

NEWS AND COMMENTARY

Cause of extreme variation in dog morphology: mutation or selection?

Are dogs genetically special?

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Using the dog genome and the extensive variation among dog breeds to understand genetic variation in other species is becoming a reality (Lindblad-Toh *et al.*, 2005). In a recent article in *PLoS Biology*, Shearin and Ostrander (2010) review the dog as a model for biomedical research. They propose that three particular mutational mechanisms, high variability associated with microsatellites, high levels of repeat purity due to high basal slippage rates, and the abundance of carnivore-specific short-interspersed nuclear elements, are important explanations for the high phenotypic variation in dogs. In our opinion, two of their other proposed mechanisms, intense artificial selection and rapid perpetuation of either new or standing mutations in dogs, may be more parsimonious and more likely explanations for the extreme variation observed in dogs. In addition, the huge population size worldwide and long history of domestication in dogs appear sufficient to explain their amazing phenotypic diversity.

Shearin and Ostrander (2010) suggest that there is more variation among breeds of dogs than among other domesticated animals. However, most domesticated animals are livestock, such as pigs, cattle, sheep and goats, and these animals have been selected for specific economic attributes such as meat, milk or wool production. As a result, selection in these species is constrained by increasing or conserving these economic functions. On the other hand, different dog breeds have been strongly differentially selected for many characteristics such as various working traits (hunting birds, hunting mammals and guarding livestock) or other traits such as racing, for companionship, or even because of unique morphological traits. In some dog breeds, odd forms such as dwarfism and hairlessness have been selected, while in livestock these mutant forms would be non-functional, have negative pleiotropic effects and be strongly selected against. Examination of such mutants could be informative about gene function but may not be useful in understanding the effects

of natural variants. In fact, extreme selection in dog breeds in Britain has become scandalous (Williams, 2010), with focus on appearance resulting in Cavalier King Charles spaniels with brains too large for the size of their skull and Boston terriers with heads so large that 92% of them must be born by Cesarean section.

In livestock, the variety of types of selection is generally much less, for example, selection in milk or meat breeds of cattle and meat, wool or milk breeds of sheep, and even in these cases there is some constraint, with young males of milk breeds of cattle and wool or milk breeds of sheep being used for meat. Horses have been selected for their extensive size differences, because of the large size that is useful in draft animals and the small size used for riding by children, but again there has been some constraint on selection because of the general use for riding. Because of their use as companion and show animals, horses have also been selected for their extensive variation in color and other traits.

Perhaps domestic cats would be an appropriate species for comparison with dogs because they are mainly companion animals (selection as mousers is generally not related to specific phenotypes). In fact, the number of color and coat mutants in domestic cats rivals that in dogs. However, as cats are already small, size mutants for dwarfism or miniaturism would make cats too small and large-size mutants might make them too dangerous. In addition, cats do not have the extreme domesticated behavior of dogs, which is one reason why breeding for particular traits may be more difficult in cats. There is an old saying illustrating this behavioral difference, 'dogs have owners, cats have employees.'

Chickens may be somewhat closer to dogs in the variety of size, color and other variation that has been selected. Beyond selection for meat (broilers) and eggs (layers), chicken breeders and fanciers have selected for a variety of morphological traits, a diversity that was recognized by Charles Darwin. An excellent illustration is the remarkable

selection response that has been obtained in the high-growth and low-growth selection lines (Figure 1) that have been developed from a single founder population of limited size variation and where the two selection lines have been maintained with an estimated effective population size of ~35 (Dunnington and Siegel, 1996). After 52 generations of divergent selection, the two populations now show a 13-fold difference in body weight at 8 weeks and dramatic differences in appetite and body composition (PB Siegel, personal communication). In fact, this remarkable selection response has been obtained because it is a pure selection experiment with no constraints with regard to the productivity of the animals and, therefore, it resembles the selection scenario for some dog breeds. For chickens, it is not thought that unique mutational mechanisms are part of the explanation for the diversity but that large amounts of standing variation and intensive selection are mainly responsible for the success of artificial selection.

The data discussed in the paper by Shearin and Ostrander in fact argue against a high mutation rate as a major factor underlying the phenotypic diversity in dogs. They refer to previous studies that have shown that the same *IGF1* haplotype is associated with small size across breeds, that the same retro-gene insertion is associated with short legs across breeds and that the same mutations at only three genes are associated with changes in fur texture across breeds (also, the same 3-bp deletion at *CBD103* results in the dominant black phenotype throughout dog breeds; Candille *et al.*, 2007). This type of widespread occurrence of a single mutation with specific effects is frequently observed in domestic animals and reflects the strong phenotypic selection leading to rapid selective sweeps (Andersson and Georges, 2004). Illustrative examples of this pattern in other domestic animals include mutations in *STX17* causing graying with age in horses (Rosengren Pielberg *et al.*, 2008), in *IGF2* causing increased muscle growth in pigs (Van Laere *et al.*, 2003) and in *SOX5* causing the peacomb phenotype in chickens (Wright *et al.*, 2009). If dogs differed from other domestic animals with regard to their intrinsic mutation rate, we would expect to find more genetic heterogeneity at the molecular level in this species, but this does not appear to be the case.

Although examining the genetic basis of particular dog morphologies is important and will give insight into the



Figure 1 The low-growth and high-growth selection lines shown were developed by Professor Paul B Siegel at Virginia Polytechnic Institute and State University from a common ancestral population. The picture shows the dramatic selection response obtained after 40 generations of selections for low or high growth. The selection experiment is still ongoing and has reached the 52nd generation.

functioning and control of certain genes, it would be surprising if these studies lead to the conclusion that dogs are substantially different in their mutational mechanisms than other species. In fact, a great strength of model species, such as dogs, is that they can provide details of mechanisms widespread in related and even unrelated species that cannot be examined in such detail.

Conflict of interest

The authors declare no conflict of interest.

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