Review

Deciphering the genetic basis of animal domestication

Pamela Wiener* and Samantha Wilkinson

The Roslin Institute and Royal (Dick) School of Veterinary Studies, University of Edinburgh, Easter Bush, Midlothian EH25 9RG, UK

Genomic technologies for livestock and companion animal species have revolutionized the study of animal domestication, allowing an increasingly detailed description of the genetic changes accompanying domestication and breed development. This review describes important recent results derived from the application of population and quantitative genetic approaches to the study of genetic changes in the major domesticated species. These include findings of regions of the genome that show between-breed differentiation, evidence of selective sweeps within individual genomes and signatures of demographic events. Particular attention is focused on the study of the genetics of behavioural traits and the implications for domestication. Despite the operation of severe bottlenecks, high levels of inbreeding and intensive selection during the history of domestication, most domestic animal species are genetically diverse. Possible explanations for this phenomenon are discussed. The major insights from the surveyed studies are highlighted and directions for future study are suggested.

Keywords: animal domestication; breed differentiation; selective sweep; population bottleneck

1. INTRODUCTION

Understanding the history of domestication has been of interest to biologists at least since Darwin. He appreciated the wide variation within domesticated species, and throughout *On the origin of species* [1] (and later, in his two volumes of *Variation under domestication* [2]) he used them as examples of his theories. It is now well accepted that the process of animal domestication has involved a combination of human-imposed selection and non-selective forces, the latter including various forms of interference with the demography and mating programme of these species.

It is only recently, with advances in genetic and statistical technologies, that the genetic changes that have accompanied animal domestication and breed development can be characterized. A rapidly increasing number of species now have full-genome sequences. High-density, genome-wide single nucleotide polymorphism (SNP) panels have been produced for humans, as well as many other plant and animal species. A variety of statistical techniques have concurrently been developed to analyse this data. One of the key aspects of this analysis is to use genomic data in order to make inferences about the selective and demographic forces that have operated on individual species.

This review discusses the contribution that genetic data have made to our understanding of both selective and non-selective processes of evolutionary change in domesticated animal species, and the insights into the domestication process that have been revealed by these studies. Applications of various population genetic-based methods for the detection of genomic regions under selection are presented, as well as methods for elucidating non-selective processes; many of these, if not all, were first developed for human genetic analysis. This article does not attempt to review all the relevant literature, but rather to use specific examples to illustrate common themes. The examples presented are primarily taken from cattle, pigs, chickens and dogs, where the most advanced genetic resources are available.

2. SELECTIVE FORCES

The assumption underlying the detection of signatures of selection in the genome is that selection is locus-specific. By comparison, the effects of other evolutionary forces (random genetic drift, mutation and inbreeding) should be expressed genome-wide. Under this premise, the methods for detecting selected loci attempt to identify those at which allele frequencies have changed in a pattern consistent with positive selection. The methods differ in the information they use to find such loci (particularly as there are very few data on historical allele frequencies), which will be outlined further.

(a) *Candidate gene studies*

One approach adopted in domestication genetics is to examine patterns of diversity around candidate genes that, based on their function, are likely to have been targets of selection. Two such genes are growth differentiation factor 8 (*GDF-8*), associated with muscle conformation, and melanocortion 1 receptor (*MC1R*), associated with coat colour.

GDF-8 (myostatin) is a negative regulator of skeletal muscle growth, and naturally occurring mutations in this gene have been associated with increased levels of muscle conformation in cattle, dogs, sheep and humans. There is
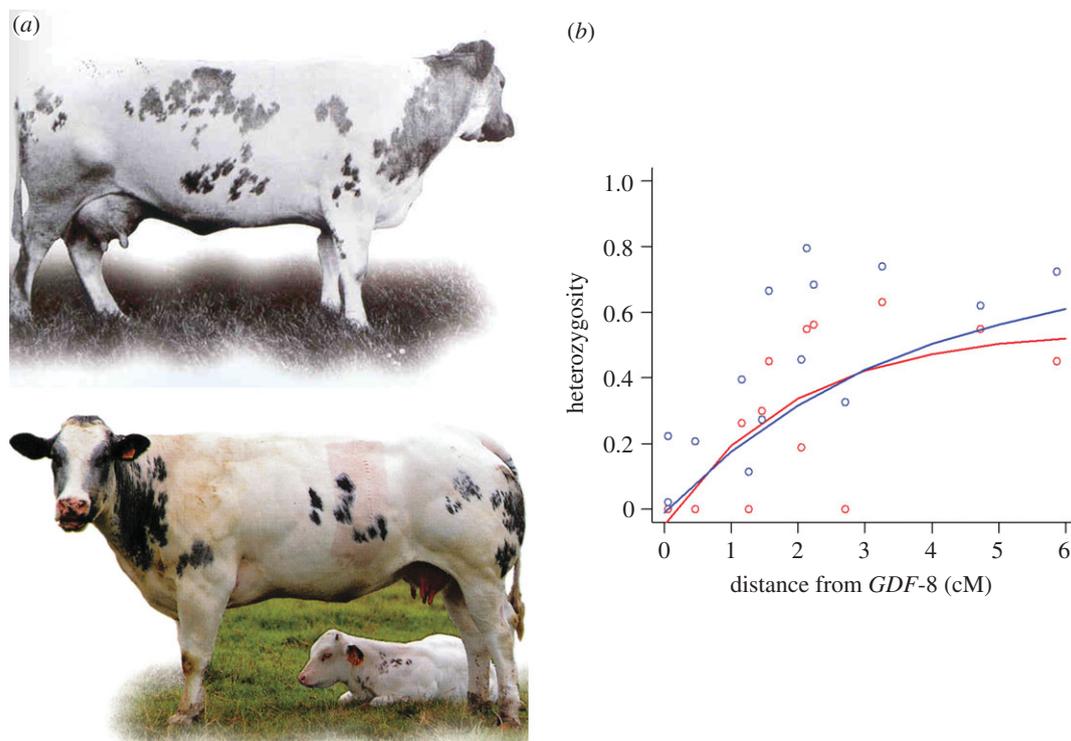
Figure 1. Selection for muscle conformation in cattle. (*a*). Belgian Blue cows from early (top) and late (bottom) in the 20th century (photos reprinted from Compere *et al.* [5]; stitches in the more recent photo indicate that the calf was delivered by caesarean section, which is common in Belgian Blue cattle and associated with the large size of double-muscled calves [5]). (*b*). Relationship between heterozygosity and genomic distance from the *GDF-8* (myostatin) gene for Belgian Blue and South Devon cattle homozygous for the 11 bp deletion (MH/MH) associated with double muscling (data from Wiener *et al.* [6] and Wiener & Gutierrez-Gil [7]). Blue circles, Belgian Blue; red circles, MH/MH South Devons.

substantial diversity in *GDF-8* across cattle breeds [3,4], including, at the extreme, two independent loss-of-function mutations that are associated with the 'double muscling' phenotype, in which animals have highly exaggerated muscle conformation. At the beginning of the twentieth century, the majority of Belgian Blue cattle had conventional conformation, and were used for both milk and beef production [5] (figure 1*a*). However, after less than a century of animal breeding, the double muscling phenotype is now nearly fixed in the breed, suggesting that there has been strong selection in favour of this trait, presumably owing to the increased amount of derived meat [8,9]. Analysis of microsatellite diversity in the region flanking the *GDF-8* gene revealed a significant decrease in heterozygosity with increasing proximity to *GDF-8* in three primarily double-muscled breeds, including the Belgian Blue, as well as in the sub-group of double-muscled South Devon cattle [6,7] (figure 1*b*), which was not seen in most non-double-muscled breeds. The pattern of heterozygosity in both Belgian Blue and South Devon cattle is consistent with strong selection on this gene. While evidence of a signature of selection near myostatin has not yet been published for other species, it is likely to exist as variation in this gene has been shown to influence traits of economic interest in breeds of dogs [10] and sheep [11].

