Modern use of molecular genetics in determining the origin of dogs and cats

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Modul no. 4: Precision Livestock Farming

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Molecular genetics fot determination of the origin

- Domestication of plants and animals are rightly considered as major human cultural innovations, which rank alongside the production of tools, mastery of fire or development of verbal language.
- Animal domestication has fascinated biologists since Charles Darwin first drew the parallel between evolution via natural selection and human-mediated breeding of livestock and companion animals.
- Molecular genetics can be used to determine the origin of dogs and cats.

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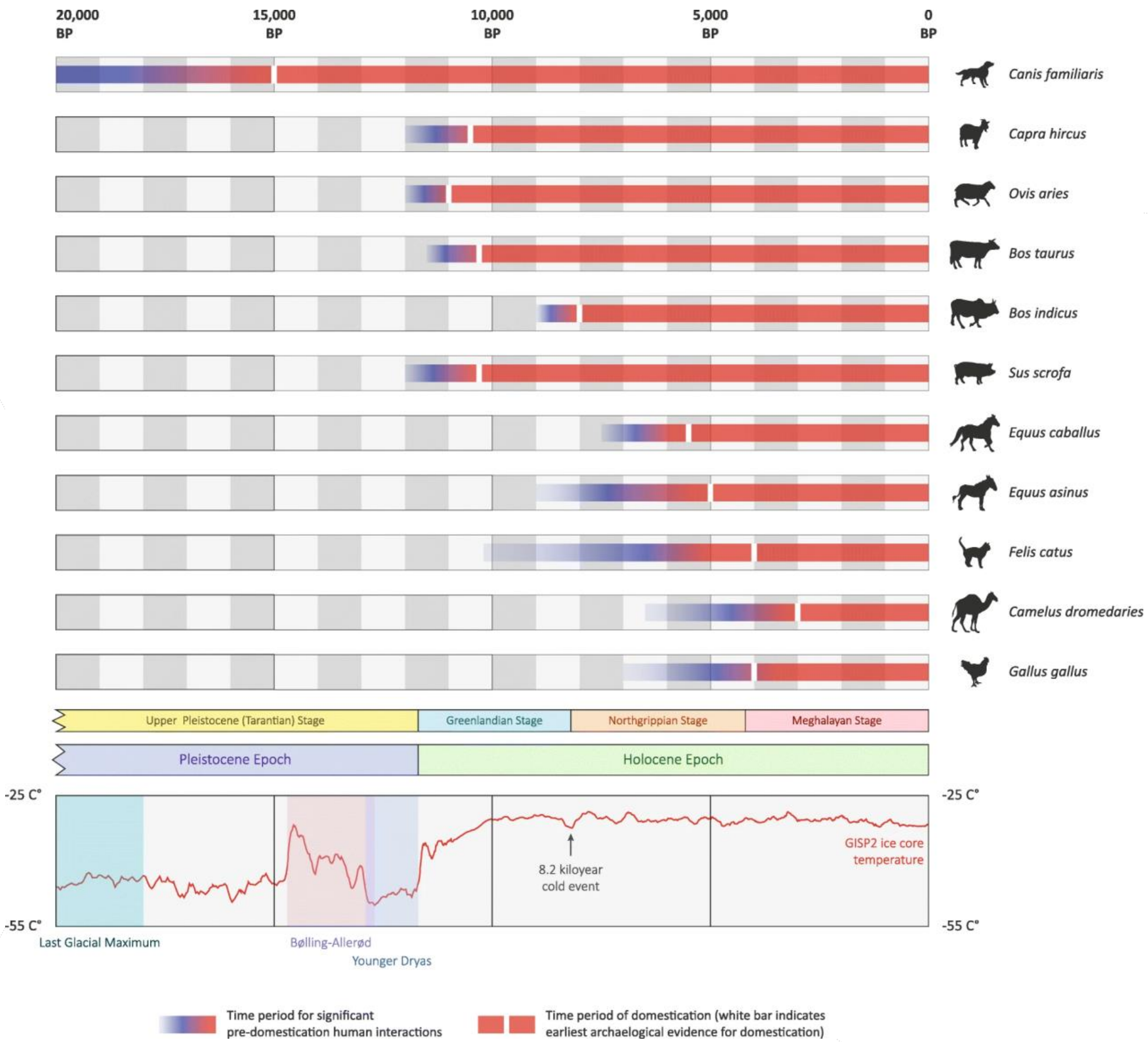
Timelines of domestication for 11 animal species with relevant stratigraphy and climate chronologies

After the appearance of the domestic dog (Canis familiaris) in archaeological finds, the domestication of crops and livestock followed relatively soon after, allowing humans to greatly expand the food available for hunting and gathering. As a result, during the Neolithic transition - the archaeologically documented transition from hunter-gatherer food production to crop and animal husbandry - increasingly sophisticated agricultural societies developed in many parts of Eurasia, North Africa and South and Central America.



