As time progressed, and methods of DNA sequencing improved, sequencing moved to larger and larger genomes. Although sequencing the human genome was contemplated quite early on, and sequencing of the *Caenorhabditis elegans* worm genome was begun as a continuation of the mapping program, what emerged next were the sequences of bacterial genomes, and the sequence of yeast, the latter accomplished by a European group effort. The sequence of the yeast genome was published in 1997, that of *C. elegans* in 1998 and, now, in three reviews in this issue (pages 2185, 2196, and 2204), we have the complete sequence of the 125-megabase genome of the fruit fly *Drosophila* (*1*–*3*).

When large-scale sequencing projects were first discussed in the mid-1980s, it was clear that a resource much larger than the average research laboratory, as well as improvements in technology, would be required. Walter Gilbert was the first to suggest a sequence factory—I seem to remember the number of 250 for the technicians that would be needed—but most of our colleagues were bitterly opposed to this idea. One, I remember, advocated the cottage industry model, hoping that the sequence of the genomes of organisms would be accomplished by many scientists working on individual genes. However, building factories with increased automation and very large computer resources has provided an answer to large-scale genome sequencing.

In their review, Adams *et al.* (*1*) provide a list of gene functions in *Drosophila*, classified by the proteins deduced from the genomic sequences into the now familiar classes (of which "unknown" and "hypothetical" are the most common). Rubin and colleagues (*3*) compare the *Drosophila* genome sequence with that of yeast and *C. elegans*, the only other eukaryote genomes sequenced so far. It should be noted that the fly has fewer genes than the worm; the genome sequence predicts about 14,200 proteins for *Drosophila* as opposed to 18,400 for *C. elegans*.

Old geneticists knew what they were talking about when they used the term "gene", but it seems to have become corrupted by modern genomics to mean any piece of expressed sequence, just as the term algorithm has become corrupted in much the same way to mean any piece of a computer program. I suggest that we now use the term "genetic locus" to mean the stretch of DNA that is characterized either by mapped mutations as in the old genetics or by finding a complete open reading frame as in the new genomics. In higher organisms, we often find closely related genes that subserve closely related, but subtly different, functions. Thus, vertebrate genomes contain three different genetic loci specifying three different aldolase enzymes. In *Drosophila*, we have one aldolase "genetic locus" that produces three different aldolases by variable splicing of the messenger RNA. Indeed, this is clearly part of the genomic style of the fly. *Drosophila* has one myosin locus that produces all of the different heavy chains by variable splicing; in contrast, *C. elegans*, with simpler muscle systems, has four different myosin genes. We have to appreciate this before we can make sense of gene numbers. It also leads one to be cautious about the commonly accepted generalization that it takes four invertebrate genomes to make a vertebrate. The science of genomics is still in its infancy, and we will have to acquire far more sophisticated views of genomes and their evolution before we can answer such questions as why the fly has 352 zinc-finger genes but the worm has only 132.

The analysis of genome sequences gives us a comprehensive protein parts list and it short-cuts the massive amount of work that would have been required to characterize each protein individually. But there is one important piece of information that is almost totally missing: the sequence information that specifies when and where and for how long a gene is turned on or off. This switching information—which I call the left-hand value of the gene by analogy with the address of a computer location—cannot be deduced from the sequence. It is absolutely essential information because in complex organisms, evolution does not proceed by enlarging the protein inventory but rather by modulating the expression of genes.

The functional properties assigned to the protein products of genes are centered on what might be called molecular functions. These can be specified whenever a protein is found to be similar to one for which the function has been determined by conventional biochemical methods. It is the way one learns to speak a natural language by listening to other speakers, and is not the result of some elaborate computation. Quite often there is little connection between these molecular functions and the classical assignments of function by phenotype (which are at the level of the organism). The middle ground—that is, the participation of proteins in the physiology of cells and how cells contribute to the function of the organism—is a gap that still remains to be closed.