Coat colour and pattern are key traits in the development of livestock and companion animal breeds, as they were under selection well before breed development [12]. A number of genes have been associated with coat colour in mammals, including the *MC1R* gene. *MC1R* influences the relative levels of eumelanin (black/brown) and phaeomelanin (yellow/red) pigments, and appears to have been a target for selection in pigs and other domesticated animal species. For example, there has been independent evolution of black coat colour in Asian and European pigs, and selection for this phenotype appears to have been particularly strong in Chinese pigs, where animals with the black coat were used preferentially in animal sacrifice rituals during the Neolithic period, because they were considered sacred [13]. Asian wild boar (the closest relative to the domestic pig) show extensive nucleotide variation at *MC1R*; however, nearly all European and Asian wild boar genotyped so far express the same *MC1R* protein, with genotypes differing primarily by synonymous substitutions [13,14]. This wild-type protein allows complete expression of both eumelanin and phaeomelanin pigments, and produces a coat in variable shades of brown [15]. In contrast, in domestic pigs, there is reduced synonymous variation relative to wild boar but at least nine different *MC1R* proteins in addition to the wild-type [14], which are associated with coat colour phenotypes ranging from red to black and including a variety of spotting patterns (white coat and spotting are determined by a different gene, *KIT*) (figure 2). Therefore, it appears that wild boar have been subject to purifying selection for a camouflaged coat, whereas a relaxation of this form of natural selection in combination with human-mediated selection for distinctive coat patterns has occurred in domestic pigs [14].

(b) *Differentiation-based approaches*
Changes within breeds have occurred on an evolutionarily short timescale compared with natural animal populations; however, there is considerable phenotypic

Figure 2. Coat colour variation in pig breeds. Clockwise from top-left: Berkshire, British Saddleback, Gloucestershire Old Spots, Large Black, Middle White and Tamworth (photos: S. Wilkinson).

variation between domesticated animal breeds, particularly in dogs. Recent studies in various species have applied an approach where markers with strong evidence of genetic differentiation (e.g. high levels of Wright's F_{ST}, a measure of genetic differentiation between populations, or allele-frequency differences) are taken as signals of differential selection across populations. This approach originated in the days when genetic markers were limited and sparse, and the focus was on specific markers [16,17], but in the current environment of dense, genome-wide markers for many species, genome scans of differentiation have become a viable strategy to identify selected genes or genomic regions using the tails of the genome-wide F_{ST} distribution to define the significance threshold [18]. For this and other approaches, it has been recognized that instead of using single-locus statistical values, a sliding window analysis removes the stochastic variation between loci, and thus better highlights regions with signals of selection [19,20]. Although the population-differentiation approach was developed originally for analysis of human data (and is still used in this context [18,21]), this technique is possibly even better suited to studies of domesticated animals because breeds are in general genetically similar entities and the differences that do exist may reflect the relatively recent selection for breed-specific characteristics.

Akey *et al.* [22] conducted an F_{ST} scan of the genome for 10 dog breeds and identified outliers, which they argued were candidates for targets of selection. This interpretation of the results was supported by the fact that five genes that had previously been mapped through association with 'hallmark' breed traits were among the 155 outlier SNPs (including the insulin-like growth factor 1 gene—*IGF1*, associated with body size—and several coat colour genes). Regarding the other outlier SNPs identified in their study, one of the highest F_{ST} values was only found in the Shar-Pei breed, which is characterized by its distinctive skin-folding phenotype. The region where the high F_{ST} signal was found contains several genes, including HAS2, the expression of which had previously been associated with skin wrinkling in this breed [23]. A recently discovered duplication upstream of this gene appears to be responsible for the wrinkling phenotype [24]. A separate study looking at genetic differentiation between 79 domestic dog breeds found that the top 11 F_{ST} values measured across all

breeds were found in genomic regions associated with morphological traits, including body size, skull and snout shape, coat characteristics and ear type [25].

For cattle, the genetic-differentiation approach has highlighted genomic regions that include genes encoding coat features or body size/conformation. Several studies have identified high levels of between-breed genetic differentiation near coat colour loci, including *MC1R* (see §2*a*) and the Charolais dilution factor (Dc locus), indicating that these genes have been important in the establishment of cattle breeds [26,27]. Another gene that has been implicated as a possible target of selection based on allele-frequency differences between cattle breeds is the growth hormone receptor (*GHR*) gene [26–28].

Although it is clear that large qualitative effects have been detected using these methods, there are known to be limitations to F_{ST}-based methods for detecting genes with small or moderate effects. Wiener *et al.* [27] found the overall correlation between F_{ST} and the statistical signal from linkage mapping analysis (see §2*e*) to be low in a study of two cattle breeds. While genes associated with coat colour could be detected as regions of large allele-frequency differences, the signals for loci associated with quantitative traits were generally weaker.

(c) Frequency spectrum-based approaches

A common approach to test for selection in human and wild plant and animal populations is to use 'frequency spectrum' tests in which empirical allele distributions are compared with those predicted under a neutral model. One set of methods involves searching the genome for regions with allele-frequency patterns that differ either from background (genome-wide) patterns or from those predicted by a neutral model [29,30]. These methods involve calculation of a composite log likelihood (CLL) for sliding window sets of genotypic data and testing significance based on a likelihood ratio test [29,30] or by permutation testing [31]. This approach has recently been applied to genome-wide SNP data for the 19 cattle breeds characterized by the Bovine HapMap Consortium [32]. In a follow-up analysis of this dataset, Stella *et al.* [31] calculated the difference for each SNP between the major allele frequency for a group of breeds defined by phenotype and the overall frequency across all breeds. For

black-coated breeds, there was a very strong signature of selection on BTA18 for windows that include the *MC1R* coat colour locus (see §2*a*). A signature of selection was also observed for polled (hornless) breeds on BTA1 within a region previously associated with presence/absence of horns. For dairy breeds, 699 putative signatures of selection were identified across the genome, with the highest (negative) CLL value on BTA6 near the *KIT* gene, which is associated with the level of white coat spotting in cattle. To make sense of the large number of significant results, the authors looked for cases where genes from the same gene family were at the centre of the significant window (e.g. potassium channel genes, integrins and arginine-/serine-rich splicing factors), arguing that these gene families may have been under selection during dairy cattle breeding.

