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Trait Relationships and Genetics in Dogs

Mapping the genetic relationships between physical traits in purebred dogs

By

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Dogs come in countless shapes and sizes and exhibit more diversity than any other land mammal on earth, a fact that makes them especially appealing to geneticists. In the last decade, scientists working at more than 100 laboratories worldwide have made significant progress in painting a detailed picture of the complex relationships between physical traits, behavior and disease in purebred dogs, and the ways genes contribute to the striking differences seen across breeds.

Searching for related traits isn't a new idea. Literature indicates that as far back as the fourth century BC, people were looking for something physical, like tail carriage or ear length, to predict something intangible — courage or sagacity, for example. The Greek philosopher Xenophon, describing the interests and values of sporting men, said that tan-colored dogs with black muzzles were esteemed as the best hunters. Early 16th-century New World explorers differentiated Indian dogs from wolves by the curve of

their tails and their vocalizations. The 1785 edition of the Sportsman's Dictionary advised serious huntsman: "Coal black dogs prove incomparable hounds." On the other hand, the future was dubious at best for those dogs unlucky enough to be covered with spots: "Forego white hounds with black spots as they are never the best hare hunters."

New genetic research indicates that yesteryear's cynologists were on the right trail, but barking up the wrong trees. Dog breeds are not mix-and-match combinations of thousands of small parts; rather, they are more like combinations of genes prepackaged in bundles and shuffled around.

So, yes: traits are linked to one another, but with caveats. As scientists and statisticians note, correlation is not causation — just because two phenomena are related, it doesn't necessarily mean one causes the other. Sometimes, it's merely coincidence. The rooster crows when the sun comes up, but contrary to what the big chicken thinks, he isn't the reason it rises.

Molecular Conversations

Genetic interactions are less like a game of marbles, in which one gene strikes another and something happens, and more like a Rube Goldberg contraption: something seemingly simple is actually the result of a long list of intricate, complicated and extraneous events. Of the thousands of genes in the genome (dogs have about 19,000, compared to humans' approximately 23,000), an inordinate number are involved in communicating with one another, sending information that either activates or represses a "dimmer switch" in other genes. Although numerous genes act alone, thousands play multiple roles during development, telling the cells of an embryo what kind of living creature it is to become.

This molecular maneuvering isn't readily visible in most mammals. For instance, a human with a genetic variant that codes for extra height may grow to be 10 percent taller than the population average. But dogs are an entirely different story. The same type of genetic code in *Canis lupus familiaris* may result in a dog that's 40 percent taller than the population norm.

Coded for Variety

Mapping a genome is like revealing the image on the front of the jigsaw-puzzle box. You know it's a picture of a Boxer, but you don't know how all the interlocking pieces fit together to make the picture. Some solutions may be fairly clear, but, for the most part, our understanding of the way genes function is still based on a lot of guesswork.

In simple terms, geneticists use mega-computers to compare and contrast DNA patterns, looking for discrepancies. Patterns with omissions, transpositions or substitutions provide more precise information to help scientists assign meaning to genomic variations. They then match the anomaly in the DNA to the trait of interest.

This is how researchers identified genetic deviations that account for breed differences. In 2004, Heidi Parker, Elaine Ostrander and their colleagues at the Washington-based Fred Hutchinson Cancer Research Center published data indicating that as much as 30 percent of the dog's genetic material accounts for breed variation (Parker et al. 2004). Whether it codes for breed-specific size, shape, behavior or disease, or the 57 parts that make up the Heinz mutt, the metaphorical genetic needle hides out in one-third of the genomic haystack.

Foundation Traits

Depending on how much time is attributed to a generation and how many generations are

involved, scientists can determine breed age. Although closely related to one another (some more closely than others), breeds can be identified as distinct based on the way their DNA segregates, or separates during gamete formation. Data suggest that the most ancient breeds are dogs that looked similar to modern-day Basenji, Saluki, Afghan Hound, Tibetan Terrier, Lhasa Apso, Chow Chow, Pekingese, Shar-Pei, Shih Tzu, Akita, Shiba Inu, Alaskan Malamute, Siberian Husky and Samoyed. All the others — from Affenpinscher to Slovakian Rough-haired Pointer to Yorkshire Terrier — were created in the last 400 years.

