

The Near Eastern Origin of Cat Domestication

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The world's domestic cats carry patterns of sequence variation in their genome that reflect a history of domestication and breed development. A genetic assessment of 979 domestic cats and their wild progenitors (*Felis silvestris silvestris* – European wildcat; *F. s. lybica* – Near Eastern wildcat; *F. s. ornata* – Central Asian wildcat; *F. s. cafra* – sub Saharan African wildcat; and *F. s. bieti* – Chinese desert cat) indicated that each wild group represents a distinctive subspecies of *Felis silvestris*. Further analysis revealed that cats were domesticated in the Near East, likely coincident with agricultural village development in the Fertile Crescent. Domestic cats derive from at least five founders from across this region, whose descendants were subsequently transported across the world by human assistance.

The domestic cat may be the world's most numerous pet, yet little is certain of the cat's origin (1–9). Archaeological remains and anthropological clues suggest that, unlike species domesticated for agriculture (e.g., cow, pig, sheep), or transport (horse, donkey), the cat began its association with humans as a commensal, feeding on rodent pests infesting grain stores of the first farmers (1). The earliest evidence of cat–human association involves their co-occurrence in Cyprus deposits aged at 9500 years ago (6). Domestic cats are generally considered descendant of the Old World wildcats but differ from these hypothesized progenitors in behavior, tameness, and coat color diversity (9, 10). Further, domestic cats appear to lack neotenous characteristics typical of other domesticated species (11).

Felis silvestris, from which domestic cats were derived, is classified as a polytypic wild species composed of three or more distinct inter-fertile subspecies: *F. s. silvestris* in Europe, *F. s. lybica* in Africa and the Near East, and *F. s. ornata* in the Middle East and Central Asia (1, 2, 12–15) and possibly the Chinese desert cat, *F. s. bieti* (inset Fig. 1A). The domestic cat is sometimes considered an additional subspecies, *F. s. catus*, possibly derived from wildcats in the Middle East or Egypt (1, 12, 14, 15). The imprecise subspecific status of *F. silvestris* populations, and relationship of

the domestic cat within this assemblage stems from morphological similarities among these groups (1, 13). A feral domestic cat with a “wild-type” mackerel tabby pattern is difficult to distinguish visually from a “true” wildcat (15, 16) which is further confounded by ongoing admixture (16–19). Furthermore the relationship between *F. silvestris* and the Chinese desert cat, which may be a separate *Felis* species, *Felis bieti* or a wildcat subspecies *F. silvestris bieti* (9, 12), is uncertain. The sand cat, *F. margarita*, a distinct species of *Felis* which ranges across North Africa and the Middle East, is the closest outgroup of the *F. silvestris/bieti* complex on the basis of morphological and molecular data (12, 13, 20).

To investigate the relationships among domestic cats, their indigenous wild progenitors and related species of the genus *Felis*, we collected tissue from 979 individuals (fig. S1; see table S1 for breakdown of number of cats tested for different genetic markers) including putative wildcats and feral domestic cats on three continents (N = 629), fancy breed domestic cats (N = 112), sand cats (*Felis margarita*, N = 11), and Chinese desert cats (*F. s. bieti*, N = 5). We extracted DNA and genotyped 851 cats for 36 variable short tandem repeat (STR) or microsatellite domestic cat loci (21) variable in *F. silvestris*, *F. s. bieti*, *F. margarita*, and domestic cats, and sequenced 2604 bp of mitochondrial DNA (mtDNA) genes *ND5* and *ND6* from 742 cats.

