



# “The Taming of the Cat Stephen J. O’Brien



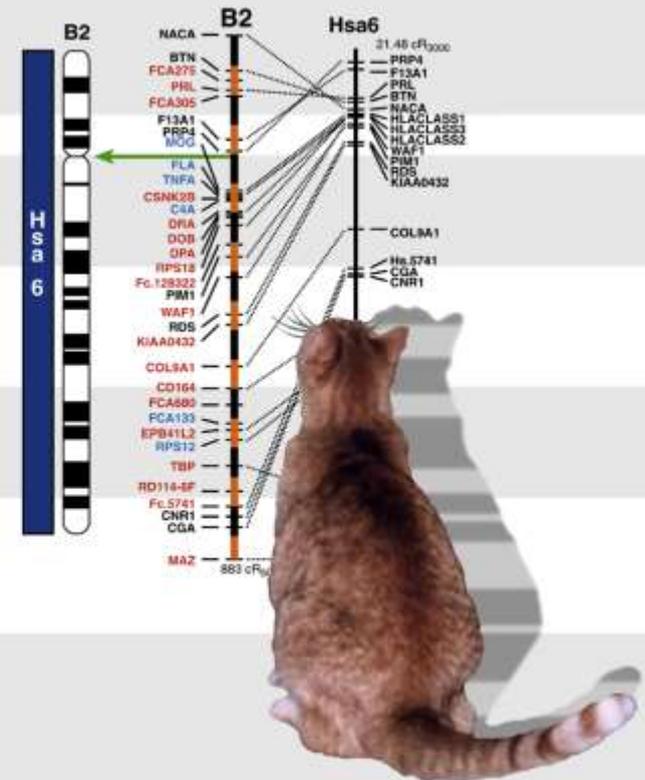
## BELYAEV CONFERENCE

a triumphant event in commemoration  
of the centenary of the birth of

Academician

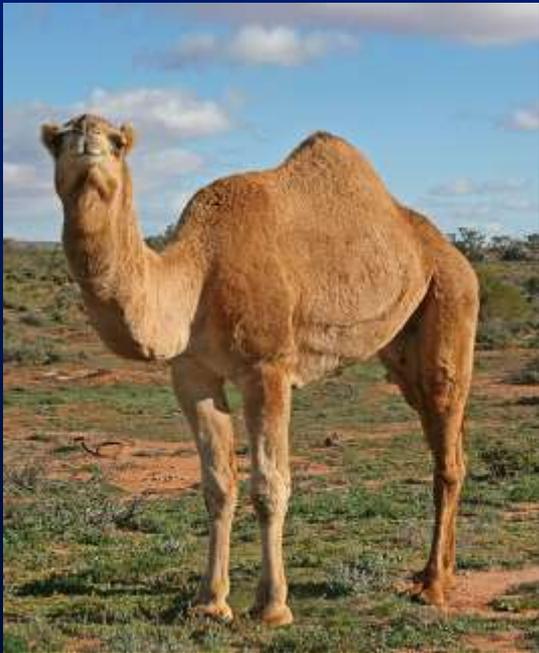
**Dmitri Belyaev**

## Some Pictures and Some Stories











Beauceron



Berger Allemand



Borders Collies



Westie



Yorkshire



Bouvier Bernois



D. Bordeaux



Epagneul Breton



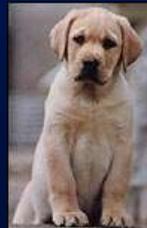
Cocker Anglais



Caniche moyen



Coton de Tuléar



Labrador



Lhasa-Apso



Shih Tzu



Setter Gordon



**The Dog and Its Genome**  
edited by Elaine A. Ostrander, Urs Giger  
& Kerstin Lindblad-Toh  
Cold Spring Harbor Laboratory Press: 2005.  
584 pp. \$135, £80

**Stephen J. O'Brien**  
Genome technology has found its way into the living room with the completion of the whole-genome sequence of the domestic dog *Canis familiaris*, from a female boxer called Tasha. Finished just a year after its initiation in 2003, the remarkably complete sequence (representing an estimated 99% of the dog's 2.4 billion base pairs) achieves 7.5-fold coverage of the genome and is a major advance over the 1.5-fold sequence of a poodle published by Celera in 2003. The dog is now a front-line model for



Boxer tricks: Tasha's genome will help researchers



Whippet



Boxer



Pointer

As stated many times  
A cat is not a dog



Persian



Maine Coon



Siamese



Turkish



Scottish Fold



Bengal



Felix Bluebird



Bambino



Burmese



Sphynx



British Shorthair



Chartreux



Bicolor Fingert



Birman

20 breeds of cats



Cornish Rex



Black



Russian Blue



Himalayan



Scottish Fold



Turkish Van



May 2003  
ISSN 1089-9021

# GENOME RESEARCH

Volume 10 Number 5

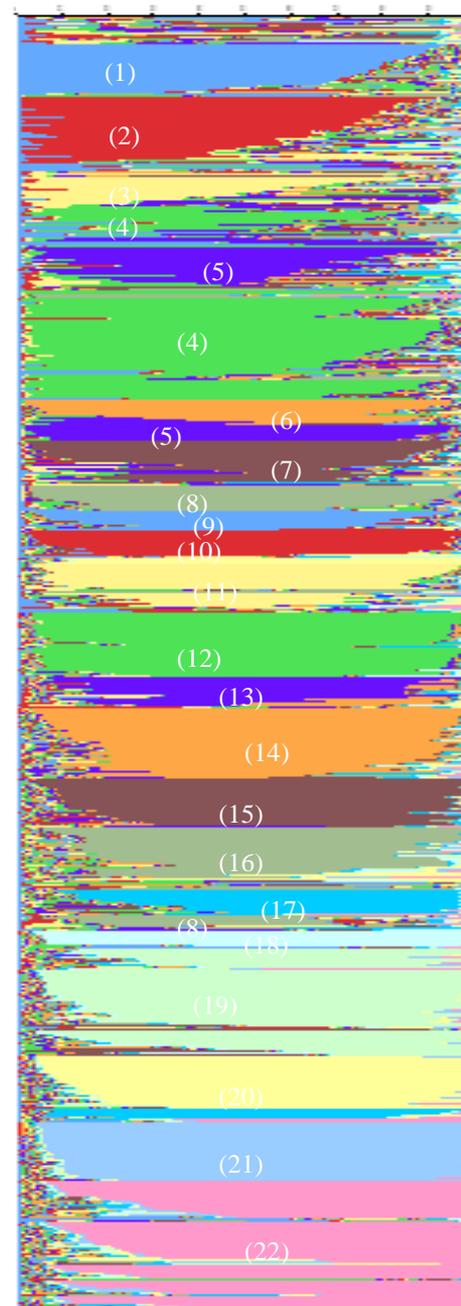
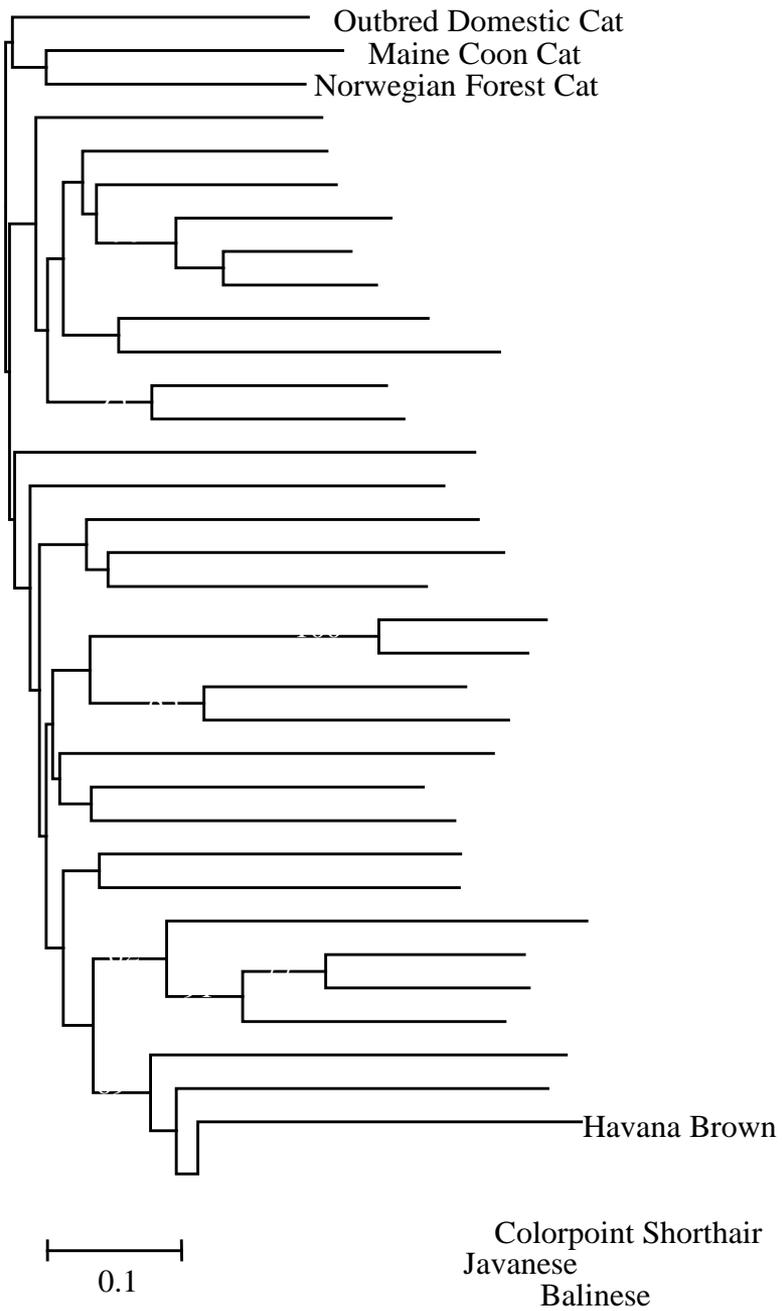
Cat Genome Radiation Hybrid Map • Human-Mouse Comparative Mapping with Human Chromosome 7 • Nuclear Lamin Mutation Associated with Partial Lipodystrophy with Diabetes • Evolution of *Mhc-DRB* Genes in Primates, Platyrrhines, and Carnivorhines • *C. elegans* and Human Comparative Proteomics

CRC Spring Harbor Laboratory Press



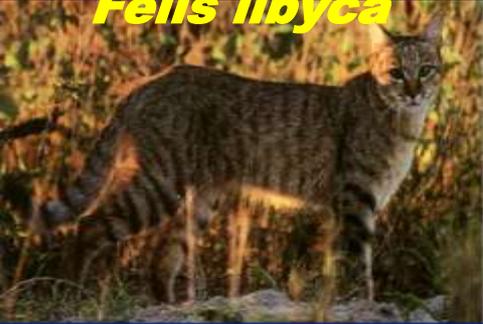
A lingering question  
... 'where did the  
domestic cat come  
from????'





**African wild cat**

***Felis libyca***

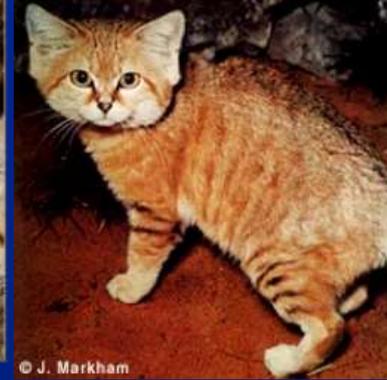


**Chinese mountain cat,**

***Felis bieti***



**Sand cat, *Felis margarita***



**European wild cat**  
***Felis silvestris***



**Domestic cat**  
***Felis catus***



**Black-footed cat**  
***Felis nigripes***



**Jungle cat,**  
***Felis chaus***

# DOMESTIC CAT LINEAGE



**European**  
***F. silvestris silvestris***



**Asiatic**  
***F. s. ornata***



**African/Mid East**  
***F. s. libyca***

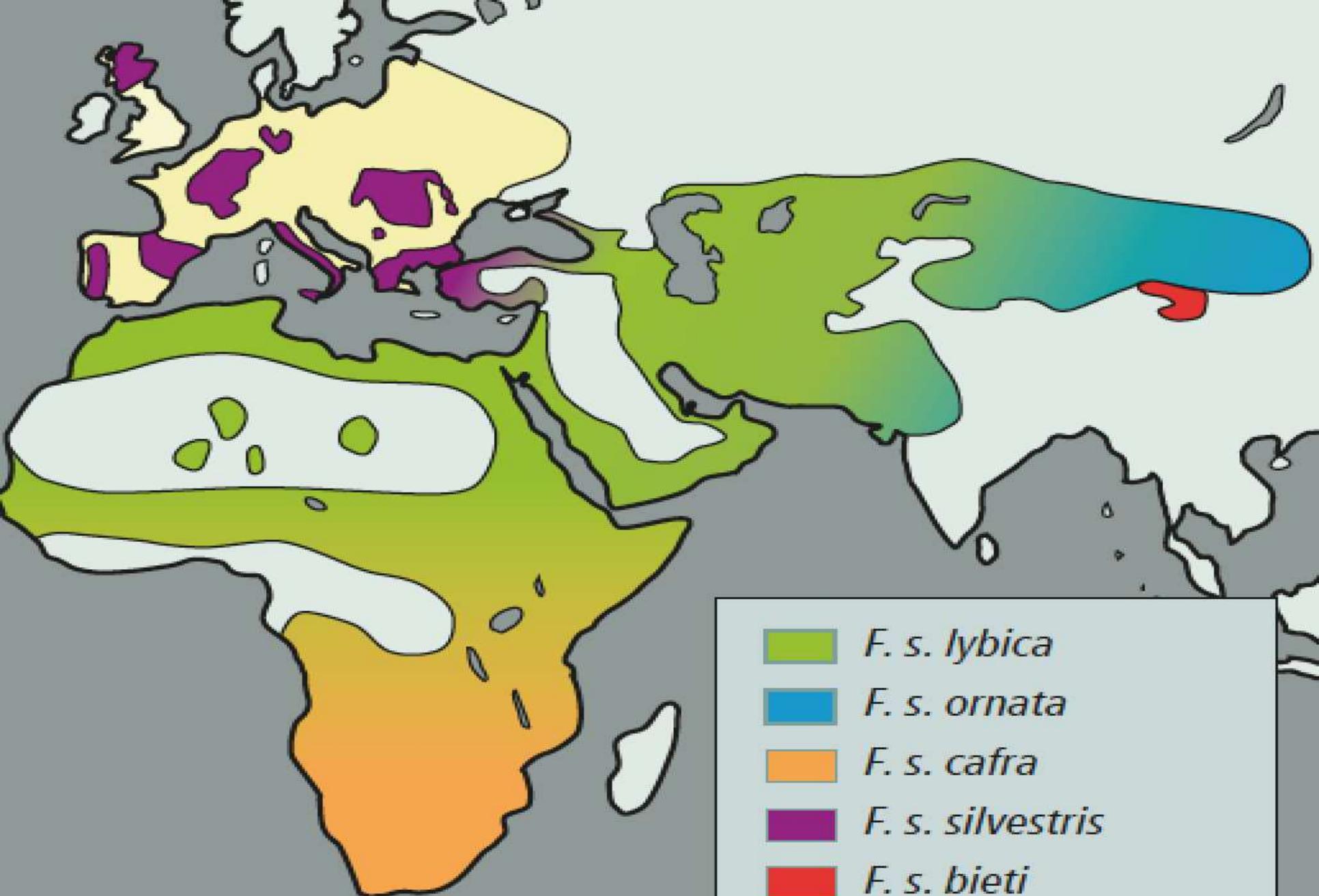
**Chinese**  
***F. s. bieti***

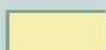


**So African**  
***F. s. caffra***



© Peter Jarkenn



-  *F. s. lybica*
-  *F. s. ornata*
-  *F. s. cafra*
-  *F. s. silvestris*
-  *F. s. bieti*
-  Historic distribution



a common site around human settlements  
in the Fertile Crescent

---

**3,600 YEARS AGO** Artists paint  
domesticated cats from Thebes, Egypt; oldest  
clear evidence of fully domesticated cat

---

◀ **2,900 YEARS AGO** Cats become  
"official deity" of Egypt in the form of  
the goddess Bastet; huge number of cats  
sacrificed and mummified in her sacred city  
indicates that Egyptians were breeding  
domestic cats

---

**2,300 YEARS AGO** The height of  
cat worship in Egypt; the Ptolemeic rulers  
maintain strict bans on the export of cats

# Science



## The Near Eastern Origin of Cat Domestication

Carlos A. Driscoll,<sup>1,2\*</sup> Marilyn Menotti-Raymond,<sup>1</sup> Alfred L. Roca,<sup>3</sup> Karsten Hupe,<sup>4</sup> Warren E. Johnson,<sup>1</sup> Eli Geffen,<sup>5</sup> Eric H. Harley,<sup>6</sup> Miguel Delibes,<sup>7</sup> Dominique Pontier,<sup>8</sup> Andrew C. Kitchener,<sup>9,10</sup> Nobuyuki Yamaguchi,<sup>2</sup> Stephen J. O'Brien,<sup>1\*</sup> David W. Macdonald

