Cats are not small dogs - dogs are not big cats!

Leslie A. Lyons, PhD

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Veterinary Medicine & Surgery
University of Missouri

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Lyons Feline Genetics Laboratory Support

Lyons	Cat	Genomics	NIH-NCRR National Center for Research Resources	LD, $RH_{Rad13,000}$ Map, Database, Animal model colony support, 74K DNA array
		Disease Mapping	Winn Feline	Blindness, cardiac, kidney
		Behavior	NIH-NICHD	Genes affecting behavior with autistic children
		Domestication	WALTHAM	Genes affecting domestication
			National Geographic	Domestication, cat mummy sequencing
		Phenotypic Traits	UC Davis CCAH	Coat colors, fur types, morphology genes
		Allergy response	Morris Animal	Hypoallergenic cats

Acknowledgements

Reuben Buckley, PhD

Tom Juba, MS

Inbread cats
- naturally occurring biomedical models
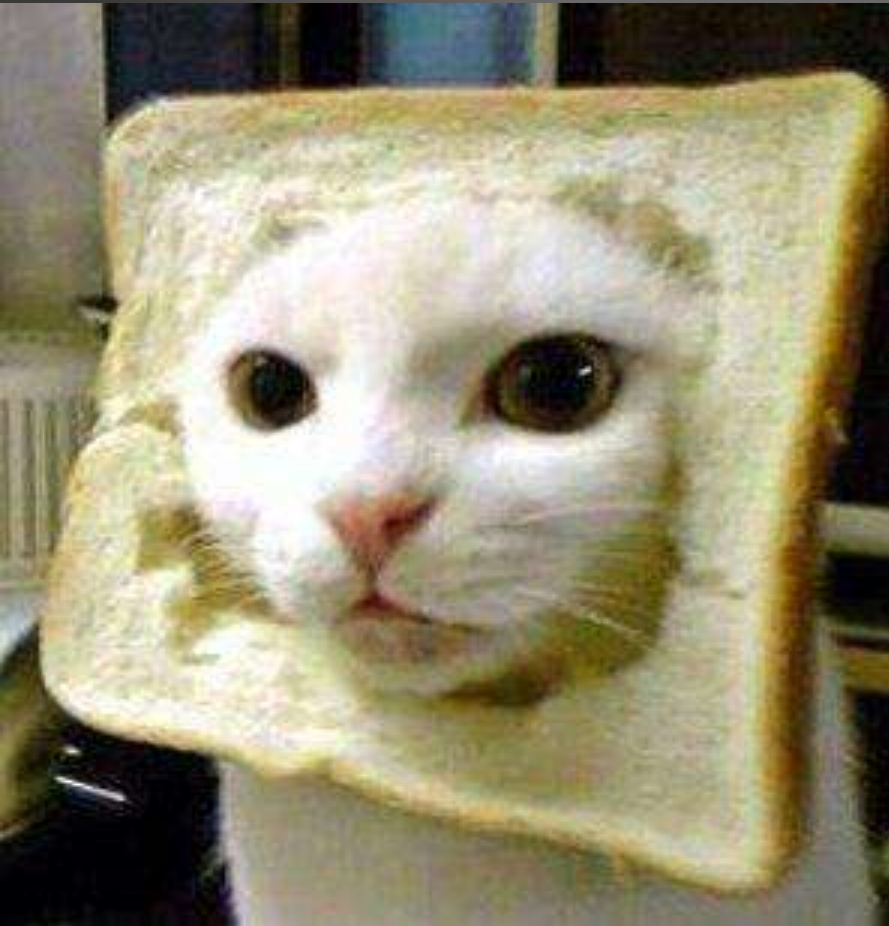
Cat Cloning & Transgenics

Rainbow – egg donor

Cc – Copy cat

Feline Polycystic Kidney Disease
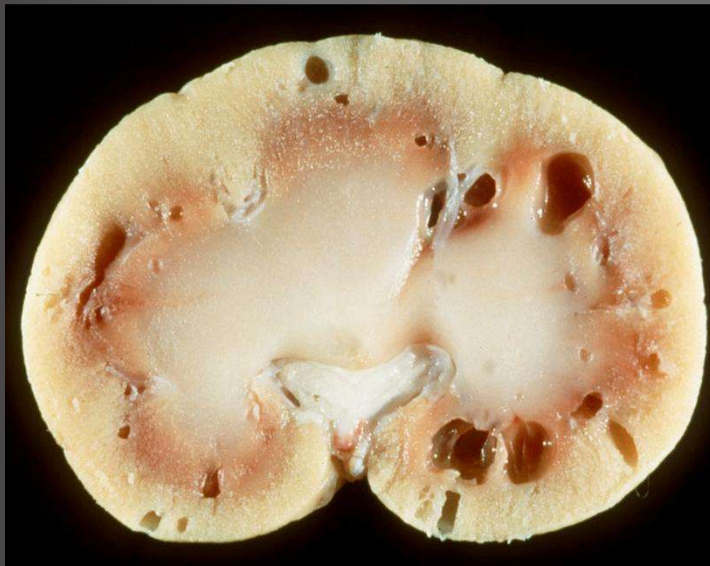
🐾 **In 2004, most common disease in registered cats!**

Lyons et al. (2004). Feline polycystic kidney disease mutation identified in *PKD1*. J Am Soc Nephrol 15, 2548-2555

Known DNA Variants in Domestic Cats

201 known DNA variants in _Felis catus_

Phenotypic Traits – 67 variants

Diseases in Breeds – 36 variants

Diseases in Random Breds – 73 variants

https://www.dailypaws.com/cats-kittens/behavior/what-is-a-group-of-cats-called

Precision / Genomic (P4) Medicine

🐾 **an emerging approach for disease treatment & prevention considering individual variability in genes, environment, and lifestyle**

🐾 **Precision Medicine Initiative® (PMI) Obama SOTU 2015**

🐾 **Understand the complex mechanisms underlying a patient's health, disease, or condition, and to better predict which treatments will be most effective – not the average or average for an ethnic group!**

Cat Breed Populations

~ 2000 – 2025

Bengals
Maine Coons
Siberians
Sphynx

Persian 70%
10 breeds 3%
Manx 1%
Cornish Rex 1%
Birman 1%
Burmese (US) 3%
Abyssinian 4%
MaineCoon 5%
Siamese 10%
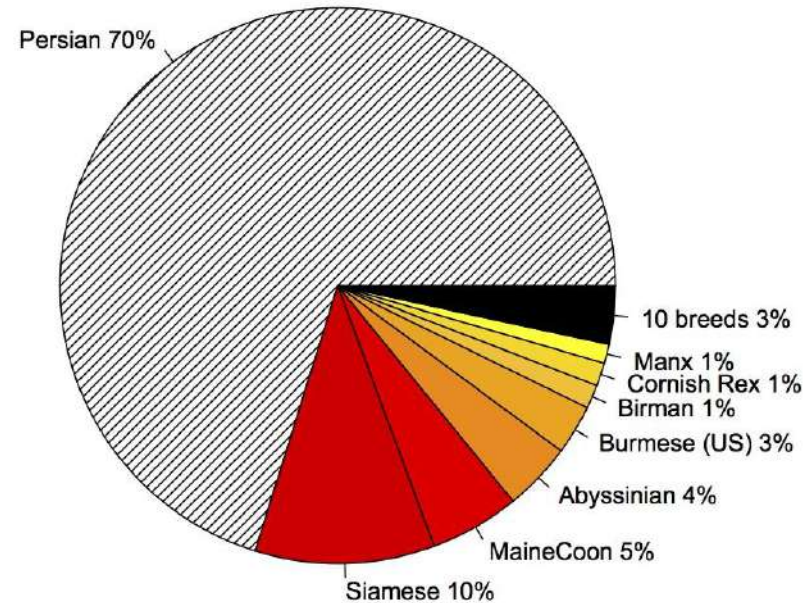
- 🐾 **> 94 million cats in the USA**

- 🐾 **33% of homes have a cat**

- 🐾 **Each household has ~ 2.2 cats**

- 🐾 **Vast no. of ferals**
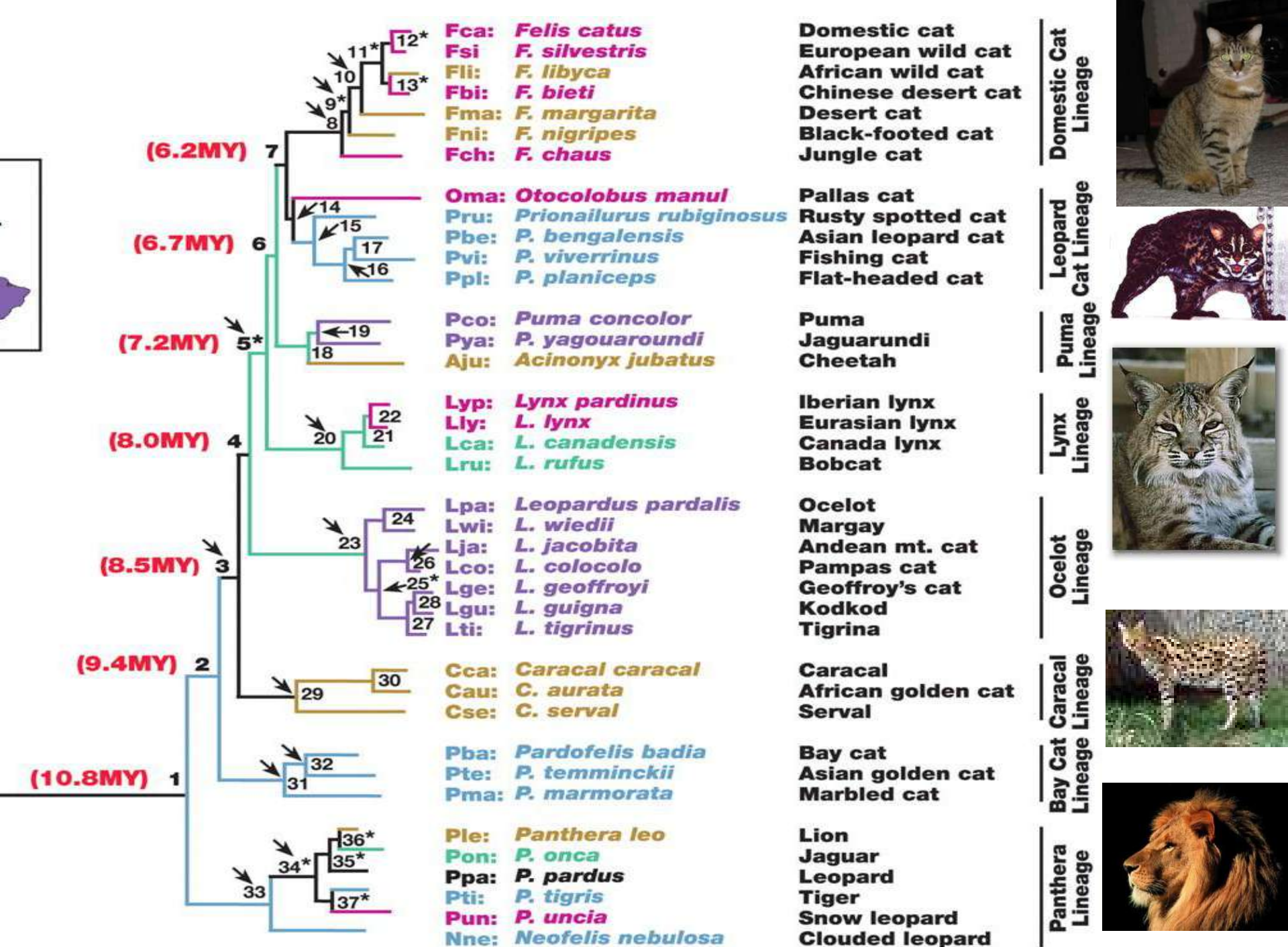
- 🐾 **< 10% breeds**

Age of Mammals
~65 millions year ago till present
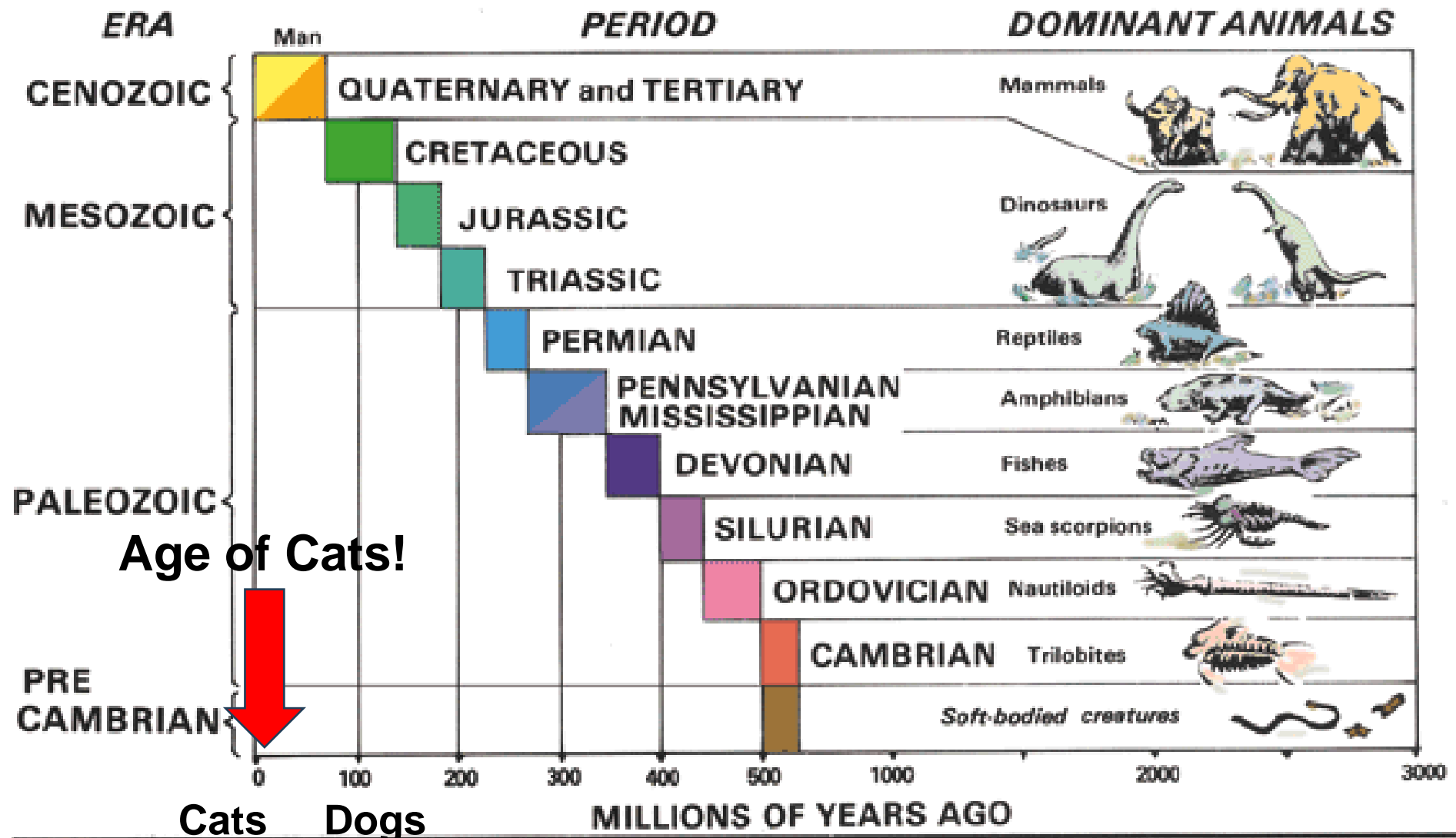
Major divisions of geologic time.

