

## Correspondence

# Mitochondrial Genomes of Extinct Aurochs Survive in Domestic Cattle

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Archaeological and genetic evidence suggest that modern cattle might result from two domestication events of aurochs (*Bos primigenius*) in southwest Asia, which gave rise to taurine (*Bos taurus*) and zebuine (*Bos indicus*) cattle, respectively [1-3]. However, independent domestication in Africa [4-5] and East Asia [6] has also been postulated and ancient DNA data raise the possibility of local introgression from wild aurochs [7-9]. Here, we show by sequencing entire mitochondrial genomes from modern cattle that extinct wild aurochs from Europe occasionally transmitted their mitochondrial DNA (mtDNA) to domesticated taurine breeds. However, the vast majority of mtDNAs belong either to haplogroup I (*B. indicus*) or T (*B. taurus*). The sequence divergence within haplogroup T is extremely low (eight-fold less than in the human mtDNA phylogeny [10]), indicating a narrow bottleneck in the recent evolutionary history of *B. taurus*. MtDNAs of haplotype T fall into subclades whose ages support a single Neolithic domestication event for *B. taurus* in the Near East, 9-11 thousand years ago (kya).

Fifty-six mitochondrial genomes from autochthonous taurine breeds across Southern Europe and the Near East were sequenced and compared with 50 sequences available in GenBank (Supplemental data). A mitochondrial genome from

American bison was also completely sequenced and, together with a complete yak mtDNA sequence, was used to root the phylogeny (Figure 1 and Supplemental data). Except five *B. indicus* sequences that formed clades I1 and I2, almost all the remaining sequences (98 out of 101) departed from a central T haplotype by an average sequence divergence in the coding region of only  $5.04 \pm 1.00$  substitutions. This corresponds to a maximum likelihood (ML) estimate of a divergence time of  $\sim 16.0 \pm 3.2$  kya when using an evolutionary rate estimate of  $2.043 \pm 0.099 \times 10^{-8}$  base substitutions per nucleotide per year (Figure 1 and Supplemental data). However, the tree also reveals exceptions that radiate much earlier than the T node. MtDNAs #98 and #99 harbour identical sequences (both from the Cabannina – an endangered breed from Liguria, northern Italy) belonging to a novel haplogroup (Q) whose ML time estimate from the QT node is  $52.2 \pm 8.0$  kya. Sequence #100 radiates even earlier from the PQT node ( $74.4 \pm 9.7$  kya) and was detected in one animal from Korea, generically classified as ‘beef cattle’. Strikingly, the control region of this mtDNA harbours the mutational motif of haplogroup P – the marker of the extinct aurochs of Northern and Central Europe [8].

Macro-haplogroup T shows an initial split into two sister subclades, T1'2'3 and T5. The latter is a newly identified haplogroup, while T1'2'3 is formed by the previously defined haplogroups T1, T2 and T3 (Figure 1). Both T1 and T3 are poorly defined, with only one (recurrent) distinguishing mutation in the control region, while T2 is better characterized (Supplemental data). In any case, T1, T2 and T3 diverge in a star-like fashion, indicating a rapid population expansion from either a single founder sequence or at most some founder sequences with very little variation for each haplogroup. Even by assuming the most restrictive scenario of just one founder per haplogroup, the estimated ML times are very low and similar to the ML ages for T5 and haplogroups I1 and I2 (Figure 1; Supplemental data) of *B. indicus*. The T4 control-region motif (16042-16093-16302) also characterizes a star-like branch, but this is within an internal clade (T3a) of T3. Thus, only six major clades of

the phylogeny (T1, T2, T3, T5, I1 and I2) encompass almost all mtDNAs observed in modern taurine and zebuine breeds. This is consistent with a bottleneck associated with a domestication event that occurred most likely during the Neolithic considering the coalescence age estimates.

As for the number of domestication events, the molecular divergence of the taurine and the zebuine lineages ( $332.4 \pm 24.0$  ky) is compatible with the formation of geographically and genetically distinct aurochs populations and, therefore, with two distinct events of domestication; one for the T (taurine) founding lineages in the Fertile Crescent and the other for the I (zebuine) founding lineages in Baluchistan – although the data do not rule out a single source. The phylogeny (Figure 1 and Supplemental data) allows one also to evaluate the possibility that T1 and T4 were domesticated independently from aurochs populations living in Africa and East Asia, respectively [4, 6]. The ancestor of T1 differs by only one mutation (16113) from the ancestor of T1'2'3 and by only two mutations (16113 and 16255) from the ancestor of T3, therefore a domestication of T1 in Africa would require that the *B. primigenius* populations of North Africa had accumulated no sequence variation in their entire mtDNA (except the T1 marker 16113) relative to the Near Eastern stocks – an unlikely scenario. As for T4, the finding that it is a derived clade within T3 suggests an origin from either the same genetic source as the T3 founder sequence(s), or at most from a genetically (and geographically) closely related population of aurochs – a scenario poorly compatible with a domestication of T4 in Eastern Asia.

In conclusion, our analysis supports the scenario of a single Neolithic origin of all T haplogroups in the Fertile Crescent but also reveals that a certain amount of gene flow occurred with *B. primigenius*. The introgression of haplogroup P most likely took place either in Northern or Central Europe, while haplogroup Q was possibly acquired from a different population of aurochs that might have ranged only south of the Alps [9].