### The Taming of the Cat



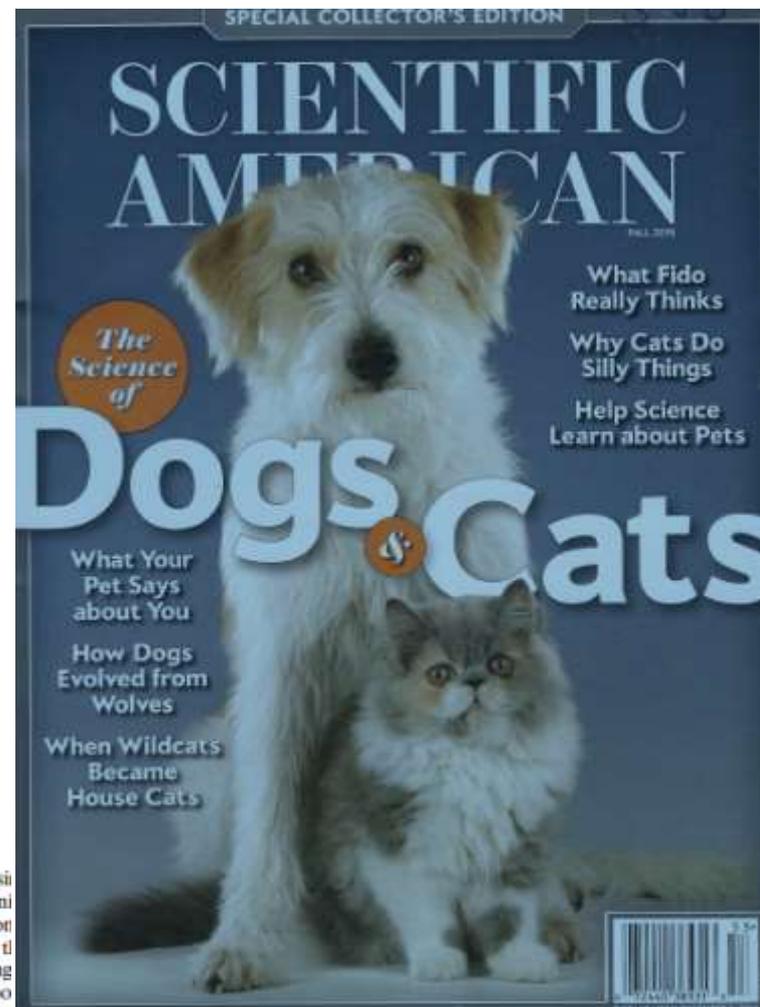
### From wild animals to domestic pets, an evolutionary view of domestication

Carlos A. Driscoll<sup>a,b</sup>, David W. Macdonald<sup>a</sup>, and Stephen J. O'Brien<sup>b,1</sup>

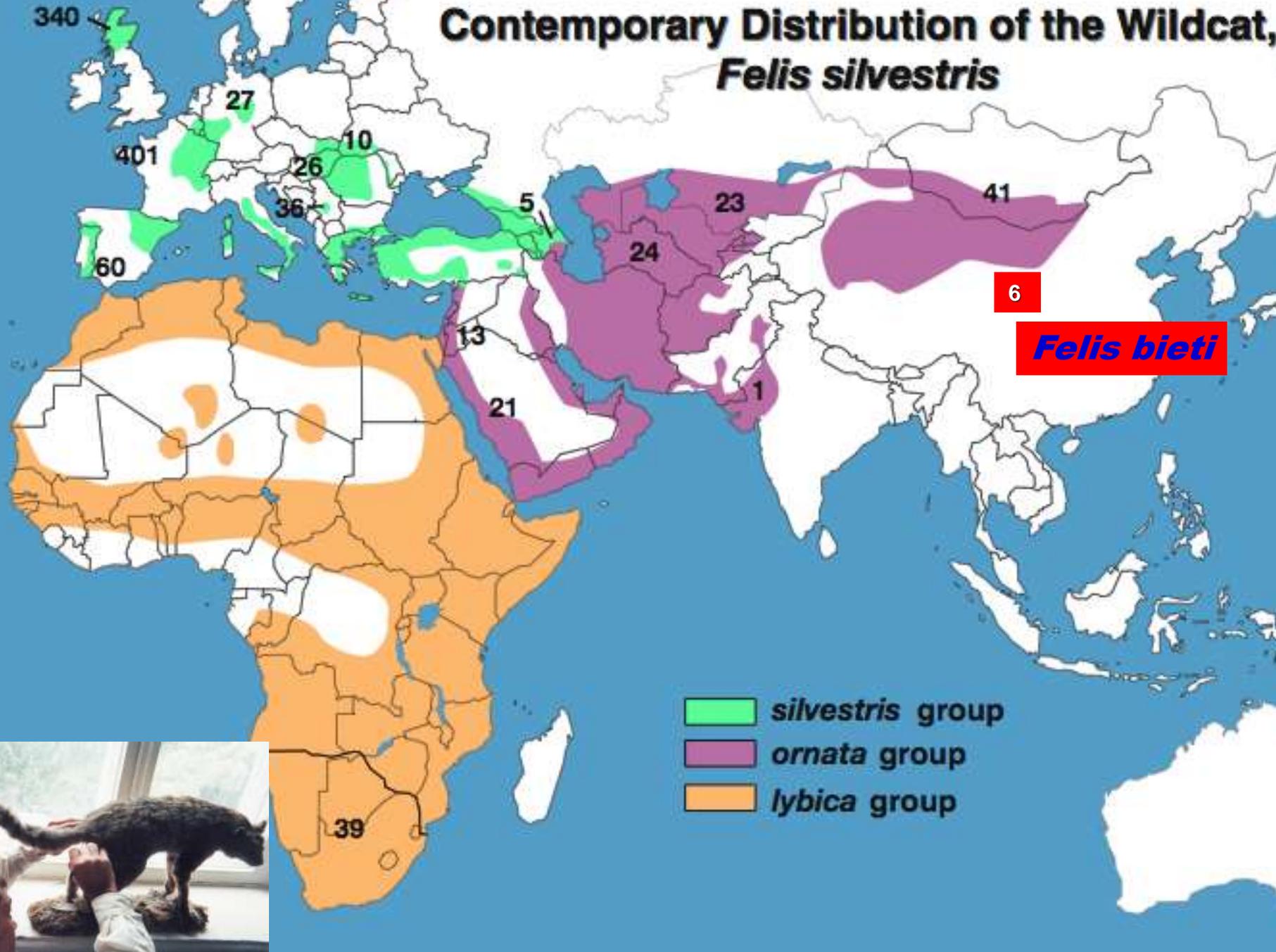
<sup>a</sup>Wildlife Conservation Research Unit, Department of Zoology, University of Oxford, Tubney House, Abingdon Road, Tubney, Oxon OX13 5QL, United Kingdom; and <sup>b</sup>Laboratory of Genomic Diversity, National Cancer Institute, Frederick, MD 21702.

Artificial selection is the selection of advantageous natural variation for human ends and is the mechanism by which most domestic species evolved. Most domesticates have their origin in one of a few historic centers of domestication as farm animals. Two notable exceptions are cats and dogs. Wolf domestication was initiated late in the Mesolithic when humans were nomadic hunter-gatherers. Those wolves less afraid of humans scavenged nomadic hunting camps and over time developed utility. Initially as guards warning

development of urban life and a suite of innovations encompassing most of what we today think of as culture (4, 5). Much of modernity is an indirect consequence of artificial selection. The plow has come to symbolize the Neolithic Revolution, but viewing history in the light of evolution we see that it was intelligently designed change to the genetic composition of natural biota that made the real tool. In some sense, Neolithic farmers were the first geneticists as domestication uses the lineage with which they engaged the most



# Contemporary Distribution of the Wildcat, *Felis silvestris*



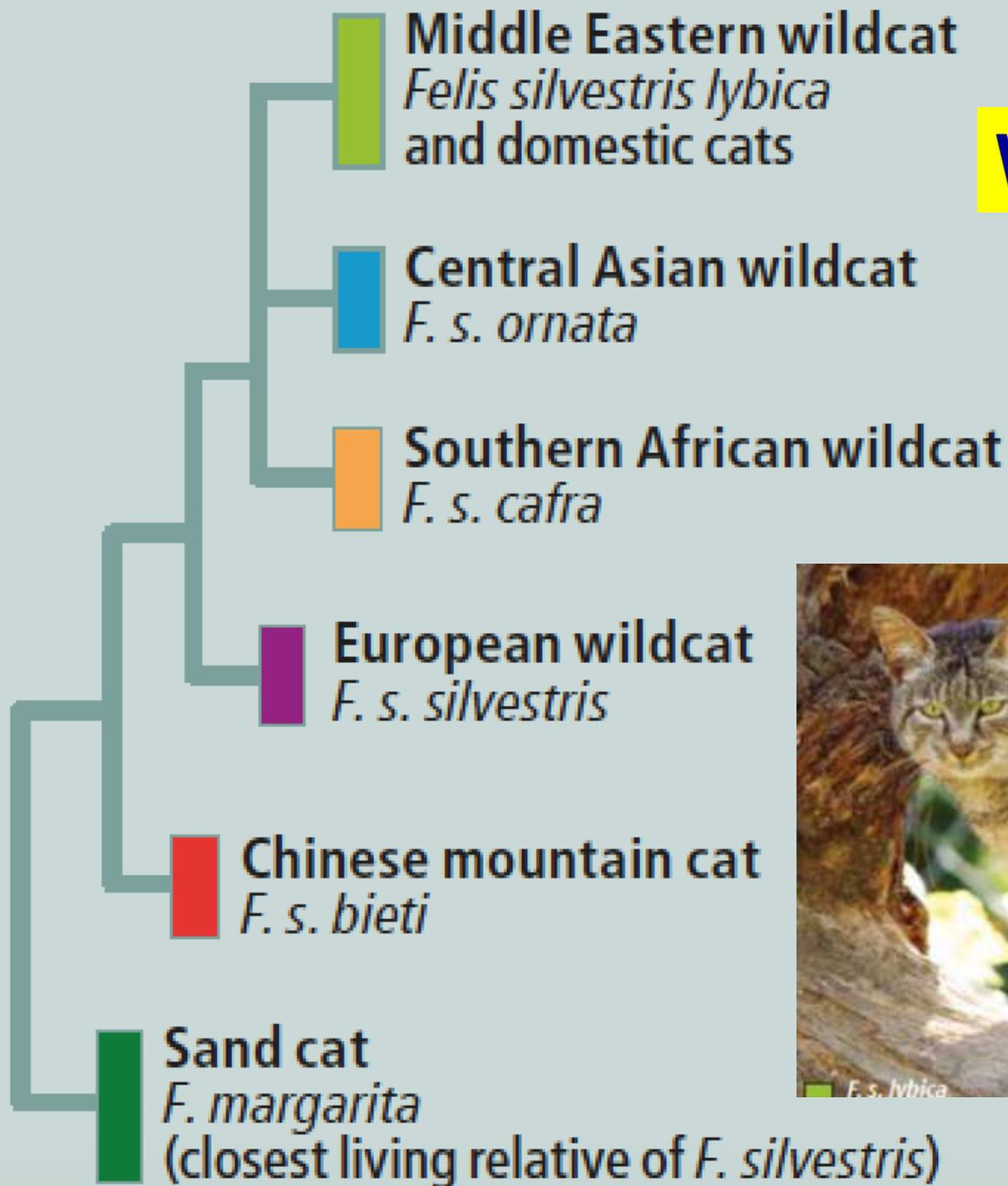
# Mitochondrial DNA-Phylogeny

- ND5 & ND6
- 2604 total characters
- 186 variable, informative
  - Mr. Bayes, NJ, MP, ML result in identical tree topology
- Coalescent dating estimates

# Microsatellite Loci

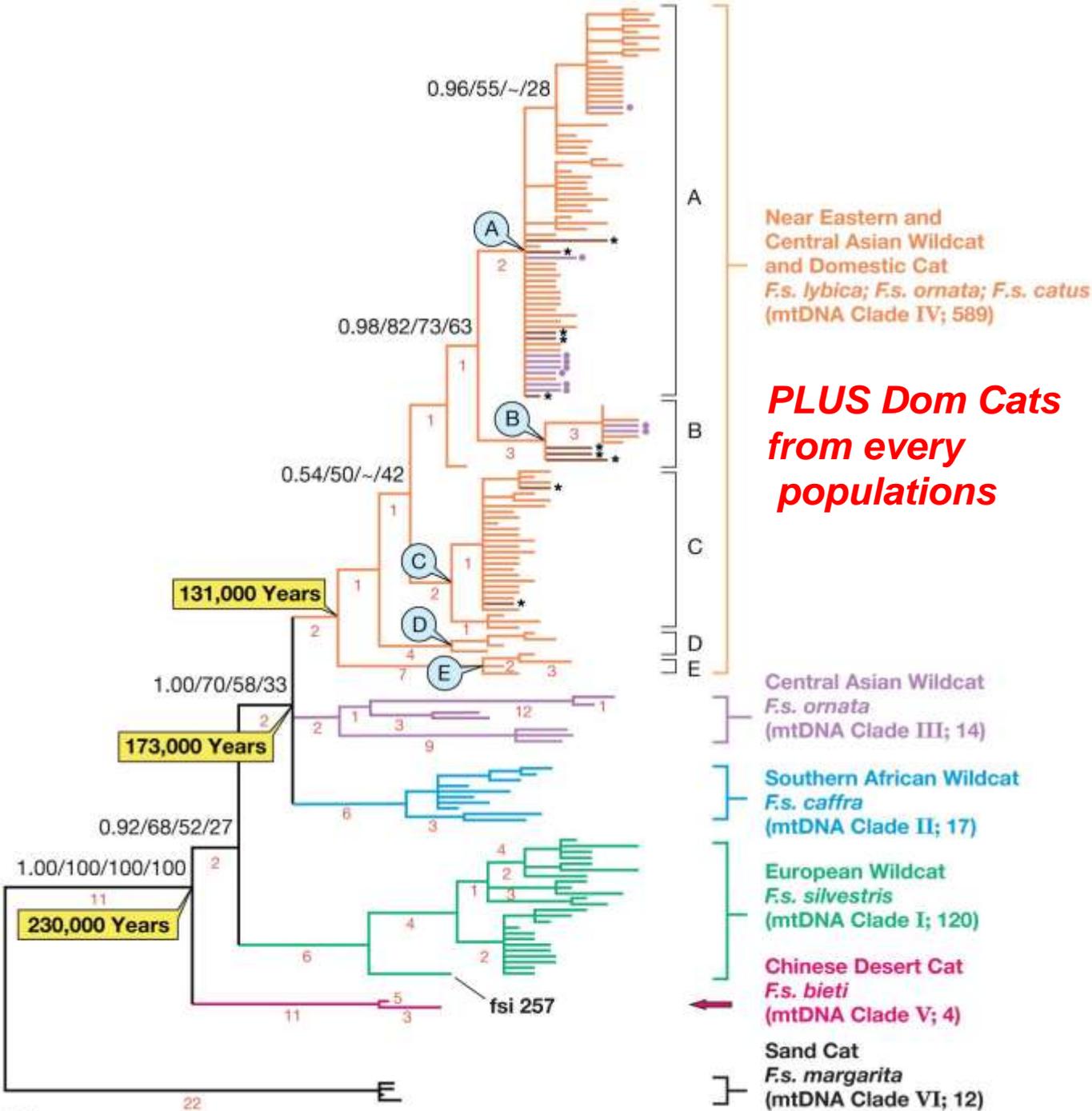
- 36 loci mapped to 16 chromosomes
- STRUCTURE Population genetic analyses
- Phylogenetic Analyses
  - Dkf, Dps result in identical tree topology

## What Carlos saw



Detail

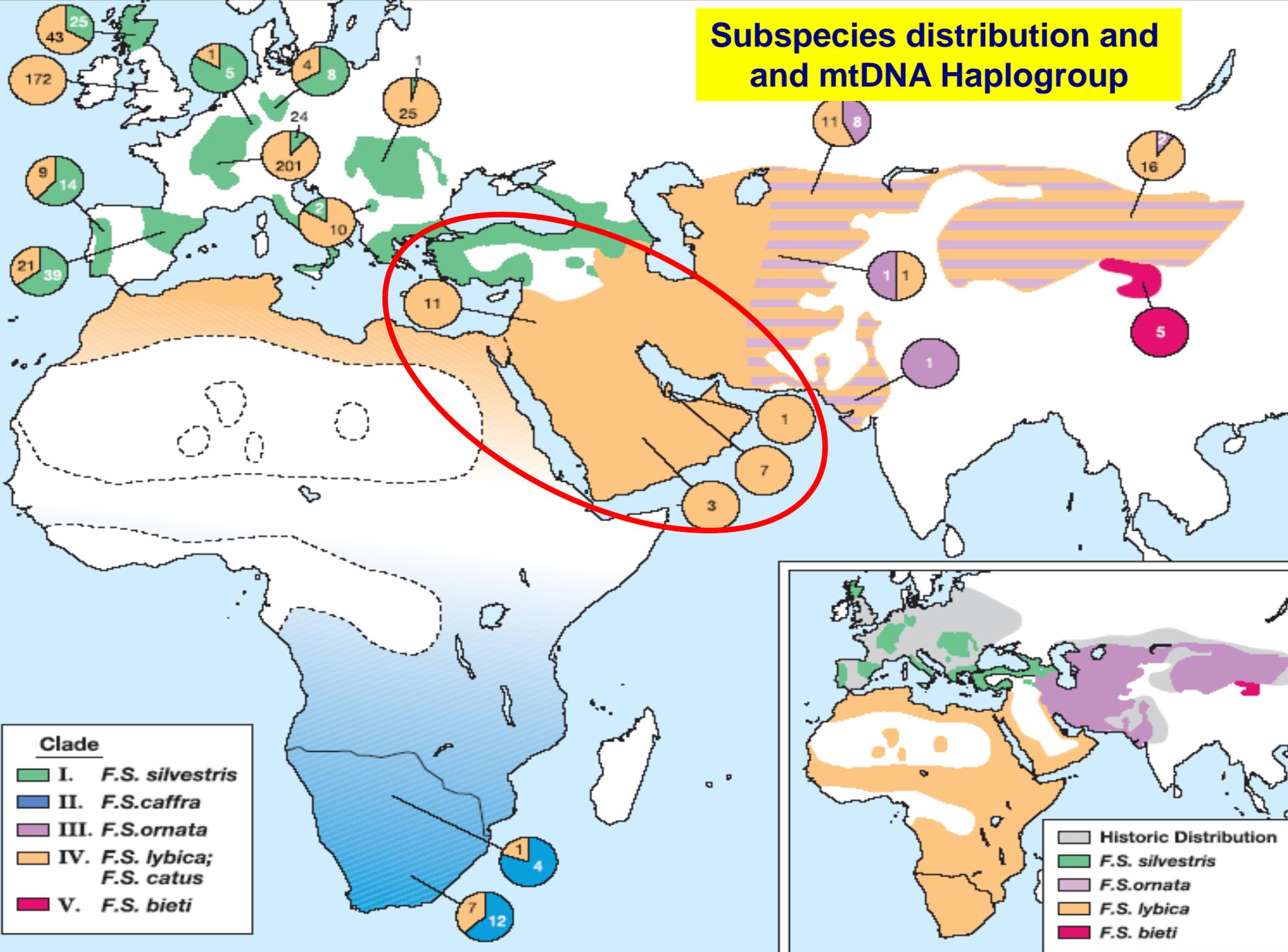
s



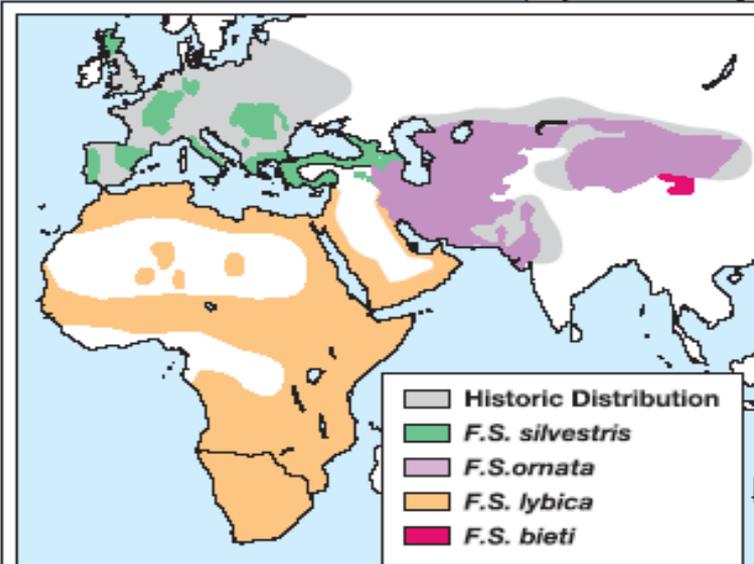
Mitochondrial genotype of wildcats across the world