Feliform – cat-like

~ 65 mya

Fca:	***Felis catus***	**Domestic cat**	
Fsi	***F. silvestris***	**European wild cat**	
Fli:	***F. libyca***	**African wild cat**	
Fbi:	***F. bieti***	**Chinese desert cat**	Domestic Cat Lineage
Fma:	***F. margarita***	**Desert cat**	
Fni:	***F. nigripes***	**Black-footed cat**	
Fch:	***F. chaus***	**Jungle cat**	
Oma:	***Otocolobus manul***	**Pallas cat**	
Pru:	***Prionailurus rubiginosus***	**Rusty spotted cat**	Leopard Cat Lineage
Pbe:	***P. bengalensis***	**Asian leopard cat**	
Pvi:	***P. viverrinus***	**Fishing cat**	
Ppl:	***P. planiceps***	**Flat-headed cat**	
Pco:	***Puma concolor***	**Puma**	
Pya:	***P. yagouaroundi***	**Jaguarundi**	Puma Lineage
Aju:	***Acinonyx jubatus***	**Cheetah**	
Lyp:	***Lynx pardinus***	**Iberian lynx**	
Lly:	***L. lynx***	**Eurasian lynx**	Lynx Lineage
Lca:	***L. canadensis***	**Canada lynx**	
Lru:	***L. rufus***	**Bobcat**	
Lpa:	***Leopardus pardalis***	**Ocelot**	
Lwi:	***L. wiedii***	**Margay**	
Lja:	***L. jacobita***	**Andean mt. cat**	
Lco:	***L. colocolo***	**Pampas cat**	Ocelot Lineage
Lge:	***L. geoffroyi***	**Geoffroy's cat**	
Lgu:	***L. guigna***	**Kodkod**	
Lti:	***L. tigrinus***	**Tigrina**	
Cca:	***Caracal caracal***	**Caracal**	
Cau:	***C. aurata***	**African golden cat**	Caracal Lineage
Cse:	***C. serval***	**Serval**	
Pba:	***Pardofelis badia***	**Bay cat**	
Pte:	***P. temminckii***	**Asian golden cat**	Bay Cat Lineage
Pma:	***P. marmorata***	**Marbled cat**	
Ple:	***Panthera leo***	**Lion**	
Pon:	***P. onca***	**Jaguar**	
Ppa:	***P. pardus***	**Leopard**	Panthera Lineage
Pti:	***P. tigris***	**Tiger**	
Pun:	***P. uncia***	**Snow leopard**	
Nne:	***Neofelis nebulosa***	**Clouded leopard**	

(6.2MY) 7
(6.7MY) 6
(7.2MY) 5*
(8.0MY) 4
(8.5MY) 3
(9.4MY) 2
(10.8MY) 1

11* 12* 10 9* 8 13*
14 15 17 16
19 18
20 22 21
24 23 26 25* 28 27
29 30
32 31
34* 36* 35* 37* 33

Historical Wildcat Ranges
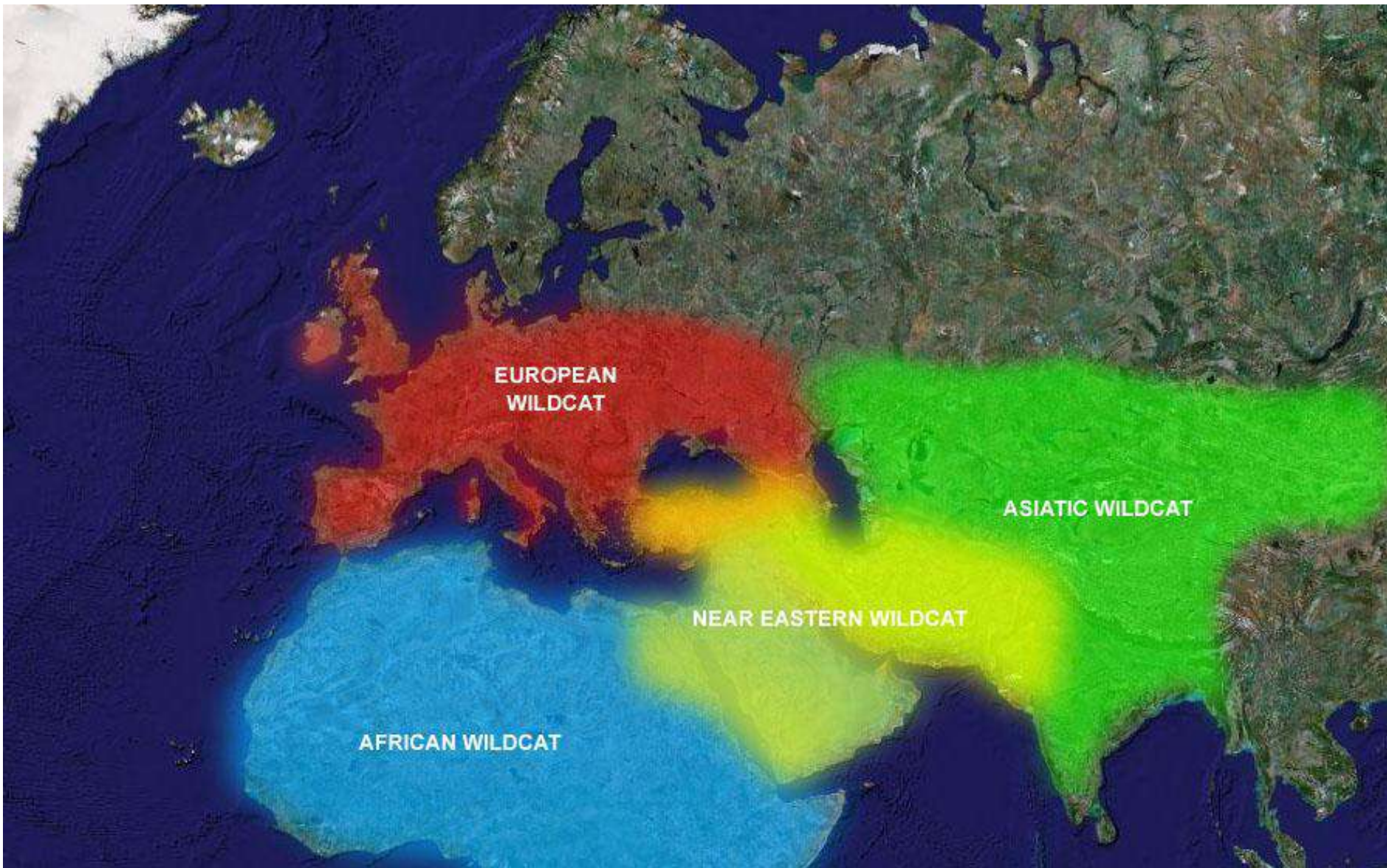
Feral cats around the world

Natural Vermin control

Cat Genetic Population Studies

Cat Genetic Diversity

- STRs
- STRs & SNPs
- Future

Created with mapchart.net
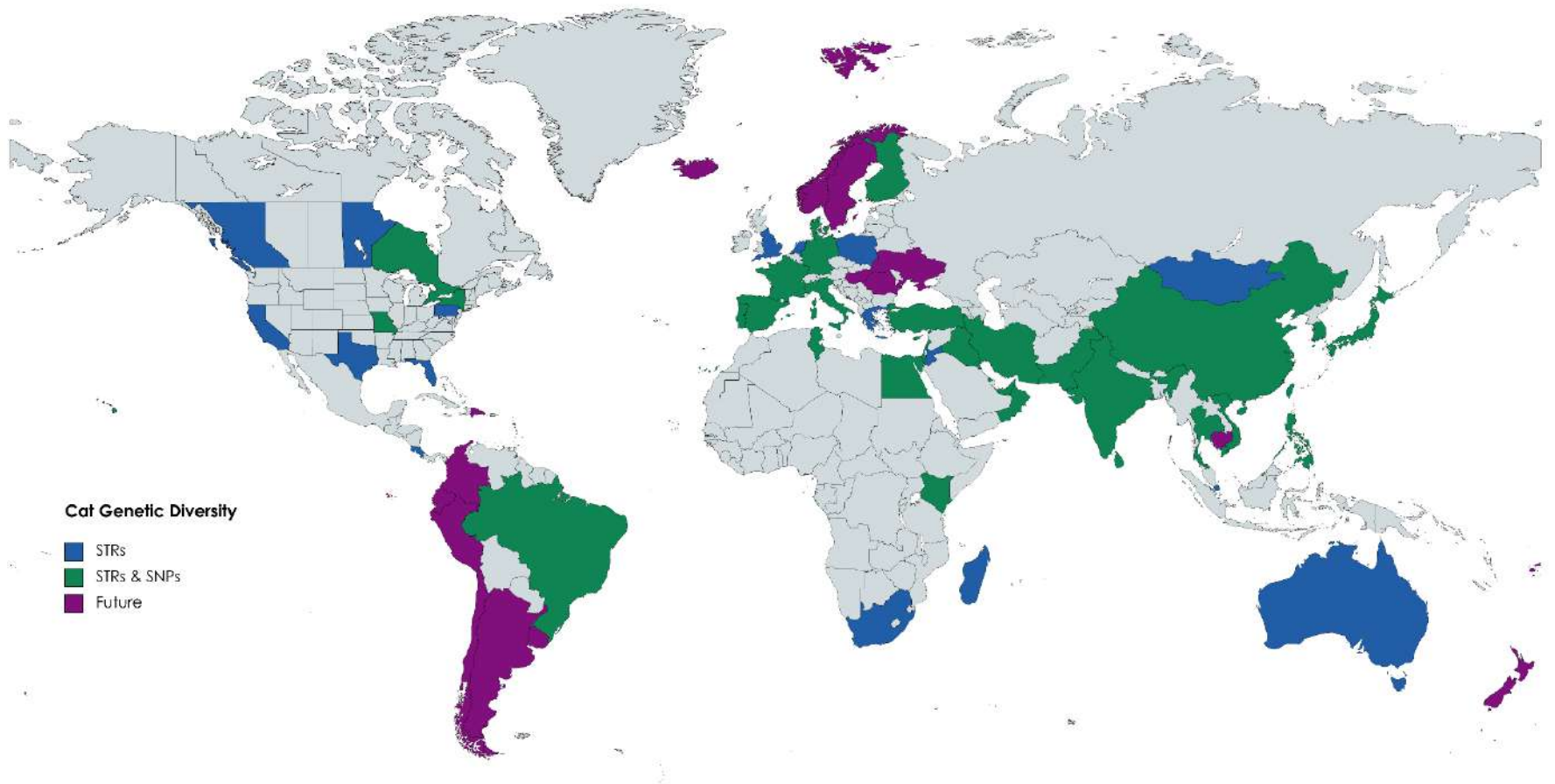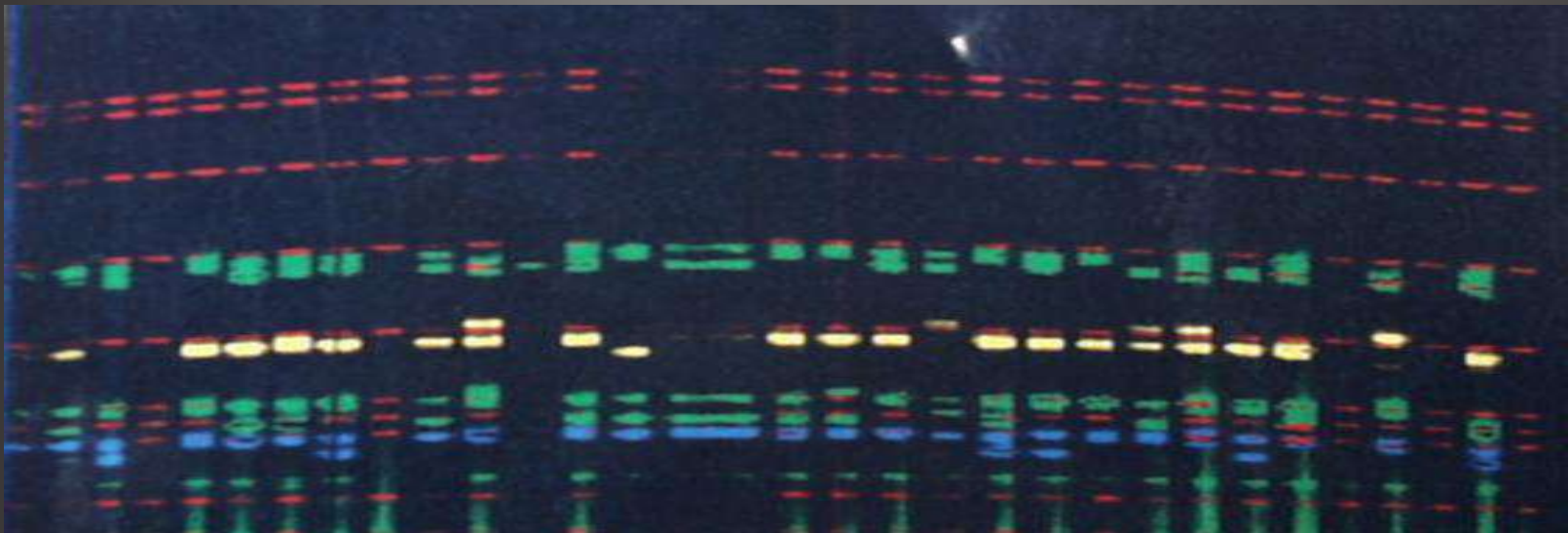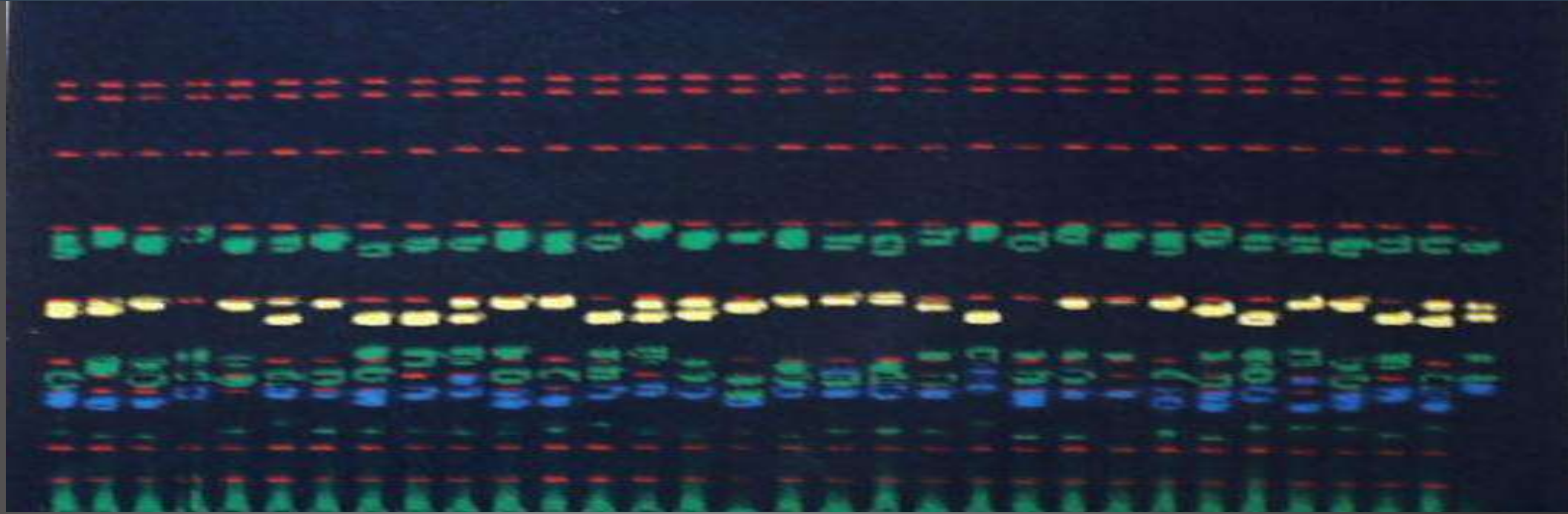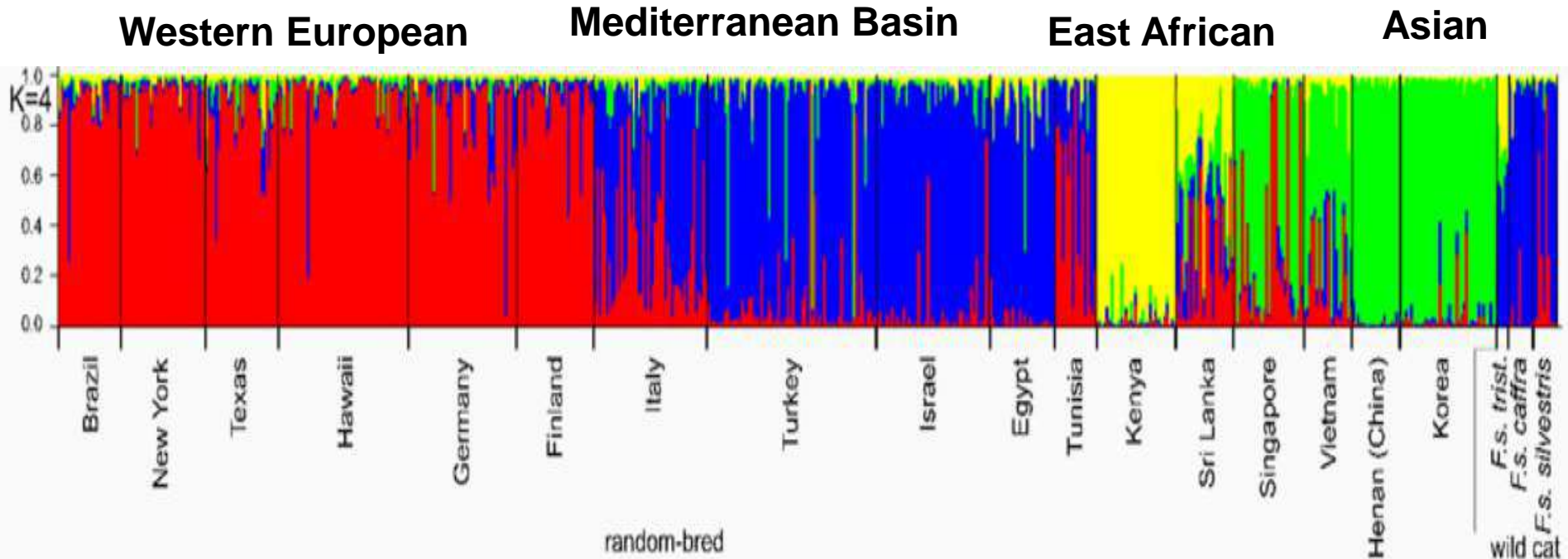
DNA markers determine genetic variation (STRs)

