Proceeding, 10th World Congress on Genetics Applied to Livestock Production

Cat Domestication & Breed Development

L. A. Lyons

Department of Veterinary Medicine & Surgery, College of Veterinary Medicine, University of Missouri, Columbia, MO USA

ABSTRACT: The dynamics of cat domestication is like no other species. Cat "domestication" is associated with the development of societies, 10,000 - 12,000 years ago. One site of origin seems definitive, the Near East, however, as there were independent sites of agricultural development and various wildcat species inhabited those regions, multiple domestications seem likely for the cat. The most ancient archeological finds place cats within human societies at 5,000 ybp in China and 9,000 ybp in Cyprus. Controlled breedings were evident in Egypt $\sim 2,500 - 3,000$ ybp. Cat breeds were developed in the late 1800s. Cats from the Orient and Western Europe were clearly different and other fur and color varieties demarcated a few other "breeds". Today, although over 50 breeds are declared, far fewer are genetically unique. Presented is the evidence supporting cat domestication and breed development.

Keywords: Felis silvestris catus; mutations; phenotype

Introduction

The earliest archeological evidence for cat associations with humans has been dated to over 3,000 -6,000 BC in Cyprus,¹⁻³ Egypt⁴ and most recently, China.⁵ Whether cats migrated to these different regions with trade and agriculture, or if regional wildcats were independently domesticated in different parts of the Old World remains an unresolved mystery. Since these early times, cats have continued their friendship with humans, having a symbiotic relationship - providing vermin control for humans, while gaining low energy expenditure for meals.^{1,6-8} Hence, as soon as cats were somewhat tamed, they expanded and migrated around the world as man's constant but often inconspicuous As trade and exploration opened new companion. opportunities and resources for man, the cat too expanded its territory around the world.^{9,10} However, like peoples that have formed ethnic groups and races, complete panmictic (random), worldwide breeding has not been possible for the cat, limited by natural boundaries, few founders and sporadic migrations. Thus, mutations and allele frequencies do differ between cat populations, forming races and breeds, as like races and ethnic groups of humans. Genetic studies of worldwide feral populations and breeds have shed light into the population structure of domestic cats,¹¹ providing important clues to their genetic identity and genetic health management.

Genetic Races of Domestic Cats

The domestic cat likely derived from one or more subspecies of wildcat (*Felis silvestris*).¹² At least one

domestication event for the cat was very likely to have been the Near East,¹³ however, independent domestications may be plausible due to the significant genetic distinction of cats in the Far East and the recent archeological find in China that associates cats with humans in an ancient agricultural site.³ Different domestication events from many and perhaps different subspecies of wildcats implies high genetic diversity for the founding populations(s) of domestic cats, which should support health and the ability to adapt to different niches and physiological insults. Without archeological samples with sufficient DNA, only the present day populations of cats can be examined to evaluate genetic diversity and population differentiations. This genetic data can allow the potential extrapolation back to the number and different sites of cat domestication. However, regardless of the cat's ancient history, the extant, present day feline populations are the concern of owners, breeders and veterinarians.

World-wide cat populations have been genetically examined to define the differences that may be important for genetic-based health management.¹¹ Different genetic markers, such as mitochondrial DNA (mtDNA),¹⁴ short ¹⁴ short tandom repeats (STR, a.k.a. microsatellites)¹⁵ and single nucleotide polymorphisms (SNPs),¹⁶ all have different "genetic clocks" and examine different time points in domestic cat history and evolution.^{13,17} The combined analysis of these different markers then paints a picture of the present geographical demarcations and genetic distinction of cat populations. To date, several published studies have examined breeds but only one has extensively examined feral cat populations.¹¹ This previous study of feral cats has been expanded to include additional world-wide populations, refining the genetic races of feral cat populations. Figure 1 depicts groupings of cats based on genetic differentiation. The DNA variants used for population studies are not supposed to be under any type of selection, thus are usually random DNA variants that are not important to health or how the cat looks. However, one can infer that other genetic variants, such as those causing specific phenotypes, diseases or health concerns, would have similar frequencies in the Since the three different genetically-like populations. populations tested in Japan have similar allele frequencies and "cluster" as a common population, health concerns, such as the gangliosidosis, a rare genetic condition that has been documented in feral Japanese domestic shorthair cats,¹⁸⁻²⁰ should be more highly prioritized on a possible list of differentials for sick cats in the region. Cats from the UK have basically the same genetic composition as cats in the USA and Canada, due to their recent Old World to New World migrations in the past 500 years. Trade and colonization has broken the extensive, natural barrier of the