Difficulties in applying frequency-spectrum-based tests to SNP data have been raised because of the bias towards high-frequency alleles inherent in SNP ascertainment, and thus interpretation of results can be problematic. While a number of solutions have been proposed to deal with this issue [33], in the long term the best remedy will involve use of full-genome sequence data in place of SNP data. Developments in next-generation sequencing are now making this a reality for many species (see §2*d*).

(d) *Extended homozygosity approaches*

Another population-genetic approach for the detection of selective sweeps has been to look for extended homozygous genomic regions. This approach is based on 'hitch-hiking' theory [34], in which neutral variants increase in frequency owing to linkage disequilibrium (LD, the statistical association between allele frequencies at different loci) with alleles at a selected locus, resulting in reduced diversity across the region.

One particularly convincing example of reduced diversity near a selected locus relates to chondrodysplasia (shortened limbs) in dogs. A genome-wide SNP analysis revealed a 24 kb region of reduced heterozygosity on chromosome 18 in chondrodysplastic breeds (e.g. Dachshunds) relative to non-chondrodysplastic breeds [35]. This region includes an insertion of a retrogene encoding fibroblast growth factor 4 (*FGF4*) in the chondrodysplastic dogs, the expression of which may result in altered activation of one or more fibroblast growth factor receptors. A similar pattern of reduced heterozygosity near the *IGF1* gene was observed in small dogs [36].

A number of statistical methods aim to distinguish the length of homozygous segments generated by selection from those generated by neutral processes, which extends the analysis beyond the heterozygosity of individual markers. One of the first methods introduced to exploit the hitch-hiking phenomenon in the context of high-density genotype data was the long-range haplotype (LRH) test [37]. In this method, the age of each core haplotype in a genomic region is assessed using the length of extended haplotype homozygosity (EHH). Unusually, high EHH values suggest a mutation that increased more quickly than expected under a neutral model. In an alternative approach, the logarithm of the ratio of EHH for an ancestral allele to that for a derived allele (iHS) is used as the test statistic [38], such that large negative (positive) values of iHS indicate selection for the derived (ancestral) allele.

The extended haplotype-based methods have been applied mainly to human genetic data, but they have also been implemented for several cattle datasets. Studies by Hayes *et al.* [28,39] found high values of iHS for SNPs in several regions of bovine chromosome 6, including one region with the *ABCG2* gene, associated with several dairy traits. The Bovine HapMap Consortium [32] also applied the iHS test across the genomes of 19 breeds and found high iHS values in one or more breeds on most chromosomes; these included regions on BTA2 near *GDF-8*, on BTA6 near *ABCG2*, and on BTA14 near a region associated with intramuscular fat. There were many other regions where a specific gene could not be implicated as a selection target. More recently, Qanbari *et al.* [40] applied the LRH test to denser (50 K SNP) data from Holstein dairy cattle. Although there were significant or nearly significant signals of selection for SNPs associated with some dairy-related candidate genes (e.g. the casein gene cluster encoding milk proteins and the *DGAT1* gene associated with milk fat percentage), of the SNPs with greatest significance levels, none were found near these candidates.

The advent of whole-genome sequencing opens up new possibilities for the detection of selection signatures. Rubin *et al.* [41] sequenced whole genomes of eight pools of chickens representing commercial lines, experimental lines and breeds selected for specific traits. The genome was searched for regions of low diversity by calculating a normalized pooled heterozygosity measure in sliding windows. One of the lowest statistics (suggestive of positive selection) was found in the region of the beta-carotene dioxygenase 2 (*BCDO2*) gene, which is associated with skin colour in chickens. One or more regulatory mutations that inhibit expression of the *BCDO2* gene appear to be responsible for the yellow skin phenotype [42]. Most chickens used for commercial egg and meat production in industrialized countries (as well as many local breeds worldwide) have the yellow skin phenotype and are homozygous for the recessive *yellow skin* allele locus, whereas other local chicken breeds have white skin and carry the dominant wild-type allele. The yellow skin allele appears to have been derived from a different ancestral species (possibly the grey junglefowl) than most of the commercial chicken genome (for which the red junglefowl is the presumed wild ancestor), suggesting a hybrid origin of commercial chickens (see §3*b*) [42].

The region with the lowest heterozygosity score across all domestic lines included the locus-encoding thyroid stimulating hormone receptor (*TSHR*) gene [41], which is involved in metabolic regulation and reproduction. This region was almost completely fixed over a 40 kb segment. Further analysis of this locus in domestic chickens from a number of countries revealed that each animal carried at least one copy of the derived haplotype (264/271 were homozygous). The role of *TSHR* in the domestication of chickens is still unknown; however, the authors suggest that it may be involved in the loss of seasonal reproduction present in non-domesticated relatives.

(e) *Genotype–phenotype association analyses*

A powerful approach for gene mapping in livestock species is linkage mapping, in which regions of the genome associated with particular traits (quantitative trait loci, QTL) are

identified. Populations generated by breed or line crosses have proved to be particularly useful for identifying the regions of the genome that distinguish the population founders. Although this technique generally identifies fairly wide intervals that include a large number of genes, in some cases it has led to the identification of individual genes that influence physical traits related to domestication, breed development or breed improvement (e.g. *IGF2* in pigs [43], *DGAT1* [44] and *GHR* [45] in cattle).

QTL-encoding physical traits may also be associated with behavioural traits. One such instance is the *PMEL17* gene encoding plumage colour in chickens, which was identified from a cross between red junglefowl and the commercial White Leghorn. A 9 bp insertion in exon 10 acts in a dominant fashion, such that birds homozygous for the ancestral junglefowl allele (*i*) are black, whereas those carrying the White Leghorn allele (*I*) are white (heterozygotes sometimes have minor pigmentation). It has been demonstrated that there are substantial behavioural differences between birds carrying the junglefowl and White Leghorn alleles, such that *i/i* individuals birds are more vocal, have lower activity levels in a test measuring fear of humans, and are more aggressive, social and explorative [46–48] than *I/I* birds, suggesting either that *PMEL17* has pleiotropic effects on behaviour or the existence of a closely linked behavioural locus [48]. This locus may also be associated with feather-pecking, a bullying behaviour that can result in severe damage to the victim [49]. Darker birds tend to suffer more from feather-pecking compared with their white counterparts [46,50]. However, it remains unresolved whether the effect on feather-pecking is due solely to the plumage colour or whether the behaviour of *i/i* birds makes them more likely to be targets of pecking.