Neighbor-joining phylogenetic analyses for STR genotypes with kinship coefficient (*D_{kf}*) and proportion of shared alleles (*D_{ps}*) genetic distance estimators provided concordant topologies that specified six clusters (Fig. 1B; referred to here as “clades” as also specified mtDNA phylogenetic analyses; see below) corresponding to the following subspecies designations: 1) *F. s. silvestris* wildcats from Europe, (STR-Clade I-green in Fig. 1); 2) *F. s. ornata* wildcats from central Asia east of the Caspian Sea (STR-Clade III-purple); 3) *F. s. lybica*, wildcats from the Near East (STR-Clade IV-beige); 4) *F. s. cafra* wildcats from Southern Africa (STR-Clade II-blue); 5) *F. s. bieti*, Chinese desert cats (STR-Clade V-red); and 6) *F. margarita*, sand cat (STR-Clade VI-black). *Felis cafra* was first named in 1822 and renamed as *Felis lybica cafra* subspecies in 1944 on the basis

of a description of a wildcat specimen captured near Kaffraria, South Africa (9), an area from whence our sub-Saharan African wildcat samples derive.

The composite STR genotypes of all known domestic house cats, fancy cat breeds, and feral domestic cats occurring in the wild populations all fell within a large monophyletic group (Clade IV-beige) that also included wildcats from the Near East. The phylogenetic tree suggests that domestication occurred in the near East where STR-Clade IV wildcats live today. This inference was further explored by examining mtDNA variation, STR variation, and ongoing admixture hybridization in the study areas (17–19).

Phylogenetic analysis of *ND5* and *ND6* sequence reveals 245 parsimony informative sites specifying 176 distinct mtDNA genotypes (Fig. 2A, fig. S2, and table S2). The mtDNA haplotypes were analyzed with Bayesian Monte Carlo-Markov chain (MCMC), maximum parsimony, Maximum Likelihood (ML), and distance based methods (22, 23). All methods resulted in identical topologies for the principal groupings corresponding to both geographic origins and STR clade designations. The consensus mtDNA gene tree (Fig. 2A), rooted with *F. margarita*, shows *F. s. bieti* basal to *F. silvestris*, as inferred from morphology. However, the short branch lengths and relatively weak bootstrap support for the node separating *F. s. bieti* from *F. silvestris* (27–68% bootstrap-BS) indicates a close genetic relationship between these two taxa, supporting the grouping of *F. s. bieti* and *F. silvestris* as a single species, *F. silvestris*.

The *Felis silvestris* mtDNA haplotypes fall into specific geographic locales (Fig. 2A). A basal lineage (Clade I - *F. s. silvestris* – European wildcat – green), is found in European populations from Scotland and Portugal in the east, to Hungary and Serbia in the west, and is sister to *F. silvestris* from Asia, Africa, and domestic cats. An early/basal European versus Africa/Asia divergence supported by recent morphological studies of fossil specimens of wildcats (15, 24) may reflect a post-glacial re-population of Europe from Iberian founders as previously suggested (9, 15, 24).

Beyond Europe, mtDNA clades II, III and IV correspond with geography and STR analysis (Fig. 2A). Within mtDNA Clade IV we identified five principal lineages of mtDNA haplotypes (A-E; Fig. 2A) with no obvious phylo-geographic association among these lineages. Domestication appears to have occurred within the Near Eastern region where Clade IV wildcats are currently extant (beige, Fig. 2A) since clade IV wildcats and domestic cats are monophyletic.

Due to hybridization of wildcats and feral domestic cats, domestic cat mtDNA haplotypes (Clade IV-beige in Fig. 2A) are commonly found in European, African and central Asian populations along with indigenous wildcat haplotypes (Fig. 1A). The observed genetic admixture may be explained by the presence of feral domestic cats or by hybridization between wildcats and domestic cats. Hybrid individuals carrying one mtDNA Clade genotype but a different STR-Clade genotype can be identified. Such cyto-nuclear discordant individuals were common in our dataset (Figs. 1B and 2A). Of cats sampled for both STR and mtDNA genotypes, seven of the 472 cats in STR-Clade IV are discordant, with a wildcat mtDNA type (Fig. 1B). However, among 108 putative European wildcats (on the basis of STR genotype; Fig. 1B), 28 carry the Clade IV (domestic) mtDNA type as do 3 of 13 southern African (STR-Clade II) wildcats.

