EMBO reports

The genetics of domestication

Research into the domestication of livestock and companion animals sheds light both on their "evolution" and human history

Philip Hunter

Since the dawn of civilization, humans have domesticated animals for their own purposes—food, clothing, protection, hunting or as companions. Not surprisingly, biologists have for decades taken a keen interest in the particular evolution of domesticated animals both to better understand the history of domestication itself and its effects on contemporary livestock and companion animals. The bulk of research is focused on the earlier history of human–animal co-evolution with a general consensus that domestication began during the early Neolithic Period around 11,000 years ago, with the possible exception of dogs, which may have first been domesticated at least 30,000 years ago. The extreme goal-directed breeding—often for cosmetic purposes—to which some animals, especially dogs, have been subjected is in fact a relatively recent phenomenon of the past two centuries; before that, the evolution of domestic animals was governed by adaptation to the different diet and conditions of expanding human settlements, and relaxed selection resulting from diminished exposure to predators. The latter sometimes reduced positive selection for the "flight" response for example.

> *"The extreme goal-directed breeding [...] to which some animals, especially dogs, have been subjected is in fact a relatively recent phenomenon of the past two centuries ..."*

Domestic animal evolution research is a highly integrative field that combines the study and dating of archaeological remains with historical records and analysis of both modern and ancient DNA, which has so far been mostly mitochondrial DNA. Although limited, it has yielded a number of insights, for instance that pigs were first domesticated in SW Asia and, around 8,500 BC, migrated into Europe along with humans. These results are based on analysis of mitochondrial signatures the pigs had acquired from local wild boar populations along the way [1] (Fig 1). Such mixing with local wild animals was indeed a common feature of most domesticated animals earlier in civilization before either reproductive isolation evolved or humans began to confine them to protect against loss or predation. "Overall, recent studies have made it clear that in pigs, a commensal domesticate, the process of domestication was long and complex, and that 'domestic' animals were not kept in isolation from their wild counterparts," explained Claudio Ottoni from the University of Oslo in Norway, and co-author on that study. "In Europe, domestic pigs were probably allowed to roam freely in the forests thus having chances to mix with wild boars, and only from the late Middle Ages stricter reproductive isolation processes were put in place. [...] It seems clear that such gene flow was asymmetrical, basically more 'wild boar' genome flew into the domestic stock than the other way around. This recurrent admixture had the effect of homogenising the genomes of wild and domestic populations, but this was counterbalanced by positive human selection on domestic pigs which eventually led to emergence of the typical morphological and behavioural differences between wild boars and domestic pigs."

Yet, mitochondrial data have limitations, and recent advances in nuclear genome sequencing have provided more conclusive information about the origins of particular domestic populations and gene flows within them as well as with wild relatives. To date, it has identified far more genes associated with domestication of plants than animals, which may reflect how the former were selected for more specific traits from the outset. "This is indeed a curious dichotomy," acknowledged Dorian Fuller at the University College London Institute of Archaeology, whose research has spanned both plant and animal domestication. "Mainly I think it is about how easy they are to isolate. In a population of cereals, you can easily control cross pollination and just as Mendel himself did with peas isolate morphologically distinct genotypes over a few generations in a few years."

> *"... the changes associated with the domestication of animals were less obvious and often involved gradual adaptation to humans and greater population densities."*

Moreover, the changes associated with the domestication of animals were less obvious and often involved gradual adaptation to humans and greater population densities. "Domestication in plants is focused on morphological adaptations that are mostly fairly obvious, and controlled by a few genes or networks of genes," Fuller explained. "In animals, many key changes are developmental and behavioural and I guess they are less obvious, and generation times and controlled

Freelance journalist in London, UK. E-mail: ph@philiphunter.com
DOI 10.15252/embr.201745664 | Published online 15 January 2018

© 2018 The Author

Figure 1. European wild boar *Sus scrofa*. © Wildlife GmbH/Alamy Stock Photo.

breeding are rather harder and longer term to engineer." He added that most breeds are already 1,000s of generations after the initial domestication took place, and formative genetic changes may have been lost amid the more forced selection that took place later.

A change of colour

There are though a few non-behavioural traits associated with domestic animals, mostly related to coat colour, tooth shape and disease resistance; in fact, coat colour is about the only domestic trait that was subject to early selection by humans. As a result, it yields the most valuable genetic markers for identifying domestic animal remains from archaeological sites—historical records confirm that coat colours of various livestock species were different from their wild relatives at least 5,000 years ago. There was initial speculation that these changes resulted from relaxed selection for camouflage alleles since these were no longer needed to protect against predation.

But this idea was scotched by a 2009 study, which provided evidence that deliberate selection for colour had already occurred in the early stages of domestication [2]. The authors found that domesticated animals accumulated mutations in the melanocortin receptor 1 (MCR1R) gene, which has been associated with coat colour variation in many animals including horses, cattle, foxes, pigs, sheep, dogs and chickens. Such alleles are usually eliminated in the wild population because the animals are more visible to prey, but they appeared to be subject to positive selection in domesticated animals. The study also found that the mutations had occurred since domestication, because there was not time for them to have arisen and become fixed in the relatively small number of generations involved. This also largely disproved an alternative to the earlier camouflage theory—that coat colours changed because they were associated with some behavioural traits such as tameness—as there is no evidence that MCR1 has anything to do with behaviour.