The case of *PMEL17* is particularly interesting in that it demonstrates the possibility of selection for correlated traits in domesticated animals. It is likely that the behavioural traits associated with *PMEL17* were not the target traits in the development of the White Leghorn breed but may have been co-selected owing to selection for white plumage. Association between behavioural traits and coat colour appears to be a common phenomenon. Genes in the melanocortin system (including *MC1R* and the *agouti* gene) have been associated in mice and other vertebrate species (e.g. lions, lizards and birds) with both coat colour and various behavioural traits, including aggressiveness, sexual behaviour and learning behaviour [51]. Eumelanin-based coloration is generally associated with more aggressive behaviour. In her treatise on cattle breeds, Felius [12] claims that the Romans and later Europeans also associated coat colour with cattle performance traits: a red coat (the most common phenotype) was associated with a 'fiery' and hard-working character, whereas the rare white coat was associated with a sluggish and lazy disposition. However, the genetic association between behavioural traits and coat colour is not universal, as demonstrated by a study on rats in which 'tameness' QTL (see below) were on different chromosomes from a QTL segregating for white coat spotting [52].

In some cases, correlated selection appears to go in the other direction, such that selection for behavioural traits may result in associated changes in more visible phenotypes, as has been seen in the well-described selection experiment involving the silver fox (the 'farm-fox experiment') [53]. Initiated in 1959 in Novosibirsk, Siberia, the original fox population showed continuous variation for tameness/aggressiveness. A breeding programme was established with 100 females and 30 males, from which foxes were selected for their tameness using severe selection criteria [54]. The resulting population of tame foxes behaved much like domestic dogs. Behavioural traits other than tameness also evolved (e.g. tail wagging, licking). Moreover, in addition to the changes in behaviour, other morphological changes also occurred, some of which are reminiscent of dog breeds. For example, traits such as floppy ears, curly tails and shortened snouts appeared in some foxes. Recent development of a linkage map for the silver fox [55] has allowed QTL analysis of backcross and intercross populations derived from the tame population and an unselected (aggressive) population. QTL for several tameness-related behavioural traits map to fox chromosome 12; however, it is still unclear whether these are associated with a single locus [56]. Furthermore, inconsistencies between results from different crosses suggest a complex inheritance pattern (e.g. strong epistatic interactions) for these traits.

The study of silver foxes suggests that laboratory selection for behavioural traits can emulate the process of domestication. Other researchers from Novosibirsk conducted an experiment selecting for reduced or enhanced aggression to humans in a population of wild-caught rats [57]. Like the silver fox, this population has recently been exploited using genetic techniques to map regions of the genome associated with 'tameness' (as referred to above), defined by a linear combination of a set of behavioural traits [52]. QTL analysis indicates that more than one region is involved in the evolution of tameness in these rats [52] and that individual QTL may comprise multiple sites [58].

Modification of behaviour is believed to have been one of the key aspects of animal domestication, including selection for 'reduced fear, increased sociability and reduced anti-predator responses' (p. 5 in [59]). As dog breeders and owners know well, behaviour is also associated with breed differences. In an investigation of four composite personality traits (playfulness, curiosity/fearlessness, sociability and aggressiveness) in 31 dog breeds, Svartberg [60] found large differences between breeds for all traits. For example, popular pet breeds tended to have higher sociability and playfulness scores than less popular breeds.

3. NON-SELECTIVE FORCES

While selection has clearly been an important force in the history of animal domestication, as with wild species, other non-selective mechanisms have strongly influenced evolutionary change in these species. There are various approaches that allow inferences about demographic and mating processes using genetic data.

(a) *Human-mediated modifications to population size and structure*

One important advance with the advent of dense markers is the ability to exploit the relationship between LD and effective population size (N_e, the number of individuals in an idealized population that would have the same rate of genetic drift as the actual population), such that N_e and r^2 (the correlation between allele frequencies

at two loci) are inversely related [61–63]. Hill [63] also recognized that LD between tightly linked markers reflects older N_e than the LD between loosely linked markers. Specifically, assuming linear population growth, LD between loci with recombination rate c reflects the N_e of $1/2c$ generations in the past [64]. With dense genotype data, this relationship can now be exploited to make inferences about population demographic history [64,65].

Using this approach, the Bovine HapMap Consortium [32] found that LD declined rapidly with increasing physical distance between markers, but the rate of decline varied between cattle breeds. Overall LD levels for cattle were between those seen for humans (generally low) and dogs. N_e appears to have declined recently for all breeds, presumably owing to bottlenecks associated with domestication and breed formation. Comparing LD–distance relationships across breeds can be used to understand the different breed histories. Three *Bos indicus* (humped cattle, originating in the Indian subcontinent) breeds examined had lower LD than the *Bos taurus* (humpless cattle, originating in the Middle East) breeds at short distances and intermediate values at long distances, indicating a relatively large ancestral population compared with the taurine breeds [32]. This characterization of *B. indicus* breeds is consistent with findings of higher nucleotide diversity in *B. indicus* than in *B. taurus* breeds [32,66]. Estimates of current N_e in several commercial taurine cattle breeds are very low (≤ 150), and the pattern of LD suggests a severe recent contraction consistent with breed formation and modern breeding practices such as artificial insemination [64,67,68].

Population contraction has also featured in the demographic history of dogs, as LD patterns suggest at least two bottlenecks: one at the time of domestication and another at the time of breed formation [69,70]. However, there are known difficulties in getting precise N_e estimates using LD patterns [71], and studies have therefore differed in their estimates of the magnitude and timing of the domestication bottleneck. The study of Lindblad-Toh *et al.* [69] suggests a substantial domestication-related bottleneck approximately 9000 generations ago, whereas that of Gray *et al.* [70] supports a more modest contraction approximately 5000 generations ago. In any case, the high level of LD over extended regions within dog breeds is consistent with a more severe contraction at the time of breed-creation events [69,70]. Long runs of homozygosity (ROHs) are also common in most dog breeds, indicating recent inbreeding [25]. There is variation in levels of LD between breeds of dogs. For example, Labrador retrievers have relatively low levels of LD (similar to that of some wolf populations), presumably because of high N_e [69,70].

A severe contraction in size will also lead to a reduction in the level of genetic diversity within populations. Muir *et al.* [72] used high-density SNP data in chickens to estimate the proportion of ancestral alleles that are absent from commercial chickens. In comparing the distribution of alleles from commercial lines with that of various non-commercial and ancestral breeds, they estimated that at least 50 per cent of the diversity in ancestral breeds is missing from commercial lines owing to bottlenecks early in the commercialization process, continued inbreeding and industry consolidation.

There is clear evidence of declining N_e in commercial animal breeds, and in some cases this has resulted in extremely low variability. A feral British breed, Chillingham cattle, was found to be homozygous at 24 out of 25 microsatellite loci [73], which is strikingly low when compared with other British cattle breeds [74]. The high levels of homozygosity in the Chillinghams presumably result from a very severe bottleneck and absence of immigration. Looking over a longer timescale, ancient *B. taurus* DNA has revealed a reduction in diversity at several cattle genes over the last 4000 years [75]. It is not yet clear whether this is a genome-wide or loci-specific pattern.