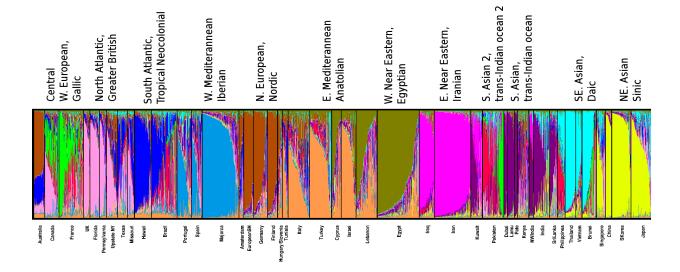


Figure 1. Genetic Structuring of World Cat Populations. The figure presents individual cats and their contributions from different genetic groupings. Each cat with similar genetic contributions are clustered in the figure, producing the groups. After the analysis, the groups are labeled with the country of origin of each cat and the group depicted with a color. For example, the cats from Majorca are genetically similar to cats from Spain and Portugal, but different from other world populations. The cats in these countries do show some mixture with cats from different regions, but are significantly similar. Twelve groupings are significantly distinct, suggesting twelve worldwide races of cats. (Figure courtesy of R. Khan, University of California, Davis)

Atlantic Ocean, thus cats in Australia, Kenya and the Americas show the marks of the past from various European invasions and colonizations. However, cats in close proximity can have different genetic origins, such as the Iberian peninsula and France. The Pyrenees mountain chain has apparently been an ecological barrier to cats, and like other species,²¹ cats of Portugal and Spain appear to be genetically different from the remaining European continental cats. Overall, twelve different groupings, clusters or races of cats can be genetically defined from the various locations that have been sampled. Some island populations appear to have similar genetic signature to the mainland, such as Majorca and Iberia, while other island populations are more distinct, such as San Marcos, an island off the coast of California. Distinct island populations are likely unique when cat migrations are very limited or forbidden, such as the case of San Marcos, and the island is small and likely had limited founders to the population historically. Specific cats from several of the "races" have been extracted to develop our pedigreed fancy breeds.

Genetic Distinction of Cat Breeds

Breeds of cats act similar genetically to ethnic groups of humans. Previous studies have shown that cat breeds have been developed from Western European, the Mediterranean, the Arabian Sea and Southeast Asian populations.¹¹ Ongoing studies may suggest that breeds like the Norwegian Forest cat can now be refined to more specific populations, such as the Northern European / Nordic race of cats. Thus, cat breeds will share health concerns and genetic traits in common with their races of origin. The same types of genetic analyses that were used to compare feral, randomly bred populations of cats have also been used to compare different cat breeds. Table 1 presents a listing of popular cat breeds. Over three dozen breeds have been have been genetically examined with the same genetic markers as the cat races. Approximately 24 breeds appear to be genetically distinct, while the remaining breeds are derived from a specific breed family, such as the Persian, the Siamese or the Burmese families. These "parent" breeds have been bred to produce slightly different cat groups that are often declared a different breed, but are genetically different by perhaps only one genetic mutation. For example, the Persian family is composed of the Persian, Exotic, Selkirk Rex, Scottish Fold and British Shorthair breeds.²² Exotics are different from Persians by having shorthair,²³ Selkirk Rex differ by having curly hair,²⁴ and Scottish Fold differ by having folded ears. Each difference is caused by a single gene mutation, which is not truly sufficient to affect the overall genetic constitution of the breed. Although the definition of cat breeds is arbitrary and of no major consequence, the health of the new and derived breeds can be significantly impacted by the individuals used to found and propagate the new breed. Selkirk Rex and Scottish Folds are new derivatives of Persians have historically been riddled with Persians. polycystic kidney disease (PKD).²⁵⁻³³ Each derivative breed should be monitoring the same health and genetic issues as found in the parent breed, such as PKD in the Persian derived breeds. Any breeds produced from Burmese need to be leery of craniofacial defects,^{34,35} feline oral facial pain,^{36,37} hypokalemia³⁸ and diabetes.^{39,40} Breeds associated with Abyssinians should be cognizant of progressive retinal atrophies and pyruvate kinase deficiency.⁴¹⁻⁴³ Additional reviews on cat mutations have been previously published.44-46