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Origin of dogs by analysis of coat colour gene *ASIP*

- Distinctive colour patterns in dogs are an integral component of canine diversity.
- Colour pattern differences are thought to have arisen from mutation and artificial selection during and after domestication from wolves but important gaps remain in understanding how these patterns evolved and are genetically controlled

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Coat colour genes

- specific colour patterns arise through differential regulation of *Agouti* (*ASIP*), which encodes a paracrine signalling molecule and antagonist of the *melanocortin 1 receptor* (*MC1R*) that causes hair follicle melanocytes to switch from making eumelanin (black or brown pigment) to pheomelanin (yellow to nearly white pigment)

The five pattern types caused by *ASIP* regulatory variation

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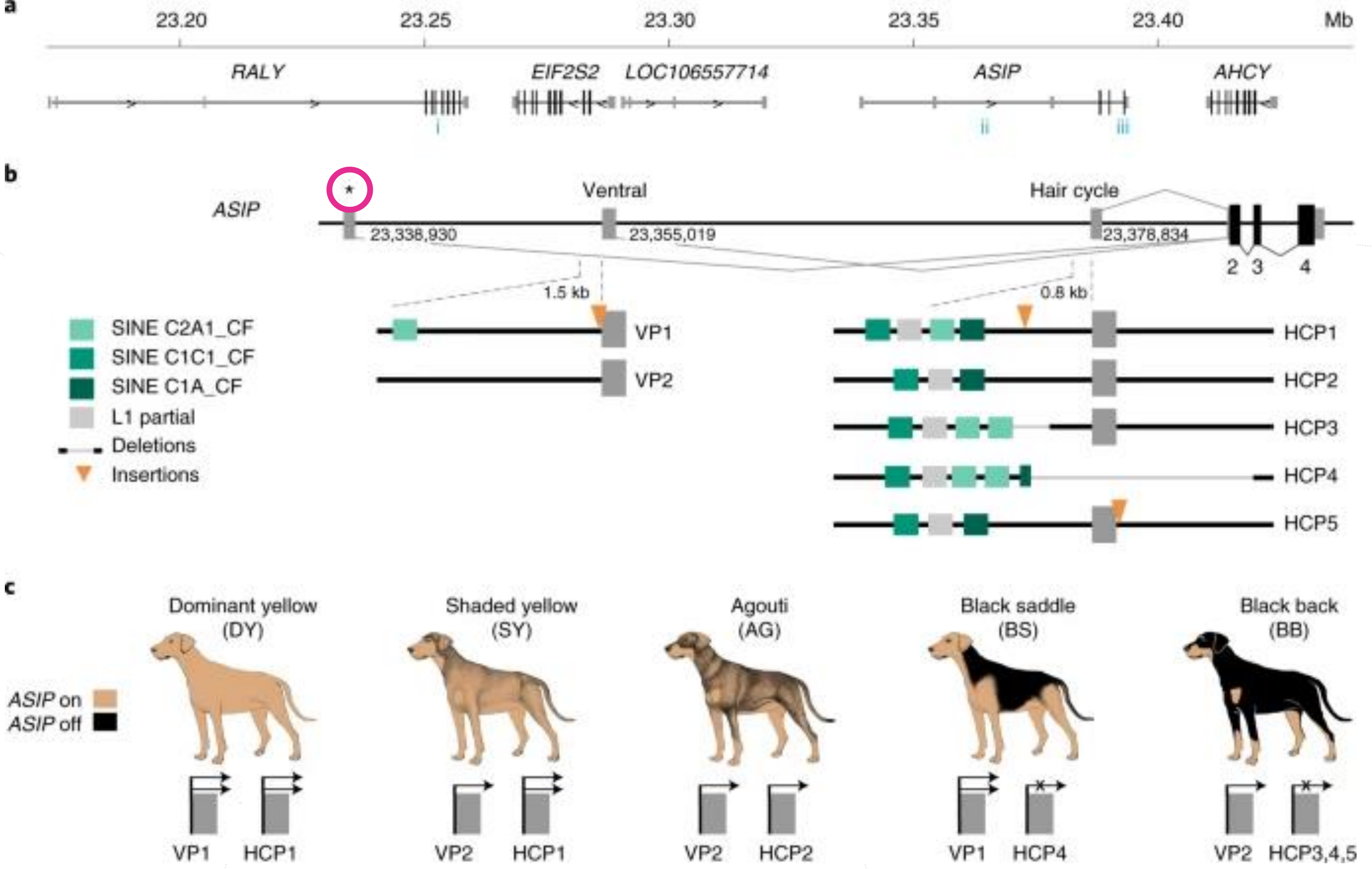
Genomic contest of *ASIP*

The canine *ASIP* gene has three alternative promoters and 5′-non-coding exons (nucleotide coordinates denote their 3′-ends. Structural variation within 1.5-kb sections of the **v**entral- (**VP**) and **h**air **c**ycle-specific **p**romoters (**HCP**) explains five different colour patterns in dogs.

Two different VP haplotypes and five different HCP haplotypes are schematically indicated.

The asterisk represents the third promoter and non-coding exon that is not related to *ASIP* pattern.