2606 bp;  
245 PI sites  
176 genotypes

# Subspecies distribution and mtDNA Haplogroup



- Clade**
- I. *F.S. silvestris*
  - II. *F.S. caffra*
  - III. *F.S. ornata*
  - IV. *F.S. lybica*; *F.S. catus*
  - V. *F.S. bieti*



Near Eastern Wildcat  
and Domestic Cat  
*F.s. lybica*; *F.s. catus* STR IV  
(mtDNA Clade IV, 465; I, 3;  
II, 2; III, 2)

PLUS Dom. Cats  
from every  
population

European Wildcat  
*F.s. silvestris* STR-I  
(mtDNA Clade I, 80; IV, 28)

Southern African Wildcat  
*F.s. caffra* STR-II  
(mtDNA Clade II, 10; IV, 16)

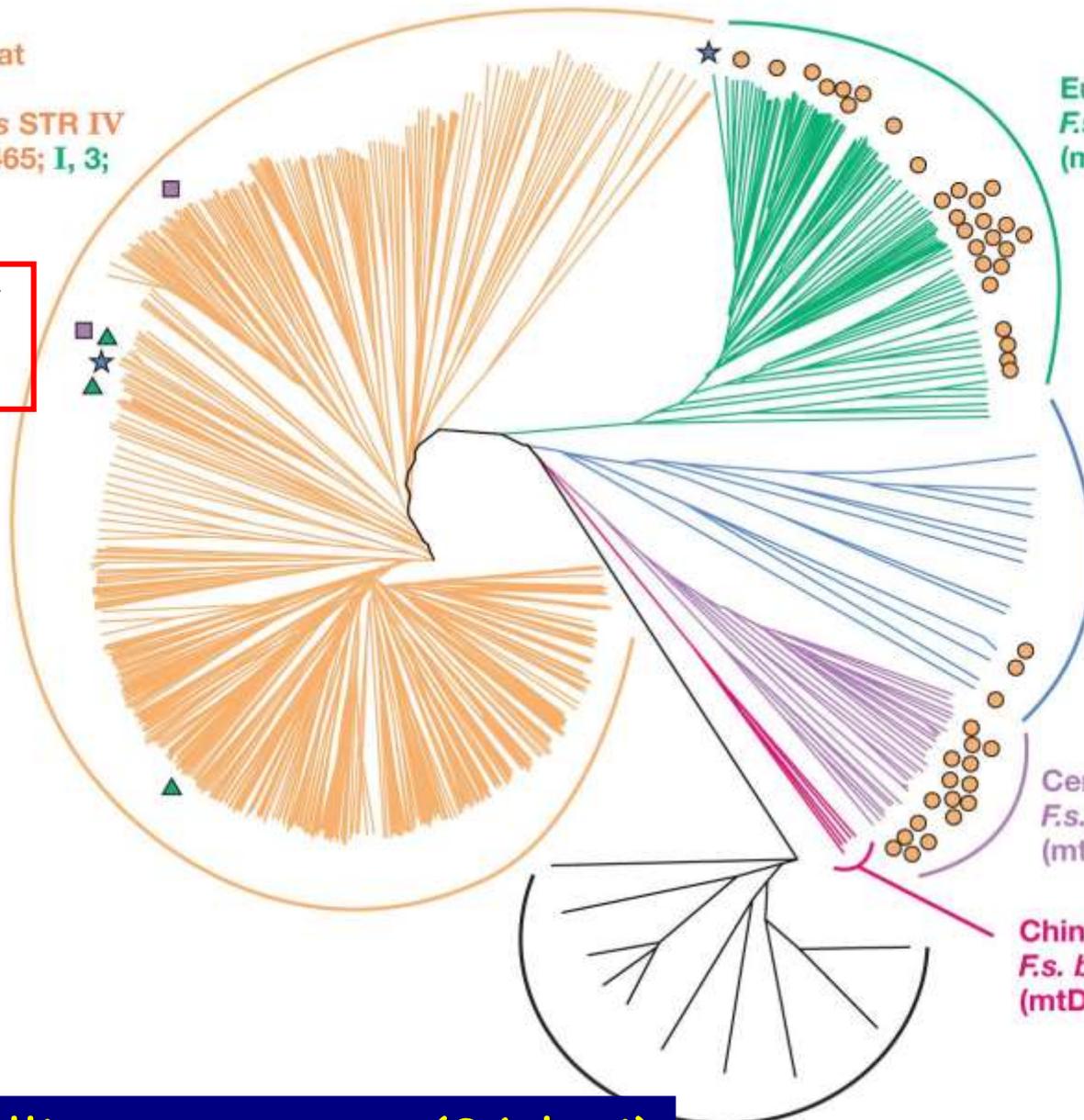
Central Asian Wildcat  
*F.s. ornata* STR-III  
(mtDNA Clade III, 11; IV, 16)

Chinese Desert Cat  
*F.s. bieti* STR-V  
(mtDNA Clade V, 4)

Ind Cat  
*F.s. margarita* STR-VI  
(mtDNA Clade VI, 10)

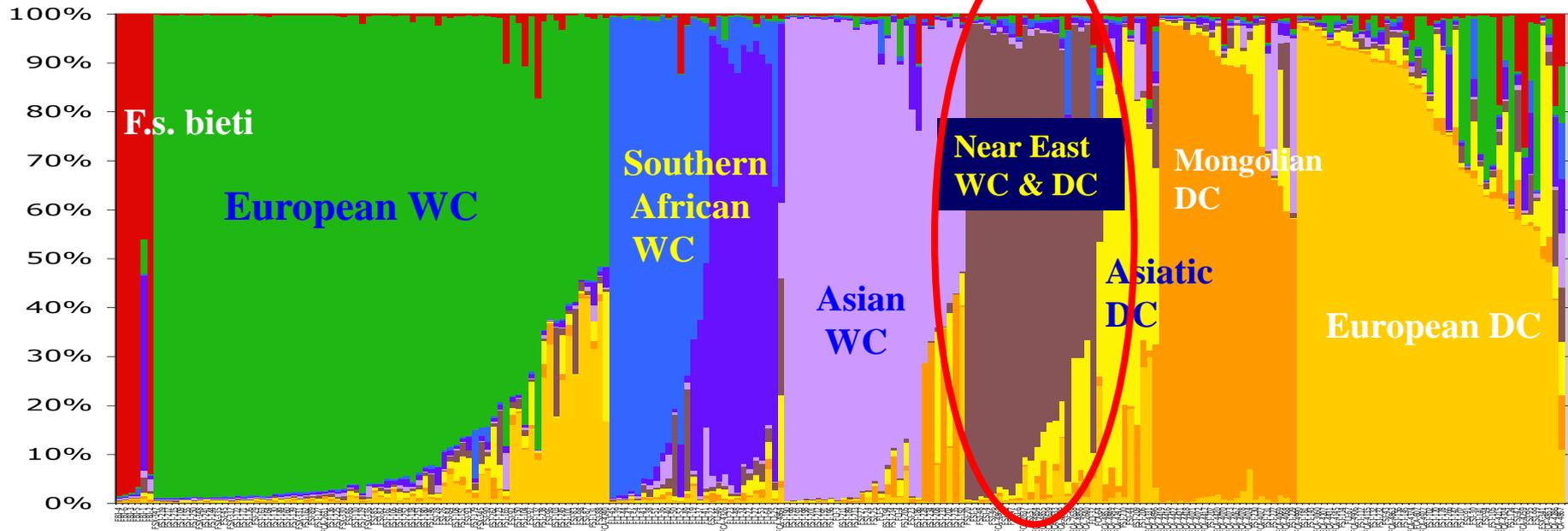
Symbols are cyto-nucleo-  
discordant cats

Microsatellite genotypes (36 loci)  
of wildcats and domestic cats



# Wildcats

# Domestic cats



# STRUCTURE

( LD and HWE based for microsatellites)

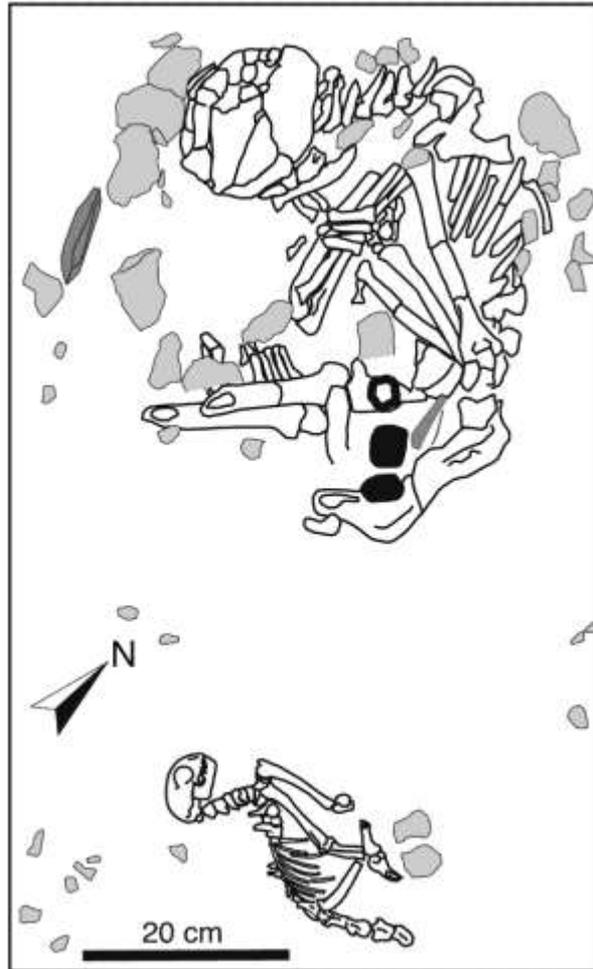
# Some Archaeology

**CHILD**



**CAT**

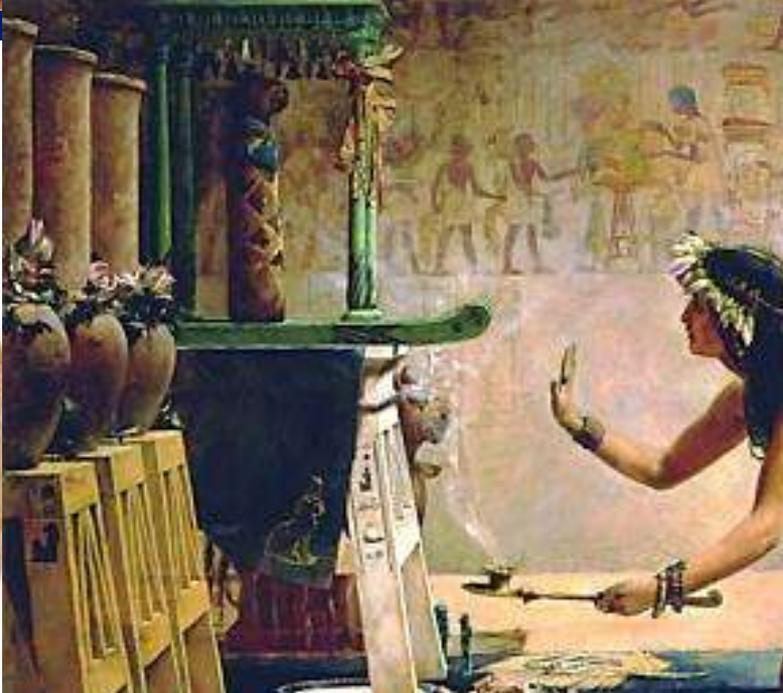
- Human burial in Cyprus with cat skeleton, bottom, that is estimated to be 9,500 years old.
- *Jen-Denis Vigne*  
*Museum Nat Hist.*  
*Paris 2004*

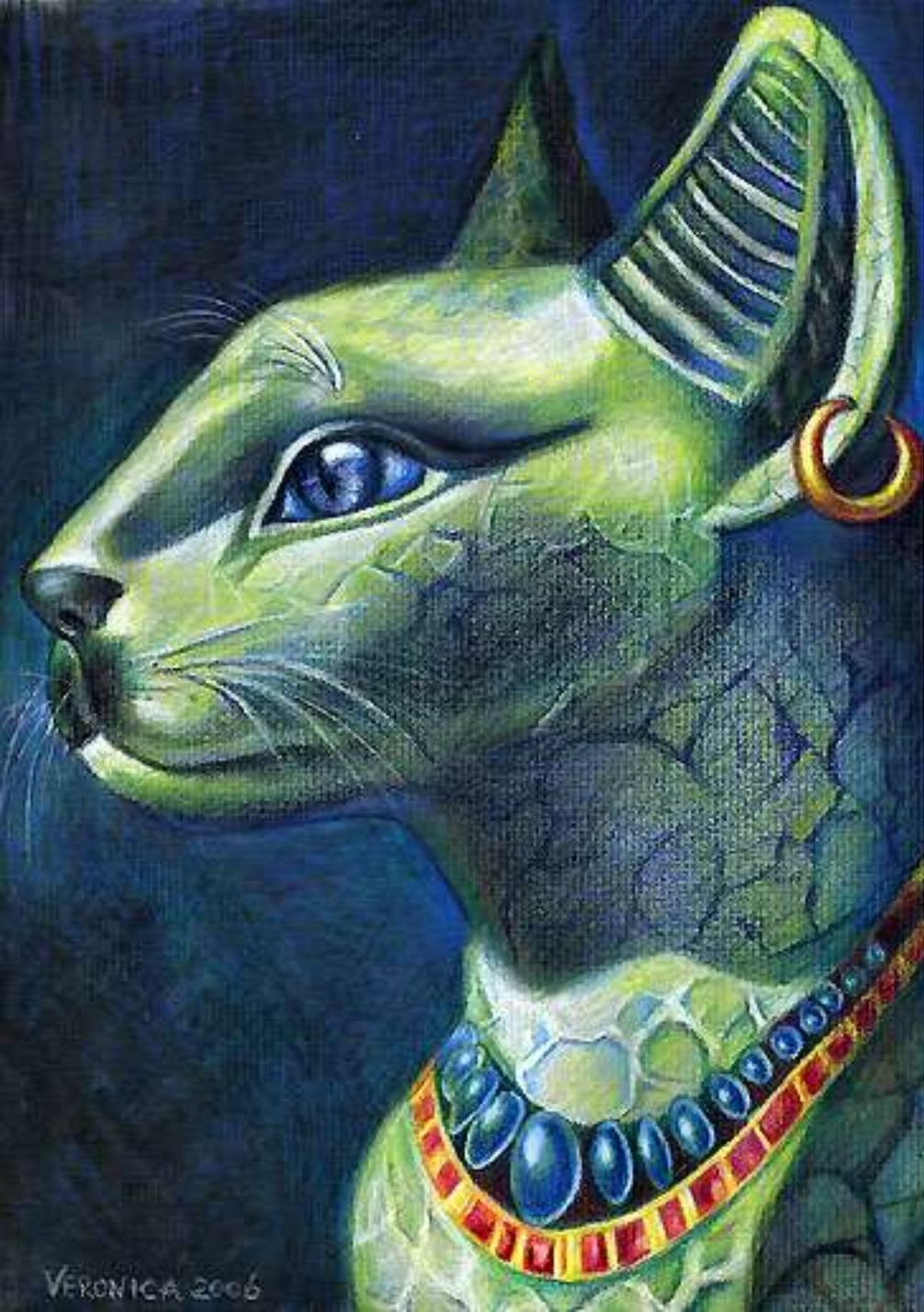


Stone Flint Green stone axes Ochre - hematite

The research team of National Museum of Natural History in Paris uncovered the carefully buried cat on Cyprus, placed just inches from a human burial that also contained polished stones, shells, tools and jewelry