Random Bred Racial Populations

The Ascent of Cat Breeds: Genetic Evaluations of Breeds and Worldwide Random Bred Populations

Monika J. Lipinski[a], Lutz Froenicke[a], Kathleen C. Baysac[a], Nicholas C. Billings[a], Christian M. Leutenegger[b], Alon M. Levy[c], Maria Longeri[d], Tirri Niini[e], Haydar Ozpinar[f], Margaret R. Slater[g], Niels C. Pedersen[b], and Leslie A. Lyons[a],*

Genomics, 2008

Feral "Races" of Cats
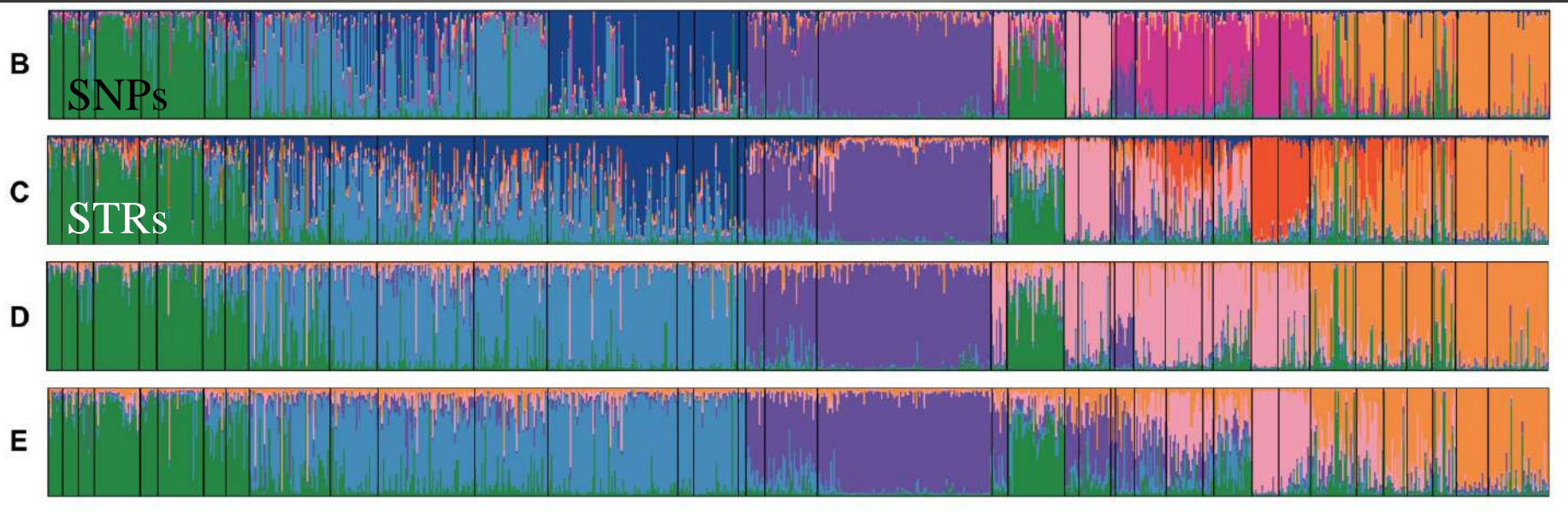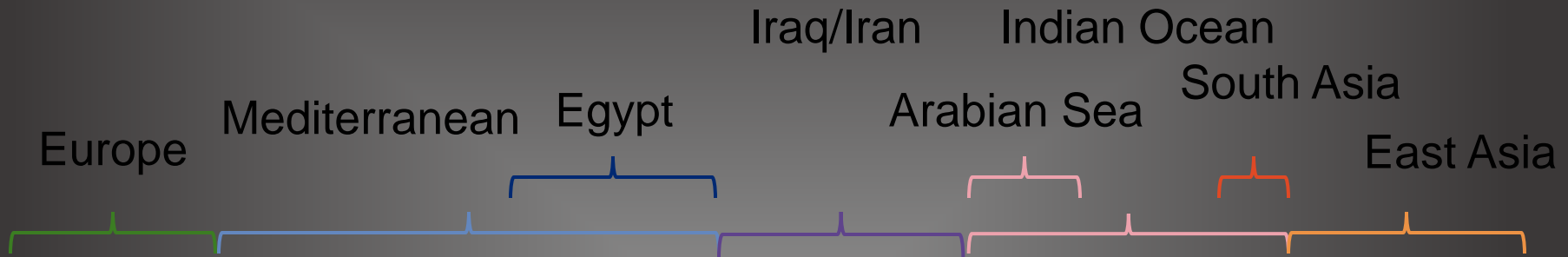
38 STRs and 148 SNPs

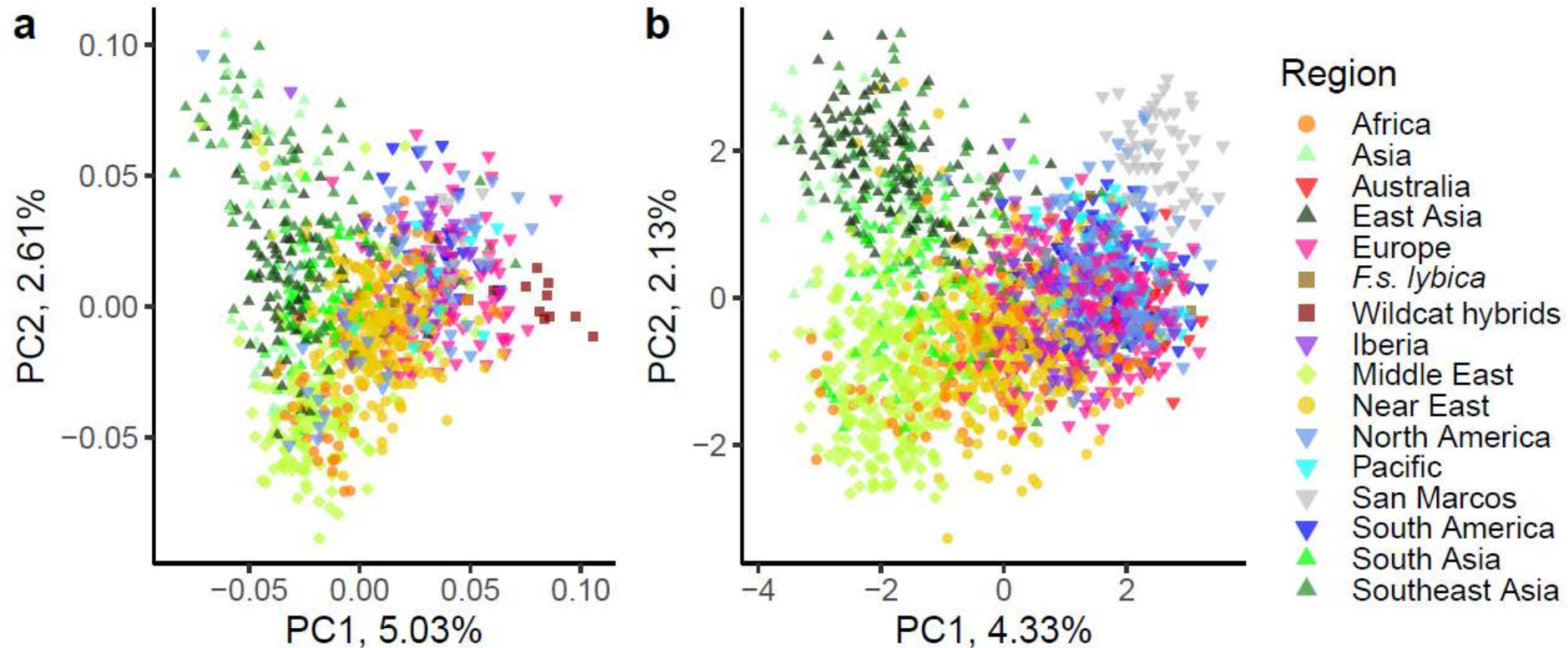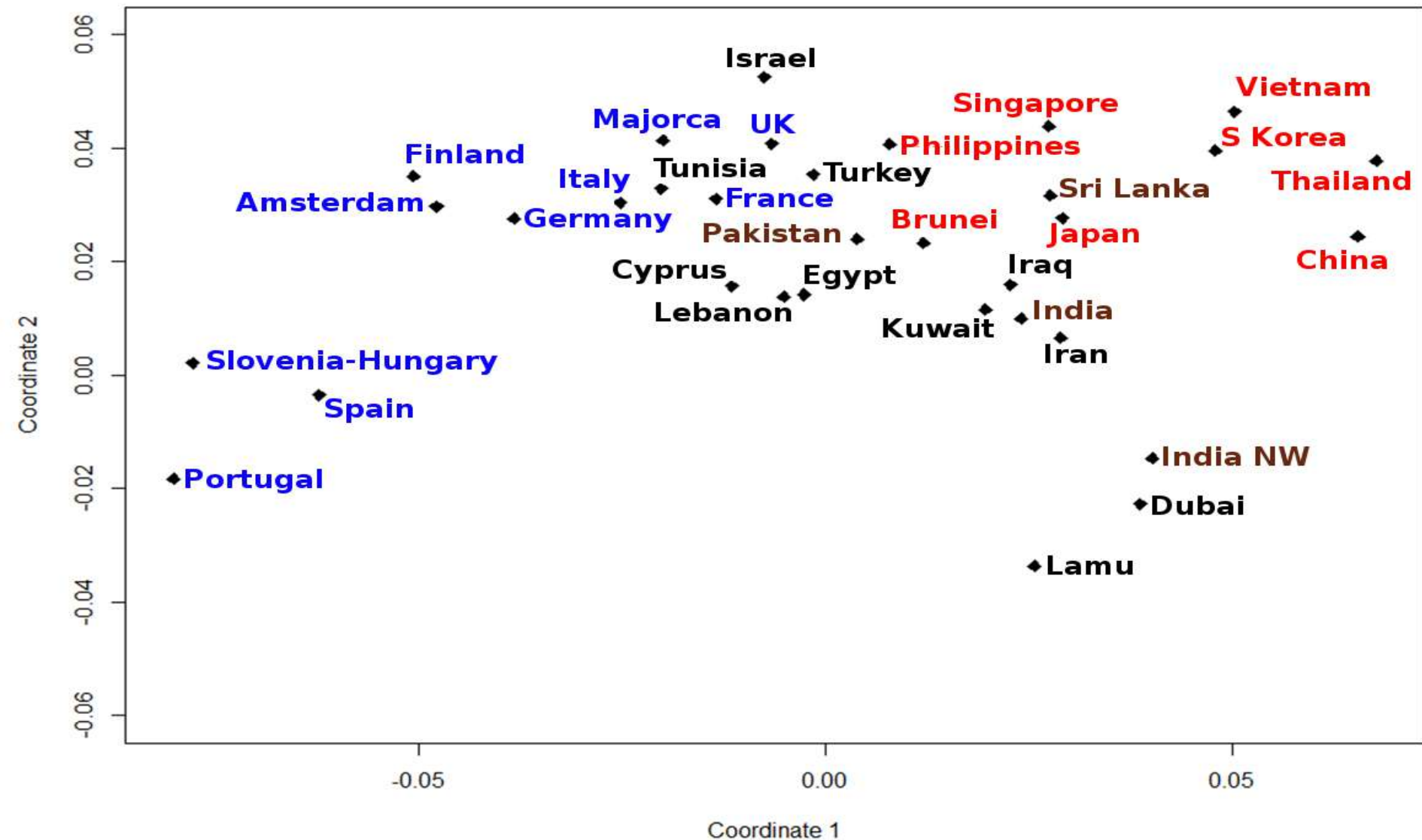World Distinct Cat Populations, K = 7
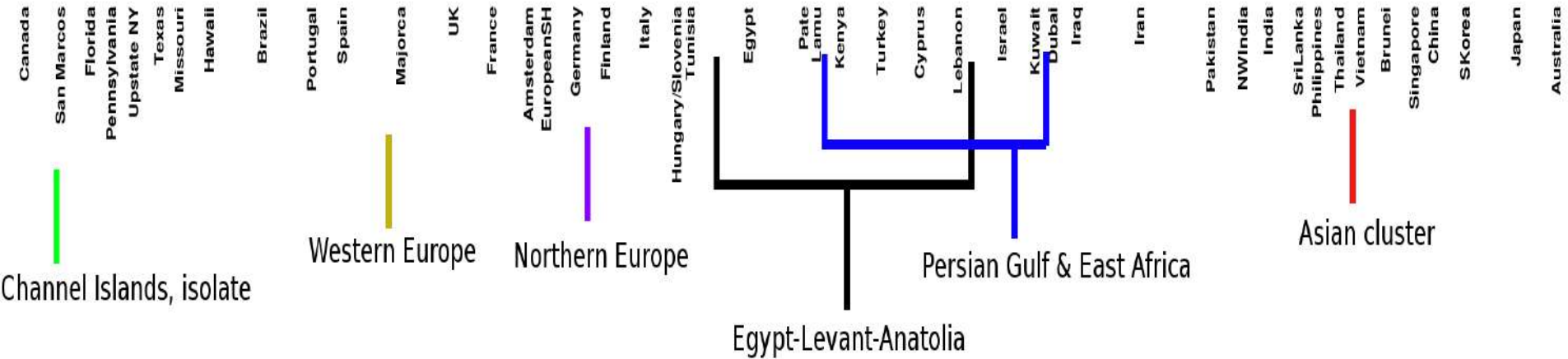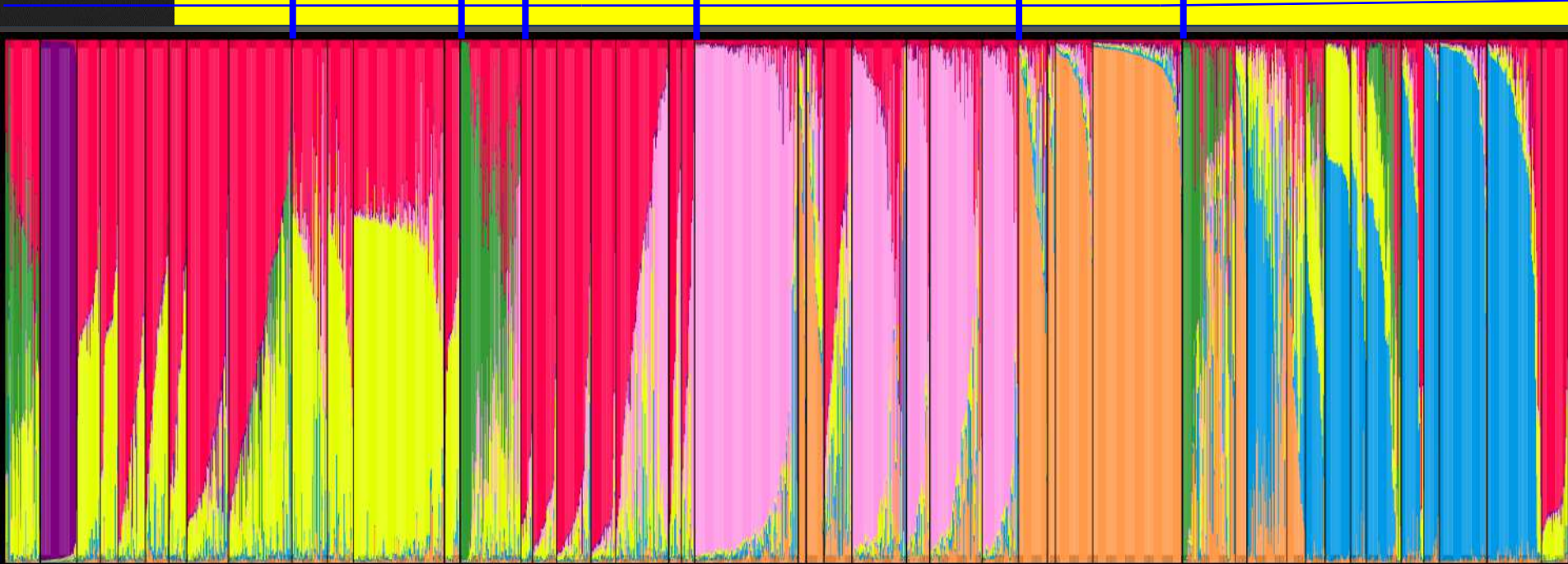
Cats are cats – Isolation by Distance