The problems faced by pre- and post-genomic genetics are therefore much the same—they all involve bridging the chasm between genotype and phenotype. Genome sequencing represents only a new beginning and not an end in itself. It is useful to have and will help us to answer the many questions that still lie ahead. Yeast, *C. elegans*, and *Drosophila* have large constituencies of researchers who will make good use of the genome sequence and, in the coming years, will tell us what it all means.

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PERSPECTIVES: ANTHROPOLOGY

Age, Sex, and Old Goats

Curtis W. Marean

The Zagros mountains that run through western Iran and northeastern Iraq are a harsh highland environment of craggy and precipitous limestone ridges and deeply incised valleys. Few large mammal species find this habitat attractive—that is, apart from wild goats and sheep that nimbly negotiate these rocky crags. About 40,000 years ago, Neanderthals started to hunt goats and sheep at some sites in the Zagros mountains. After they became extinct, their human successors continued this hunting pattern. But at some point, there was a critical shift in the relation between hunters and hunted, resulting in the gradual domestication of wild animals. Exactly when this shift happened has been hotly debated. Now, Zeder and Hesse, reporting on page 2254 of this issue (*1*), persuasively argue that humans began to domesticate wild goats about 10,000 years ago (see the figure). With modern goat skeletons as a guide, they examined assemblages of ancient goat bones from the Zagros and assigned them an age at death and a sex.

Our human ancestors began to domesticate wild animals through herd management. They first controlled the movements of animals, and then introduced selective breeding and regulation of the sex ratio and age structure of the herds. With time and efficient selective breeding, domesticated species underwent shifts in the frequency of certain groups of genes, resulting in anatomical changes. In the case of goats, this included changes in horn shape, the

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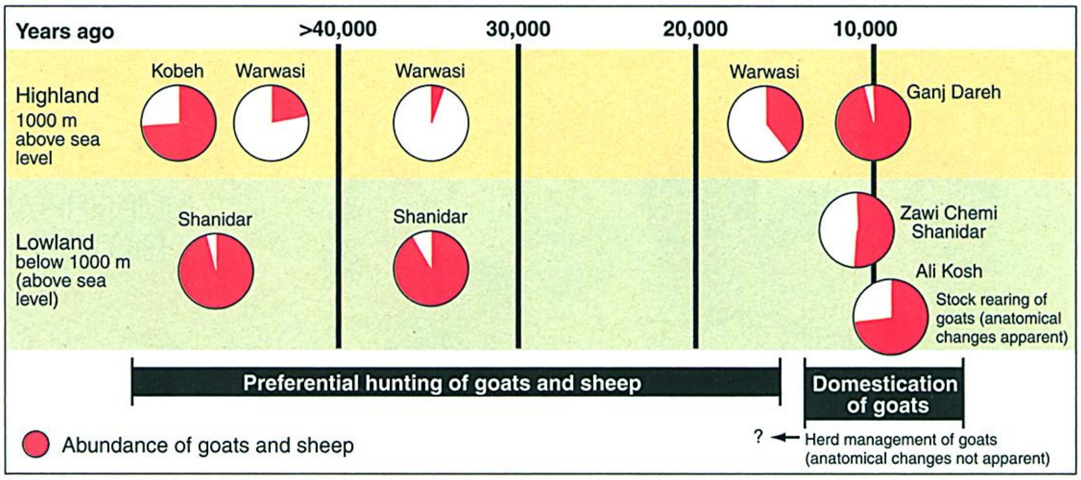
length of limbs, and coat coloration. Archaeologists have traditionally examined changes in overall size (diminution with domestication) and shifts in horn shape to identify the time period when animals were first domesticated. But, as Zeder and Hesse correctly point out, body size is sensitive to a host of factors, such as temperature and environment, and so is not an accurate marker of domestication. Similarly, changes in sexually selected traits, such as horn shape, are often found late in the domestication process, or not at all, particularly if there were regular infusions of wild genes (which could happen if managed females were allowed to breed with wild males). Thus, size and horn shape only allow us to view domestication after the first steps have already taken place. To overcome this difficulty, Zeder and Hesse decided to examine the age at death of male and female goats. From this information they were able to reconstruct the culling pattern (young males were selectively harvested), allowing them to detect human manipulations of the goat population before changes in anatomy became apparent.