# EGYPT





# On the Origin of CATS!!

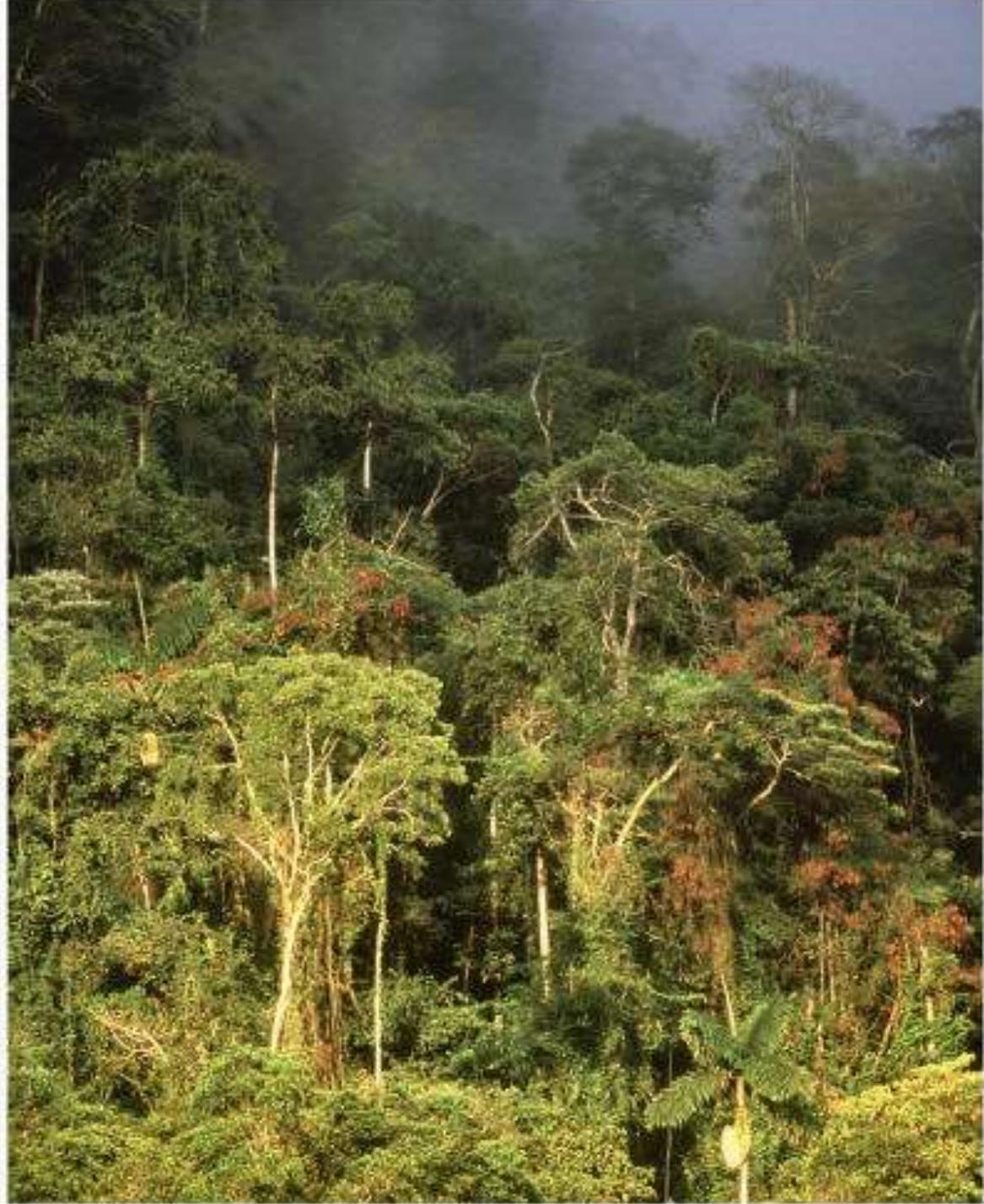
- Five *Felis silvestris* continental subspecies form a closely related five-way radiation that dates to 230,000 years ago:
  - *Felis silvestris silvestris* European wildcat
  - *Felis silvestris cafra* African wildcat
  - *Felis silvestris ornata* Central Asian wildcat
  - *Felis silvestris bieti* East Asian wildcat
  - *Felis silvestris lybica* Near Eastern wildcat
- Domestic cats & Near East Asia cats fall in one clade originating and living today in the **NEAR EAST Asia**
- First archaeological record of cat and people was ~10,000 years ago in Middle east (Cyprus).
- Cats were domesticated along with plants and farm animals in the early agricultural villages in the Near East
- **> 5 matrilineal events dating to 130,000 yrs**
  - No geographic structure to 5 mtDNA lineages

So How did

cat

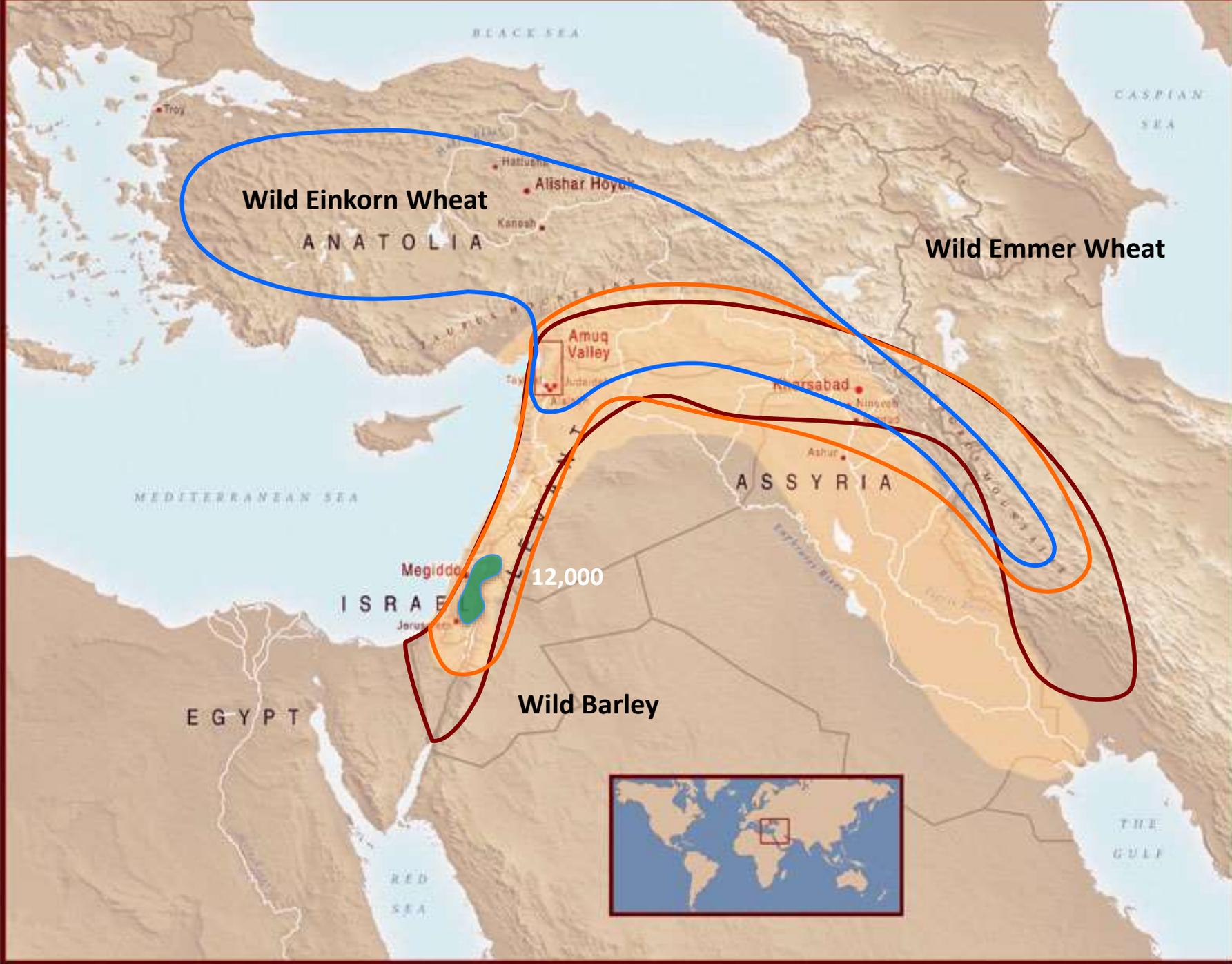
domestication

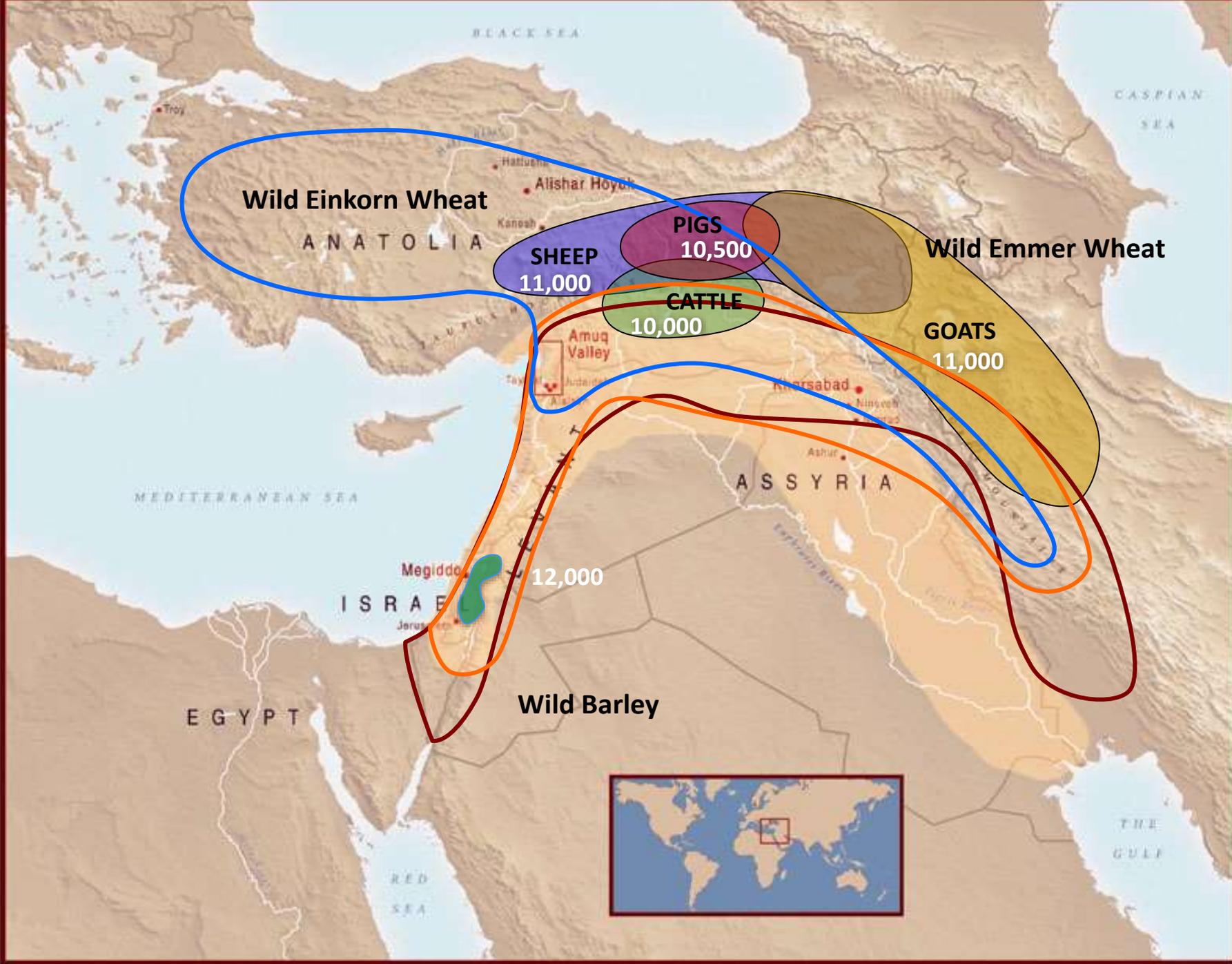
happen?

