* gene in several sheep breeds by sequencing the *ASIP* locus and measuring gene expression. "Surprisingly what we found was in fact that the genetic cause of domestic white and black sheep involves a novel tandem duplication affecting the ovine agouti gene and two other neighboring genes, *AHCY* and *ITCH*," explains Dr. Belinda Norris, lead author of the study. "We discovered a novel mechanism in which the dominant white sheep is caused by the ubiquitous expression of a duplicated agouti coding sequence located immediately downstream of a duplicated *ITCH* gene promoter region." It was found that recessive black sheep harbor only poorly expressed non-duplicated agouti alleles, likely a result of a defective single-copy ancestral agouti gene promoter. The researchers also studied the *ASIP* locus in Barbary sheep, an ancient species exhibiting a tan body and pale belly. They confirmed in this ancient sheep that expression of a single-copy agouti gene determines coat color patterning, similarly to findings previously described in mice and pigs.

Norris notes that this work will aid in the development of gene copy number detection and analysis methods in the mapping and association of heritable traits in livestock animals. For sheep raisers, this could ultimately mean a genetic test that would identify carriers of the black non-agouti allele. Furthermore, these findings will help to unravel the events leading to the domestication of sheep, and future work may be able to pinpoint when the dominant Agouti mutation occurred, and whether it occurred as single or multiple events.

Source: Cold Spring Harbor Laboratory

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