Breed /	Place founded	Derived Breed /	Ocicat		Abyssinian
Family		grouping*	Oriental	Variant	Siamese Family
Abyssinian	Founder—India?	Somali	Persian	Founder—Europe	Exotic
American	Natural mutation	United States—		Mutation	Russian—random
Bobtail		random breds	Peterbald		breds, Don Sphynx
	Natural mutation	United States—		Crossbreed hybrid	Manx, Japanese
American Curl		random breds			Bobtail, United
American	Founder—United				States—random
Shorthair	States	American Wirehair	Pixie-bob		breds
American	Natural mutation	American	1 1110 000	Founder—United	United States—
Wirehair	i tuturur muturom	Shorthair	Ragdoll	States	random breds
Australian	Crossbreed hybrid	Burmese – Persian	Russian Blue	Founder—Europe	fundom ofodb
Mist	erossoreed hybrid	derived	Savannah	Species hybrid	Serval × domestic
Balinese	Variant	Siamese Family	Savaillall	Natural mutation	United Kingdom—
Buillese	Species hybrid	•		Inatural inutation	random breds,
	Species hybrid	Leopard cat ×	Scottish Fold		British SH, Persian
Bengal		Egyptian Mau,	Scottisti Fold	Natural mutation	,
	E I.	Abyssinian		Natural mutation	United States—
	Founder—		0.11 ¹ .1 D		random breds,
Birman	Southeast Asia	D	Selkirk Rex	E	Persian
	Variant	Burmese,	<i>a</i> :	Founder—	a: 1 :i
		Singapura,	Siamese	Southeast Asia	Siamese Family
Bombay		Tonkinese		Founder—Europe	Russian—random
British	Founder—Europe		Siberian		breds
Shorthair		Scottish Fold		Variant	Bombay, Burmese,
	Founder—	Bombay,	Singapura		Tonkinese
	Southeast Asia	Singapura,		Founder—Arabian	African—random
Burmese		Tonkinese	Sokoke	Sea	breds
Burmilla	Crossbreed hybrid	Burmese, Persian	Somali	Variant	Abyssinian
Chartreux	Founder—Europe		Sphynx	Natural mutation	Devon Rex
Colorpoint	Variant			Variant	Bombay, Burmese,
Shorthair		Siamese Family	Tonkinese		Singapura
	Natural mutation	United Kingdom—	Turkish	Founder—	
Cornish Rex		random breds	Angora	Mediterranean	
	Natural mutation	United Kingdom—		Founder—	
		random breds,	Turkish Van	Mediterranean	
Devon Rex		Sphynx	*Modified from genetic studies based on 29 tetranucleotide short tandem repeat markers, 39 dinucleotide short tandem repeat markers, and		
	Founder—				
Egyptian Mau	Mediterranean		unpublished data (I	LA Lyons)	
European	Founder—Europe				
Exotic	Variant	Persian		G	
Havana Brown	Variant	Siamese Family		Summary	
Japanese	Founder	Sidillese I dilling			
Bobtail				ling the relationship of	
Javanese	Variant	Siamese Family	origin and their breed families can be predictive for health care issues. Genetic testing can provide definitive answers for many health concerns and can predict risk for certain diseases.		
	Founder—	Shamese F anniy			
Korat	Southeast Asia				
Kurilean	Natural mutation	Eastern Russia,		cine is improving hum	
Bobtail	ratural mutation	Kuril Islands		e for the domestic ca	
	Natural mutation	United States—		educe the costs of ge	
LaPerm	Natural mutation			to perform large batt	
	Foundar United	random breds	and eventually whole genome sequencing. Veterinarians will have more predictive powers for health concerns and will be able to implement proper interventions. As the genetic data becomes more readily available, veterinarians will be		
Maine Coon	Founder—United				
	States	TT. '. 1 TZ' 1			
	Natural mutation	United Kingdom—			
Manx		random breds		les in health care mana	
	Natural mutation	United States—		lations. Genetic coun	
Munchkin		random breds		medicine, bringing tog	
	E. 1. E.				
Norwegian Forest Cat	Founder—Europe		individual into co	nsideration with the g	genetic diversity and

live longer and higher quality lives, so too will our furry companion felines.

Acknowledgements

This project was funded in part previously by the National Center for Research Resources R24 RR016094 and is currently supported by the Office of Research Infrastructure Programs OD R24OD010928.