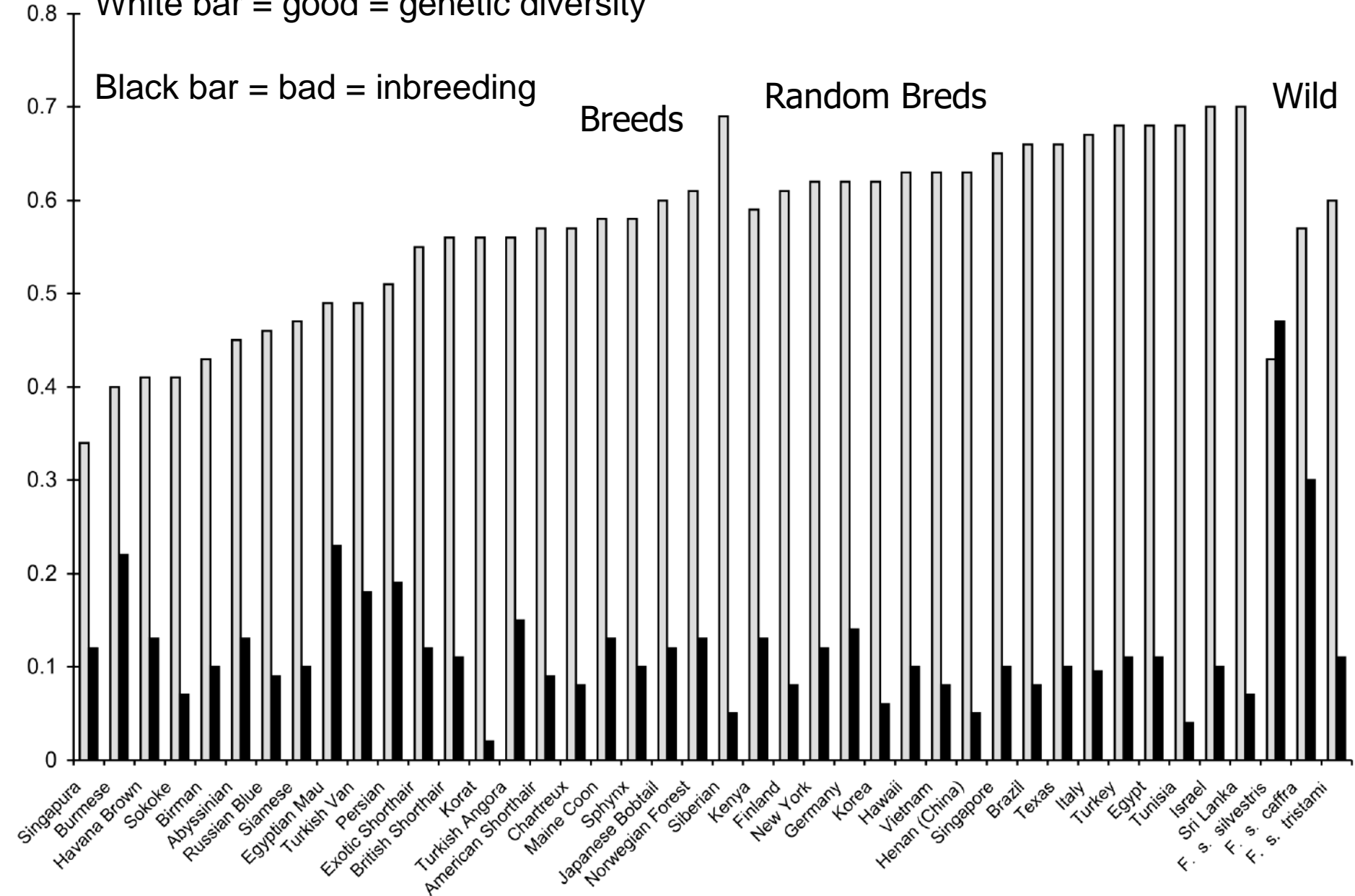# Overall Genetic Relationship of Cat Populations
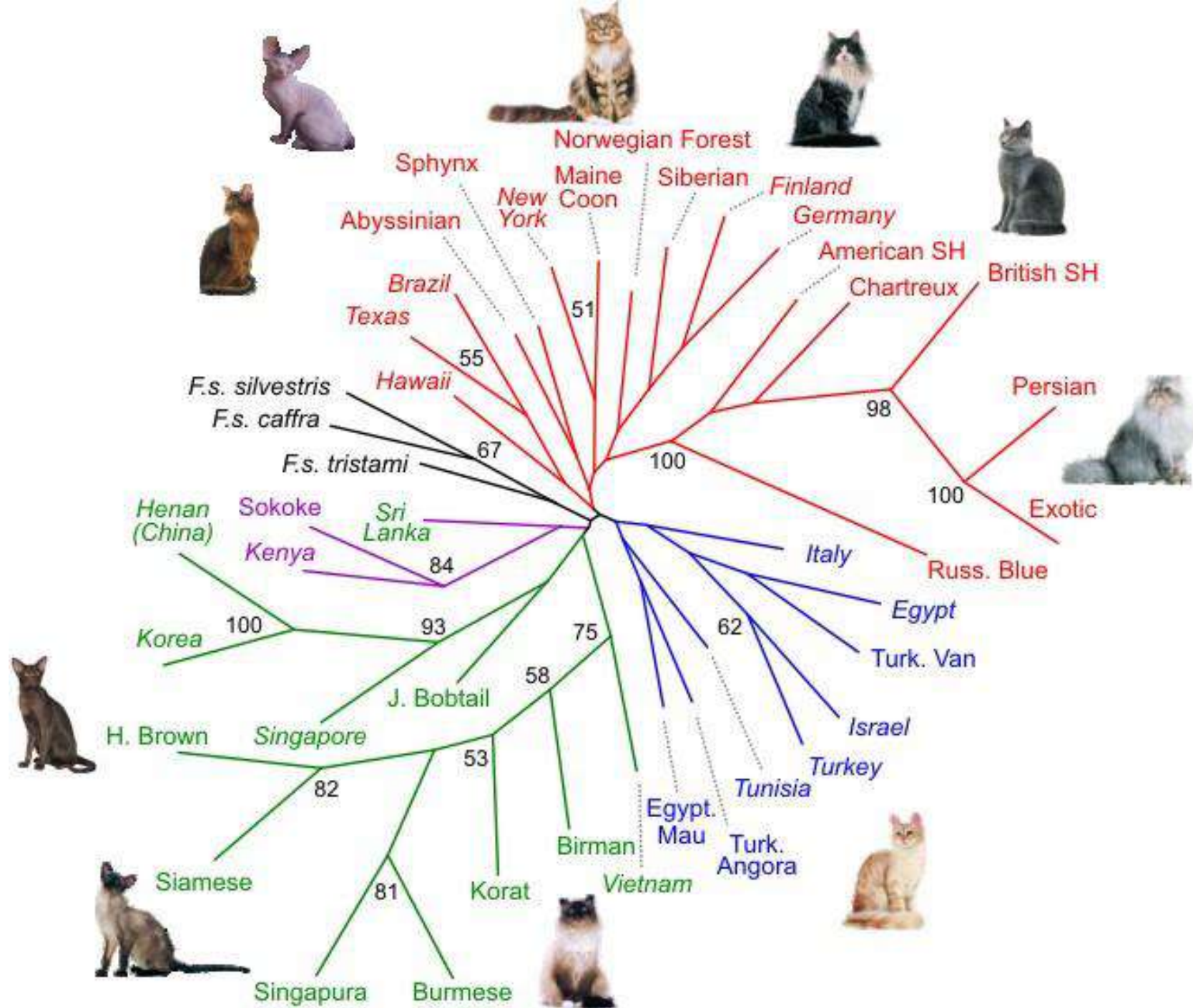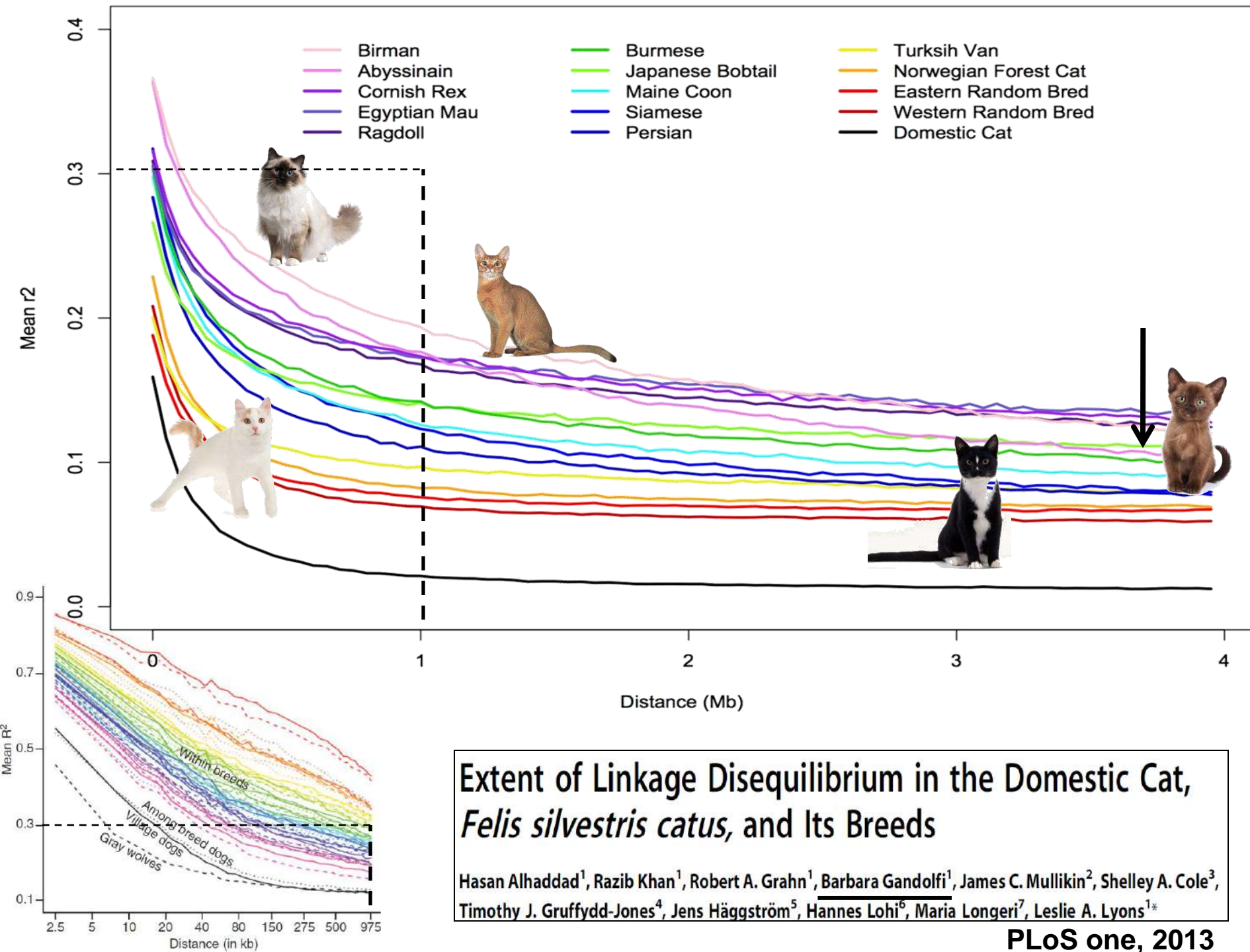