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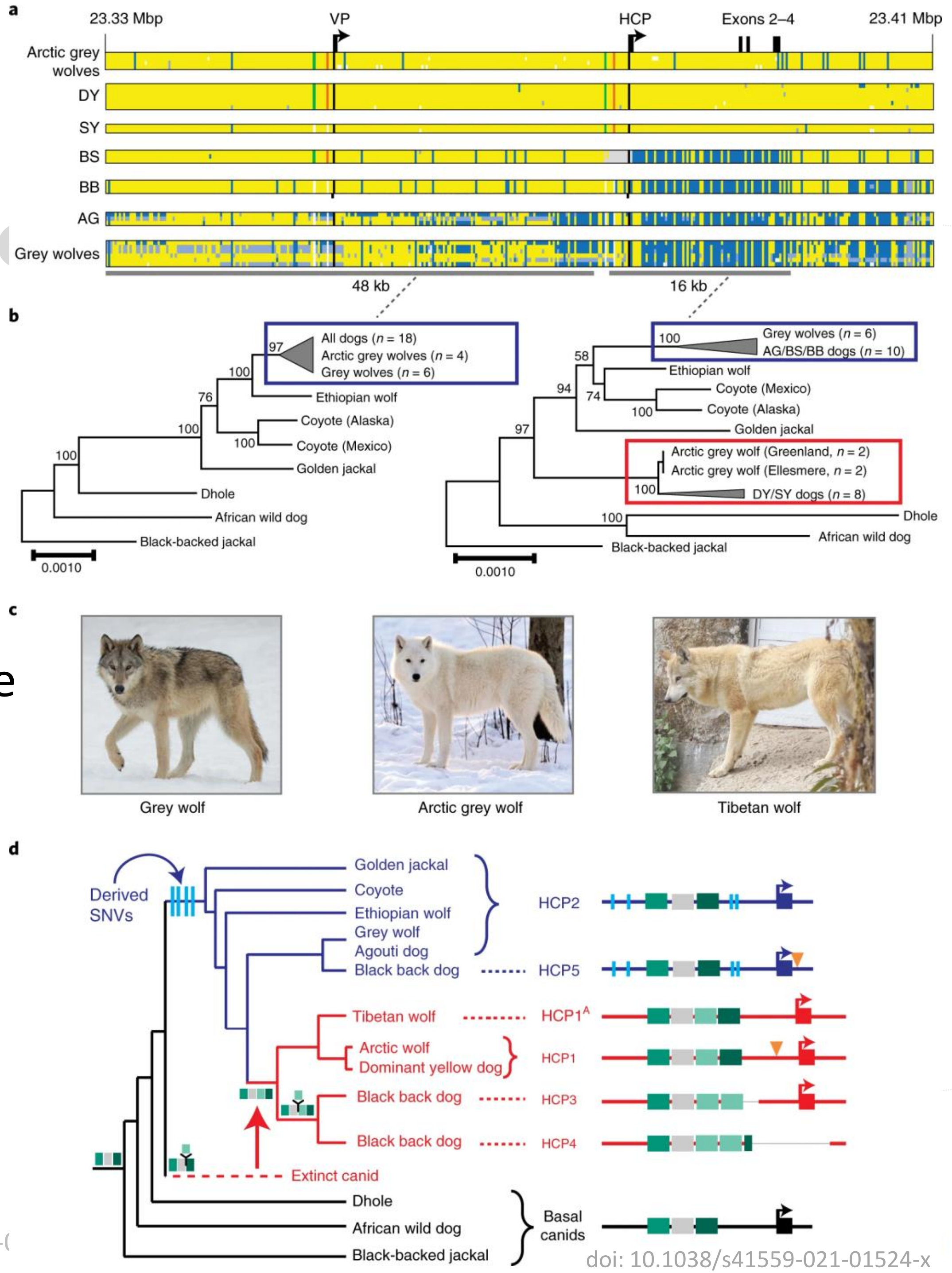
Yellow dogs and white wolves share an ancient HCP haplotype

a, Genotypes at 377 SNVs (columns) at the *ASIP* locus in grey wolves and dogs (rows), coded for heterozygosity (light blue), homozygosity for the reference (yellow) or the alternate (dark blue) allele or as missing genotypes (white). Alternate first exons (arrows) and nearby DY-associated structural variants (SINE insertions, green; polynucleotide expansions, orange) are included for reference.

b, Maximum likelihood phylogenies, including seven extant canid species and the dog, from 48- and 16-kb intervals upstream or downstream of the HCP, respectively. Grey wolf/dog phyletic clades are highlighted with boxes to indicate relationships that are consistent (blue) or inconsistent (red) with genome-wide phylogenies.

c, Images of a grey wolf, Arctic grey wolf and Tibetan wolf.

d, A phylogeny representing distinct HCP evolutionary histories inferred from genetic variation in extant canids. Structural variants and derived SNVs (cyan) distinguish wolf-like canid (blue), ghost lineage (red) and basal canid (black) haplotypes.