This leaves the question of why early farmers bothered to select for coat colour, with one possible explanation that it made it easier to keep track of livestock when they are not camouflaged. Coat colour could also have been seen as a metaphor for the improved characteristics of livestock, although that is less likely given that it does not appear to be linked to the other desirable traits. A third possibility is that early farmers simply preferred or enjoyed some of the early coat colours and selected for them accordingly, which is plausible given that this appears to have happened more recently among primitive farming communities. Whatever its evolution, this colour marker can help to identify animal remains via its DNA. "If you find, say, the variant for a black and white coat in a Neolithic sample, you know they are domestic animals,"

 © 2018 The Author

explained Keith Dobney at the University of Liverpool, UK.

The value of genomic DNA

In many cases though identification of domestic animals from archaeological remains requires a combination of techniques, including dating, study of historical records and genetic analysis, Dobney added. This is particularly the case where only mitochondrial DNA data are available, since it only reveals phylogenic relationships and not genetic factors associated with given phenotypes such as domestication. "Mitochondrial DNA is a neutral marker since a domestic animal has a signature that's the same as a wild one," Dobney said. "But we can infer domestication has occurred when you find these signatures in different places, especially where they otherwise shouldn't be."

While data from nuclear DNA can yield a lot more information, including about gene flows between domestic and wild relatives or phenotypic changes associated with domestication, Dobney insisted that integrative studies remain essential to root genetic studies accurately and ensure they align with archaeological, cultural and historical information. This has helped to better understand specific cases of domestication such as the pig, but also changed more general perceptions, such as the notion and importance of evolutionary bottlenecks during which almost all genetic variation within a given population is wiped out. Numerous cases of such bottlenecks have been cited in the literature, but most of these are wrong or at best misleading, according to Greger Larson at the University of Oxford, UK. It has been proposed that domestication of some animals can be traced back to such a bottleneck event, but Larson argues that, in practice, numbers were rarely if ever reduced to a sufficiently small number. "The bottleneck is the last sacred cow of domestication," he said. "If you take the modern rabbit genome, you do not even find a signature of myxomatosis, even though that disease knocked out 99.9% of rabbits on three separate continents. You would surely expect to see some kind of residual signature on the genome, slightly longer fragment lengths perhaps or haplotype blocks, but no, it's not there at all." Although a huge proportion of rabbits were eliminated, a sufficient number was still left to preserve a significant amount of genetic variability. "You need to get down to 6, 10 or say 15 individuals to see bottlenecks, or perhaps a few more but sustained for a longer period of time and then followed by rapid population growth," Larson explained.

Recent findings have also played into the ongoing debate over exactly how to define animal domestication. As Larson pointed out, human civilization has had a measurable genetic impact on a wide range of animals, including insects and wild animals. Domestication should therefore be seen as a continuum rather than an exclusive category, with even the case of dogs—which "evolved" from wolves drawn to human settlements (Fig 2)—less clear-cut than is often thought. "Our entire perception of dogs is coloured massively by the last 100–150 years since the creation of dog breeds," Larson explained. "In fact, more than two-thirds of the 1 billion dogs on the planet are street dogs without names, which are tolerated but not cared for. [. . .] Admittedly a lot of that extreme variation has occurred only quite recently, which is the case for most animals regarded as domestic." He therefore argues to dispense with long-established views over what domestication is. "We must understand that it is a long term rather fluid process," Larson said. "Variation exists along a continuum rather than within nice neat boxes with which we like to order the world."

> *"One reason cats were not subjected to selection by humans [..] is that they were already good at hunting rodents and there was no need to improve upon that"*

Nonetheless, some basic facts about the history of domestication can be established. According to Dobney, it broadly began during the earlier Neolithic when humans started to live in larger, relatively fixed settlements and cultivated cereal crops, which attracted a variety of animals. But this required the animals themselves to thrive in larger population densities, which led to a general rule about domestication: that the animals must be relatively social in the first place. Subsequent selection may make them more social but they would generally only encroach on human settlements in significant numbers if they could live in groups at the outset. Indeed, animals such as horses, or cattle that humans co-opted from wild aurochs, were already accustomed to living in herds.

Figure 2. Eurasian wolf *Canis lupus lupus*. © Naturfoto-Online/Alamy Stock Photo.