The wildcats in central Asia (STR-Clade III – purple) include the highest frequency of discordant individuals (mtDNA clades III and IV; Fig. 1B), perhaps due to incomplete lineage sorting or recent gene flow between adjacent populations (Fig. 2A).

We implemented the Bayesian population genetic analysis program STRUCTURE which assesses population subdivision (25) and characterizes genomic evidence of recent hybridization. STRUCTURE analyses of the 851 STR genotypes placed cats into discrete population clusters corresponding to European, African, and Central Asian wildcats and identified subdivision of domestic cats from different regions (Fig. 2B). Interestingly we identified a discrete population of wild and domestic cats from Near East Asia (brown group in Fig. 2B) distinct from the other *F. silvestris* subspecies and three subgroupings of domestic cats. These 15 individuals have concordant mtDNA and STR phylogenies identical to domestic cats and were collected in remote deserts of Israel, United Arab Emirates, Bahrain, or Saudi Arabia. These data suggest that these Near Eastern wildcats may represent the ancestral founder population of domestic cats supporting a domestication origin in the Near East.

Identification of hybrids ($Q < 0.8$) revealed that some (~22%) of the identified cyto-nuclear discordant cats in Figs. 1B and 2A showed evidence of recent hybridization. Because of this we removed 81 hybrid cats defined by STRUCTURE and generated new phylogenies combining the STR genotypes of cats grouped within the distinct populations (Fig. 2C). This analysis re-affirms the recognition of the major *F. silvestris* subspecies groups illustrated in Fig. 1A and the distinctiveness of Near East wildcats as the closest group to all domestic cats. The results also suggest a close affinity between *F. s. bieti* (Chinese desert cat) and the Asian wildcats (Clade III and IV), plus paraphyly of other *F. silvestris* subspecies with respect to *F. s. bieti* in support of the recognition of *F. s. bieti* as a subspecies of *F. silvestris* (Fig. 2C).

The coalescence-based age of mtDNA ancestral nodes for domestic cats (Clade IV) and all *Felis silvestris* mtDNA lineages was estimated with the linearized tree method (26). After fulfilling the requirement for molecular clock rate homogeneity across all lineages (table S4) we constructed a NJ algorithm on the basis of the linearized tree with Kimura two-parameter distances. We adopted a sequence divergence rate of 2.24 bp/MY, specific for the *ND5* and *ND6* genes (27) expecting one new variant (0–2) in the most recent 17,000 year period of domestic cat ancestry (see SOM text). Indeed 90% of the domestic cats within the five lineages (A-E in Fig. 2A) share haplotypes that are 0–3 bp apart, reflecting modest mutation accumulation within lineages. By contrast, the estimated coalescent date on the basis of the mtDNA data for all *Felis silvestris* (including *F. s. bieti*) subspecies is 230,000 years ago while the estimated age for the ancestor of *F. s. lybica* and domestic cats is 131,000 years. Other methods of date estimation suggested a range from 107,000 to 155,000 years (SOM text). These estimates are all greater by an order of magnitude than archaeological evidence for cat domestication (6). The persistence of five well supported mtDNA lineages dating back a hundred thousand years prior to any archaeological record of domestication would suggest

that domestic cats originated from at least five matrilineal mtDNA haplotypes.

The variation described here is important for conservation and management of free ranging cat species for (16, 28). In table S6 we present a full list of population specific (private) STR alleles as well as mtDNA population specific site genotypes suitable for assessment of a wildcat's population, subspecies of origin and distinction from domestic cats. The domestication of wild species to complement human civilization stands as one of the more successful 'biological experiments' ever undertaken. For cats, the process began over 9,000 years ago as the earliest farmers of the Fertile Crescent domesticated grains and cereals as well as livestock animals (1, 3, 4, 29–31). In parallel the endemic wildcats of the region may have adapted by both regulating the rodents in the grain stores and abandoning their aggressive wild-born behaviors. The archaeological imprints left in the genomes of living cats here weigh into inferences around the timing, steps and provenance of domestication, a dynamic exercise depicted in art, in history, and in human cultural development since recorded evidence began.