Tips on goat management. The abundance of goats and sheep, as a percentage of total ungulates, in a sample of archaeological bone assemblages from the Zagros mountains. From 40,000 to 20,000 years ago, goats and sheep were the predominant wild animal hunted by humans in both highland and lowland regions. Early domestication in the form of herd management began about 10,000 years ago in the Ganj Dareh highland region. Separation of managed and wild populations and selective breeding occurred 1000 years later in the lowland areas of Ali Kosh.

Anatomical changes would only become apparent after separation of wild and managed goats, which effectively erected a "genetic firewall" between the two populations. This separation could have been enforced through extermination of the wild population, fencing in of the managed population, or relocation of the managed herd away from the natural range of the wild population. Zeder and Hesse report that at Ganj Dareh—a 10,000-year-old settlement in the Zagros highlands where modern wild goats still roam—they were unable to find changes in anatomical features in archaeological goat remains. They suggest that at this site managed goats might still have been interbreeding with wild populations and that domestication had not yet progressed to separating wild and managed herds (see the figure). Ali Kosh—a lowland site 300 m above sea level and outside the preferred range of modern wild goats—may be one of the earliest sites where managed populations were genetically isolated, leading to the anatomical changes characteristic of more recent domestic goats.

The Zeder and Hesse findings provide archaeological support for a theory of animal domestication proposed by Ingold in 1974 (*2*). He conducted fieldwork among the Lapps in Finland, who herd reindeer. Ingold observed changes in the relation between reindeer and people that resulted from complex shifts in reindeer population levels, pasture quality, technology, and social conditions. This led him to propose that the domestication process had a fluid quality, and perhaps continued for a long time before the introduction of selective breeding.

Ingold's theory of domestication accommodates the possibility that societies shifted between symbiotic pastoralism and pure hunting several times before they finally began herd management. The Zagros record may provide evidence for this in the form of a long history of interactions between humans and goats. In the Zagros highlands the archaeological record shows that humans hunted goats and sheep more than 40,000 years ago at Shanidar Cave (*3*) and Kobeh Cave (*4*) (see the figure). At other, ecologically similar sites, such as Warwasi, red deer and gazelle were the predominant prey. It seems that at some locations humans preferentially hunted goats, whereas at others they did not. This ancient and patterned focus on sheep and goats raises the possibility that people managed goats even earlier than 10,000 years ago, a proposition that we can now test with the Zeder and Hesse method.

The implications of the new work range far beyond the Zagros mountains for two reasons. First, by documenting early herd management prior to anatomical changes, the authors forced us to accept the possibility that animal domestication may have occurred elsewhere. Second, they provide a method for archaeologists seeking to test this possibility. There are many areas of the world where this may apply. For example, the North African archaeological record shows intriguing similarities to the Zagros record. For more than 40,000 years, North Africans preferentially hunted Barbary sheep to the near exclusion of other species. Around 20,000 years ago, at Tamar Hat in eastern Algeria, the remains of Barbary sheep completely dominate the archaeological assemblage of animal bones. The excavator, Saxon (*5*), argued that the age structure of the sheep resembled that of a managed population, and he even detected size differences that led him to propose that the inhabitants of Tamar Hat were preferentially killing young males and old females in their flocks. He concluded that North Africans had already domesticated Barbary sheep 20,000 years ago. However, it should be noted that the Barbary sheep were never domesticated to Ingold's stock-rearing end point because no changes in anatomical features (that would have resulted from selective breeding) have been found. Also, Saxon's study has been widely ignored by the scholarly community. The Zeder and Hesse report forces us to reevaluate this and other studies, as well as the accepted understanding of the location, process, and timing of the origins of pastoralism. More specifically, their findings firmly establish that the first steps in goat domestication occurred at least 10,000 years ago in the Zagros mountains.

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