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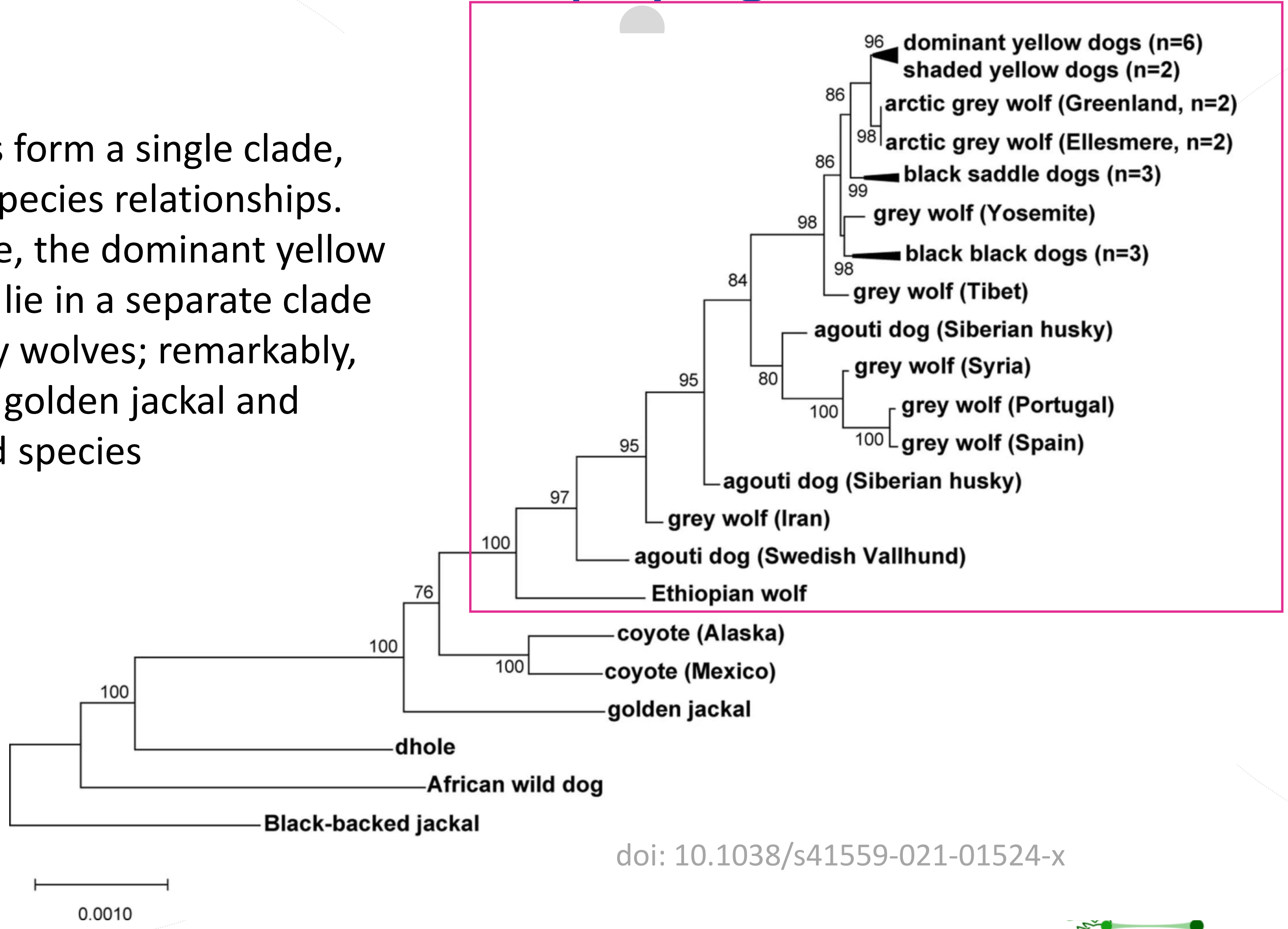
The evolutionary origin of *ASIP* haplotypes was explored by constructing maximum likelihood phylogenetic trees

All dogs and grey wolves form a single clade, consistent with known species relationships. However, in the HCP tree, the dominant yellow and shaded yellow dogs lie in a separate clade together with Arctic grey wolves; remarkably, this clade is basal to the golden jackal and distinct from other canid species



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Distribution of *ASIP* alleles in ancient dogs and wolves, and an evolutionary model for dominant yellow acquisition