References and Notes

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Supporting Online Material

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SOM Text
Tables S1 to S6
Figs. S1 and S2
References

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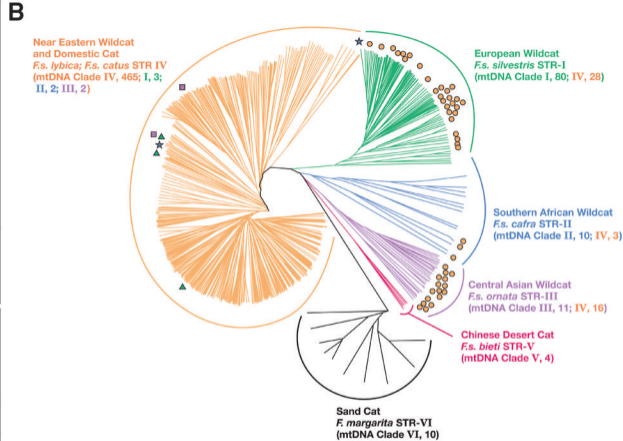
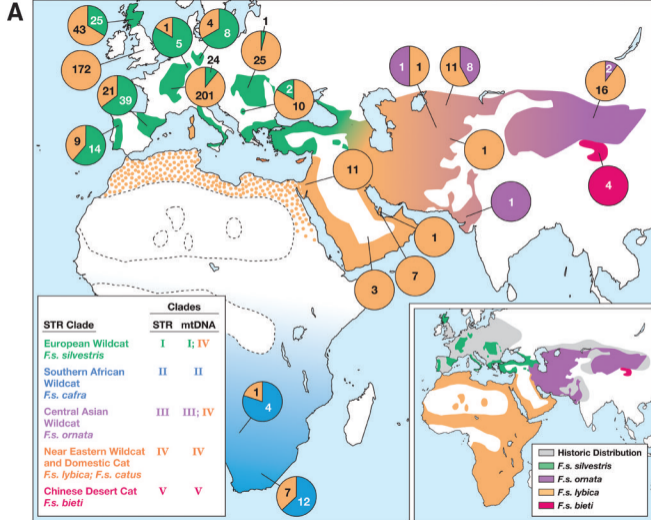
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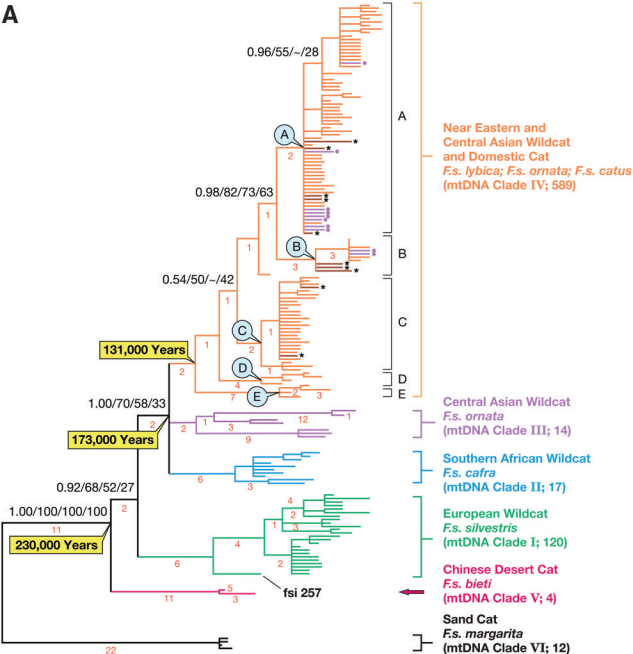
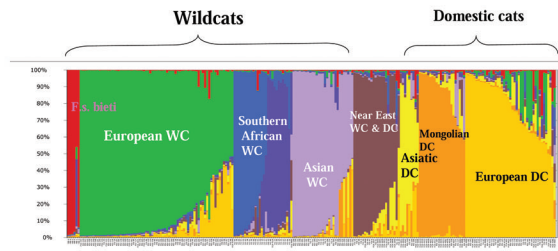
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Fig. 1. (A) Current range of *Felis silvestris*, and areas of sample collection. Colored regions reflect the location of capture of individuals carrying different STR clade genotypes (defined in box at lower left). Mitochondrial DNA (mtDNA) haplotype frequencies are indicated in pie charts specifying the number of specimens carrying each mtDNA haplotype clade. Central Asian indicates Asian cats east of the Caspian Sea. Near East indicates Israel, Saudi Arabia, Bahrain, and the United Arab Emirates. European include specimens collected west of the Caspian Sea. Domestic cats, *F. s. catus* are distributed world wide and overwhelmingly carry Clade IV mtDNA haplotypes (beige). Inset: Current and historic range of *F. silvestris* subspecies on the basis of traditional morphology based taxonomy (2, 12, 13). The Chinese desert cat, is referred to throughout as a wildcat subspecies, *F. silvestris bieti* (9, 12) as supported by data presented here. **(B)** STR based phenogram of 851 domestic and wild specimens created on the basis of short tandem repeats (STR) Dps genetic distance and minimum evolution (Neighbor Joining) algorithm. Color groups correspond to geographic locales specified in A. Solid symbols indicate cyto-nuclear discordant individuals which contain a STR composite clade of the