Multidimensional scaling of F_{st}

Gene Pool Health of Breeds

White bar = good = genetic diversity

Black bar = bad = inbreeding

Breeds

Random Breds

Wild

Extent of Linkage Disequilibrium in the Domestic Cat, *Felis silvestris catus,* and Its Breeds

Hasan Alhaddad[1], Razib Khan[1], Robert A. Grahn[1], Barbara Gandolfi[1], James C. Mullikin[2], Shelley A. Cole[3], Timothy J. Gruffydd-Jones[4], Jens Häggström[5], Hannes Lohi[6], Maria Longeri[7], Leslie A. Lyons[1]*
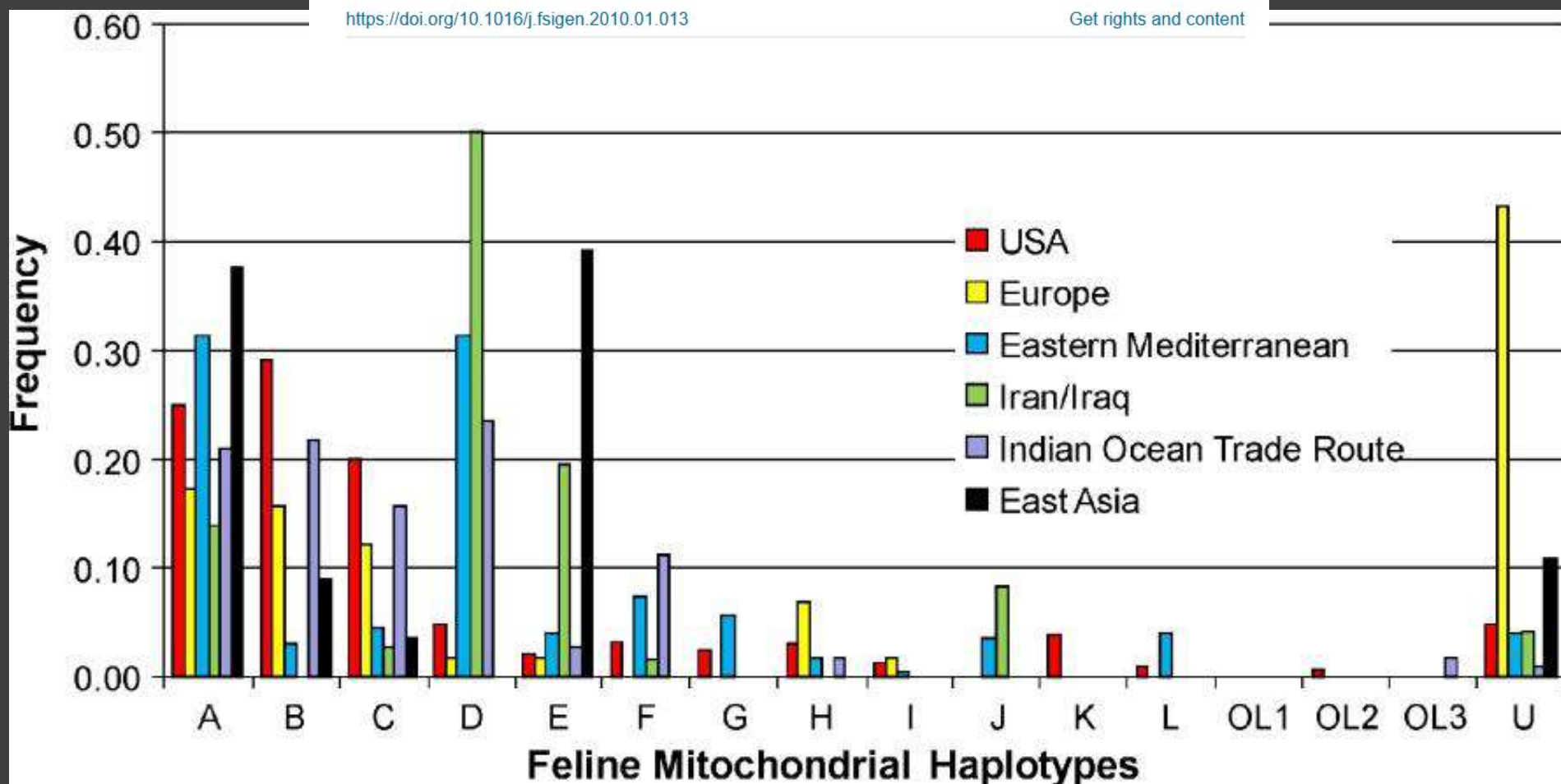
Feline non-repetitive mitochondrial DNA control region database for forensic evidence

R.A. Grahn[a], J.D. Kurushima[a], N.C. Billings[a], J.C. Grahn[a], J.L. Halverson[b], E. Hammer[a], C.K. Ho[a], T.J. Kun[c], J.K. Levy[d], M.J. Lipinski[a], J.M. Mwenda[e], H. Ozpinar[f], R.K. Schuster[g], S.J. Shoorijeh[h], C.R. Tarditi[a, c], N.E. Waly[i], E.J.
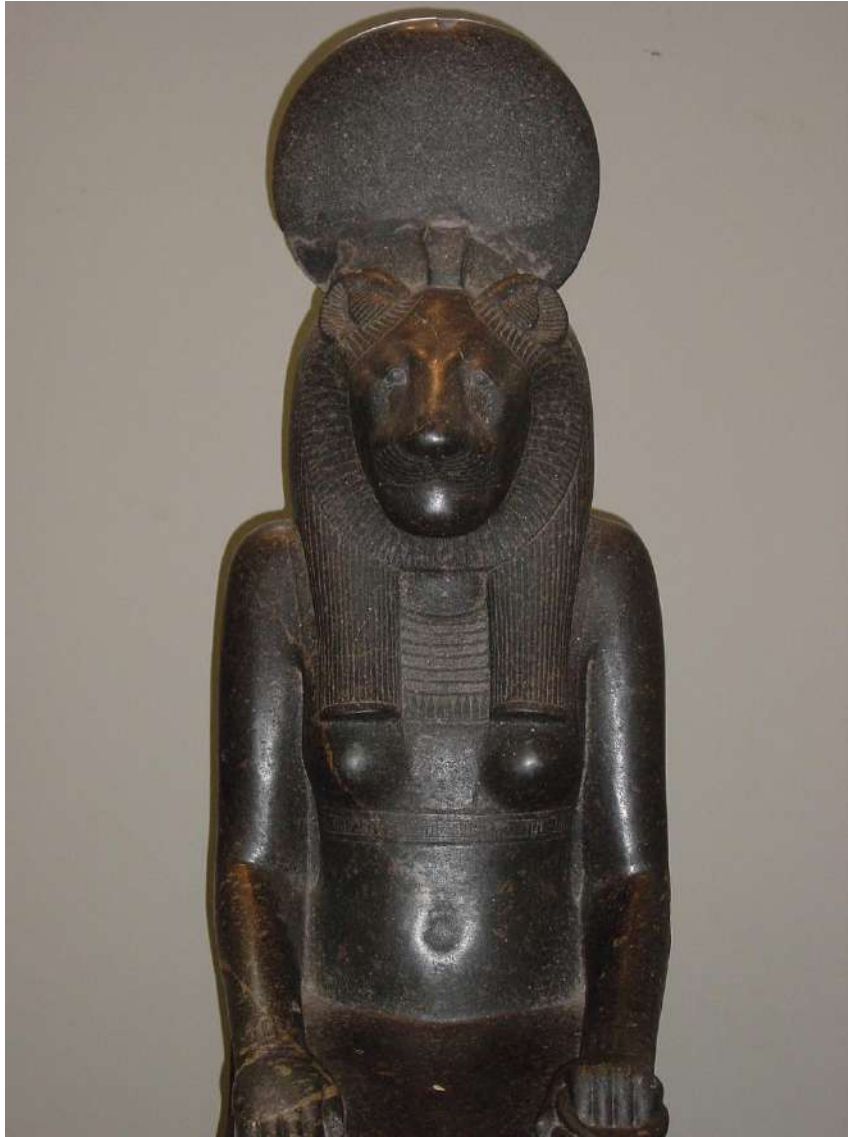
⊞ Show more

Network of Cat mtDNA CR

- **~800 bp mitotype**

- **4 common types**

- **5 minor types**

- **4 derived**

- **20% unique**

Cats of the Pharaohs: Genetic Comparison of Egyptian Cat Mummies to their Feline Contemporaries

Jennifer D. Kurushima,[a] Salima Ikram,[b] Joan Knudsen,[c] Edward Bleiberg,[d] Robert A. Grahn,[a] and Leslie A. Lyons[a,*]

Population Genetics & Mummies

Published in final edited form as:
J Archaeol Sci. 2012 October ; 39(10): 3217–3223. doi:10.1016/j.jas.2012.05.005.

Cats of the Pharaohs: Genetic Comparison of Egyptian Cat Mummies to their Feline Contemporaries

Jennifer D. Kurushima[a], Salima Ikram[b], Joan Knudsen[c], Edward Bleiberg[d], Robert A. Grahn[a], and Leslie A. Lyons[a,*]
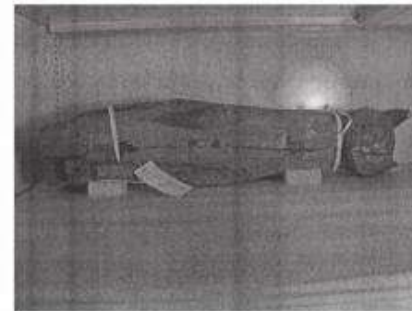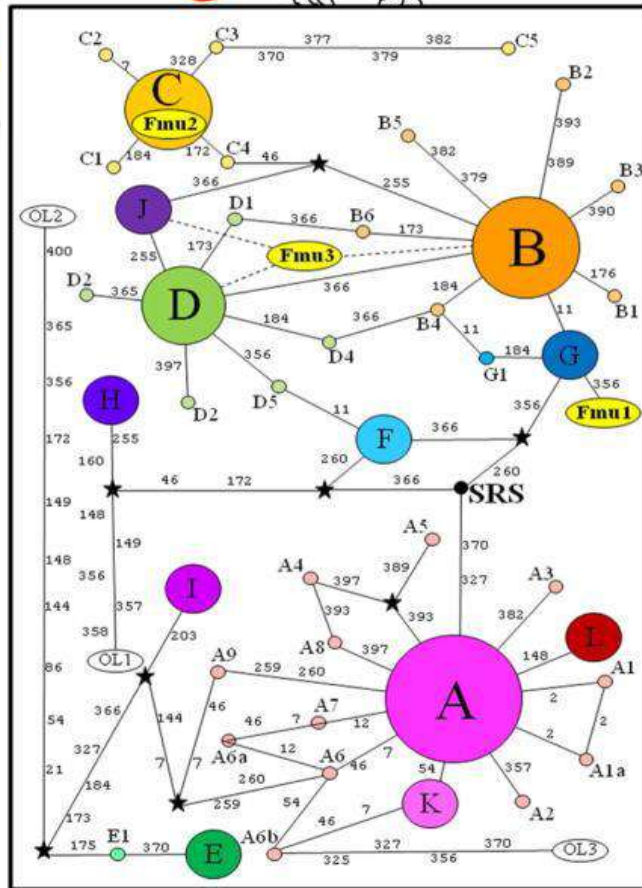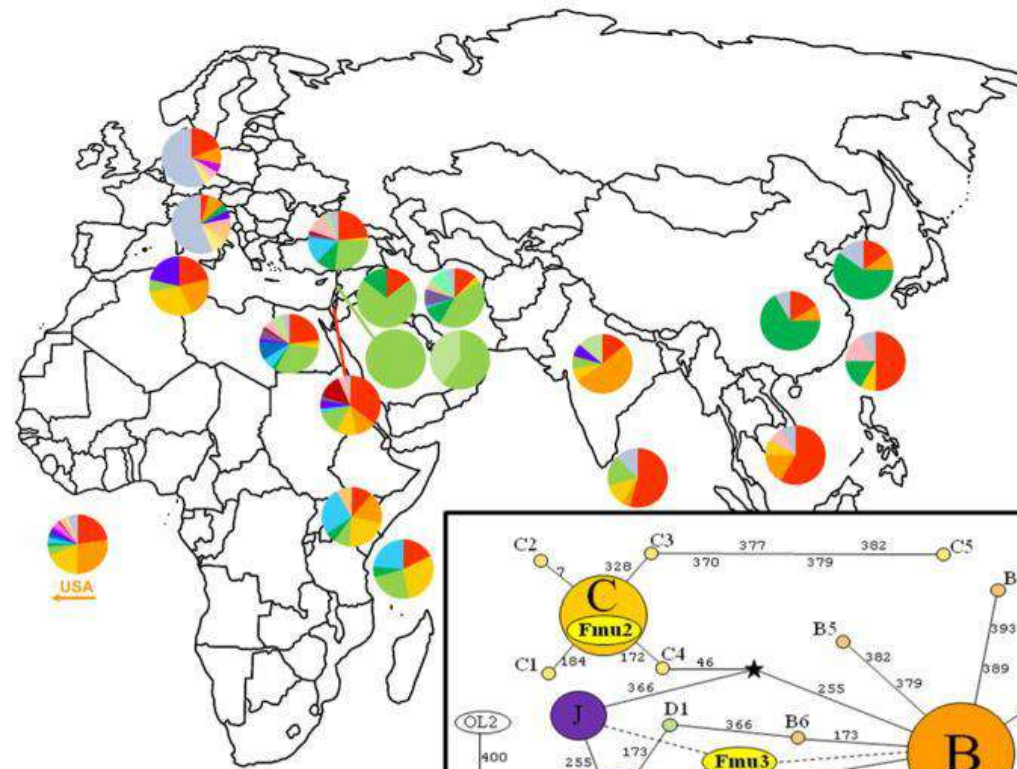