(b) Introgression

Another human-related phenomenon that is manifested in the architecture of genomes is that of introgression between breeds. Animal breeders may practice crossbreeding to introduce certain desirable traits for breed improvement. In the case of pig breeds, past human activity has influenced the genetic composition of European breeds. In the 18th and 19th centuries, Asian alleles were introduced into certain British pig breeds to promote traits such as fattening and earlier maturation [2]. Breeds that experienced genetic introgression included Berkshire and Middle White, and Asian morphological characteristics such as the squashed face of the Middle White are still evident (see figure 2). Molecular studies have since provided genetic evidence of the introgression from Asia to Europe. A study examining mitochondrial diversity in pigs revealed that a number of European commercial pig breeds carry Asian-like mtDNA haplotypes [76]. The levels of Asian genetic introgression were highly variable, depending on the breed and commercial line, with an average of 29 per cent frequency of Asian mtDNA haplotypes across European breeds. Genetic introgression can also be non-human-mediated, such as gene flow from wild relatives into the domestic pool and *vice versa*. For example, a Chinese wild boar genotyped by Fang *et al.* [14] carried an *MC1R* allele common in European domestic pigs, which must have resulted from gene flow. It is not clear whether the introgression of grey junglefowl into the primarily red junglefowl background of commercial chickens, suggested by the presence of the yellow skin phenotype [42] (see §2d), was a human-mediated event.

4. LEVELS OF GENETIC DIVERSITY

One of the most interesting and somewhat surprising findings arising from genetic studies of domesticated animals is that despite the role of intensive selection, inbreeding and population bottlenecks, many domesticated animal species are characterized by a high degree of genetic diversity. Cattle, particularly *B. indicus* breeds, have substantial nucleotide diversity [32], indicating a large ancestral effective population size. There is also evidence from a number of individual genes that nucleotide variation is relatively high in domesticated pigs [77], where sustained gene flow with their wild boar relatives (see §3b) appears to play an important role [78]. Despite the extensive bottleneck and associated loss of alleles that accompanied the commercialization of broiler and layer lines [72], domestic chickens have extensive sequence diversity [79], again presumably owing to a very large ancestral population which had even

greater levels of diversity (as also seen in present-day red junglefowl [80]). These high levels of genetic diversity contribute to the continuing ability of breeders to select for production traits. Despite the very low effective population size of the Holstein, average milk yield has continued to increase [81]. Similarly, heritability for growth in broiler chickens has remained at a similar level despite intensive selection over the last 50 years [82].

Certain livestock breeds with particularly low population size (such as Chillingham cattle, discussed in §3*a*) and some purebred dogs appear to be exceptions to this pattern. Many dog breeds were established with very low initial sizes, resulting in highly inbred populations and a high prevalence of inherited diseases (e.g. syringomyelia in Cavalier King Charles Spaniels and atopic dermatitis in various breeds [83]), presumably owing to the high frequency of individuals homozygous for recessive alleles. This is reflected in the low level of nucleotide diversity seen in the dog, when compared with chickens and cattle (electronic supplementary material, table S1).

While there are many indicators to show that genetic variation is being lost in domesticated animals, this appears to be operating within an overall context of high levels of diversity in most cases, and therefore can be counteracted by informed breeding decisions. This is not to suggest that conservation and breed management is not required, but rather that animal breeding has not yet reached a point of no return.

5. CONCLUSIONS

(a) *Preliminary insights from genomic analyses*

Although identification of the genes important in animal domestication and breed development is still in its early stages, some common themes have emerged. One is that there are clearly strong signatures of selection near a number of genes associated with coat colour and pattern (e.g. *MC1R*, *KIT*). This should not be surprising in that these visible phenotypes provide a clear-cut mechanism for farmers and breeders to distinguish their animals from others, and in some cases have served a cultural role. Coat colour and pattern remain important features of breeds and are still under selection. For example, Red Angus cattle breeders have formed separate breed societies from Black Angus in a number of countries in part because the red coat (an *MC1R* variant) is thought to be more heat- and sun-tolerant than black.

There are also genomic indicators that suggest selection on genes related to growth and body composition. There is clear evidence in several cattle breeds for selection on the myostatin gene, associated with muscle composition, and several studies also suggest that there may have been selection on the *GHR* gene, associated with growth rate and various production traits. In dogs, there is also evidence of strong selection on a number of genes associated with growth (e.g. *IGF1*) and skeletal traits, many of which are related to breed-specific characteristics. The genomic picture of selection for dairy-related traits is somewhat cloudier than that seen for other cattle production characteristics. There is some indication of selection signals near the *ABCG2* and *DGAT1* genes, which have been associated with milk-production traits, but this is not consistent across studies.

Although these studies have indicated several genes that appear to have been under selection and have

highlighted demographic events, they also suggest difficulties in fully characterizing the history of animal domestication using genetic data because of the concurrent action of multiple factors. Both selective and non-selective forces have clearly played key roles in the history of most domesticated species, and it may be difficult to separate these factors. For example, extended homozygosity and increased LD can derive from population contraction and/or inbreeding as well as strong selection, leading to problems distinguishing between these causes [84].

(b) *Directions for further study*

Improvement and further development of statistical methods for identification of selection signals is an active area of investigation. In addition to the need for better ways of distinguishing between demographic and selection processes, new approaches may be required to adequately investigate the role of selection on quantitative traits such as milk yield. Low power to detect selection on quantitative traits [27] may help to explain the inconsistent picture of selection signals seen in dairy cattle.

Another important area of further research is the identification of the genes that have been selected for their impact on tameness and other domestication-related behavioural traits. While progress is currently being made in this direction, the study of the genetic basis of these traits is still in its infancy. Long-term experimental selection for tameness in the silver fox has provided valuable insight into the domestication process and promises to provide even greater understanding once genomic techniques are applied to this population. The loci underlying the rat and the fox tameness QTL do not map to orthologous regions [56], and thus these studies have already demonstrated that there are multiple genetic routes to evolving tameness.

As demonstrated by the silver fox and tame rat studies, experimental populations may provide great insight into the process of domestication. There have been several recent studies examining genetic changes over the course of experimental selection on *Drosophila* [85] and chicken [86] lines. More extensive analysis of this type of data, especially when genetic material is collected from different stages of the experiment, may allow inference of the processes of domestication that cannot be measured directly. A complementary and more direct approach involves the analysis of ancient genetic material from different historical periods. As techniques for working with these samples improve, they will increasingly provide insights into the genetic changes that have accompanied the domestication process [87].

REFERENCES

1 Darwin, C. 1859 *On the origin of species by means of natural selection, or the preservation of favoured races in the struggle for life.* London, UK: John Murray.
2 Darwin, C. 1868 *The variation of animals and plants under domestication,* vols. I and II. London, UK: John Murray.

3 Grobet, L. *et al.* 1998 Molecular definition of an allelic series of mutations disrupting the myostatin function and causing double-muscling in cattle. *Mamm. Genome* **9**, 210–213. (doi:10.1007/s003359900727)

4 Dunner, S., Miranda, M. E., Amigues, Y., Canon, J., Georges, M., Hanset, R., Williams, J. & Menissier, F. 2003 Haplotype diversity of the myostatin gene among beef cattle breeds. *Genet. Sel. Evol.* **35**, 103–118. (doi:10.1186/1297-9686-35-1-103)

5 Compere, G., Buren, R. & Hanset, R. 1996 *The Belgian Blue: the history of a cattle breed and its conquest of the world*. Tournai, Belgium: Casterman.