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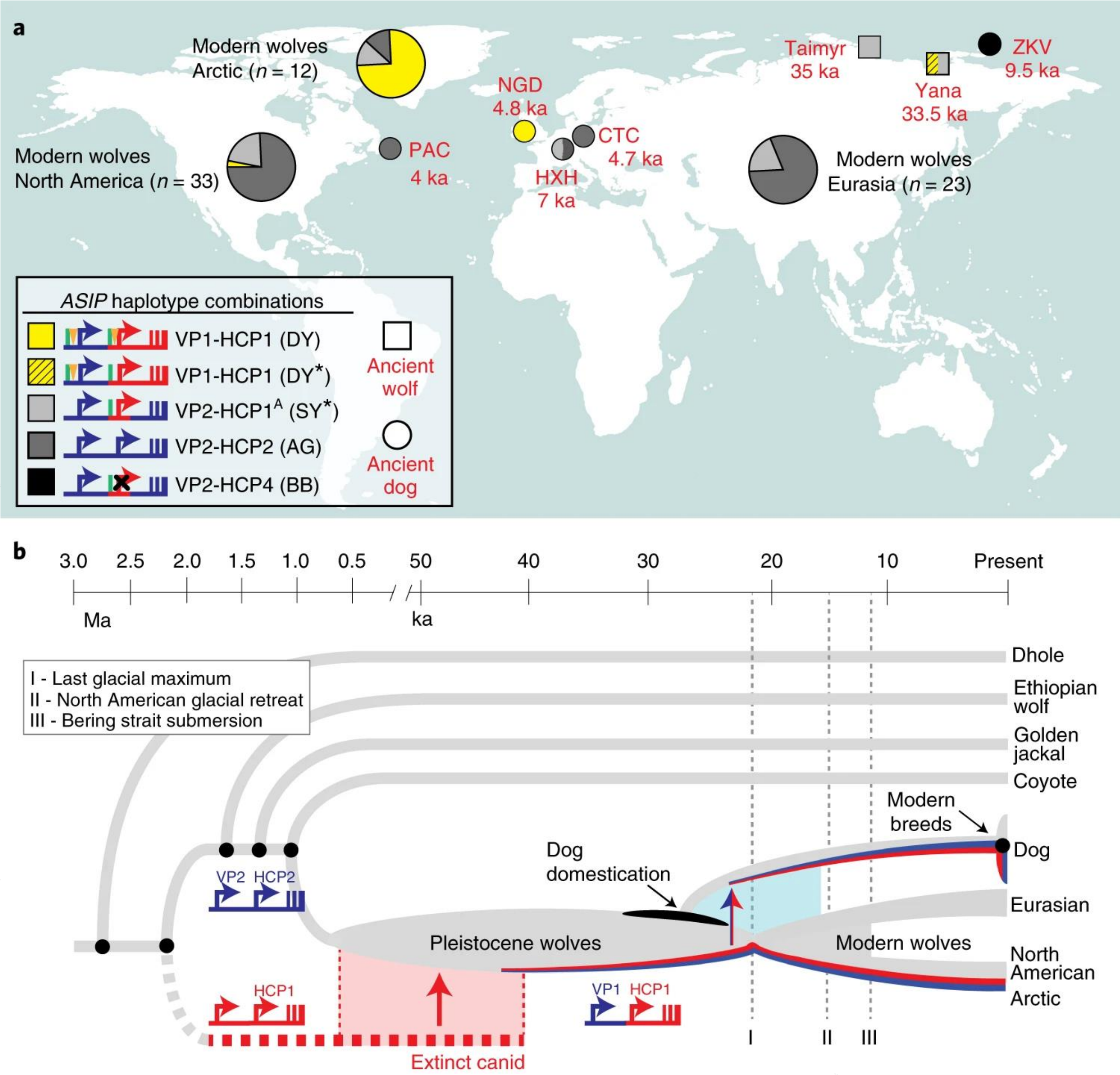
ASIP haplotypes for five ancient dogs (circles), two ancient wolves (squares) and 68 modern wolves (pie charts) found in Holarctic. Figure b) shows a model for the origin of the dominant yellow haplotype and its transmission to Arctic wolf dogs and canids, in which molecular changes in modular promoters were acquired by introgression (red, HCP1) or mutation in the gray wolf (blue, VP1).



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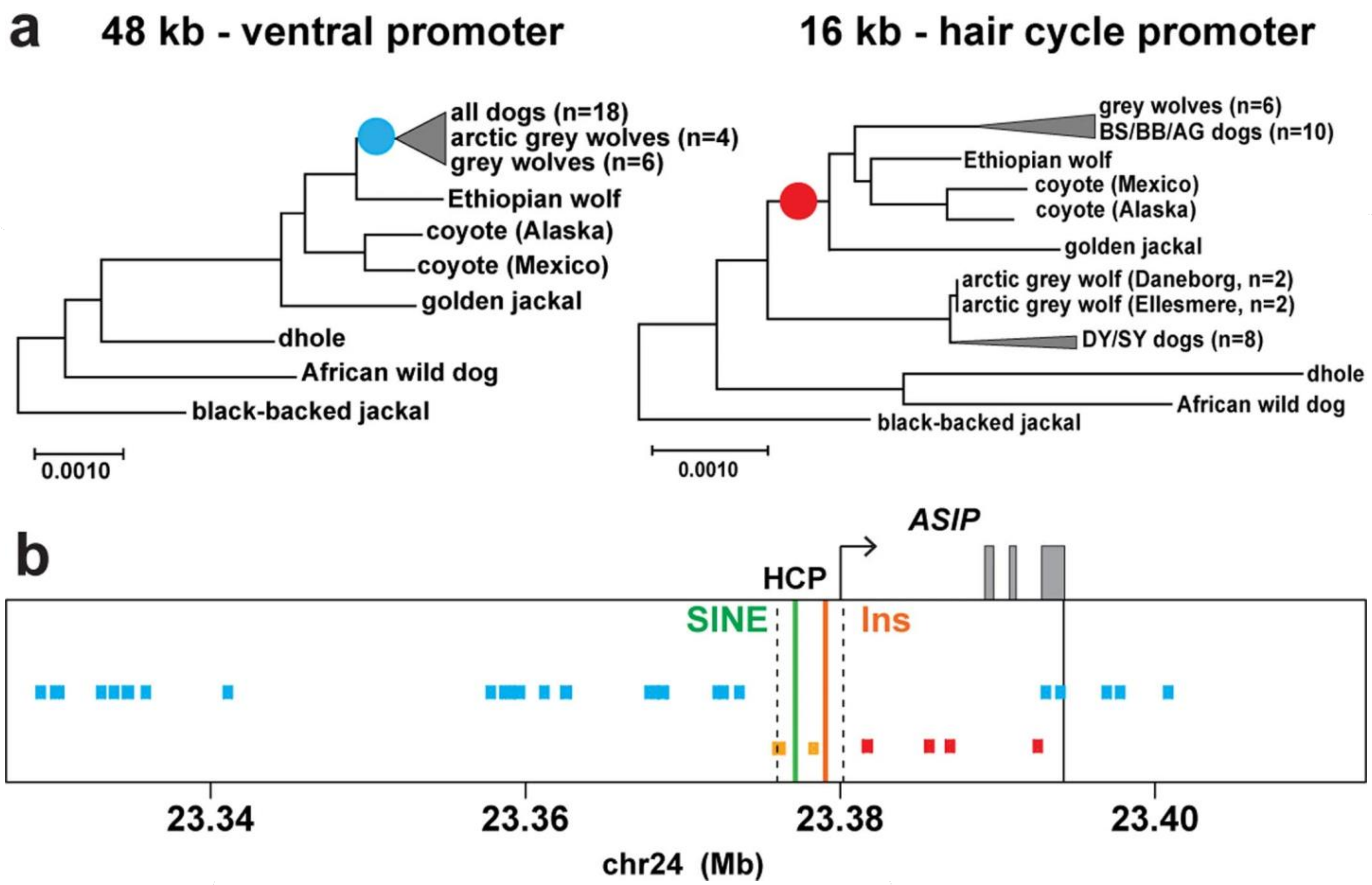
Phylogeny of canids for VP(48 kb) and HCP (16 kb)