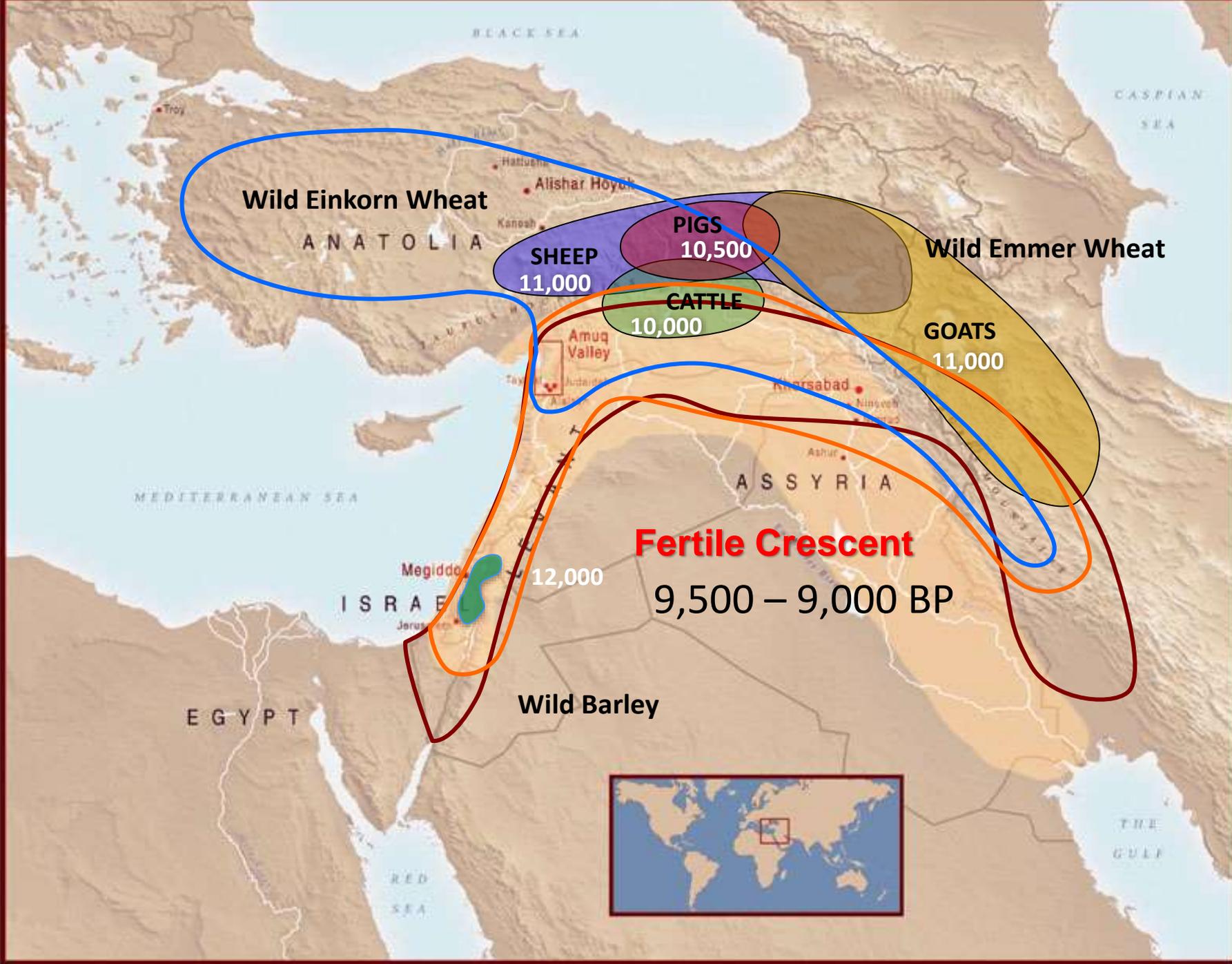






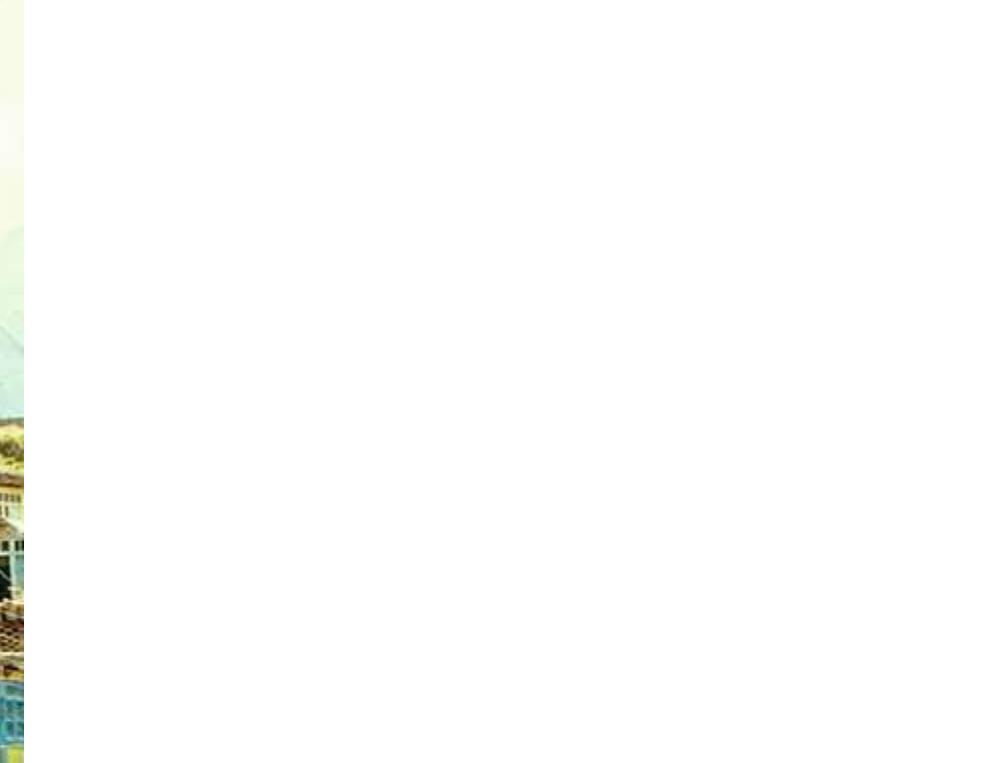














*A closing thought*

*Was cat domestication  
sympatric speciation?*

*Perhaps!*





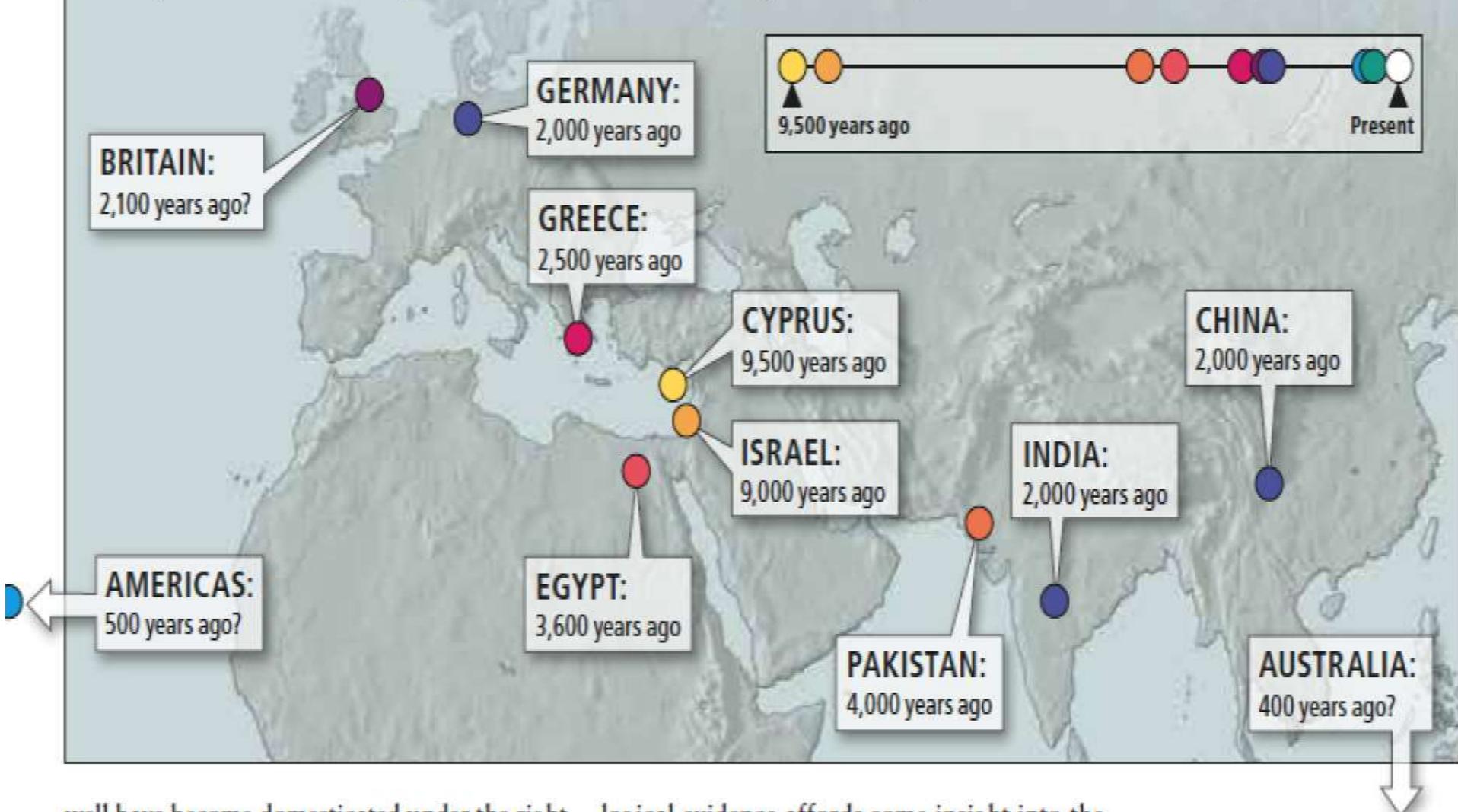




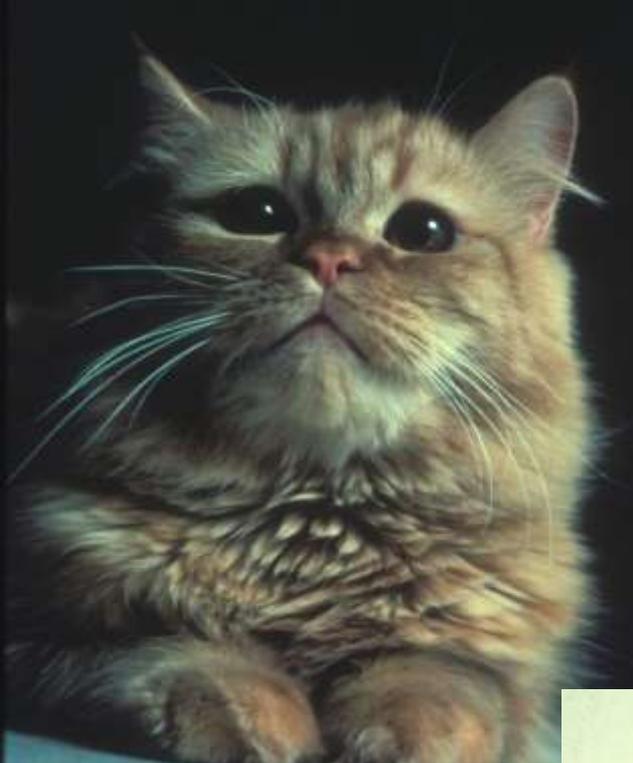
[DISPERSAL]

# HAVE CATS, WILL TRAVEL

As agriculture and permanent human settlements spread from the Fertile Crescent to the rest of the world, so, too, did domestic cats. The map below shows the earliest putative occurrences of house cats in regions around the globe.



will have become domesticated under the right... earliest evidence affords some insight into the





*How far we have come*

**Table 1. Common western domestic animals and their context**

Domestic animal		Wild ancestor		Earliest human association/domestication		
Common name	Scientific name	Common name	Scientific name	Time	Locus	First special breed formation
Dog	<i>Canis familiaris</i>	Grey wolf	<i>C. lupus</i>	13,000–17,000 BP	Central Europe	3000–4000 BP
House sparrow	<i>Passer domesticus</i>	Sparrow	<i>Passer predomesticus</i>	Earliest Neolithic	Fertile Crescent	None
Pigeon	<i>Columba livia</i>	Rock dove	Same	Upper Pleistocene?	Fertile Crescent	Unknown
House mouse	<i>Mus domesticus</i>	Grey mouse	<i>Mus musculus</i>	12,000 BP	Fertile Crescent	< 300 years
Black rat	<i>Rattus rattus</i>	Same	Same	<12,000 BP	SE Asia	None
Brown rat	<i>Rattus norvegicus</i>	Same	Same	<5500 BP	Central Asia	1856
Goat	<i>Capra hircus</i>	Bezoar	<i>Capra aegagrus</i>	11,000 BP	SE Anatolia-Zagros	>5000 BP
Sheep	<i>Ovis aries</i>	Mouflon	<i>O. orientalis</i>	12,000 BP	SE Anatolia; Iraq	6000–5500 BP
Taurine cattle	<i>Bos taurus</i>	Auroch	<i>Bos primigenius primigenius</i>	11,000–10,500 BP	SE Anatolia; Upper Euphrates	> 4500 BP
Zeboid cattle	<i>Bos indicus</i>	Auroch	<i>Bos primigenius namadicus</i>	9000 BP	NW South Asia	Unknown
Pig	<i>Sus domesticus</i>	Wild boar	<i>Sus scrofa</i>	10,500 BP	At least six; includes SE Anatolia	Neolithic
Donkey	<i>Equus asinus asinus</i>	African wild ass	<i>Equus asinus africanus</i>	4800 BP	Eastern Africa	Unknown
Horse	<i>Equus caballus</i>	European forest horse (Tarpan)	<i>Equus ferus</i>	5000–4000 BP	Pontic steppes, Central Asian steppes	> 2800 BP
Dromedary camel	<i>Camelus dromedarius</i>	Same	Same	~5000 BP	Arabia	Unknown
Bactrian camel	<i>Camelus bactrianus</i>	Same	Same	4600 BP	East Iran	Unknown
Cat	<i>F. silvestris catus</i>	Wildcat	<i>F. silvestris lybica</i>	9700 BP	Cyprus/Fertile Crescent	< 300 years

\*These species were commensals that seized advantage of anthropogenic habitat

# Cinnamon - The Genomics Cat.!!

G3-2016

## A High-Resolution SNP Array-Based Linkage Map Anchors a New Domestic Cat Draft Genome Assembly and Provides Detailed Patterns of Recombination

Gang Li,<sup>\*1</sup> LaDeana W. Hillier,<sup>1,1</sup> Robert A. Grahn,<sup>3,5</sup> Aleksey V. Zimin,<sup>\*\*</sup> Victor A. David,<sup>\*\*</sup> Marilyn Menotti-Raymond,<sup>\*\*</sup> Rondo Middleton,<sup>\*\*</sup> Steven Hannah,<sup>\*\*</sup> Sher Hendrickson,<sup>\*\*</sup> Alex Makunin,<sup>\*\*\*</sup> Stephen J. O'Brien,<sup>\*\*</sup> Pat Minx,<sup>1</sup> Richard K. Wilson,<sup>1</sup> Leslie A. Lyons,<sup>4,5</sup> Wesley C. Warren,<sup>1,2</sup> and William J. Murphy<sup>\*2</sup>

## Comparative analysis of the domestic cat genome reveals genetic signatures underlying feline biology and domestication

Michael J. Montague<sup>a,1</sup>, Gang Li<sup>b,1</sup>, Barbara Gandolfi<sup>c</sup>, Razib Khan<sup>d</sup>, Bronwen L. Aken<sup>e</sup>, Steven M. J. Searle<sup>e</sup>, Patrick Minx<sup>a</sup>, LaDeana W. Hillier<sup>a</sup>, Daniel C. Koblodt<sup>a</sup>, Brian W. Davis<sup>b</sup>, Carlos A. Driscoll<sup>f</sup>, Christina S. Barr<sup>f</sup>, Kevin Blackstone<sup>f</sup>, Javier Quilez<sup>g</sup>, Belen Lorente-Galdos<sup>g</sup>, Tomas Marques-Bonet<sup>g,h</sup>, Can Alkan<sup>i</sup>, Gregg W. C. Thomas<sup>j</sup>, Matthew W. Hahn<sup>k</sup>, Marilyn Menotti-Raymond<sup>l</sup>, Stephen J. O'Brien<sup>lm</sup>, Richard K. Wilson<sup>a</sup>, Leslie A. Lyons<sup>k,2</sup>, William J. Murphy<sup>b,2</sup>, and Wesley C. Warren<sup>a,2</sup>

Tamazian et al. *GigaScience* 2014, 3:13  
<http://www.gigasciencejournal.com/content/3/1/13>

(GIGA)  
SCIENCE

DATA NOTE

Open Access

## Annotated features of domestic cat – *Felis catus* genome

Gaik Tamazian<sup>1</sup>, Serguei Simonov<sup>1</sup>, Pavel Dobrynin<sup>1</sup>, Alexey Makunin<sup>1</sup>, Anton Logachev<sup>1</sup>, Aleksey Komissarov<sup>1</sup>, Andrey Shevchenko<sup>1</sup>, Vladimir Brukhin<sup>1</sup>, Nikolay Cherkasov<sup>1</sup>, Anton Svitin<sup>1</sup>, Klaus-Peter Koepfli<sup>1</sup>, Joan Pontius<sup>1</sup>, Carlos A Driscoll<sup>2</sup>, Kevin Blackstone<sup>2</sup>, Cristina Barr<sup>2</sup>, David Goldman<sup>2</sup>, Agostinho Antunes<sup>3</sup>, Javier Quilez<sup>4</sup>, Belen Lorente-Galdos<sup>5</sup>, Can Alkan<sup>6</sup>, Tomas Marques-Bonet<sup>5</sup>, Marilyn Menotti-Raymond<sup>7</sup>, Victor A David<sup>7</sup>, Kristina Narfström<sup>8</sup> and Stephen J O'Brien<sup>1,9\*</sup>

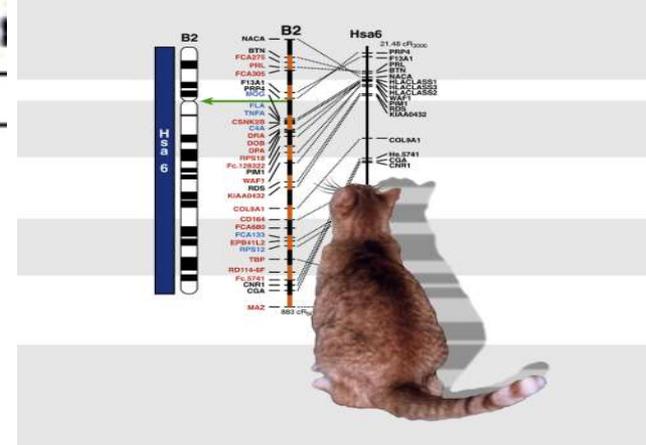
Expansion of the feline chemosensory system for detecting pheromones at the expense of odorant detection.



**Table 1 Annotated cat genome features available in GARField2**

**Feature**

- I. Assembly of *Felis catus* genome Fca-6.2
- II. GARField2 Genome Browser for domestic cat genome
- III. Gene annotation **20,343**
- IV. DNA variants
  - a. SNPs
  - b. Indels
- V. Repeats content in *Felis catus* genome (Fca-6.2)
  - a. Interspersed repeats
  - b. Tandem repeats
    - Complex Tandem Repeats
    - Short Tandem Repeats (STRs)
    - STR primer sequences
- VI. Evolutionary Constrained Elements (ECE) among mammals
- VII. Feline endogenous retrovirus-like elements
  - a. RD114
  - b. enFeLV
  - c. FERVs
  - d. Other ERV families
- VIII. Methylation Sites in the cat genome
- IX. Micro-RNA
- X. Nuclear mitochondrial segments (*Numts*) in Fca-6.2
  - a. Lopez Tandem Numt Chr-D2
  - b. Dispersed Numts
- XI. Segmental duplications in the domestic cat genome
- XII. Assisted assembly of *Felis silvestris* genome
  - a. SNPs within *F. silvestris*
  - b. SNPs between *F. silvestris* and *F. catus*

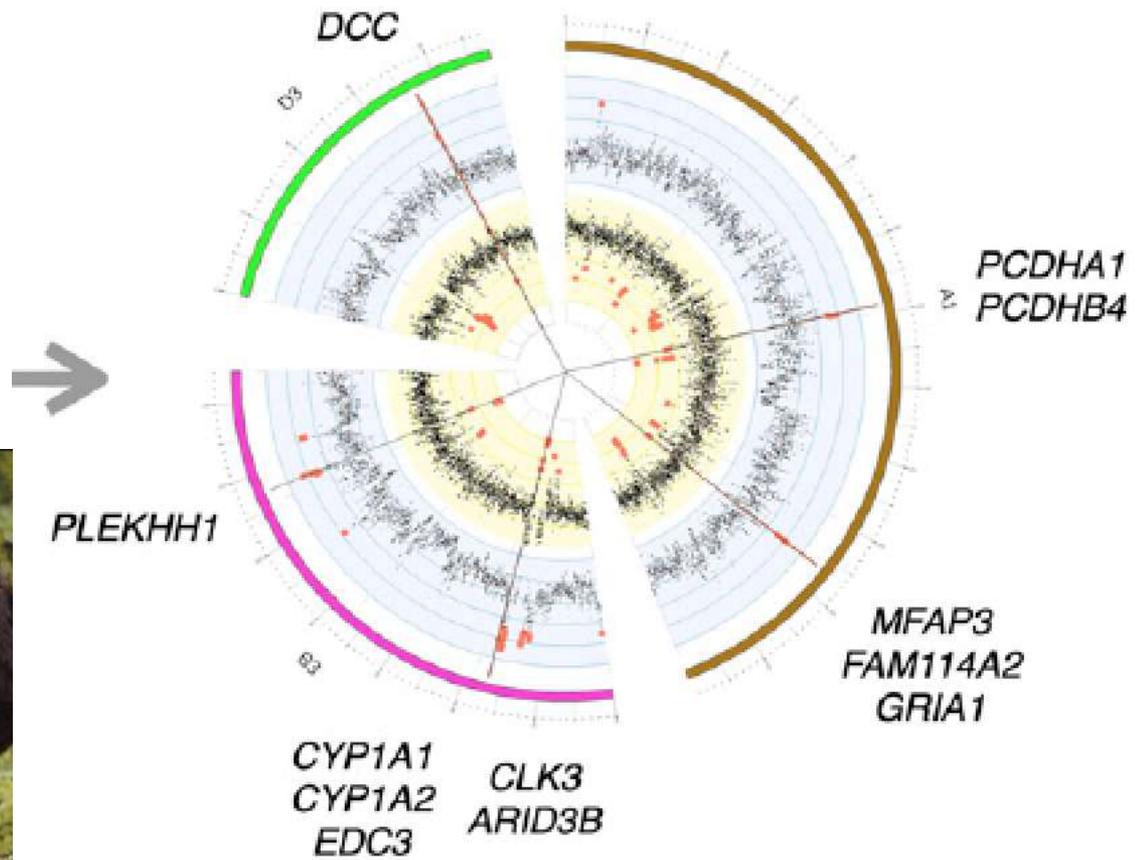


**Garfield** <http://lgd.abcc.ncifcrf.gov>

TM & © Paws, Inc. All Rights Reserved. Used by Permission. Jim Davis



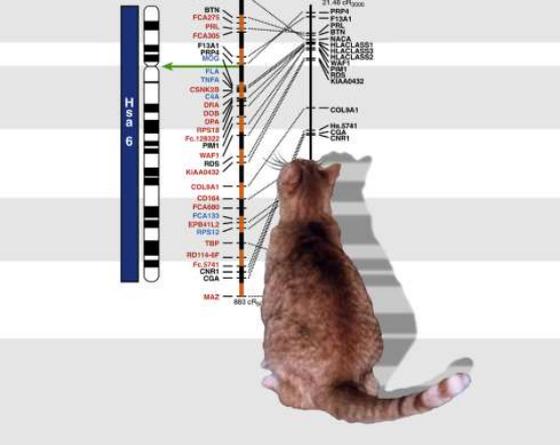
# Selected genes in 5 regions candidates for cat domestication behavior





And now I really  
would like to say  
"Thanks" to...