Scientists suspect that many foundation traits differentiating ancient dogs evolved only once. Perhaps they were embedded in the genome of the now-extinct wolf species that begat domestic dogs. For instance, achondroplasia (short-limbed dwarfism), a defining trait in 19 breeds, including Dachshunds, Corgis and Bassett Hounds, is the result of a single evolutionary event (Parker et al. 2009). This means that mongrel dogs with short limbs are not necessarily mixes of short-limbed breeds. Rather, it's the other way around: short-limbed dogs were accompanying our ancestors long before Doxies and Corgis were engineered less than 400 years ago.

Brachycephalia (disproportionate shortening of the muzzle) is another foundation trait. A Boxer wouldn't be mistaken for a Pug, nor a Bulldog for a Pekingese, but they all share brachycephalic head types. Archeological evidence from ancient gravesites indicates that brachycephalia existed long before the formation of modern breeds. And indeed, a single genetic variation causes this trait, no matter how different the breeds look (Bannasch et al. 2010).

The challenge comes in teasing out the handful of genes associated with these foundation characteristics when the breeds that share them are vastly different. To do so, researchers devised a method to map dog traits developed under extreme selection: find the marker in a single breed and it will provide a clue as to where it will be found in all dogs. Because size differences are magnified in certain breeds, looking for genes associated with size was a starting point. Information gleaned from archeological sites indicates that small stature in dogs appears to be an ancient trait.

Genetic Messengers

Diminutive breeds can be as small as six pounds, whereas some giants weigh in at just under 200 pounds, and height can vary from less than six inches to as much as three feet. Even so, all puppies are born almost the same size, with short muzzles for nursing and stout legs for pushing siblings out of the way at mealtime. Why does one turn into a calm 180-pound giant and the other into an excitable eight-pound lap dog?

Studying the genetic make-up of 526 dogs from 14 small breeds, including the Chihuahua, Toy Fox Terrier and Pomeranian, and nine giant breeds, including the Irish Wolfhound, Saint Bernard and Great Dane, scientists pinpointed a specific gene-sequence variant in the canine genetic code associated with small size (Sutter et al. 2007). They concluded that a single gene that encodes an insulin-like growth factor is common to all small breeds and is nearly absent from all giant breeds, implicating it as a major influence on small stature in dogs. But there are exceptions. Though at some stage of early growth, all little dogs get the genetic memo to stay small, some dogs, like Rottweilers, are born with the small-stature variation but grow large in spite of it, indicating that in certain cases, something overrides the message associated with small size.

This is not to say, however, that a single gene controls size. In genetics, big is not the opposite of small. In other words, a dog who doesn't carry the small gene is not necessarily destined to be big. Researchers found several other gene variants that affect size to

various degrees; large size is linked to three of them.

In science, every answer prompts new questions. Having found the genes associated with smallness, scientists were eager to find other traits that might be related to size. For example, little dogs live longer than big dogs. Or so it seems. Is there a genuine connection between size and longevity and, if so, where is the link in the DNA? Longevity has been documented only since the mid-1980s. However, because life span was never selected for by breeders, any link in the DNA between size and life span would be a result of random chance rather than artificial selection.

Researchers found no evidence indicating that the largest individuals *within* a breed die earlier than smaller ones (Jones et al. 2008; to date, studies have been done on only a few breeds. Anecdotal evidence indicates this may not be the case in other breeds). But when they mapped traits *across* certain breeds of extreme size difference, they found that the genetic subset that influences size also plays a role in longevity. As the authors wrote, “This peculiar inverse correlation between longevity and size ... is strictly a between-breed phenomenon and provides an excellent example of a trait that can be approached with across-breed mapping ... [A] subset of loci, which control body size, also contribute to longevity, with some playing a greater role in the aging process than others.”

Is temperament linked to longevity? A 1997 analysis of rates and causes of death in more than 222,000 insured Swedish dogs provided baseline mortality data on 250 breeds from birth through 10 years of age (Bonnett et al. 1997). Using the population-based study and then attributing temperament traits to breeds, researchers found evidence suggesting that a breed’s typical boldness is also related to longevity (Careau et al. 2010).

Extreme Selection

In 2003, researchers found evidence indicating that dogs engineered for the chase, with long thin legs for running, have narrow heads and long muzzles because the width of the leg bone and the length of the skull are controlled by the same group of genes (Chase et al. 2003). Recently, scientists in the same labs published additional findings (Jones et al. 2008): two aspects of size and shape of the muzzle are linked; tail length, ear erectness and size appear to be related; and ear and tail shapes are linked, as are head and neck size. In addition, they identified a candidate gene associated with the degree of tail curvature and short coat.