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Derived substitutions shared by grey wolf and dogs (cyan). Ancestral alleles on DY/Arctic wolf haplotypes (red) or BB and DY/Arctic wolf haplotypes (orange) that correspond to derived substitutions among the core group of wolf-like canids

The broken lines demarcate the HCP region (chr24:23,375,800–23,380,000). The solid line signifies the downstream boundary for phylogenetic analysis. The solid green and orange lines indicate the positions of the SINE and 24 bp insertion, respectively, associated with the DY/Arctic wolf haplotype.

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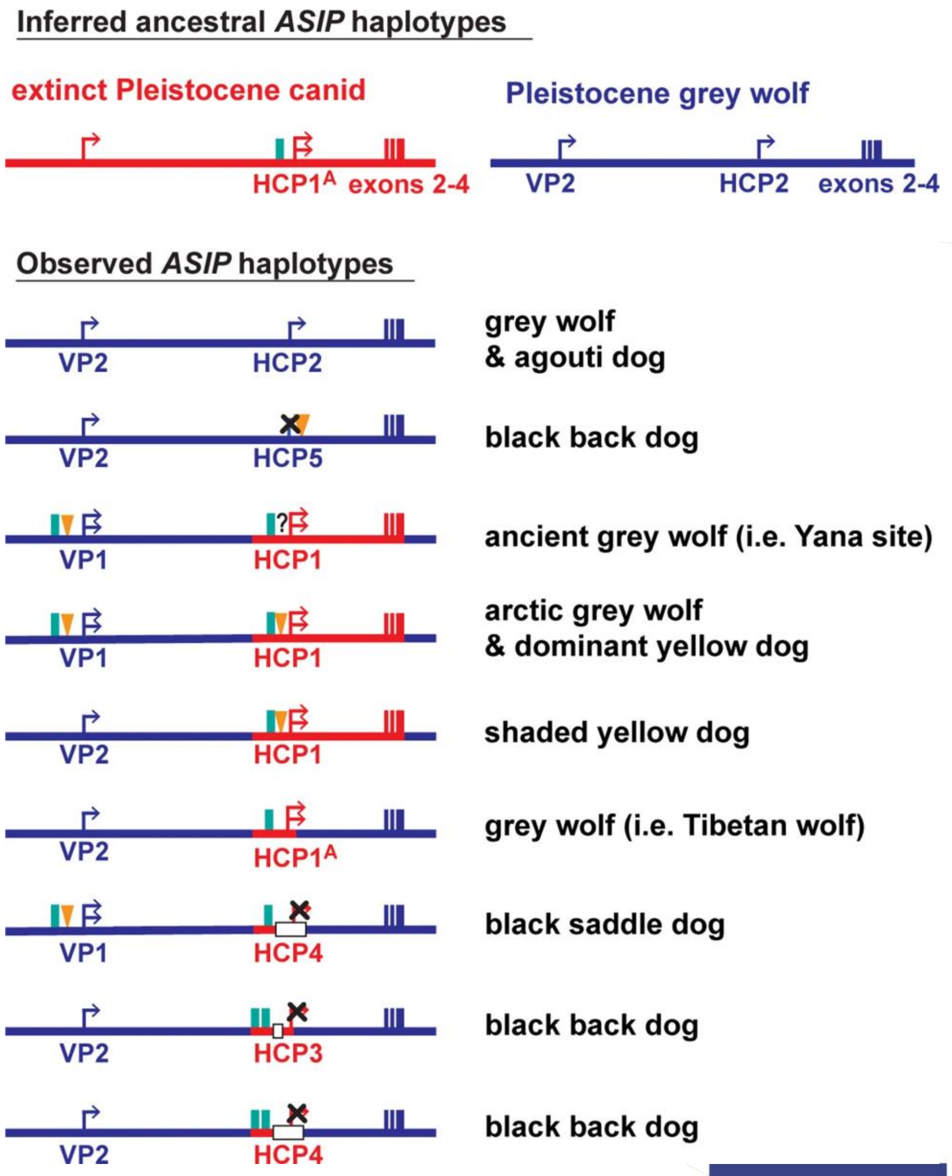
- The colour (red or blue) of *ASIP* haplotype segments indicates ancestral species of origin, inferred from phylogenetic analysis
- Relevant structural variants near the ventral (VP) and hair cycle (HCP) promoters are depicted as yellow triangles (polynucleotide expansions), green bars (SINE insertions) and white bars (deletions).
- Modified promoter activity is indicated by an X mark (no activity) or an additional arrow (elevated expression), based on RNA-seq and/or inference from coat colour



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- The wide distribution of dominant yellow across modern dog breeds from diverse locations, as well as the dingo, a feral domesticate, frequently found in Australia, suggests that the dog originated in Southeast Asia.