6 Wiener, P., Burton, D., Ajmone-Marsan, P., Dunner, S., Mommens, G., Nijman, I. J., Rodellar, C., Valentini, A. & Williams, J. L. 2003 Signatures of selection? Patterns of microsatellite diversity on a chromosome containing a selected locus. *Heredity* **90**, 350–358. (doi:10.1038/sj.hdy.6800257)

7 Wiener, P. & Gutierrez-Gil, B. 2009 Assessment of selection mapping near the myostatin gene (GDF-8) in cattle. *Anim. Genet.* **40**, 598–608. (doi:10.1111/j.1365-2052.2009.01886.x)

8 Hanset, R. 1982 Muscular hypertrophy as a racial characteristic: the case of the Belgian Blue breed. In *Muscle hypertrophy of genetic origin and its use to improve beef production* (eds J. W. B. King & F. Menissier), pp. 437–449. London, UK: Martinus Nijhoff Publishers.

9 Arthur, P. F. 1995 Double muscling in cattle: a review. *Aust. J. Agric. Res.* **46**, 1493–1515. (doi:10.1071/AR9951493)

10 Mosher, D. S., Quignon, P., Bustamante, C. D., Sutter, N. B., Mellersh, C. S., Parker, H. G. & Ostrander, E. A. 2007 A mutation in the myostatin gene increases muscle mass and enhances racing performance in heterozygote dogs. *PLoS Genet.* **3**, 779–786. (doi:10.1371/journal.pgen.0030079)

11 Clop, A. *et al.* 2006 A mutation creating a potential illegitimate microRNA target site in the myostatin gene affects muscularity in sheep. *Nat. Genet.* **38**, 813–818. (doi:10.1038/ng1810)

12 Felius, M. 1995 *Cattle breeds: an encyclopedia*. Doetinchem, The Netherlands: Misset Uitgeverij BV.

13 Li, J., Yang, H., Li, J. R., Li, H. P., Ning, T., Pan, X. R., Shi, P. & Zhang, Y. P. 2010 Artificial selection of the melanocortin receptor 1 gene in Chinese domestic pigs during domestication. *Heredity* **105**, 274–281. (doi:10.1038/hdy.2009.191)

14 Fang, M. Y., Larson, G., Ribeiro, H. S., Li, N. & Andersson, L. 2009 Contrasting mode of evolution at a coat color locus in wild and domestic pigs. *PLoS Genet.* **5**, e1000341. (doi:10.1371/journal.pgen.1000341)

15 Kijas, J. M. H., Wales, R., Tornsten, A., Chardon, P., Moller, M. & Andersson, L. 1998 Melanocortin receptor 1 (MC1R) mutations and coat color in pigs. *Genetics* **150**, 1177–1185.

16 Cavalli-Sforza, L. L. 1966 Population structure and human evolution. *Proc. R. Soc. Lond. B* **164**, 362–379. (doi:10.1098/rspb.1966.0038)

17 Lewontin, R. C. & Krakauer, J. 1973 Distribution of gene frequency as a test of theory of selective neutrality of polymorphisms. *Genetics* **74**, 175–195.

18 Akey, J. M., Zhang, G., Zhang, K., Jin, L. & Shriver, M. D. 2002 Interrogating a high-density SNP map for signatures of natural selection. *Genome Res.* **12**, 1805–1814. (doi:10.1101/gr.631202)

19 Endo, T., Ikeo, K. & Gojobori, T. 1996 Large-scale search for genes on which positive selection may operate. *Mol. Biol. Evol.* **13**, 685–690.

20 Weir, B. S., Cardon, L. R., Anderson, A. D., Nielsen, D. M. & Hill, W. G. 2005 Measures of human population structure show heterogeneity among genomic regions. *Genome Res.* **15**, 1468–1476. (doi:10.1101/gr.4398405)

21 Coop, G. *et al.* 2009 The role of geography in human adaptation. *PLoS Genet.* **5**, e1000500. (doi:10.1371/journal.pgen.1000500)

22 Akey, J. M., Ruhe, A. L., Akey, D. T., Wong, A. K., Connelly, C. F., Madeoy, J., Nicholas, T. J. & Neff, M. W. 2010 Tracking footprints of artificial selection in the dog genome. *Proc. Natl Acad. Sci. USA* **107**, 1160–1165. (doi:10.1073/pnas.0909918107)

23 Zanna, G., Docampo, M. J., Fondevila, D., Bardagi, M., Bassols, A. & Ferrer, L. 2009 Hereditary cutaneous mucinosis in Shar Pei dogs is associated with increased hyaluronan synthase-2 mRNA transcription by cultured dermal fibroblasts. *Vet. Dermatol.* **20**, 377–382. (doi:10.1111/j.1365-3164.2009.00799.x)

24 Olsson, M. *et al.* 2011 A novel unstable duplication upstream of *HAS2* predisposes to a breed-defining skin phenotype and a periodic fever syndrome in Chinese Shar-Pei dogs. *PLoS Genet.* **7**, e1001332. (doi:10.1371/journal.pgen.1001332)

25 Boyko, A. R. *et al.* 2010 A simple genetic architecture underlies morphological variation in dogs. *PLoS Biol.* **8**, e1000451. (doi:10.1371/journal.pbio.1000451)

26 Flori, L., Fritz, S., Jaffrezic, F., Boussaha, M., Gut, I., Heath, S., Foulley, J. L. & Gautier, M. 2009 The genome response to artificial selection: a case study in dairy cattle. *PLoS ONE* **4**, e6595. (doi:10.1371/journal.pone.0006595)

27 Wiener, P., Edriss, M. A., Williams, J. L., Waddington, D., Law, A., Woolliams, J. A. & Gutierrez-Gil, B. 2011 Information content in genome-wide scans: concordance between patterns of genetic differentiation and linkage mapping associations. *BMC Genomics* **12**, 65. (doi:10.1186/1471-2164-12-65)

28 Hayes, B. J., Chamberlain, A. J., Maceachern, S., Savin, K., McPartlan, H., MacLeod, I., Sethuraman, L. & Goddard, M. E. 2009 A genome map of divergent artificial selection between *Bos taurus* dairy cattle and *Bos taurus* beef cattle. *Anim. Genet.* **40**, 176–184. (doi:10.1111/j.1365-2052.2008.01815.x)

29 Kim, Y. & Stephan, W. 2002 Detecting a local signature of genetic hitchhiking along a recombining chromosome. *Genetics* **160**, 765–777.