NATIONAL GEOGRAPHIC

SCIENCE OF
CATS

As Seen On
NATIONAL
GEOGRAPHIC
CHANNEL
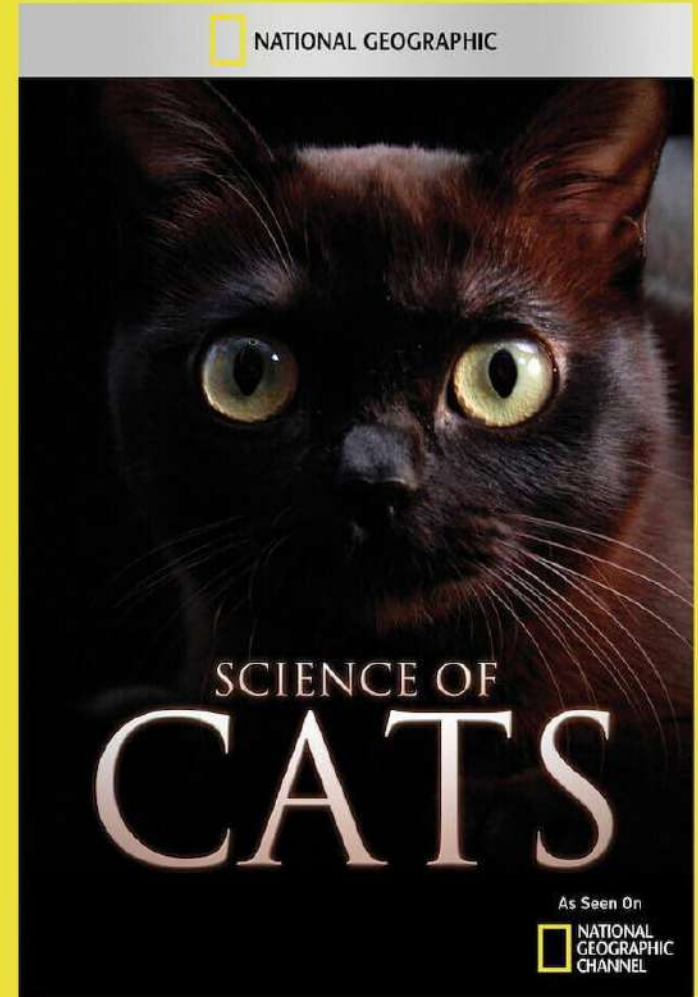
The Near Eastern Origin of Cat Domestication

Carlos A. Driscoll,* Marilyn Menotti-Raymond, Alfred L. Roca, Karsten Hupe,
Warren E. Johnson, Eli Geffen, Eric Harley, Miguel Delibes, Dominique Pontier,
Andrew C. Kitchener, Nobuyuki Yamaguchi, Stephen J. O'Brien,* David Macdonald*

correspondence should be addressed. E-mail: obrien@ncifcrf.gov;
scoll@ncifcrf.gov; david.macdonald@zoology.oxford.ac.uk

	Total	STR	mtDNA
Felis margarita	11	11	11
Felis silvestris bieti	5	5	4
Known domestic cats*	222	223	174
Fancy breed cats	112	101	55
Wild-living cats**	629	511	498
TOTALS	979	851	742

The Taming of the

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

Carlos A. Driscoll[a,b], David W. Macdonald[a], and Stephen J. O'Brien[b,1]

A

B

131,000 Years

173,000 Years

230,000 Years

0.1

Clade IV

Clade III

Clade II

Clade I

Clade V

Clade VI

C

Clade IV

Clade I

Clade II

Clade III

Clade V

Clade VI
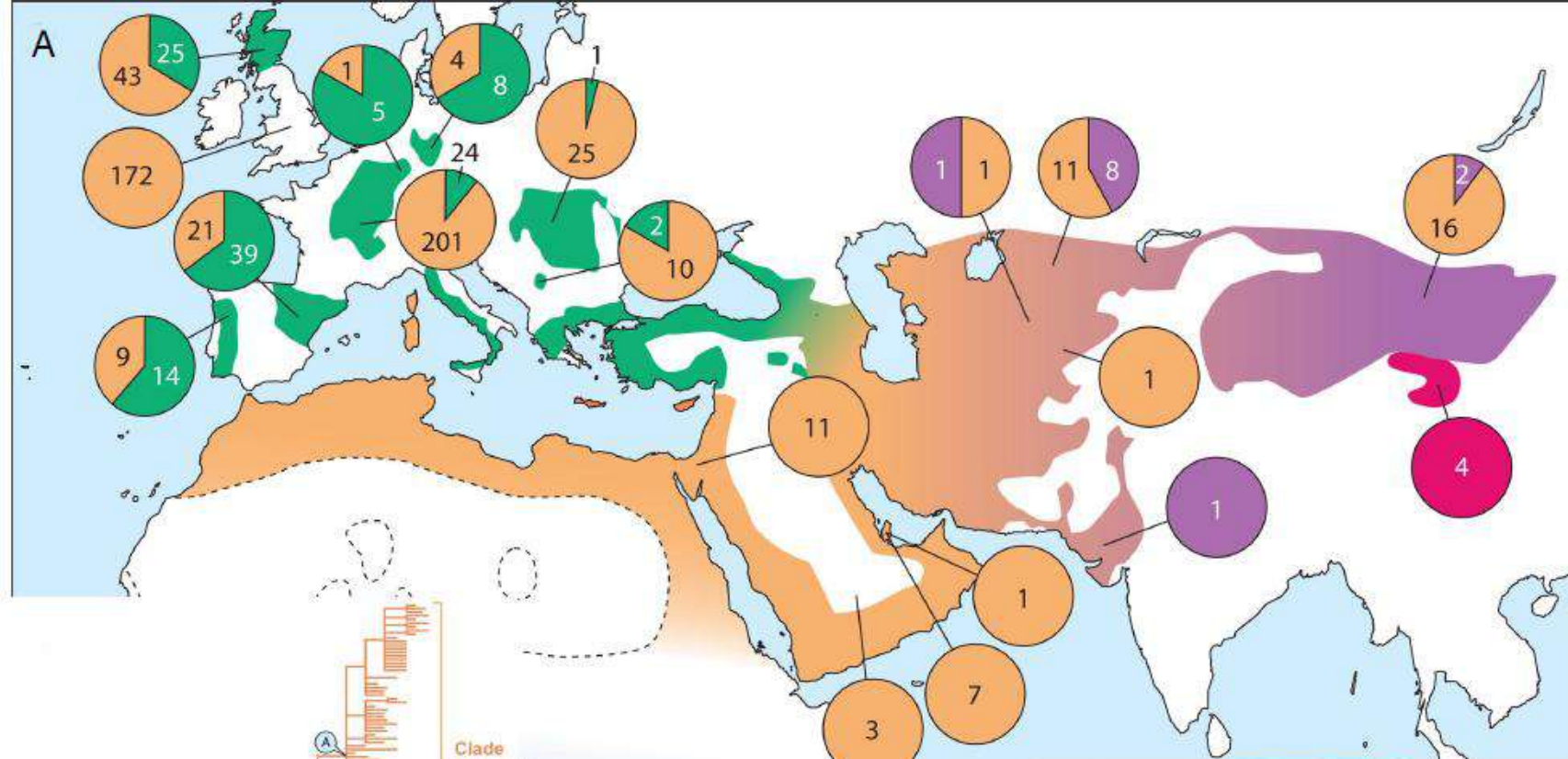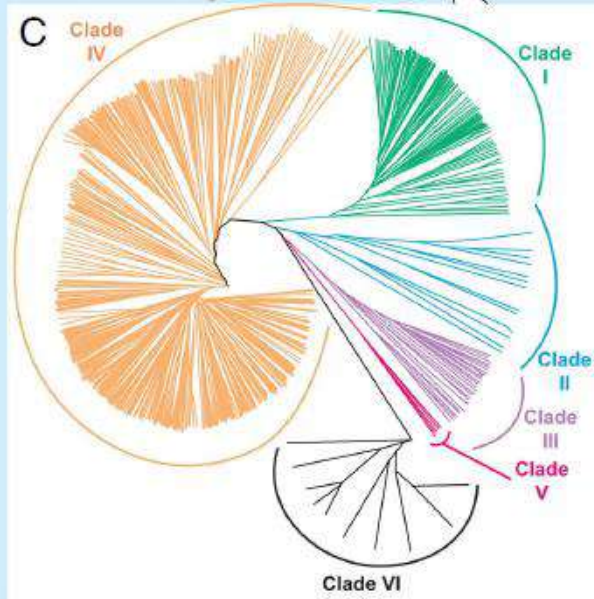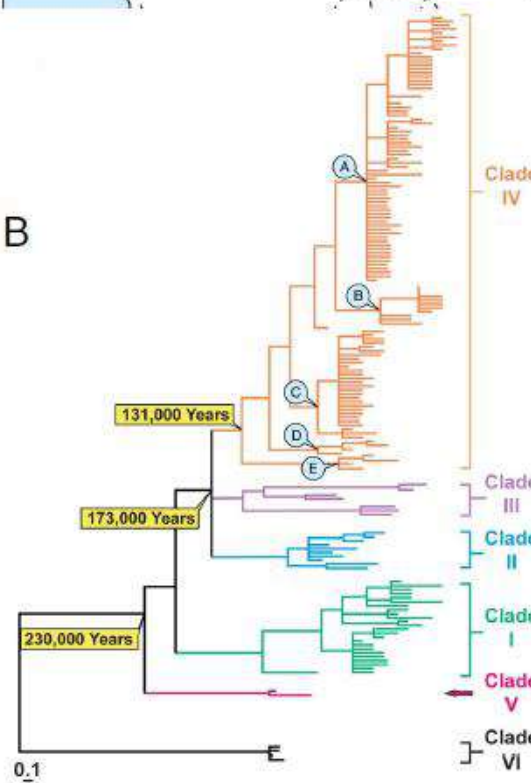
Domestication & Selection
➡ Breeds

Cat Fancy Origins

🐾 1st cat show: Crystal Palace, England in 1871

🐾 1887 National Cat Club

🐾 British, Persian, Manx, Siamese, Angora, Russian Blue
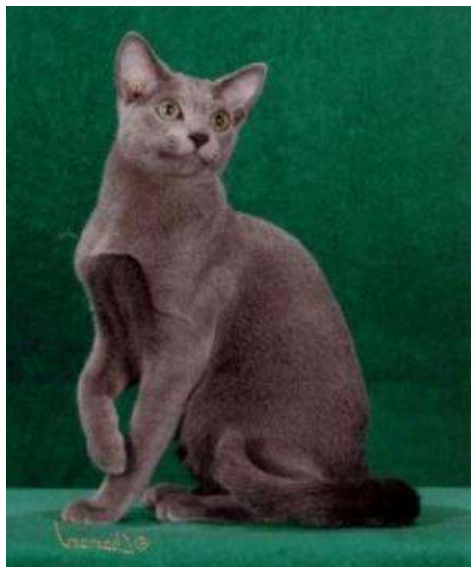
🐾 Maine Coon, USA 1905

Long hair breeds

Persian

Norwegian forest cat

Ragdoll

Birman

Maine coon

Siberian

Turkish angora

Oriental longhair

Hair Type Breeds

Devon rex

Selkirk rex

Laperm

Peterbald

Sphynx

American wirehair
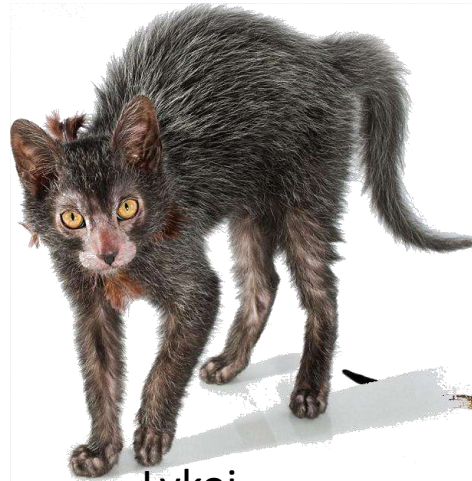
Lykoi

Cornish rex

Coat Colors & Patterns

Bengal

Bombay

Abyssinian

Turkish van

Russian blue

Toyger

Siamese

Morphological Trait Breeds

Manx

Japanese bobtail

American curl

Scottish fold

Breeds based on size

Munchkin
vs.
Maine coon

CFA Breed Distributions

- **Top 14 breeds represent ~94% of breed cats**

  - <u>**Persian / Exotic**</u> **= 1,271,301 (~65%)**

  - <u>**Siamese**</u> **= 189,791**   <u>**Maine Coon**</u> **= 72,416**
  - <u>**Abyssinian**</u> **= 67,488**   **Burmese = 51,033**
  - **American SH = 36,482**   **Scottish Fold = 21,266**
  - **Cornish Rex = 21,028**   **Birman = 20,439**
  - <u>**Manx**</u> **= 19,154**   **Russian Blue = 16,368**

*5 oldest breeds, pre - WWII

Breeds population structure

Persian, Exotic SH, British SH, Scottish Fold, Chartreux, American SH, Sphynx, Japanese Bobtail, Cornish Rex, Ragdoll, Maine Coon, Abyssinian, Siberian, Norwegian FC, Manx, Egyptian Mau, Turkish Angora, Turkish Van, Bengal, Sokoke, Ocicat, Russian Blue, Australian Mist, Burmese, Birman, Havana Brown, Korat, Siamese, Singapura
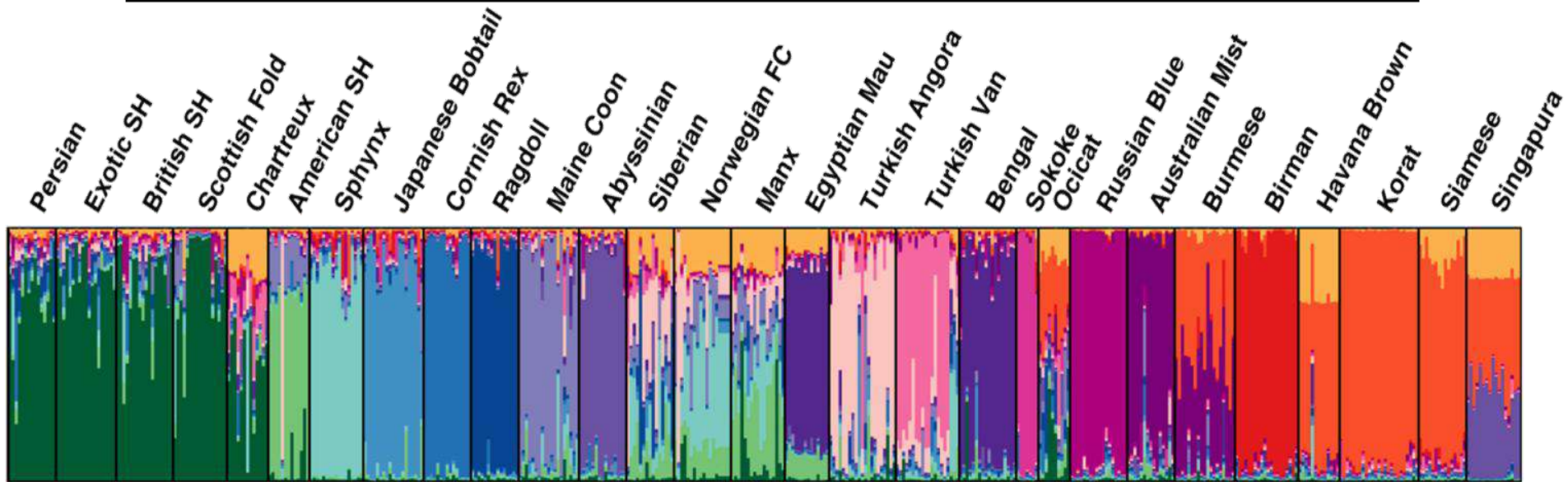
Singapura = Siamese + Abyssinian

Variation of cats under domestication: genetic assignment of domestic cats to breeds and worldwide random-bred populations

J. D. Kurushima, M. J. Lipinski, B. Gandolfi, L. Froenicke, J. C. Grahn, R. A. Grahn and L. A. Lyons
Department of Health & Reproduction, School of Veterinary Medicine, University of California – Davis, Davis, CA, 95616, USA.