- Another study published suggests that the self-domestication hypothesis can finally be rigorously tested and assessed using high-resolution comparative genomics.

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Origin of cats

- Wildcats (*Felis silvestris*) are distributed all over the Old World.
- DNA analysis suggests that cats lived for thousands of years alongside humans before they were domesticated.
- During that time, their genes have changed little from those of wildcats, apart from picking up one recent tweak: the distinctive stripes and dots of the tabby cat.
- Surprisingly, wild and domestic cats showed no major differences in their genetic makeup, and one of the few traits available for telling them apart was the **tabby** coat marking.

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- The earlier ancestors of today's domestic cats spread from southwest Asia and into Europe as early as 4400 B.C. The cats likely started hanging around farming communities in the Fertile Crescent about 8,000 years ago, where they settled into a mutually beneficial relationship as humans' rodent patrol.
- A second lineage, consisting of African cats that dominated Egypt, spread into the Mediterranean and most of the Old World beginning around 1500 B.C. This Egyptian cat probably had behaviors that made it attractive to humans, such as sociability and tameness.
- Modern genetic data analyses of nuclear short tandem repeats (STR) and 16% of the mitochondrial DNA (mtDNA) genome in extant wild and domestic cats revealed that only one of them, the north African/southwest Asian *Felis silvestris lybica*, was ultimately domesticated.

Subspecies of cats: *Felis silvestris silvestris* (European wildcat), *Felis silvestris lybica, Felis silvestris ornata, Felis silvestris cafra and Felis silvestris bieti*

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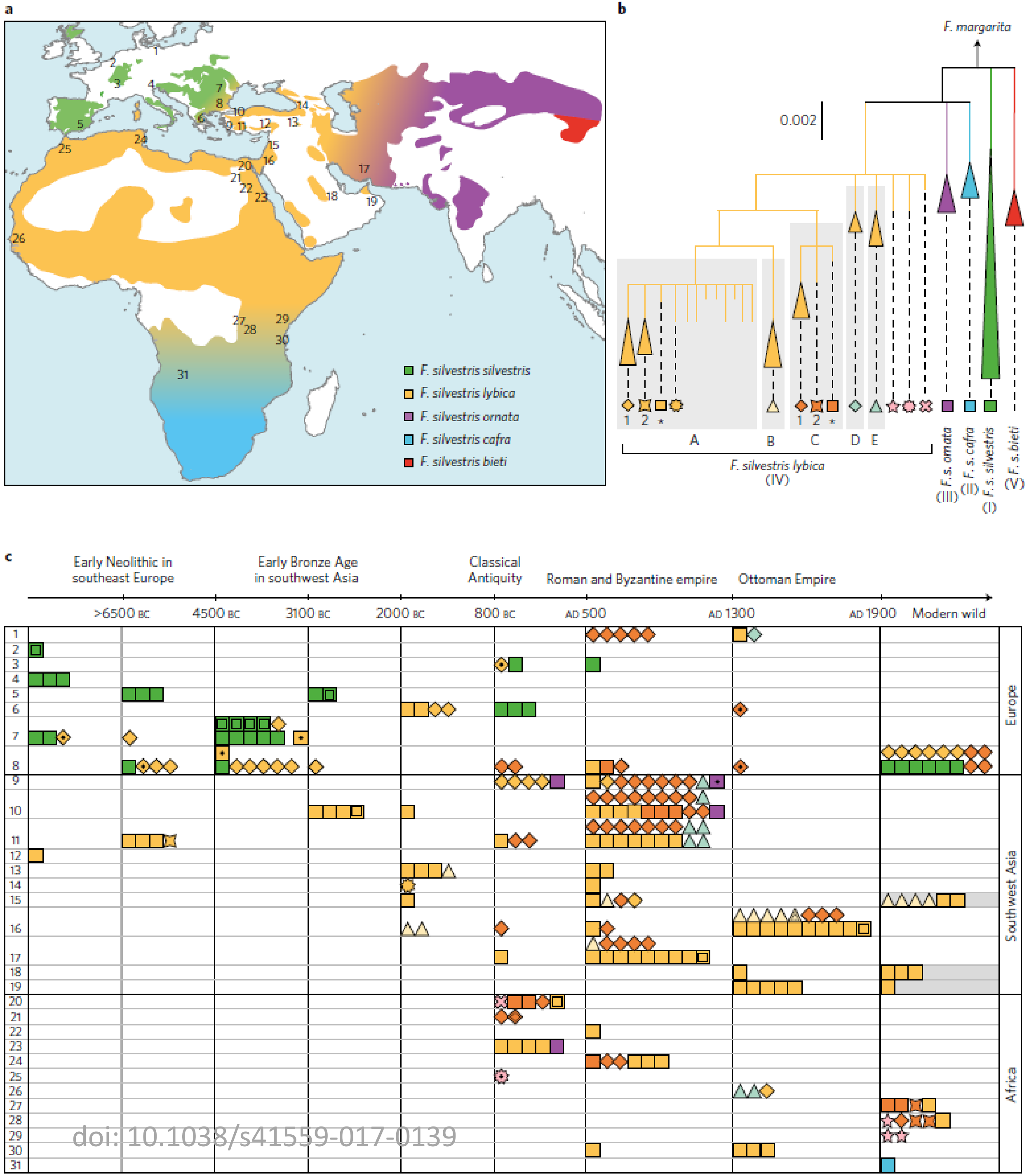

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Spatio-temporal representation of cat maternal genealogies

a) Map showing the present-day distribution of *Felis silvestris* with the geographic range of each subspecies.

b) Tree of mtDNA lineages observed in our ancient samples and in modern wild and domestic cats from literature.

c) Spatio-temporal depiction of ancient cat haplotypes as depicted with symbols from the tree in b.