30 Nielsen, R., Williamson, S., Kim, Y., Hubisz, M. J., Clark, A. G. & Bustamante, C. 2005 Genomic scans for selective sweeps using SNP data. *Genome Res.* **15**, 1566–1575. (doi:10.1101/gr.4252305)

31 Stella, A., Ajmone-Marsan, P., Lazzari, B. & Boettcher, P. 2010 Identification of selection signatures in cattle breeds selected for dairy production. *Genetics* **185**, 1451–1461. (doi:10.1534/genetics.110.116111)

32 Gibbs, R. A. *et al.* 2009 Genome-wide survey of SNP variation uncovers the genetic structure of cattle breeds. *Science* **324**, 528–532. (doi:10.1126/science.1167936)

33 Ramirez-Soriano, A. & Nielsen, R. 2009 Correcting estimators of theta and Tajima's D for ascertainment biases caused by the single-nucleotide polymorphism discovery process. *Genetics* **181**, 701–710. (doi:10.1534/genetics.108.094060)

34 Maynard Smith, J. & Haigh, J. 1974 Hitch-hiking effect of a favorable gene. *Genet. Res.* **23**, 23–35. (doi:10.1017/S0016672300014634)

35 Parker, H. G. *et al.* 2009 An expressed Fgf4 retrogene is associated with breed-defining chondrodysplasia in domestic dogs. *Science* **325**, 995–998. (doi:10.1126/science.1173275)

36 Sutter, N. B. *et al.* 2007 A single IGF1 allele is a major determinant of small size in dogs. *Science* **316**, 112–115. (doi:10.1126/science.1137045)

37 Sabeti, P. C. *et al.* 2002 Detecting recent positive selection in the human genome from haplotype structure. *Nature* **419**, 832–837. (doi:10.1038/nature01140)

38 Voight, B. F., Kudaravalli, S., Wen, X. Q. & Pritchard, J. K. 2006 A map of recent positive selection in the human genome. *PLoS Biol.* **4**, 446–458. (doi:10.1371/journal.pbio.0040446)

39 Hayes, B. J., Lien, S., Nilsen, H., Olsen, H. G., Berg, P., Maceachern, S., Potter, S. & Meuwissen, T. H. E. 2008 The origin of selection signatures on bovine chromosome 6. *Anim. Genet.* **39**, 105–111. (doi:10.1111/j.1365-2052.2007.01683.x)

40 Qanbari, S., Pimentel, E. C. G., Tetens, J., Thaller, G., Lichtner, P., Sharifi, A. R. & Simianer, H. 2010 A genome-wide scan for signatures of recent selection in Holstein cattle. *Anim. Genet.* **41**, 377–389.

41 Rubin, C. J. *et al.* 2010 Whole-genome resequencing reveals loci under selection during chicken domestication. *Nature* **464**, 587–591. (doi:10.1038/nature08832)

42 Eriksson, J. *et al.* 2008 Identification of the yellow skin gene reveals a hybrid origin of the domestic chicken. *PLoS Genet.* **4**, e1000010. (doi:10.1371/journal.pgen.1000010)

43 Van Laere, A. S. *et al.* 2003 A regulatory mutation in IGF2 causes a major QTL effect on muscle growth in the pig. *Nature* **425**, 832–836. (doi:10.1038/nature02064)

44 Grisart, B. *et al.* 2002 Positional candidate cloning of a QTL in dairy cattle: identification of a missense mutation in the bovine DGAT1 gene with major effect on milk yield and composition. *Genome Res.* **12**, 222–231. (doi:10.1101/gr.224202)

45 Blott, S. *et al.* 2003 Molecular dissection of a quantitative trait locus: a phenylalanine-to-tyrosine substitution in the transmembrane domain of the bovine growth hormone receptor is associated with a major effect on milk yield and composition. *Genetics* **163**, 253–266.

46 Natt, D., Kerje, S., Andersson, L. & Jensen, P. 2007 Plumage color and feather pecking: behavioral differences associated with PMEL17 genotypes in chicken (*Gallus gallus*). *Behav. Genet.* **37**, 399–407. (doi:10.1007/s10519-006-9125-0)

47 Karlsson, A. C., Kerje, S., Andersson, L. & Jensen, P. 2010 Genotype at the PMEL17 locus affects social and explorative behaviour in chickens. *Br. Poult. Sci.* **51**, 170–177. (doi:10.1080/00071661003745802)

48 Karlsson, A. C., Mormede, P., Kerje, S. & Jensen, P. 2011 Genotype on the pigmentation regulating PMEL17 gene affects behavior in chickens raised without physical contact with conspecifics. *Behav. Genet.* **41**, 312–322. (doi:10.1007/s10519-010-9379-4)

49 Keeling, L., Anderson, L., Schutz, K. E., Kerje, S., Fredriksson, R., Carlborg, O., Cornwallis, C. K., Pizzari, T. & Jensen, P. 2004 Chicken genomics: feather-pecking and victim pigmentation. *Nature* **431**, 645–646. (doi:10.1038/431645a)

50 Bright, A. 2007 Plumage colour and feather pecking in laying hens, a chicken perspective? *Br. Poult. Sci.* **48**, 253–263. (doi:10.1080/00071660701370483)

51 Ducrest, A. L., Keller, L. & Roulin, A. 2008 Pleiotropy in the melanocortin system, coloration and behavioural syndromes. *Trends Ecol. Evol.* **23**, 502–510. (doi:10.1016/j.tree.2008.06.001)

52 Albert, F. W. *et al.* 2009 Genetic architecture of tameness in a rat model of animal domestication. *Genetics* **182**, 541–554. (doi:10.1534/genetics.109.102186)

53 Belyaev, D. K. 1979 Destabilizing selection as a factor in domestication. *J. Hered.* **70**, 301–308.

54 Trut, L. N., Plyusnina, I. Z. & Oskina, I. N. 2004 An experiment on fox domestication and debatable issues of evolution of the dog. *Russ. J. Genet.* **40**, 644–655. (doi:10.1023/B:RUGE.0000033312.92773.c1)

55 Kukekova, A. V. *et al.* 2007 A meiotic linkage map of the silver fox, aligned and compared to the canine genome. *Genome Res.* **17**, 387–399. (doi:10.1101/gr.5893307)

56 Kukekova, A. V. *et al.* 2011 Mapping loci for fox domestication: deconstruction/reconstruction of a behavioral phenotype. *Behav. Genet.* **41**, 593–606. (doi:10.1007/s10519-010-9418-1)

57 Naumenko, E. V., Popova, N. K., Nikulina, E. M., Dygalo, N. N., Shishkina, G. T., Borodin, P. M. & Markel, A. L. 1989 Behavior, adrenocortical activity, and brain monoamines in Norway rats selected for reduced aggressiveness towards man. *Pharmacol. Biochem. Behav.* **33**, 85–91. (doi:10.1016/0091-3057(89)90434-6)

58 Albert, F. W. *et al.* 2011 Targeted resequencing of a genomic region influencing tameness and aggression reveals multiple signals of positive selection. *Heredity* **107**, 205–214. (doi:10.1038/hdy.2011.4).