Genetic Distinction of Breeds
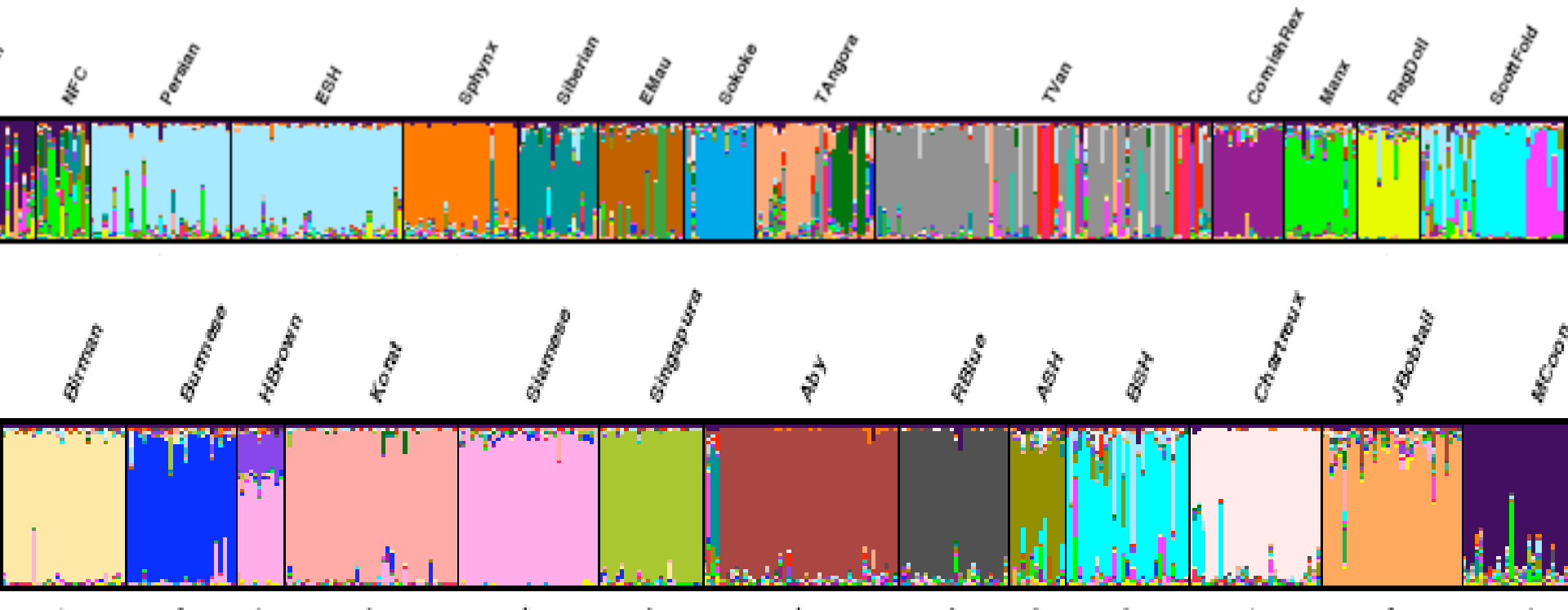
24 of 29 breeds distinct

Population structure

Legend:
- | M.Coon
- ● Persian
- % Wildcat
- × NFC
- ■ Mix-breed
- ⊕ RB
- + Abyssinian
- □ E.Mau
- ● T.Van
- ▲ C.Rex
- O Bengal
- ⬡ A.Curl
- △ J.bobtail
- ✳ Ragdoll
- ✶ Burmese
- ○ Birman
- # O.shorthair
- ◆ Siamese
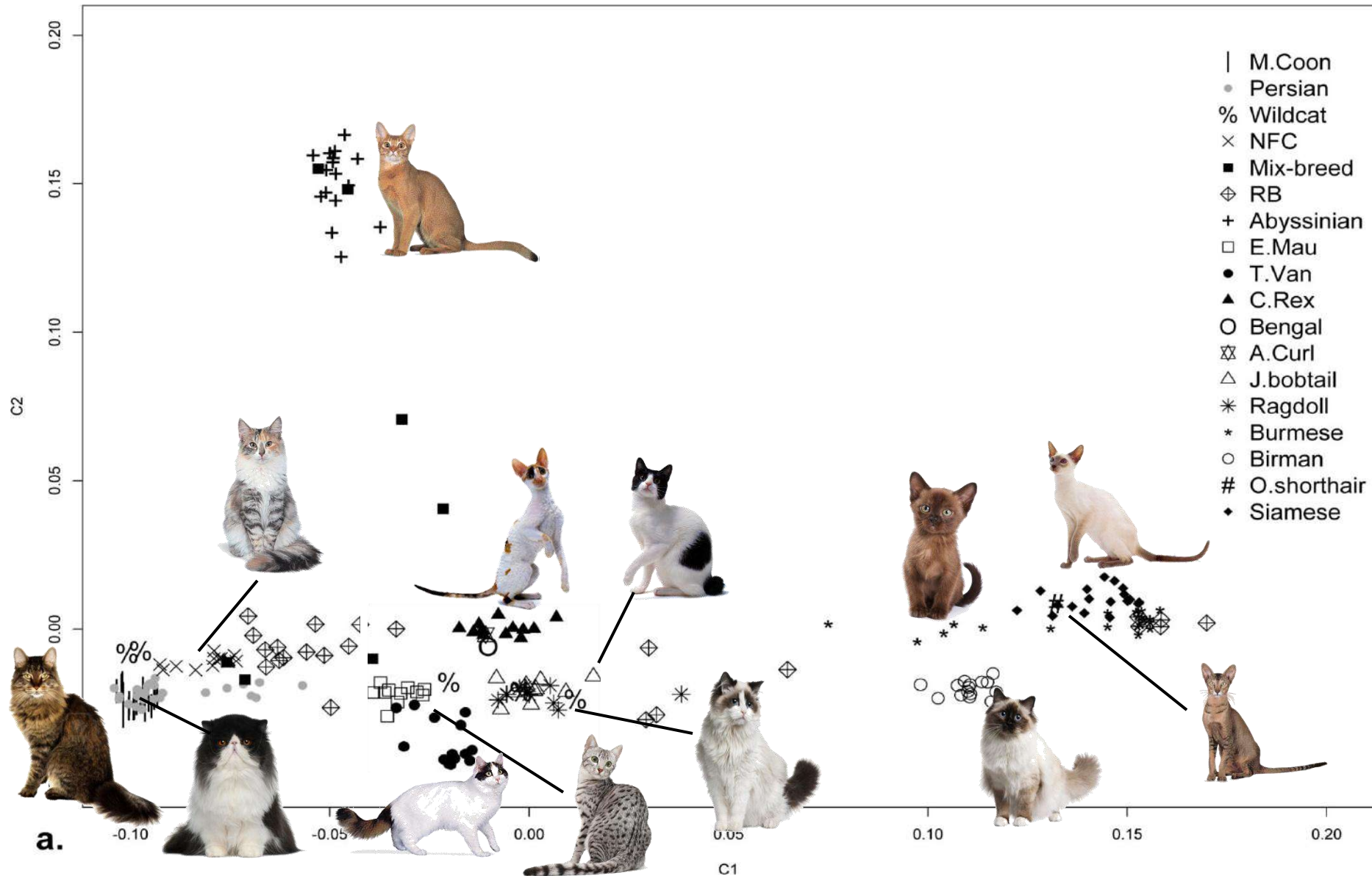
Outcrossing to increase diversity

Turkish Van Ancestry
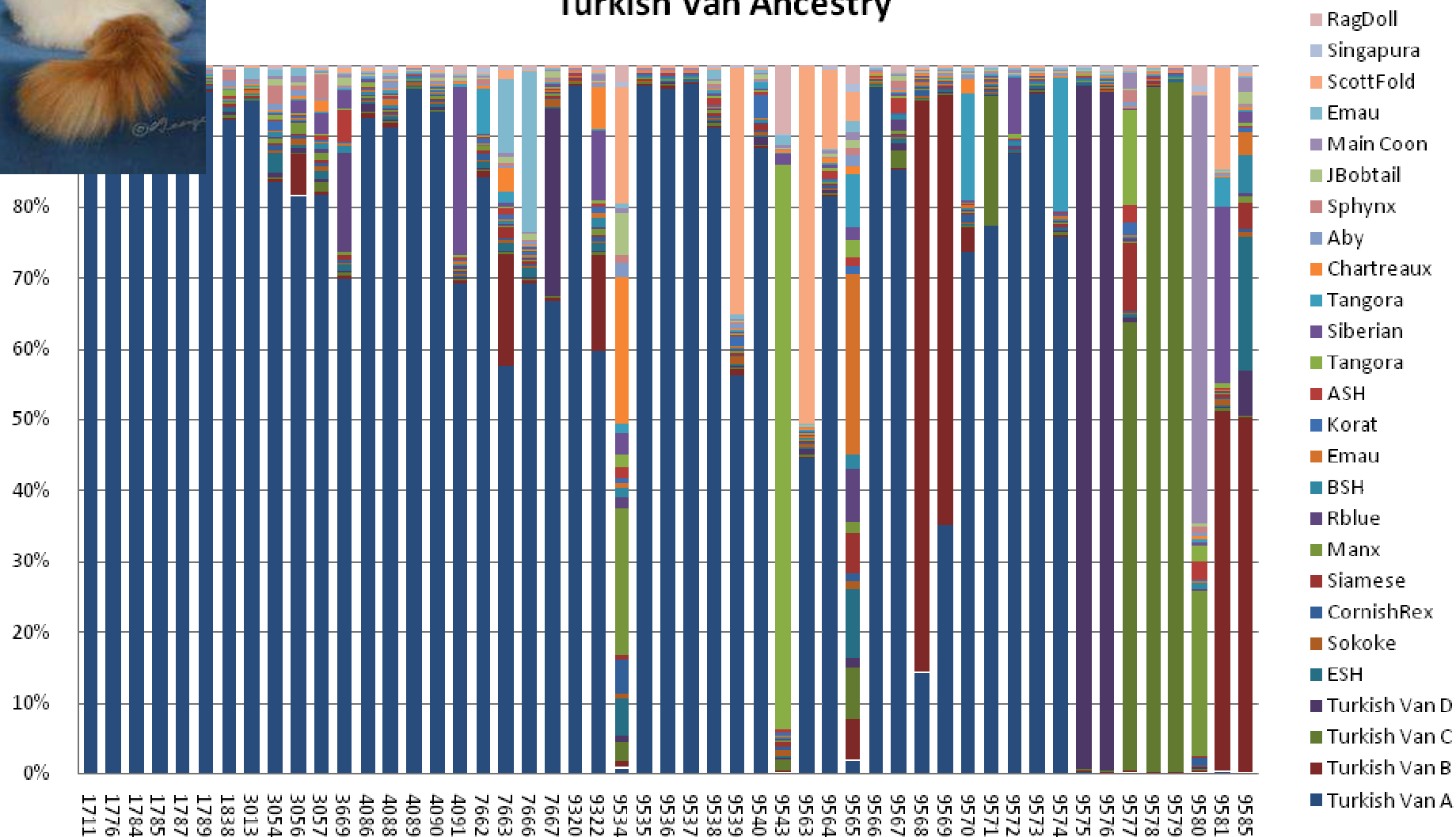
Cat Breed Genetic Health

Chart showing Heterozygosity / Inbreeding with Ho(STR) values across cat breeds: Sokoke, Burmese, Singapura, Russian Blue, Birman, Havana Brown, Korat, Siamese, Ocicat, Egyptian Mau, Abyssinian, Chartreux, Japanese Bobtail, Cornish Rex, British SH, Exotic SH, Persian, Turkish Van, Sphynx, Scottish Fold, American SH, Bengal, Australian Mist, Maine Coon, Turkish Angora, Ragdoll, Siberian, Norwegian FC, Manx.

Poor Genetic Health -------------------- Good Genetic Health

http://www.nymews.com/ourcats/giosep03.jpg

Brachycephalic

Dolichocephalic

The "Persian family"

a.

b.