LGD LGD LGD LGD EGD LGD  
 LGD LGD LGD LGD LGD LGD  
 LGD LGD LGD LGD LGD LGD



**Laboratory of Genomic Diversity**  
**Annual Retreat Boardwalk**  
**Ocean City October 2005**





# **STEPHEN J. O'BRIEN**

*For Theodosius Dobzhansky Center for Genome  
Bioinformatics*

*St. Petersburg State University*

*The Promise of Genome Bioinformatics in  
biomedical and environmental health sciences*

*South African Genetics Society*

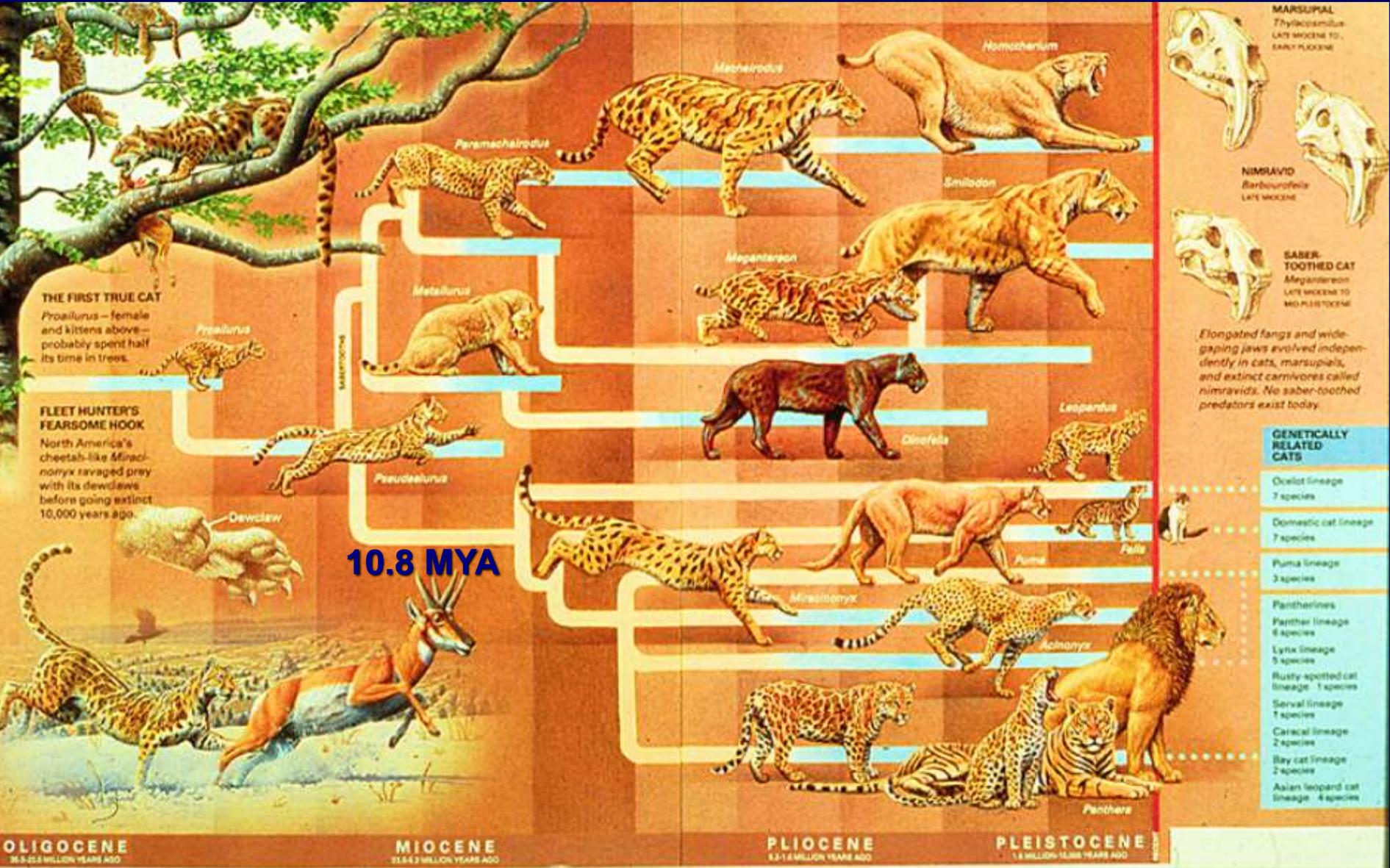
*September 21, 2016*





***Thanks !!***

# The Evolutionary History of Felidae



# Special Thanks to :

**Al Roca**

**Eduardo Eizirik**

**Warren Johnson**

**Bill Murphy**

**Bill Nash**

**Joan Menninger**

**Marilyn Menotti-Raymond**

**Victor David**

**John Page**

**Emma Teeling**

**John Arthur**

**Stan Cevario**

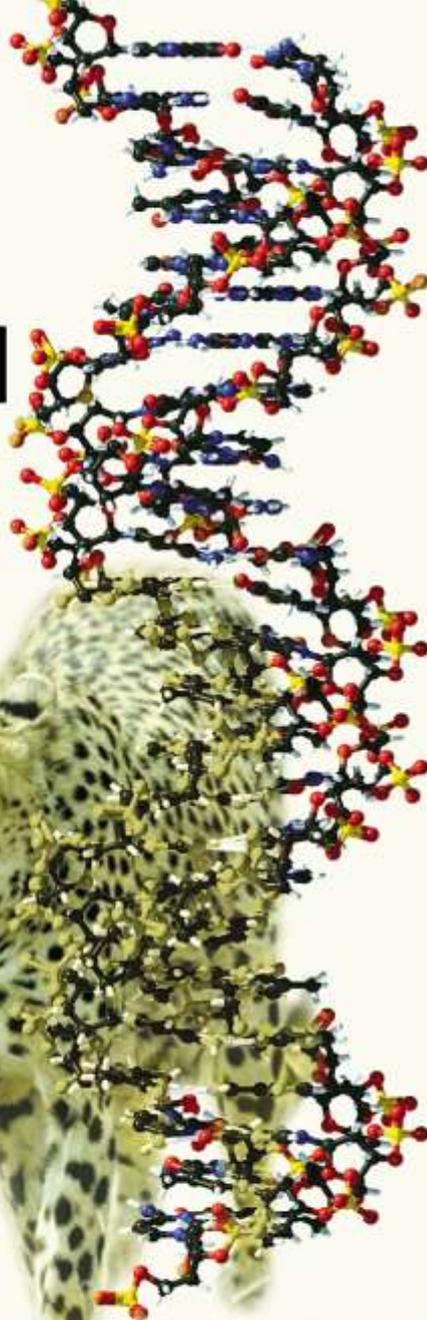
**Amy Klar**



**& Valerie Beason**

# TEARS OF THE CHEETAH

And Other Tales  
From the Genetic  
Frontier



TEARS OF THE CHEETAH is told by O'Brien with such literary mastery that one can hardly lay the book down.. O'Brien has succeeded in telling his stories in a simple language that can be understood even by the non-expert. There is no other book I have read in recent years from which I have learned and enjoyed more"

—Ernst Mayr

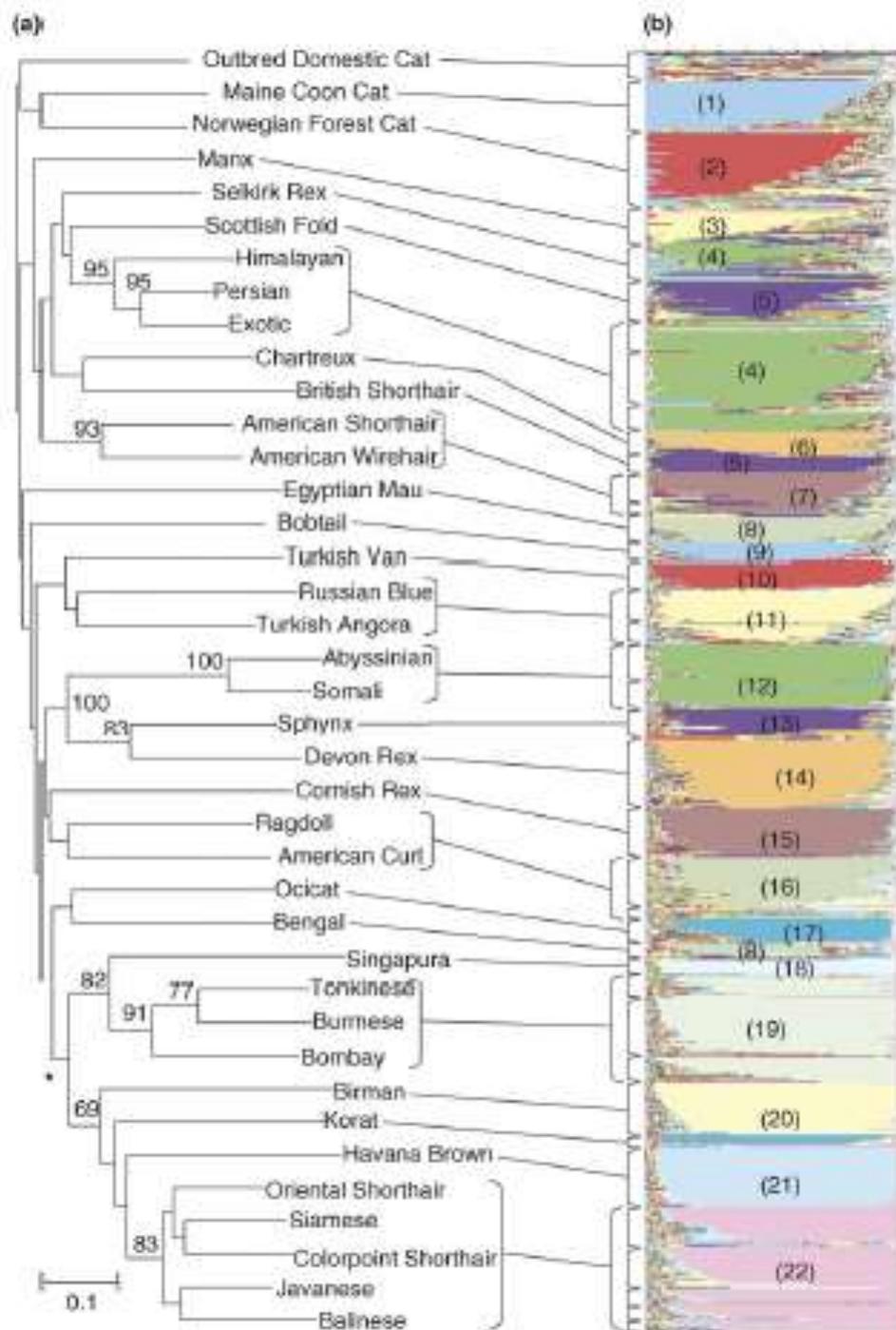
STEPHEN J. O'BRIEN

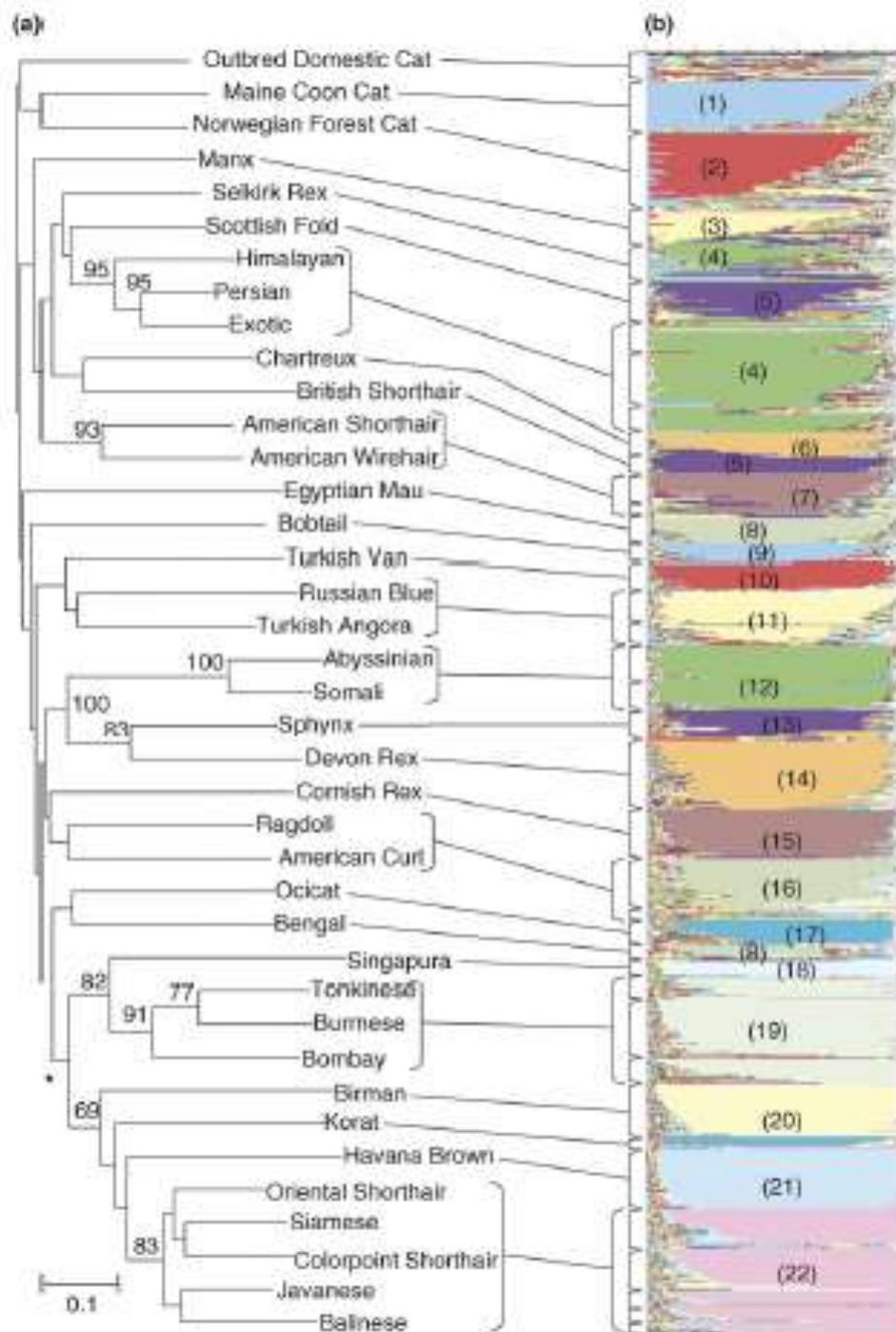
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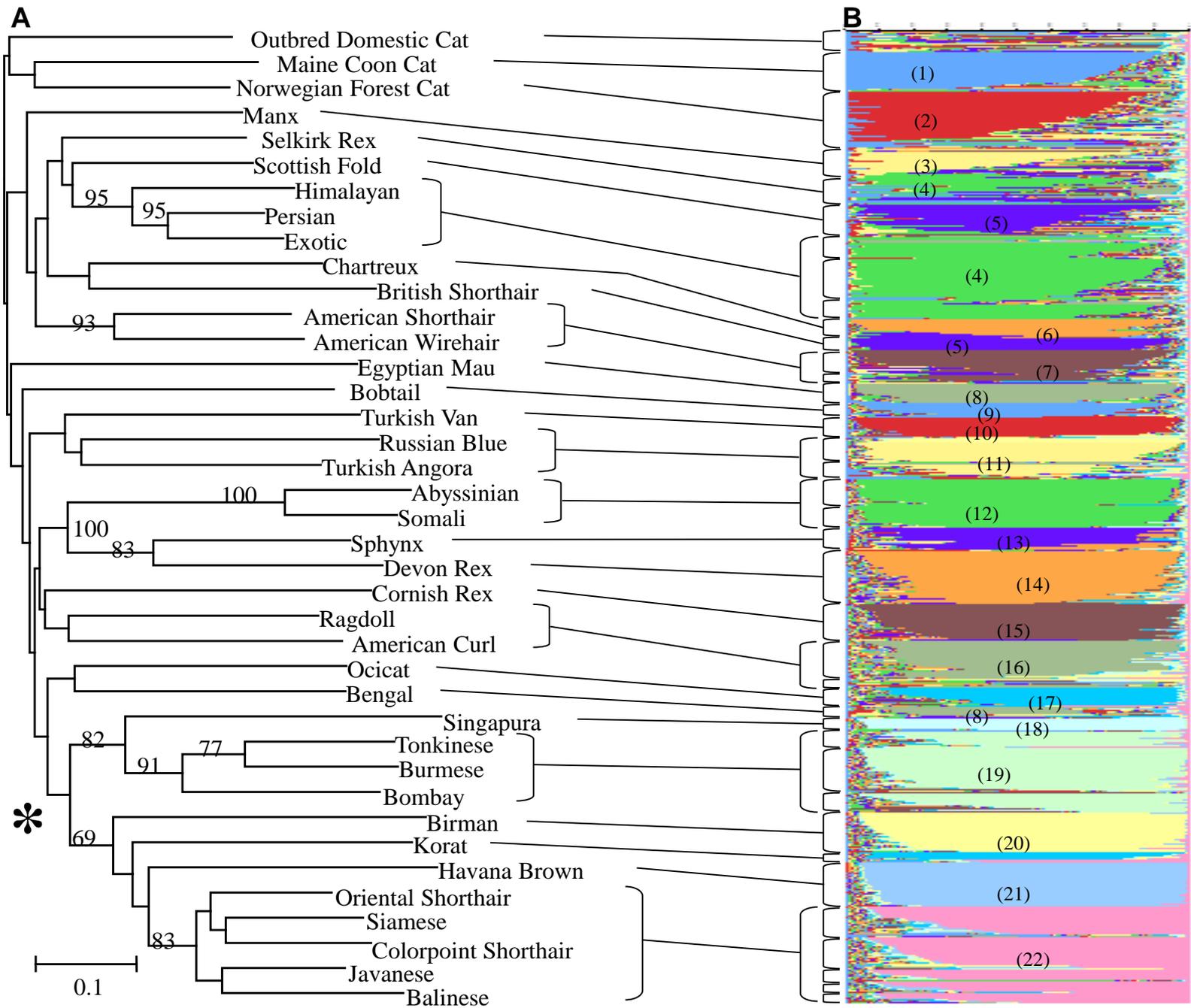