59 Jensen, P. 2006 Domestication: from behaviour to genes and back again. *Appl. Anim. Behav. Sci.* **97**, 3–15. (doi:10.1016/j.applanim.2005.11.015)

60 Svartberg, K. 2006 Breed-typical behaviour in dogs: historical remnants or recent constructs? *Appl. Anim. Behav. Sci.* **96**, 293–313. (doi:10.1016/j.applanim.2005.06.014)

61 Sved, J. A. 1971 Linkage disequilibrium and homozygosity of chromosome segments in finite populations. *Theor. Popul. Biol.* **2**, 125–141. (doi:10.1016/0040-5809(71)90011-6)

62 Hill, W. G. 1975 Linkage disequilibrium among multiple neutral alleles produced by mutation in finite population. *Theor. Popul. Biol.* **8**, 117–126. (doi:10.1016/0040-5809(75)90028-3)

63 Hill, W. G. 1981 Estimation of effective population-size from data on linkage disequilibrium. *Genet. Res.* **38**, 209–216. (doi:10.1017/S0016672300020553)

64 Hayes, B. J., Visscher, P. M., McPartlan, H. C. & Goddard, M. E. 2003 Novel multilocus measure of linkage disequilibrium to estimate past effective population size. *Genome Res.* **13**, 635–643. (doi:10.1101/gr.387103)

65 Tenesa, A., Navarro, P., Hayes, B. J., Duffy, D. L., Clarke, G. M., Goddard, M. E. & Visscher, P. M. 2007 Recent human effective population size estimated from linkage disequilibrium. *Genome Res.* **17**, 520–526. (doi:10.1101/gr.6023607)

66 Murray, C., Huerta-Sanchez, E., Casey, F. & Bradley, D. G. 2010 Cattle demographic history modelled from autosomal sequence variation. *Phil. Trans. R. Soc. B* **365**, 2531–2539. (doi:10.1098/rstb.2010.0103)

67 de Roos, A. P. W. 2008 Linkage disequilibrium and persistence of phase in Holstein–Friesian, Jersey and Angus cattle. *Genetics* **179**, 1503–1512. (doi:10.1534/genetics.107.084301)

68 Qanbari, S., Pimentel, E. C. G., Tetens, J., Thaller, G., Lichtner, P., Sharifi, A. R. & Simianer, H. 2010 The pattern of linkage disequilibrium in German Holstein cattle. *Anim. Genet.* **41**, 346–356.

69 Lindblad-Toh, K. *et al.* 2005 Genome sequence, comparative analysis and haplotype structure of the domestic dog. *Nature* **438**, 803–819. (doi:10.1038/nature04338)

70 Gray, M. M., Granka, J. M., Bustamante, C. D., Sutter, N. B., Boyko, A. R., Zhu, L., Ostrander, E. A. & Wayne, R. 2009 Linkage disequilibrium and demographic history of wild and domestic canids. *Genetics* **181**, 1493–1505. (doi:10.1534/genetics.108.098830)

71 Wang, J. L. 2005 Estimation of effective population sizes from data on genetic markers. *Phil. Trans. R. Soc. B* **360**, 1395–1409. (doi:10.1098/rstb.2005.1682)

72 Muir, W. M. *et al.* 2008 Genome-wide assessment of worldwide chicken SNP genetic diversity indicates significant absence of rare alleles in commercial breeds. *Proc. Natl Acad. Sci. USA* **105**, 17 312–17 317. (doi:10.1073/pnas.0806569105)

73 Visscher, P. M., Smith, D., Hall, S. J. G. & Williams, J. A. 2001 A viable herd of genetically uniform cattle: deleterious alleles seem to have been purged in a feral strain of inbred cows. *Nature* **409**, 303. (doi:10.1038/35053160)

74 Wiener, P., Burton, D. & Williams, J. L. 2004 Breed relationships and definition in British cattle: a genetic analysis. *Heredity* **93**, 597–602. (doi:10.1038/sj.hdy.6800566)

75 Svensson, E. M., Anderung, C., Baubliene, J., Persson, P., Malmstrom, H., Smith, C., Vretemark, M., Daugnora, L. & Gotherstrom, A. 2007 Tracing genetic change over time using nuclear SNPs in ancient and modern cattle. *Anim. Genet.* **38**, 378–383. (doi:10.1111/j.1365-2052.2007.01620.x)

76 Fang, M. Y. & Andersson, L. 2006 Mitochondrial diversity in European and Chinese pigs is consistent with population expansions that occurred prior to domestication. *Proc. R. Soc. B* **273**, 1803–1810. (doi:10.1098/rspb.2006.3514)

77 Ojeda, A., Rozas, J., Folch, J. M. & Perez-Enciso, M. 2006 Unexpected high polymorphism at the FABP4 gene unveils a complex history for pig populations. *Genetics* **174**, 2119–2127. (doi:10.1534/genetics.106.063057)

78 Ramirez, O. *et al.* 2009 Integrating Y-chromosome, mitochondrial, and autosomal data to analyze the origin of pig breeds. *Mol. Biol. Evol.* **26**, 2061–2072. (doi:10.1093/molbev/msp118)

79 Wong, G. K. S. *et al.* 2004 A genetic variation map for chicken with 2.8 million single-nucleotide polymorphisms. *Nature* **432**, 717–722. (doi:10.1038/nature03156)

80 Granevitze, Z., Hillel, J., Chen, G. H., Cuc, N. T. K., Feldman, M., Eding, H. & Weigend, S. 2007 Genetic diversity within chicken populations from different continents and management histories. *Anim. Genet.* **38**, 576–583. (doi:10.1111/j.1365-2052.2007.01650.x)

81 Brotherstone, S. & Goddard, M. 2005 Artificial selection and maintenance of genetic variance in the global dairy cow population. *Phil. Trans. R. Soc. B* **360**, 1479–1488. (doi:10.1098/rstb.2005.1668)

82 Hill, W. G. 1998 Inferences from evolutionary biology to livestock breeding In *Proc. 6th World Congress on Genetics Applied to Livestock Production,* pp. 32–39. Armidale, Australia: Organising Committee.

83 Rooney, N. & Sargan, D. 2009 *Pedigree dog breeding in the UK: a major welfare concern?* Hosham, UK: Royal Society for the Prevention of Cruelty to Animals.

84 Thornton, K. R., Jensen, J. D., Becquet, C. & Andolfatto, P. 2007 Progress and prospects in mapping recent selection in the genome. *Heredity* **98**, 340–348.

85 Burke, M. K., Dunham, J. P., Shahrestani, P., Thornton, K. R., Rose, M. R. & Long, A. D. 2010 Genome-wide analysis of a long-term evolution experiment with drosophila. *Nature* **467**, 587–590. (doi:10.1038/nature09352)

86 Johansson, A. M., Pettersson, M. E., Siegel, P. B. & Carlborg, O. 2010 Genome-wide effects of long-term divergent selection. *PLoS Genet.* **6**, e1001188. (doi:10.1371/journal.pgen.1001188)

87 Ludwig, A. *et al.* 2009 Coat color variation at the beginning of horse domestication. *Science* **324**, 485. (doi:10.1126/science.1172750)