Rows represent the approximate geographic provenance of the samples as reported in the map in a whereas the columns pertain to chronological periods, the limits of which were selected to separate the prehistoric and historical periods evenly, to unambiguously assign each sample to a single bin and to take historic events into account that could have affected human–cat interactions, as indicated on the timeline above. A dot inside the symbols indicates AMS-radiocarbon-dated samples; dashed lines inside the symbols indicate incomplete mtDNA profiles; Near Eastern modern wildcats from literature are indicated by grey-shaded bins.

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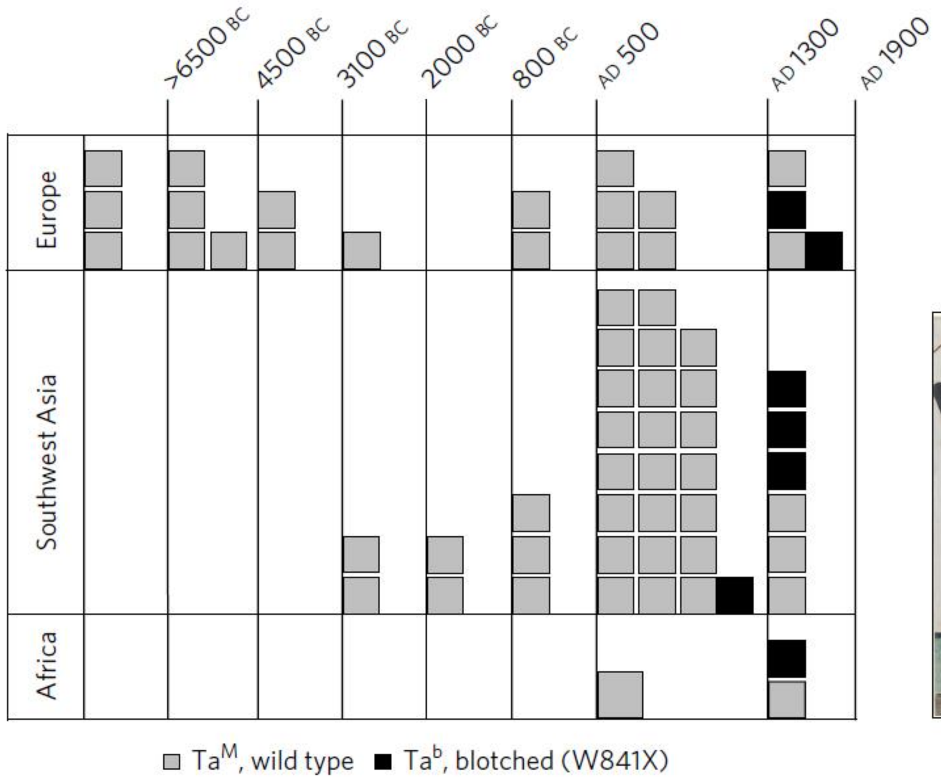
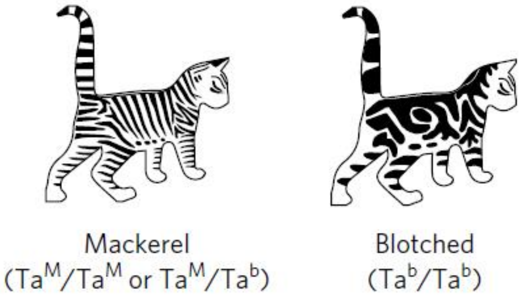
Spatio-temporal representation of the alleles determining the phenotypic variation in the shape of tabby patterns, mackerel (Ta^M) and blotched (Ta^b).

- The image from ancient Egypt shows a ‘cat under the chair’ with a tabby mackerel marking, typical of *F. silvestris lybica*





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Domestication of cats

- Cat domestication was a complex, long-term process featuring extensive translocations that allowed admixture events between geographically separated cat populations at different points in time.
- Cats became a domesticated companion of humans without changing much
- Domestic cats look similar to wildcats, but they aren’t solitary, tolerating both humans and other cats.
- This is in contrast to dogs, the first animals to be domesticated. Dogs were selected to perform specific tasks—which never was the case for cats—and this selection for particular traits is what led to dogs’ diversification to the many breeds we see today.

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Conclusion

- The vanguard of high-resolution surveys of livestock paleogenomes described in the previous section signpost the future of archaeogenetics in domestic animals.
- They point towards high-resolution studies across time and space that will reveal the genetic architecture of animal domestication and the physiological and neurobiological changes that occur as livestock and companion animals are brought under human control and subject to long-term reproductive management and artificial selection.
- It is likely that high-resolution surveys of pre-domestic and early animal paleogenomes will provide important new information on intriguing features of domestic animals and the domestication process

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