Geneticists suspect that many multiple- trait relationships were developed under extreme selection and are linked to a few single genes that regulate systems controlling most types of growth, some of which have been favored by breeders, and others — like longevity — the result of unintended consequences. Breed development is rapid because, as noted earlier, most selected traits are tied to a few big bundles of prepackaged traits; very few characteristics are offered a la carte. Unless breeds have truly unique features (like the Lundehund’s triple-jointed polydactyl toes), most breeds could be recreated by bringing together the right combination of genes from related breeds.

The Brain Game

Characterizing behavioral traits is an inexact science at best. Ask 10 experts to define fear-aggression and you’ll likely get 10 different descriptions. However, a few behaviors are magnified to the point of being easily characterized: the intense gaze and stalking movement certain herding breeds use to move livestock; the stylized position pointing dogs take to indicate the presence of game; the retrievers’ act of fetching game and returning it to the hunter. Strung together in sequence, these behaviors make up the bulk of the predatory response wolves employ to hunt and survive. But, in some amazing way, artificial

selection extracts and segregates fragments of the sequence.

Scientists wondered: if a truncated motor pattern is exaggerated in a breed, will it be amplified in the DNA? The answer appears to be yes. Findings indicate that genes associated with herding, pointing and boldness are found in areas linked to brain development (Jones et al. 2008), and two gene variants tied to herding are in the same location as genes linked to schizophrenia in humans. This is not to say that Border Collies are borderline schizophrenics. But it does stand to reason that candidate genes associated with extreme behaviors include some that may be expected to play a role in regulating those behaviors. Genes tied to pointing are in the same area as cranial nerve development, and boldness is linked to genes that encode proteins affecting specific neural connections and signal transduction (the mechanism that converts a mechanical/chemical stimulus to a cell into a specific cellular response). Whereas small dogs are genetically predisposed to excitability, boldness has no relationship to size.

Health Linkages

In canine physiology, form, function and behavior are mixed up in ways we don't fully understand, and it's becoming increasingly apparent that health is part of the formula, too. For example, just as certain cancers tend to occur at higher rates within specific breeds, certain orthopedic diseases are linked to a dog's size. Researchers found that the incidence of two specific polygenic orthopedic diseases (those affected by multiple genes) — hip dysplasia and patellar luxation — are allied with the same gene variant that's associated with size (Chase et al. 2009). Additionally, scientists discovered that pancreatitis, which occurs more commonly in small dogs such as Cocker Spaniels, is also related to the size-gene variant. Selecting for growth rates may not be the cause of disease. Rather, it's possible that size extremes upset the balance of genes that control disease.

Breeders and scientists are working hard to discover what and where the problems are and how to solve them. How much influence does any one trait have on another? Do early-onset health issues like allergies predict the debilitating illnesses dogs experience later in life, such as Addison's disease, arthritis or even cancer? In a survey of blind guide-dog handlers conducted by the Morris Animal Foundation in 2008, we discovered that working Golden Retrievers have a less than 30 percent cancer rate, compared to a 62 percent cancer rate in the general breed population. Remarkable! Guide dog schools drop 75 percent of Goldens from their programs before the age of two due to any number of health issues, including chronic allergies. It's possible that allergies are predictors of cancer, but that hypothesis hasn't yet been studied.

Breeders want to know if they can remove deleterious genes that predispose dogs to fatal diseases and still hold on to desirable traits that create the essence of a breed. Getting rid of genes responsible for disease may dramatically change the way pedigreed dogs look and behave. Consider, for instance, the possibility that eliminating spinal degenerative disease will introduce inconsistency in tail carriage and gait, or that identifying markers for elbow dysplasia and removing carriers from the breeding population will affect the width of the chest, resulting in an appearance contrary to that described by breed standards, or how a breed is expected to move and even behave. If so, will we be willing to re-examine the definition of a breed as dogs who share characteristic appearance, function and a common gene pool, a Victorian-era mandate meant to suspend change in pedigreed dogs? What scientific findings in this decade will determine the breeding of dogs in the near future? Finding genetic traits and identifying their relationships to one another will assuredly be at the top of the list.

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