© 2018 The Author

Cats are individualists

One notable exception to the social rule is the domestic cat, which was drawn into human settlements by the availability of food, namely small rodents, but was happy to keep its distance from the bipeds. However, cats' ability to hunt down vermin made them so useful that humans encouraged them to come in and kept them in a variety of settings from barns to ships. Yet, despite their long association with humans, domestic cats are genetically much more similar to their wild ancestors than most other domesticated animals, according to Eva-Maria Geigl, Research Director at the CNRS Institut Jacques Monod Epigenome and Paleogenome group in Paris, France. "Indeed, when people have compared the genomes of present-day house cats with those of present-day wildcats, there have been few changes seen," she said. "The most obvious ones concerned the neural crest [a group of pluripotent stem cells] that is involved in the establishment of the nervous system. This hints at behavioural differences between the wild and the domestic cat and is confirmed through observation since wildcats are solitary animals whereas domestic cats tolerate humans and other cats in their proximity." [3]. One reason cats were not subjected to selection by humans—until recently for cosmetic reasons—is that they were already good at hunting rodents and there was no need to improve upon that; their adaptation was purely commensal.

Geigl also studied the history of cat domestication. "Until recently it was only known that all present-day domestic cats are the descendants of the wildcat of North Africa and Southwest Asia, *Felis silvestris lybica*," [4] she explained (Fig 3). "Our data show that the cat must have entered the so-called human niche at the latest during the Neolithic since we found the Anatolian mitochondrial lineage in remains in South-east Europe in Neolithic sites. We conclude that the first farmers who migrated into Europe must have translocated the cat, which we had found in Neolithic sites in Anatolia, since it is highly unlikely that cats, territorial and hydrophobic animals, swam from Anatolia across the Bosphorus" [5]. From there, the Anatolian lineage spread all over the world. "In addition, we found a particular mitochondrial lineage in Egypt that was spread quickly and in high numbers throughout the Roman Empire, and later up to the Baltic Sea with the Vikings," Geigl added. "At present, both lineages are about equally represented in domestic cats."

Like coat colour, the lineage of cats is another example where correlation of genetic evidence with archaeological and historical data provided a more complete picture of human history and migrations. "It showed how the cat became a commensal

Figure 3. African wildcat *Felis silvestris lybica*. © Ann and Steve Toon/Alamy Stock Photo.

 © 2018 The Author

companion of humans, first of their settlements with granaries and fields infested with rodents, and later on ships that also were full of rodents, these pests being life threatening in both contexts and cats being the perfect 'antidote'," Geigl explained.

The impact on human civilization

One key aspect of domestication in general—of plants as well as animals—is the impact on human evolution itself, which is even more profound. The most quoted one is the persistence of lactose tolerance into adulthood, driven by consumption of non-human milk after weaning [6]. "That is still the locus under highest positive selection in present-day human genomes," Geigl commented. But there are other adaptations to diet and disease resistance in particular that have left their marks in the human genome. Moreover, next to the breeding of cereal crops and the domestication of livestock for producing food and clothing, the single biggest step towards modern intensive agriculture and the growth of civilizations was the recruitment of oxen as beasts of burden for ploughing fields. "Domestic oxen made agriculture much more efficient and thus increased the number of people that could be sustained," Geigl said.

> *"One key aspect of domestication in general – of plants as well as animals – is the impact on human evolution itself, which is even more profound."*

At another level, animal domestication sheds light on evolution itself by showing what happens when selective forces on species evolution are dramatically modified even in the absence of the directed breeding. As Dobney noted, it is evolution on steroids and is best regarded as an ongoing process for study rather than as a series of individual events. Such studies have a great potential in the genomics era to yield further insights both about evolution and the history of human civilization.

References

1. Ottoni C, Flink LG, Evin A, Geörg C, De Cupere B, Van Neer W, Bartosiewicz L, Linderholm A, Barnett R, Peters J *et al* (2013) Pig domestication and human-mediated dispersal in Western Eurasia revealed through ancient DNA and geometric morphometrics. *Mol Biol Evol* 30: 824 – 832
2. Fang M, Larson G, Soares Ribeiro H, Li N, Andersson L (2009) Contrasting mode of evolution at a coat color locus in wild and domestic pigs. *PLoS Genet* 5: e1000341
3. Montague MJ, Li G, Gandolfi B, Khan R, Aken BL, Searle SM, Minx P, Hillier LW, Koboldt DC, Davis BW *et al* (2014) Comparative analysis of the domestic cat genome reveals genetic signatures underlying feline biology and domestication. *PNAS* 111: 17230 – 17235
4. Driscoll CA, Menotti-Raymond M, Roca AL, Hupe K, Johnson WE, Geffen E, Harley EH, Delibes M, Pontier D, Kitchener AC *et al* (2007) The Near Eastern origin of cat domestication. *Science* 317: 519 – 23
5. Ottoni C (2017) The palaeogenetics of cat dispersal in the ancient world. *Nat Ecol Evol* 1: 0139
6. Bersaglieri T, Sabeti PC, Patterson N, Vanderploeg T, Schaffner SF, Drake JA, Rhodes M, Reich DE, Hirschhorn JN (2004) Genetic signatures of strong recent positive selection at the lactase gene. *Am J Hum Genet* 74: 1111 – 1120

© 2018 The Author