indicated cluster, but a mtDNA of an alternative locale (see text). In parentheses are the number of cats in each STR Clade that carry various mtDNA clade haplotypes.

Fig. 2. (A) Phylogenetic tree of mitochondrial DNA sequence (MinimumEvolution/Neighbor Joining phylogram of 2604 bp of the ND5 and ND6 gene) of 176 haplotypes discerned from 742 cats sampled across the range of the domestic cat, European, Asian and African wildcat, Chinese desert cat and sand cat. Trees created from Bayesian, ML and MP methods result in identical topologies for clade groupings. Confidence/bootstrap values (Bayes/MP/ML/ME) are based on 1000 iterations and are adjacent to nodes. The number of single nucleotide differences is indicated in red below the corresponding branch. Clade designations and number of individuals is indicated in parentheses following the corresponding common name and taxonomic trinomial. A through E designate lineages within mtDNA clade IV. Confidence/Bootstrap values for these nodes are as follows: A, 1.00/87/71/54; B, 1.00/82/80/80; C, 0.97/63/59/42; D, 1.00/98/99/88; E, 1.00/100/100/82 (as above). Purple and brown tree limbs within mtDNA clade IV reflect individual from two locales that bear cyto-nuclear discordant mtDNA vs. STR genotypes (see text). Beige Clade IV bearing mtDNA haplotypes are found among domestic cats, in wild potentially admixed populations in Europe, Asia, or Africa (see Fig. 1A), and in Near Eastern wildcats (see text). **(B)** STRUCTURE based populations resolved 851 cats into several wildcat groups, three domestic cat groups, plus one group (brown) which included both domestic cats and Near East wildcats. Y-axis represent Q-value, the percent representation of resolved populations (colors) within each individual (listed on X-axis). **(C)** Phylogenetic relationships among *Felis silvestris* groups as defined by composite STR genotypes based on 36 STR loci. Tree is rooted at Sand Cat. Bootstrap values at corresponding nodes from 1000 iterations with the following measures: Dps 1-(ps)/Dkf 1-(kf)/Dps-In/Dkf-In. All methods result in identical topologies. Individuals were clustered into representative populations based on STRUCTURE Q-value of 0.80 or greater with the same loci (see text). It is notable that all known domestic cats cluster into domestic-Asia, domestic-Europe or with Near East wildcats, regardless of provenance, and that these groups cluster together. Number of taxon specific alleles in red.



A**B****C**