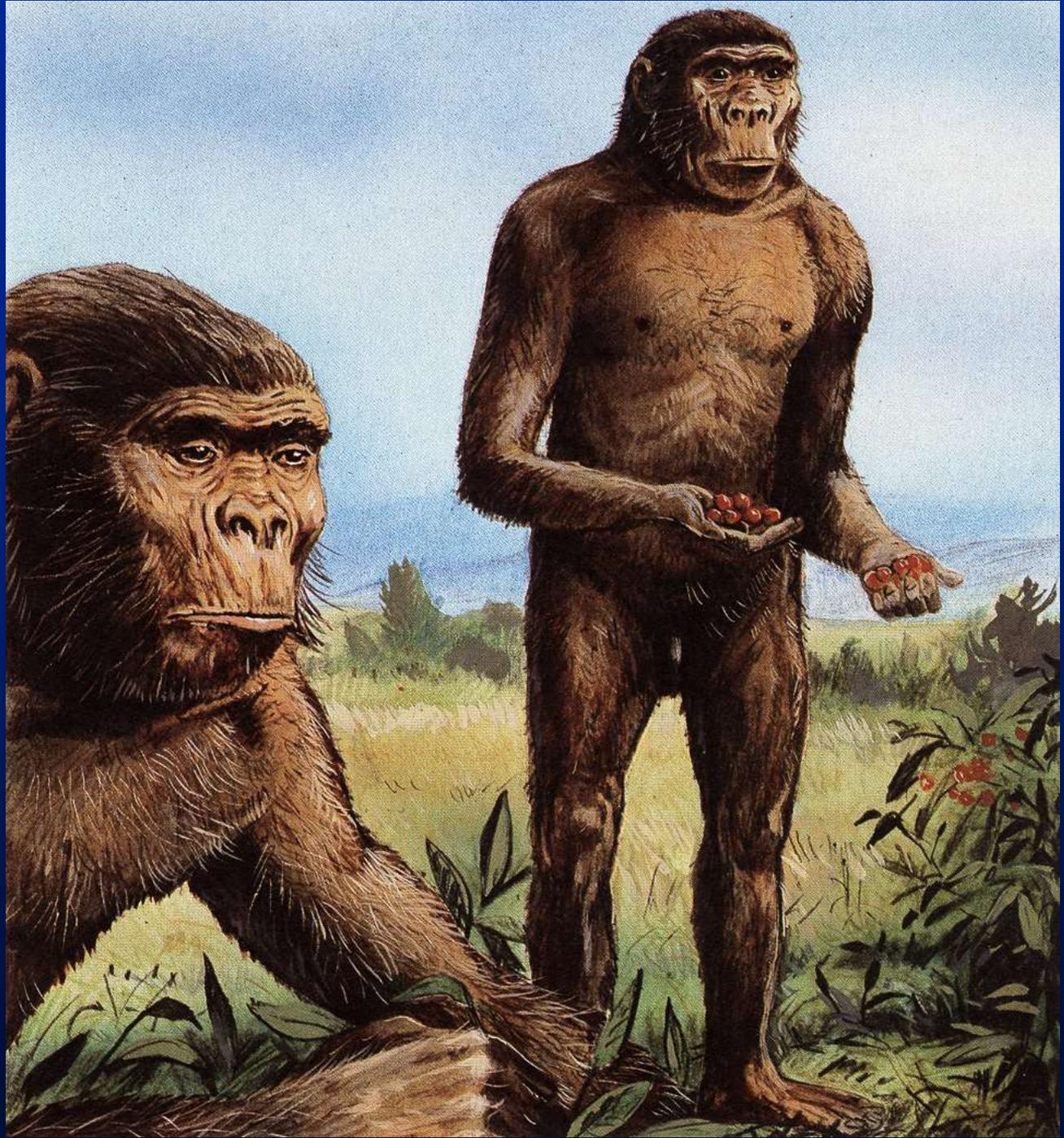
- Chapter 1 - A Mouse that Roared
- Chapter 2 - *Cheetahs Never Win* –
- Chapter 3 - *Prides and Prejudice*
- Chapter 4 - *A Run for its Life - The Florida Panther*
- Chapter 5 - *Bureaucratic Mischief*
- Chapter 6 - *A Whale of a Tale* –
- Chapter 7 - *The Lion Plague*
- Chapter 8 - The Wild Man of Borneo-
- Chapter 9 -- *The Panda's Roots*
- Chapter 10- *The Way We Were-*
- Chapter 11 -- Snowball's Chance-Pawprints
- Chapter 12 - Genetic Guardians
- Chapter 13 – Origins
- Chapter 14 - A Silver Bullet







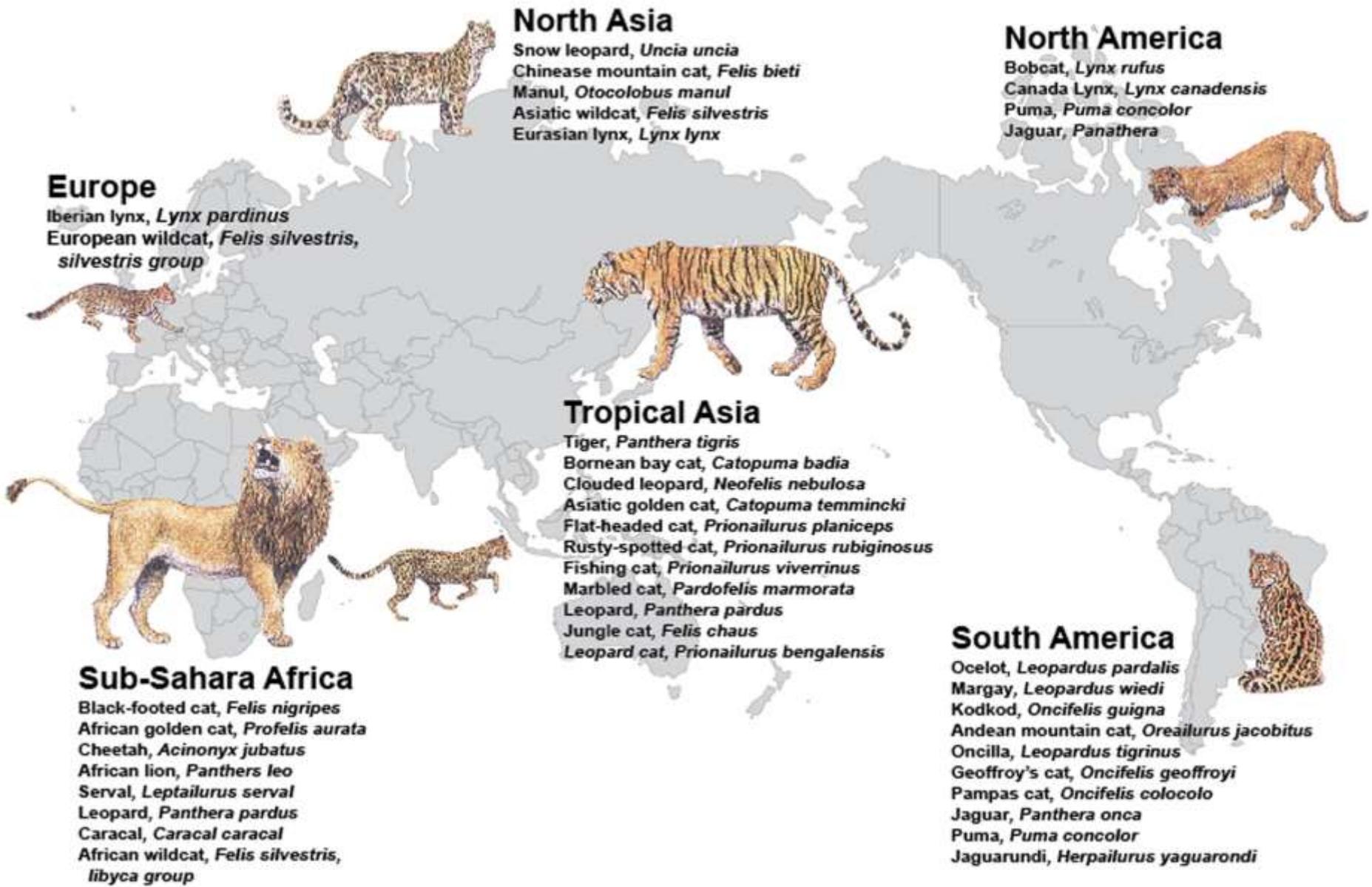






**The Felidae Family is made up of 37 species that all arose in the last ten million years**

**So where did all these cat species come from??**



# Our Strategy



**Sampling of all 37 felid species and seven outgroup species**  
**Test of 35 genes for phylogenetic congruence**

# A comprehensive gene sampling 37 Felidae species & outgroups

5 X-linked (3,230 bp):

ALAS, ATP-7A, IL2RG, PLP, ZFX

4 Y-linked (4,457 bp):

SMCY, SRY, UBEY, ZFY

6 mtDNA gene fragments (3,936 bp):

ND2, ND4, ND5, ATP8, CYTB, 16S

20 autosomal gene fragments (11,166 bp):

APP, CALB1, CHRNA1, CLU, CMA1

DGKG2, FES, GATA3, GHR, GNAZ, GNB1, HK1, NCL

PNOC, RAG2, RASA2, SIL, TCP1, TTR

• 22,789 bp (total)

Timing calibrated with

16 Felidae species' fossils

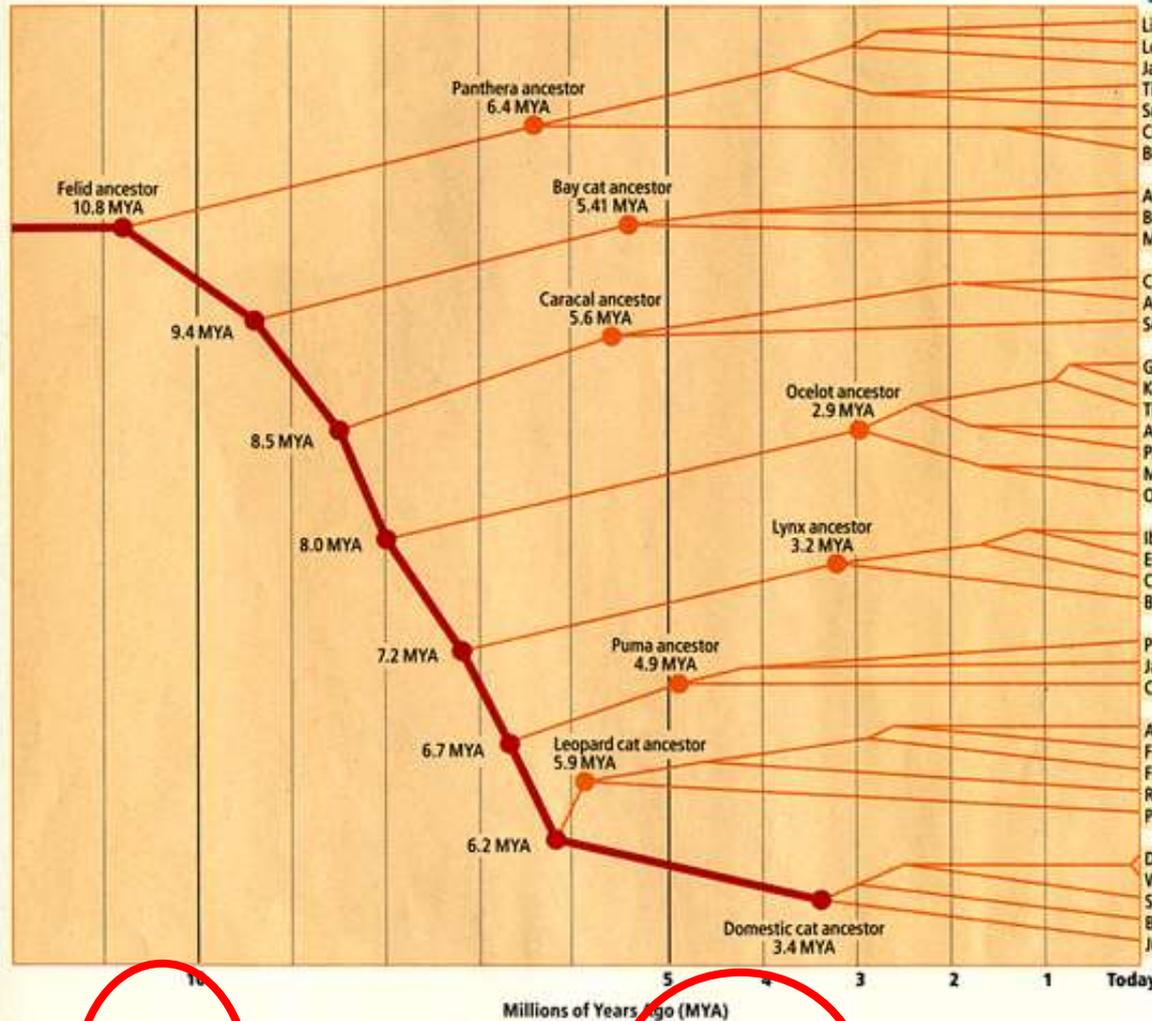
**Johnson et al Science 311:74**

**January, 2006**



# THE CAT FAMILY TREE

Scientists compared DNA sequences in all 37 species of cats to determine the tree's branches. Fossils provided dates that indicate when major branching occurred.



## 8 LINEAGES

### 1 PANTHERA

These medium- to large-sized predators in the ecosystem. The lion, tiger, jaguar, and leopard are the most famous members of this lineage. They are known for their roar. The two clouded leopards are also members of this lineage.

### 2 BAY CAT

This poorly known group of cats (two to 16 kilograms) is restricted to tropical Southeast Asia. Bay cats were not considered a separate lineage by taxonomists until recently.

### 3 CARACAL

These medium-size cats (five to 15 kilograms) were not typically grouped with other Felidae species.

### 4 OCELOT

These small- to medium-sized cats (two to 15 kilograms) are found in Central and South America. They are smaller than other Felidae species.

### 5 LYNX

These medium-size cats (six to 25 kilograms) have large ears. They live in temperate forests and tend to specialize on hares. These species have been around since the Miocene.

### 6 PUMA

These diverse cats, from the jaguarundi to the puma, originated in North America. Pumas can be locally common in some areas.

### 7 ASIAN LEOPARD CAT

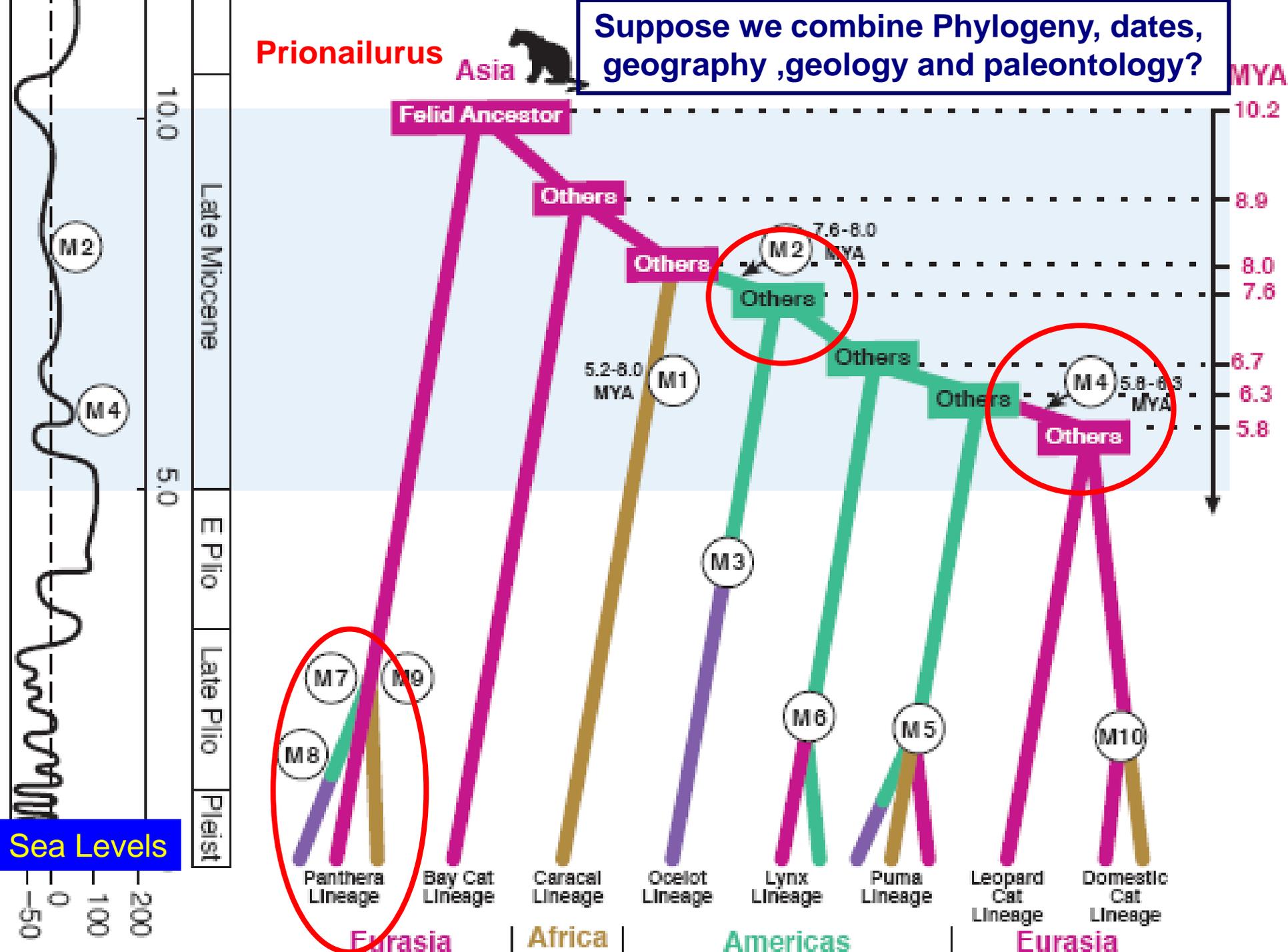
These small cats (two to 10 kilograms) live in forest to Mongolian steppe.