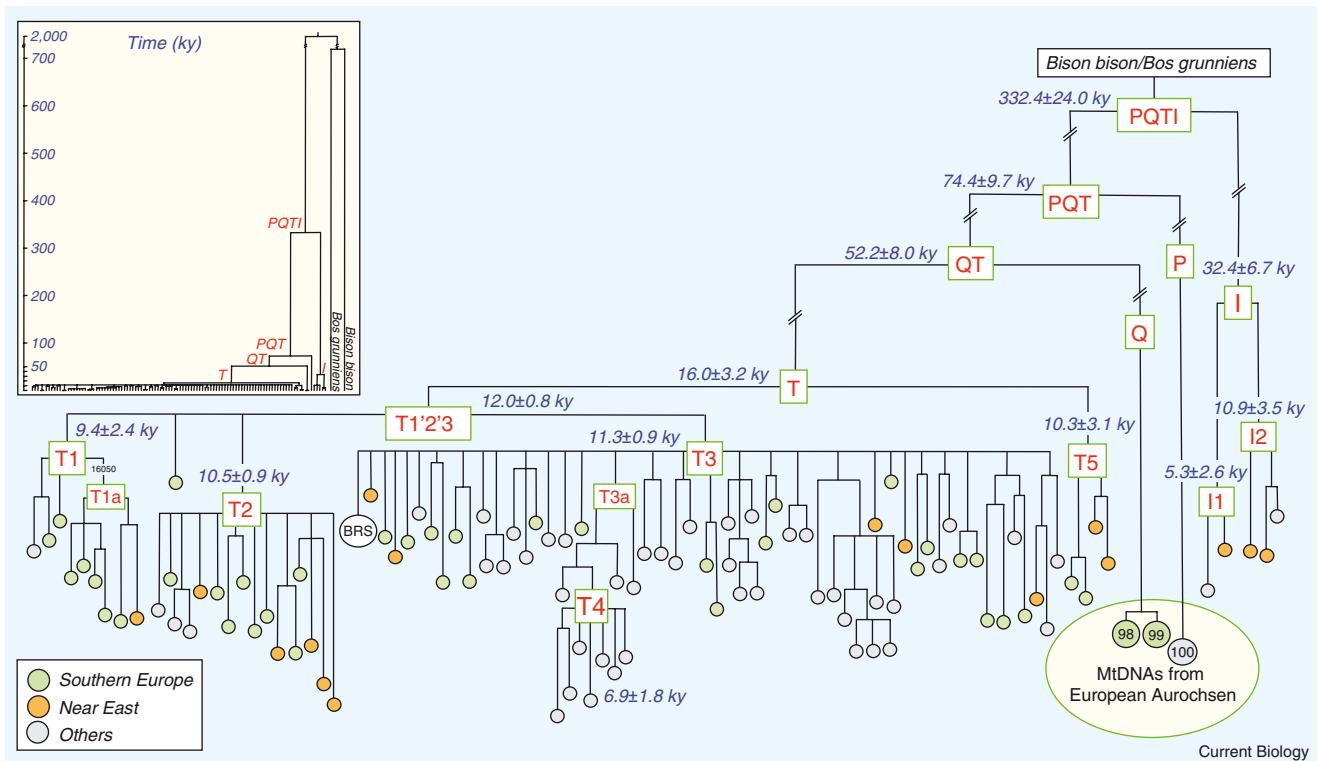


Figure 1. Tree of complete mtDNA sequences from cattle

This tree encompasses 56 novel sequences from Southern Europe and the Near East and 50 previously published sequences and was rooted by using a published *Bos grunniens* (yak) sequence and a novel *Bison bison* (American bison) sequence. Time estimates shown for clades and subclades are maximum likelihood (ML) estimates. However, the averaged distance ( $\rho$ ) of the haplotypes of a clade to the respective root haplotype, accompanied by a heuristic estimate of standard error ( $\sigma$ ) are also available in Supplemental data. BRS indicates the *Bos taurus* reference sequence [11]. The inset shows the reconstructed phylogeny based only on the coding-region sequence (from np 364 to np 15791) with an ML time scale shown on its left. Details concerning samples, mutational motifs of haplogroups and subhaplogroups as well as the protocol for sequencing entire mtDNAs are provided in Supplemental data.

#### Supplemental data

Supplemental data including experimental procedures are available at <http://www.current-biology.com/cgi/content/full/18/XXX/DC>

#### Acknowledgments

We are grateful to Mario Cancedda, Ekbal R. Hana, Mahzad Akbarpour, and Hans Lenstra for their help in the collection of the samples, and to Alan Gentry, Colin Groves, Faysal Bibi and Elisabeth Vrba for suggestions on palaeontological issues. This research received support from Progetti Ricerca Interesse Nazionale 2005 (Italian Ministry of the University) (to A.T.), Ministero degli Affari Esteri (to O.S.), Compagnia di San Paolo (to O.S. and A.T.) and Fondazione Cariplo (to A.T.). MtDNA sequences have been deposited in GenBank with accession numbers EU177815-EU177870 for cattle and EU177871 for the *Bison bison* sequence

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