Persian Family

Selkirk Rex: Morphological and Genetic Characterization of a New Cat Breed

SERINA FILLER, HASAN ALHADDAD, BARBARA GANDOLFI, JENNIFER D. KURUSHIMA, ALEJANDRO CORTES, CHRISTINE VEIT, LESLIE A. LYONS, AND GOTTFRIED BREM

Journal of Heredity, 2012

c.
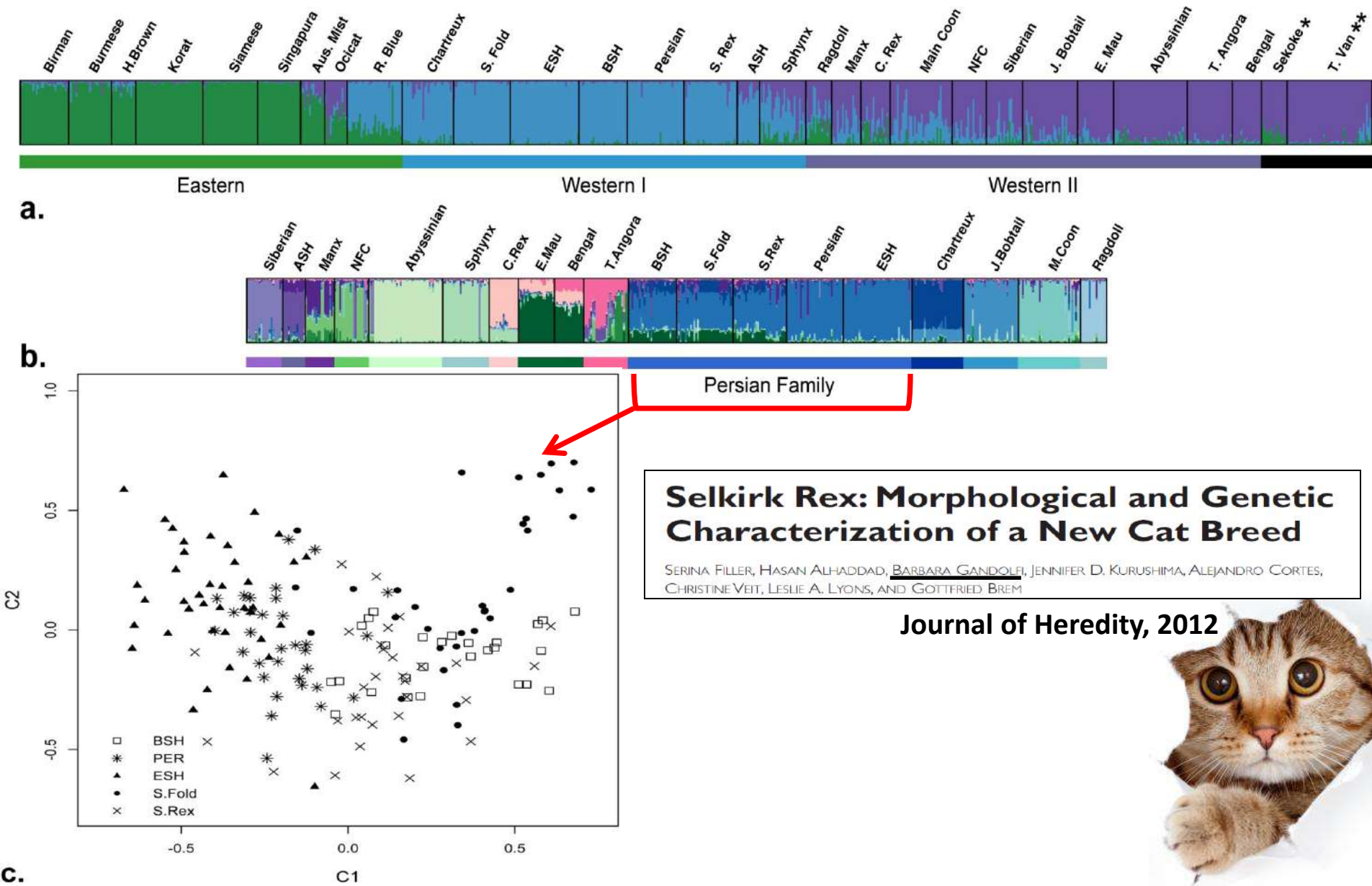
a.

b.

c.

d.

Cinnamon – MU Abyssinian

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

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

Cat genome is ~2.6 Gb

11 million SNPs total (w/ wildcat)

19,493 genes

Assembly version	Assembled size	N50 contig size	N50 scaffold size	Total gap size
Reference assembly gap sequence estimates (Courtesy Wes Warren)				
F. catus 6.2	2.36 Gb	21 kb	4.7 Mb	40 Mb
F. catus 8.0	2.6 Gb	45 kb	180 Mb	41 Mb
72x PacBio	2.5 Gb	42.5 Mb		4761 contigs

What are felid innovations compared to other carnivores?

1) Within carnivores, cats have the broadest hearing range (6 hearing genes)

2) 20 positively selected vision genes (increase low-light vision)

3) Two chemosensory gene families
      Or (olfactory receptor, detection of odorants)
      V1r (vomeronasal receptor, detection of pheromone)

Positively Selected Sensory Genes

Hearing: COL9A3, MYO15A
Night & Tunnel Vision: CABP4, CHM, PDE6B
Vision: CNGB3, CPLX4, IMPG1, MKKS, MYO3B, PPEF1, SPATA7
Taste Reception: RTP3, TAS2R38
Olfaction: OR10V1, OR13H1

Hearing: CDKN1B, PTPRQ, MYO15A
Vision: BBS7, BBS9, CA4, GJA10, GUCA1A, LRAT, MYO3B
Neurotransmitter: GRIA2, GRIN2C, NPY, PY1R

Hearing: CNGA2, COL9A3, MYO15A, MYO7A*
Vision: IQCB1, MYO9A, MERTK, MYO7A*
Taste Reception: TAS2R3
Neurotransmitter: GRIA2, NPFFR2, PCDHB4
Olfaction: CNGA2, OR2B11, OR10K1

Legend
Intact V1r Gene
V1r Pseudogene
Intact Or Gene
Or Pseudogene
Rate of Or Gene Gain
Rate of Or Gene Loss
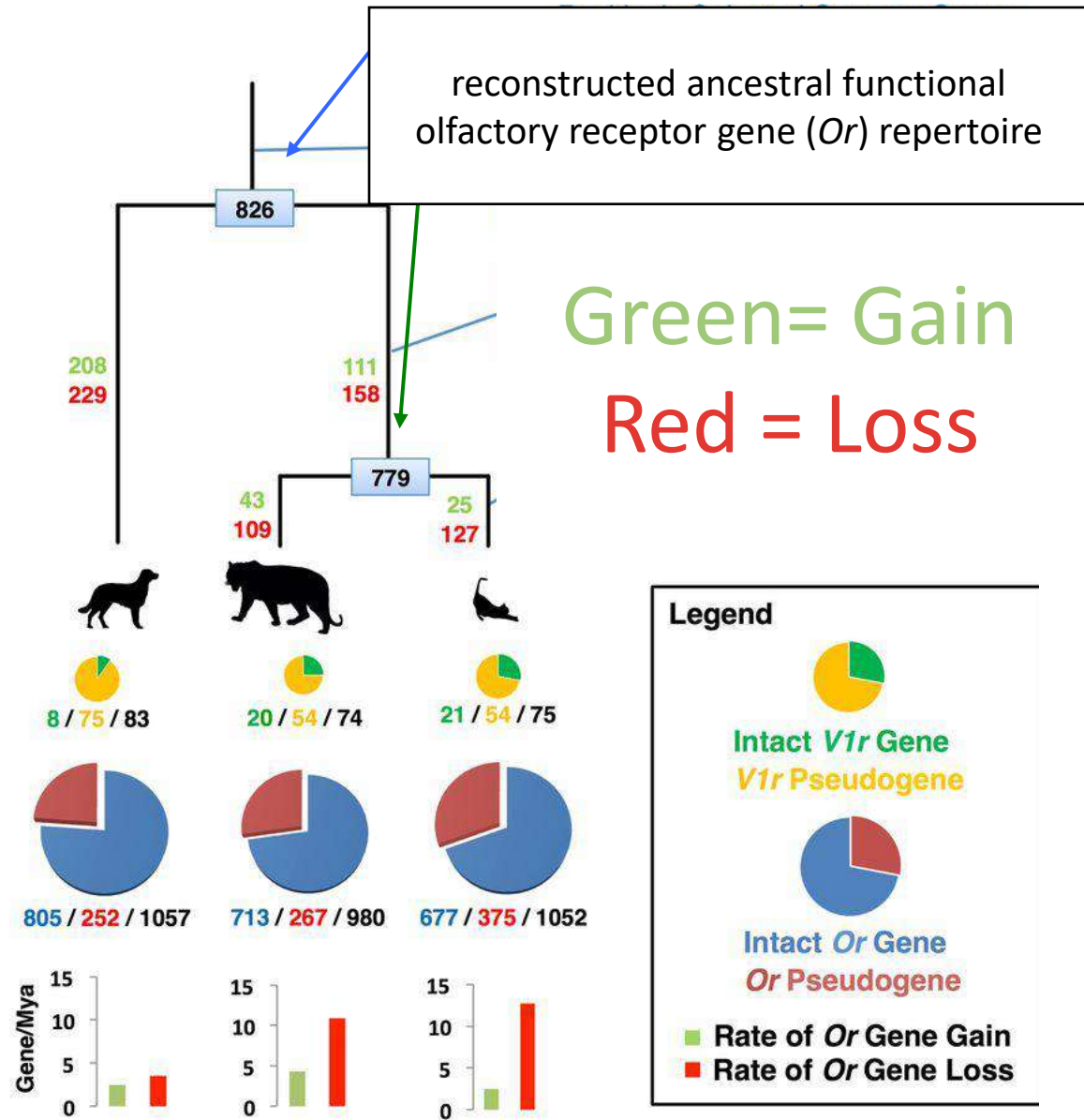
Olfactory & Vomeronasal Receptors

To identify genes families that rapidly evolve, we look for gene expansions.

Analysis of the complete **Or** gene repertoires for Cat, Tiger and Dog. Revealed decrease in felids versus dogs
~700 genes vs. > 800

Vlr gene repertoire is markedly reduced in dogs but expanded in the ancestor of the cat family.
### 8 genes vs. 21 genes

reconstructed ancestral functional olfactory receptor gene (*Or*) repertoire

Green= Gain
Red = Loss

826

208
229

111
158

779

43
109

25
127

8 / 75 / 83   20 / 54 / 74   21 / 54 / 75

805 / 252 / 1057   713 / 267 / 980   677 / 375 / 1052

Gene/Mya

Legend

Intact *V1r* Gene
V1r Pseudogene

Intact *Or* Gene
Or Pseudogene

■ Rate of *Or* Gene Gain
■ Rate of *Or* Gene Loss

What makes a cat - a cat?

- **shorter rostrums than dogs**

- **more specialized carnassials**
  - **less teeth than dogs**

- **more digitigrade**
  - **walks on toes**

- **more carnivorous**

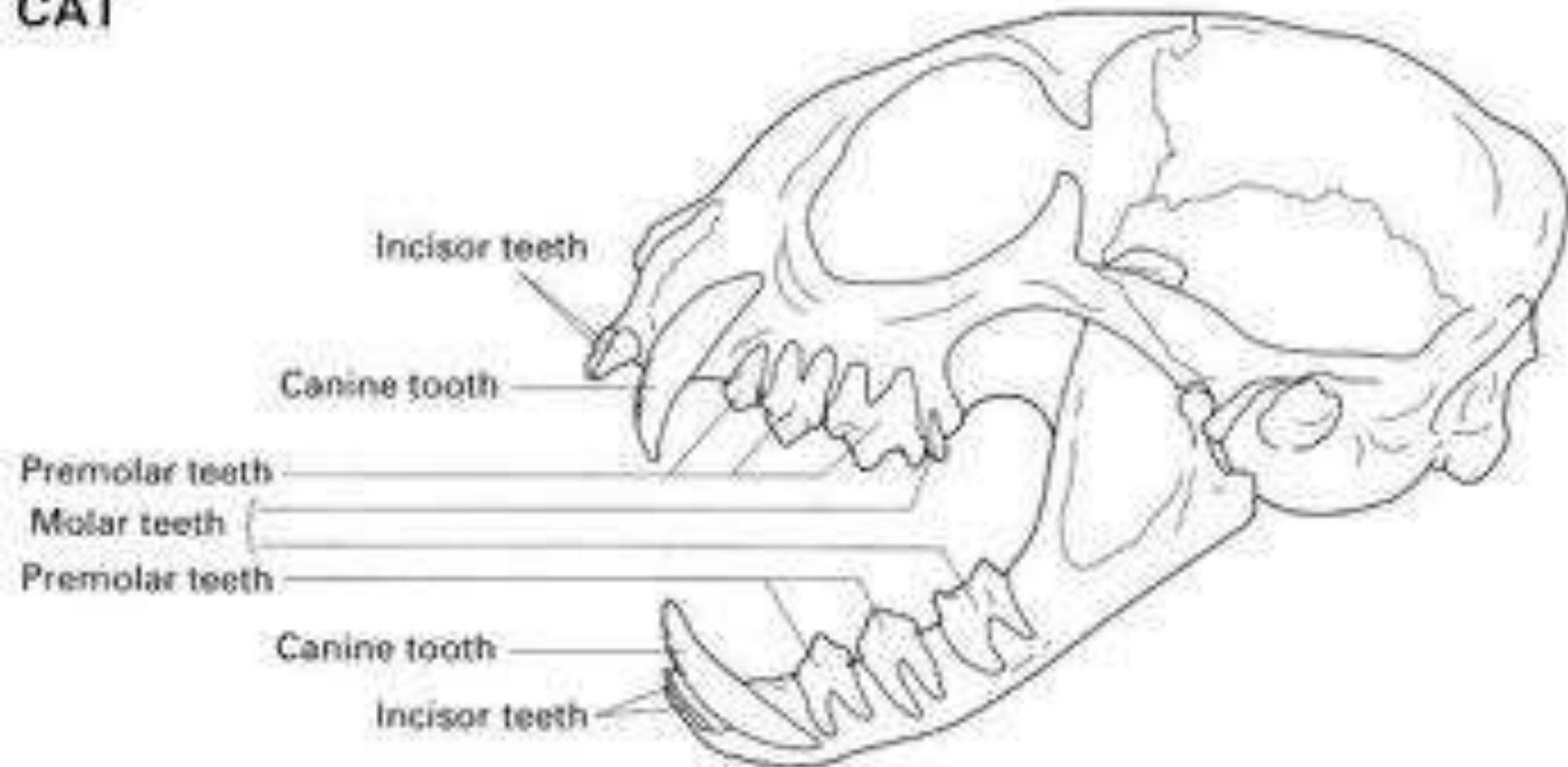- **ambush hunters, arboreal**

- **retractable claws**

Dreamstime.com
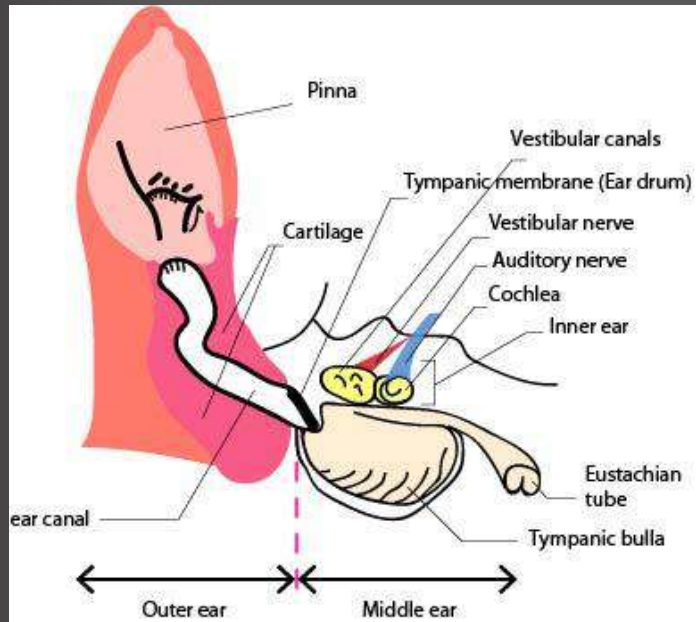
Specialized Dentition of Cats

- **Specialized teeth 2 x 3I/3I (incisors), 1C/1C (canine) , 3P/2P (Pre-molar), 1M/1M (molars)**

CAT

Incisor teeth

Canine tooth

Premolar teeth

Molar teeth

Premolar teeth

Canine tooth

Incisor teeth

Cats are not small dogs!

- ~ 65 mya last common ancestor

- Obligate carnivore vs. omnivore
  - Ambush predator

- Recent vs. more ancient domestication
  - Progenitor still exists for cats

- Mild vs. Intense Selection
  - Minimal on behavior for cats
  - Less of genome under selection
  - Fewer breeds, more recent – aesthetics - simple
  - Large random bred population

Precision Medicine

the time is meow!