References

- 1. Vigne JD. The origins of animal domestication and husbandry: a major change in the history of humanity and the biosphere. *ComptesRendus bBiologies.* Mar 2011;334(3):171-181.
- Vigne JD, Briois F, Zazzo A, et al. First wave of cultivators spread to Cyprus at least 10,600 y ago. *Proc Nat Acad Sci USA*. May 29 2012;109(22):8445-8449.
- 3. Vigne JD, Guilaine J, Debue K, Haye L, Gerard P. Early taming of the cat in Cyprus. *Science*. Apr 9 2004;304(5668):259.
- 4. Malek J. *The cat in Ancient Egypt*. Philadelphia: University of Pennsylvania; 1993.
- Hu Y, Hu S, Wang W, et al. Earliest evidence for commensal processes of cat domestication. *Proc Nat Acad Sci USA*. Jan 7 2014;111(1):116-120.
- 6. Clutton-Brock J. A natural history of domesticated mammals. London: Cambridge University Press, British Museum; 1987.
- Driscoll CA, Clutton-Brock J, Kitchener AC, O'Brien SJ. The Taming of the cat. Genetic and archaeological findings hint that wildcats became housecats earlier--and in a different place--than previously thought. *Sci Am.* Jun 2009;300(6):68-75.
- 8. Tresset A, Vigne JD. Last hunter-gatherers and first farmers of Europe. *Comptes Rendus Biologies*. Mar 2011;334(3):182-189.
- 9. Todd NB. Cats and commerce. *Sci Am.* 1977;237:100-107.
- 10. Todd NB. An ecological, behavioral genetic model for the domestication of the cat. *Carnivore*. 1978;1:52-60.
- Lipinski MJ, Froenicke L, Baysac KC, et al. The ascent of cat breeds: genetic evaluations of breeds and worldwide randombred populations. *Genomics*. 2008;91(1):12-21.
- 12. Nowell K, Jackson P. Wild cats status survey and conservation action plan. Gland: IUCN; 1996.
- Driscoll CA, Menotti-Raymond M, Roca AL, et al. The Near Eastern origin of cat domestication. *Science*. Jul 27 2007;317(5837):519-523.
- Grahn RA, Kurushima JD, Billings NC, et al. Feline nonrepetitive mitochondrial DNA control region database for forensic evidence. *Forensic Sci Int Genet*. Feb 25.
- Menotti-Raymond M, David VA, Pflueger SM, et al. Patterns of molecular genetic variation among cat breeds. *Genomics*. Jan 2008;91(1):1-11.
- Kurushima JD, Lipinski MJ, Gandolfi B, et al. Variation of cats under domestication: genetic assignment of domestic cats to breeds and worldwide random-bred populations. *Animal Gen.* Nov 22 2012.
- Driscoll CA, Menotti-Raymond M, Nelson G, Goldstein D, O'Brien SJ. Genomic microsatellites as evolutionary chronometers: a test in wild cats. *Genome Res.* Mar 2002;12(3):414-423.
- Hasegawa D, Yamato O, Kobayashi M, et al. Clinical and molecular analysis of GM2 gangliosidosis in two apparent littermate kittens of the Japanese domestic cat. J Feline Med Surg. Jun 2007;9(3):232-237.
- 19. Uddin MM, Hossain MA, Rahman MM, et al. Identification of Bangladeshi domestic cats with GM1 gangliosidosis caused by

the c.1448G>C mutation of the feline GLB1 gene: case study. J Vet Med Sci / Japan Soc Vet Sci. 2013;75(3):395-397.