### 8 DOMESTIC CAT

These small cats (one to 10 kilograms) are the most common, which is worldwide. They have been around since the Pliocene.

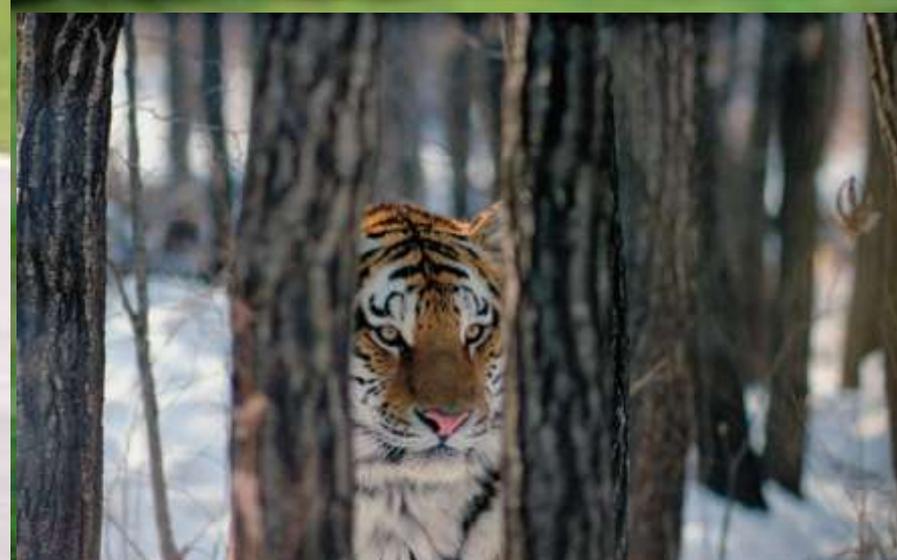
Suppose we combine Phylogeny, dates, geography, geology and paleontology?

Prionailurus Asia 

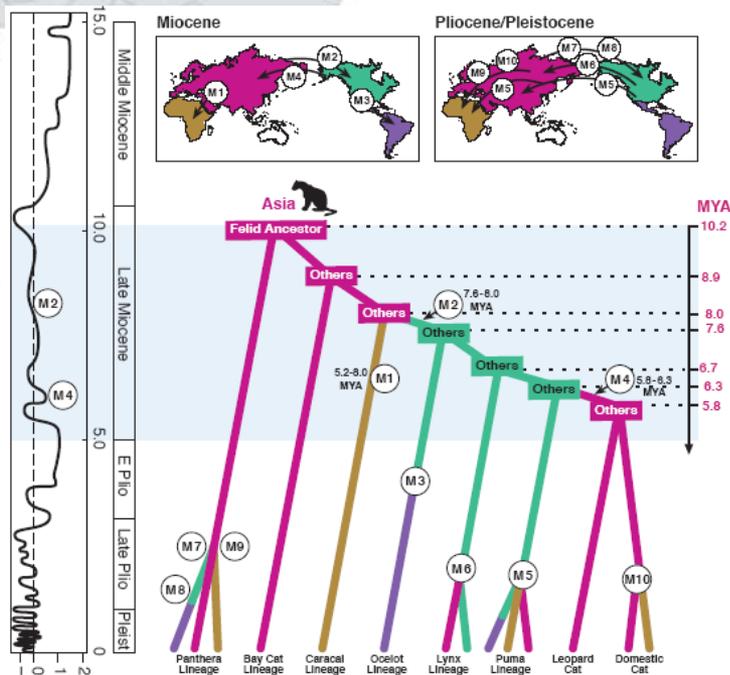
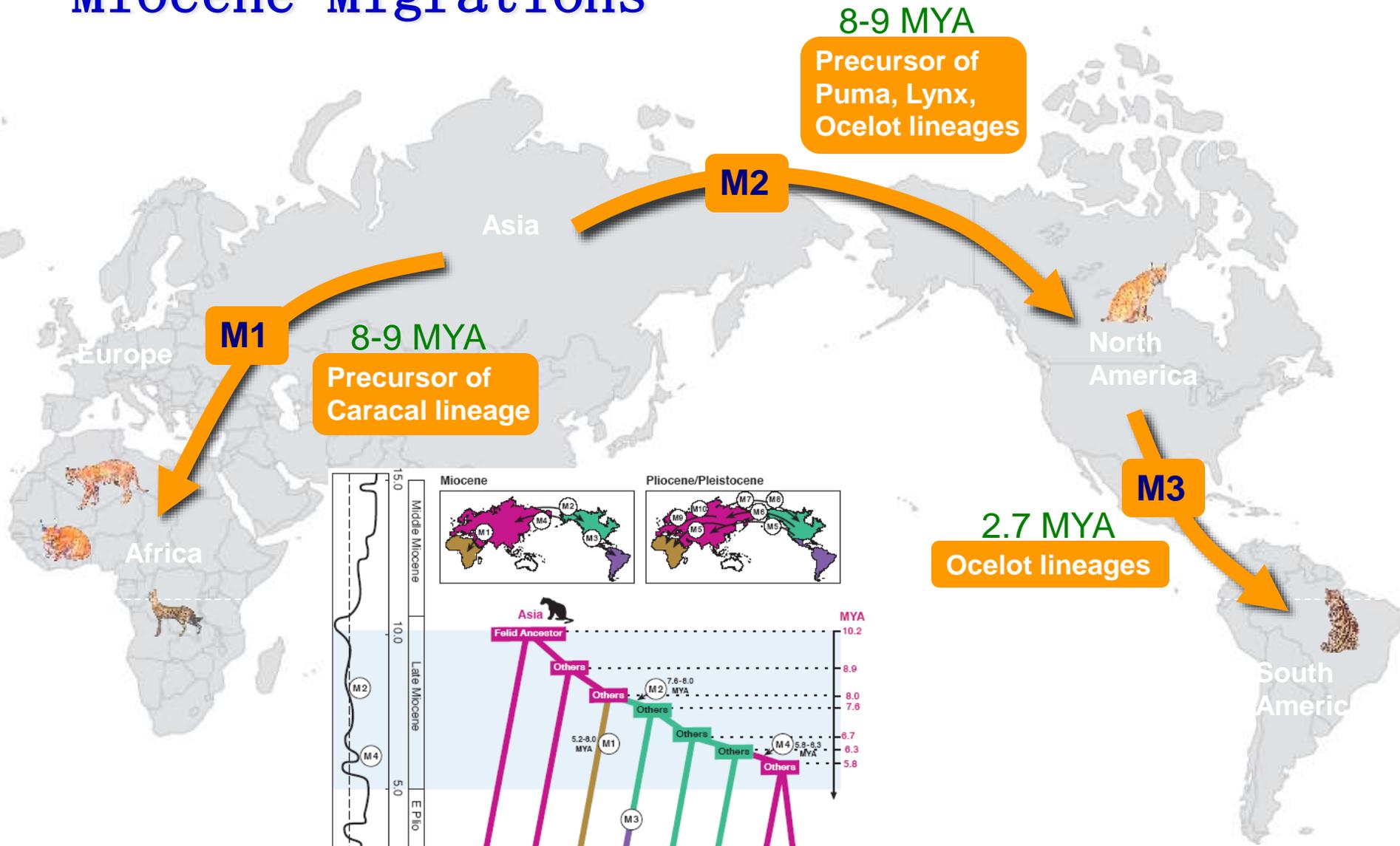


# ONE AMAZING JOURNEY

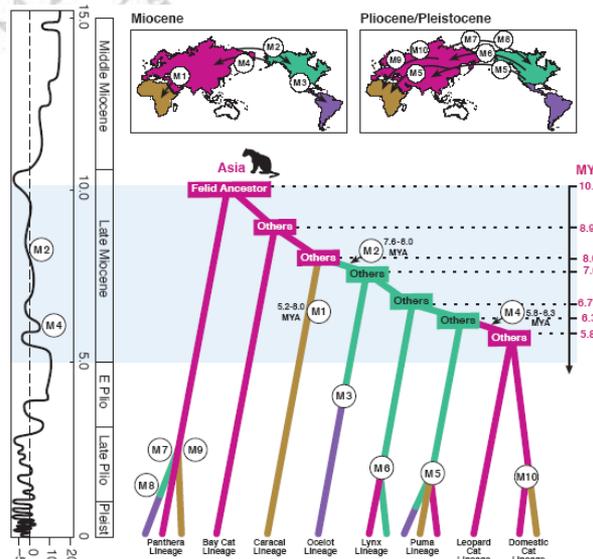
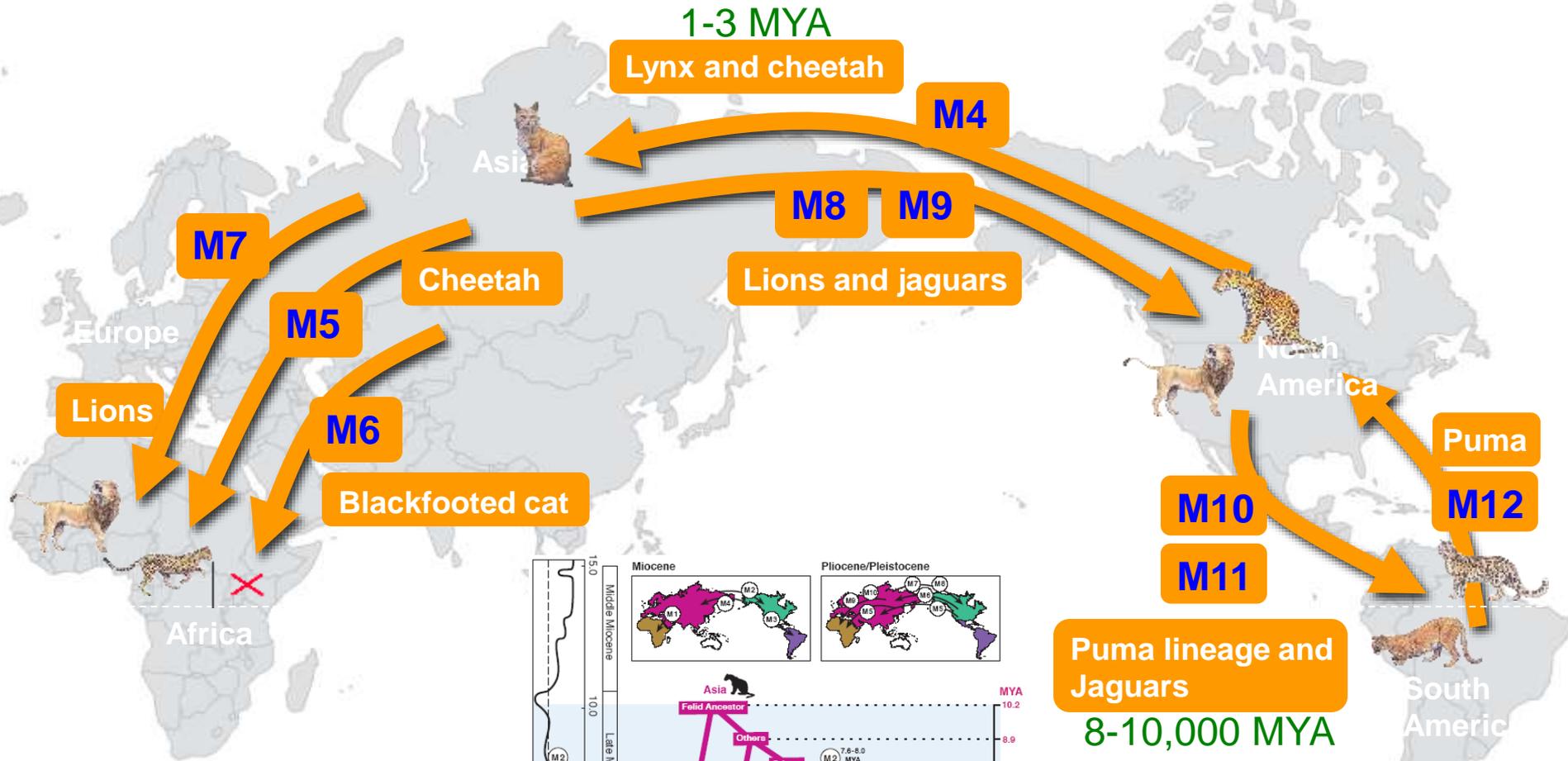
## On the Origins of Cat



# Miocene Migrations



# Late Pliocene Migrations



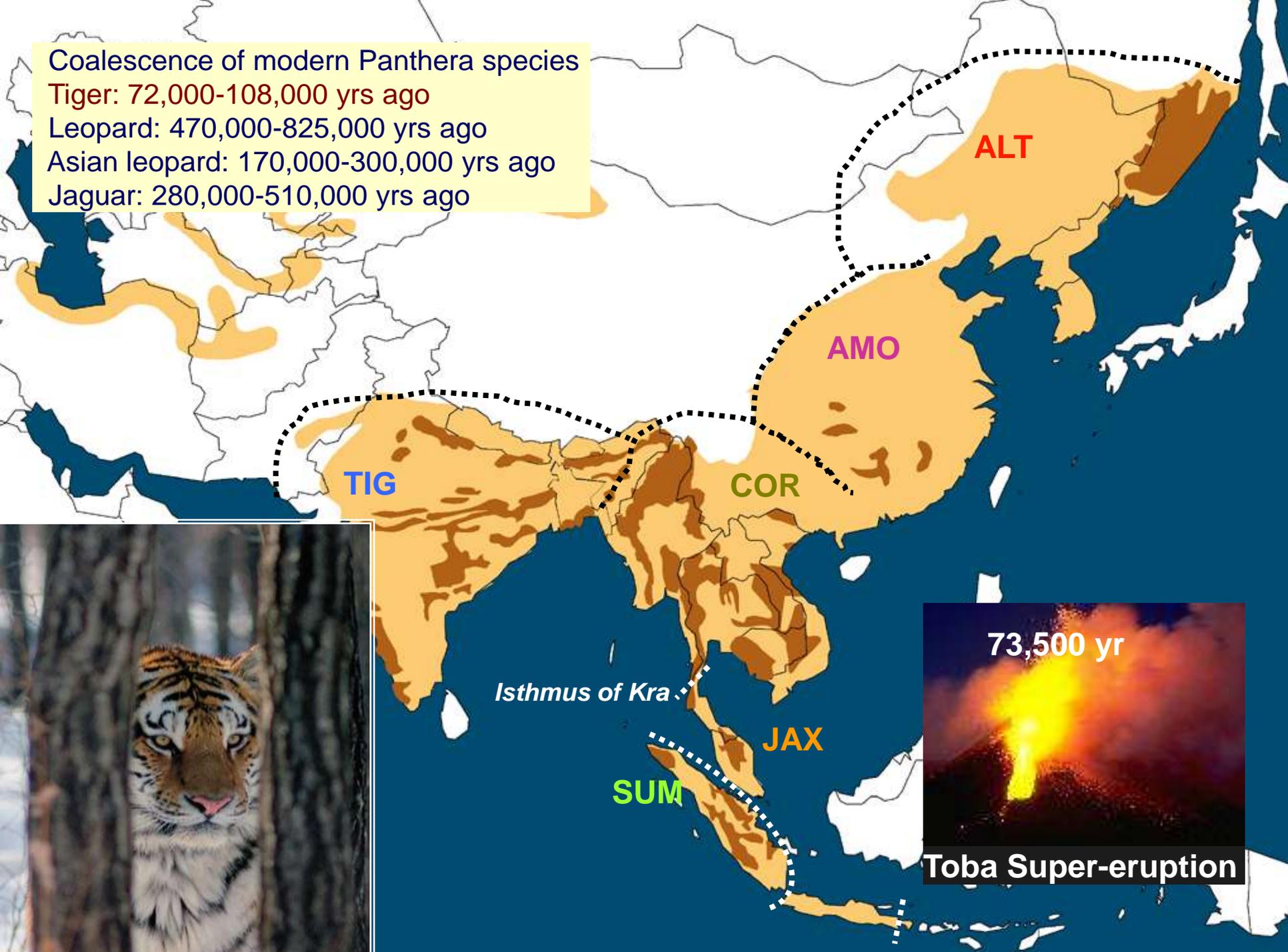
Coalescence of modern Panthera species

Tiger: 72,000-108,000 yrs ago

Leopard: 470,000-825,000 yrs ago

Asian leopard: 170,000-300,000 yrs ago

Jaguar: 280,000-510,000 yrs ago



ALT

AMO

TIG

COR

Isthmus of Kra

JAX

SUM

73,500 yr

Toba Super-eruption



*And that's How we believe the modern cats came to be*





May 2003  
ISSN 1089-9021

# GENOME RESEARCH

Volume 10 Number 5

Cat Genome Radiation Hybrid Map • Human-Mouse Comparative Mapping with Human Chromosome 7 • Nuclear Lamin Mutation Associated with Partial Lipodystrophy with Diabetes • Evolution of *Mhc-DRB* Genes in Primates, Platyrrhines, and Carnivorhines • *C. elegans* and Human Comparative Proteomics

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