- Yamato O, Matsunaga S, Takata K, et al. GM2-gangliosidosis variant 0 (Sandhoff-like disease) in a family of Japanese domestic cats. *Vet Rec.* Dec 4 2004;155(23):739-744.
- Martin-Burriel I, Rodellar C, Canon J, et al. Genetic diversity, structure, and breed relationships in Iberian cattle. *J Animal Sci.* Apr 2011;89(4):893-906.
- Filler S, Alhaddad H, Gandolfi B, et al. Selkirk Rex: morphological and genetic characterization of a new cat breed. J *Hered.* Sep-Oct 2012;103(5):727-733.
- Kehler JS, David VA, Schaffer AA, et al. Four independent mutations in the feline fibroblast growth factor 5 gene determine the long-haired phenotype in domestic cats. *J Hered.* Sep-Oct 2007;98(6):555-566.
- Gandolfi B, Alhaddad H, Joslin SE, et al. A splice variant in KRT71 is associated with curly coat phenotype of Selkirk Rex cats. *Sci Rep.* 2013;3:2000.
- Barthez PY, Rivier P, Begon D. Prevalence of polycystic kidney disease in Persian and Persian related cats in France. J Feline Med Surg. Dec 2003;5(6):345-347.
- Beck C, Lavelle RB. Feline polycystic kidney disease in Persian and other cats: a prospective study using ultrasonography. *Aust Vet J.* Mar 2001;79(3):181-184.
- Biller DS, Chew DJ, DiBartola SP. Polycystic kidney disease in a family of Persian cats. J Am Vet Med Assoc. Apr 15 1990;196(8):1288-1290.
- Biller DS, DiBartola SP, Eaton KA, Pflueger S, Wellman ML, Radin MJ. Inheritance of polycystic kidney disease in Persian cats. *J Hered.* Jan-Feb 1996;87(1):1-5.
- 29. Bogdanova N, Dworniczak B, Dragova D, et al. Genetic heterogeneity of polycystic kidney disease in Bulgaria. *Hum Genet.* Jun 1995;95(6):645-650.
- Eaton KA, Biller DS, DiBartola SP, Radin MJ, Wellman ML. Autosomal dominant polycystic kidney disease in Persian and Persian-cross cats. *Vet Pathol.* Mar 1997;34(2):117-126.
- 33. Lyons L, Biller D, Erdman C, et al. Feline polycystic kidney disease mutation identified in PKD1. *J Am Soc Nephrol.* 2004.
- 34. Zook. Encephalocele and other congenital craniofacial anomalies in Burmese cats. *Vet Med/Small Anim Clin.* 1983;78:695-701.
- Noden DM, Evans HE. Inherited homeotic midfacial malformations in Burmese cats. J Craniofac Genet Dev Biol Suppl. 1986;2:249-266.
- Rusbridge C, Heath S, Gunn-Moore DA, Knowler SP, Johnston N, McFadyen AK. Feline orofacial pain syndrome (FOPS): a retrospective study of 113 cases. *J Feline Med Surg.* Jun 2010;12(6):498-508.
- 37. Heath S, Rusbridge C, Johnson N, Gunn-Moore D. Orofacial pain syndrome in cats. *Vet Rec.* Nov 24 2001;149(21):660.
- Gandolfi B, Gruffydd-Jones TJ, Malik R, et al. First WNK4hypokalemia animal model identified by genome-wide association in Burmese cats. *PloS one*. 2012;7(12):e53173.
- Rand JS, Bobbermien LM, Hendrikz JK, Copland M. Over representation of Burmese cats with diabetes mellitus. *Aust Vet J.* Jun 1997;75(6):402-405.
- O'Leary CA, Duffy DL, Gething MA, McGuckin C, Rand JS. Investigation of diabetes mellitus in Burmese cats as an inherited trait: a preliminary study. *New Zeal Vet J.* Nov 2013;61(6):354-358.
- Menotti-Raymond M, Deckman K, David V, Myrkalo J, O'Brien S, Narfström K. Mutation discovered in a feline model of human congenital retinal blinding disease. *Invest Ophthalmol Vis Sci.* . 2010;51(6):2852-2859.
- Menotti-Raymond M, David VA, Schaffer AA, et al. Mutation in CEP290 discovered for cat model of human retinal degeneration. *J Hered.* May-Jun 2007;98(3):211-220.

- 43. Grahn RA, Grahn JC, Penedo MC, Helps CR, Lyons LA. Erythrocyte Pyruvate Kinase Deficiency mutation identified in multiple breeds of domestic cats. *BMC Vet Res.* Oct 30 2012;8(1):207.
- 44. Lyons LA. Feline genetics: clinical applications and genetic testing. *Topics Comp Animal Med.* Nov 2010;25(4):203-212.
- 45. Lyons LA. Genetic testing in domestic cats. *Mol Cell Probes*. Dec 2012;26(6):224-230.
- 46. Lyons LA. Genetic Testing in Domestic Cats. In, *Consultations in Feline Medicine*, August JR, ed, Vol 6. St. Louis, MO: Saunders Elsevier; 2010.