Genetics of Cat Populations and Breeds: Implications for Breed Management for Health!

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Introduction

Inclusive of feral domestic cats, the worldwide population of *Felis silvestris catus* is ~ 600 million and represents on the order of 99% of all living individuals of the mammalian family Felidae (Dauphiné, Cooper 2009). In the United States, 38.4 million households own cats, totaling 88 million individual animals, which incur $400 in expenditures per year per household.[4] Cats incur veterinary healthcare costs in a direct fashion, but they may be important vectors for pathogens that impact human behavior, such as *Toxoplasma gondii*. Latent infection with *Toxoplasma gondii* has been implicated in cultural variation. Associations with mental illness and infected status have also been reported. Thus, the management of cat populations is increasing in the public interest. Understanding their genetic relationships helps to manage their healthcare and predict and prevent unwanted genetic diseases and traits.

Wildcat Origins

The domestic cat, *Felis catus,*[25,38] is one of 38 species in the cat family Felidae*,* being a member of the *Felis* lineage.[52] The *Felis* lineage is composed of three small African felids and four small felids that may be the progenitors of the domestic cat, including *Felis lybica* (African wildcat), *Felis silvestris* (European wildcat), *Felis ornata* (Asian wildcat), and *Felis bieti* (Chinese desert cat).[28,32] The domestic cat and the wildcat species can interbreed, producing fertile hybrids;[26] thus, their demarcation as subspecies and even distinct species can be disputed. Because the common housecat is a domesticated derivative, the term *Felis catus* has been readopted and does not clearly denote the genetic relationship to the progenitor wildcats or their subspecies.[25] The relationship of the African, European, and two Asian wildcats is somewhat controversial; currently, 21 subspecies are defined within these groupings.[34] Other than the South African subspecies of African wildcat, *Felis lybica cafra,* most species of wildcat and their associated subspecies may be the progenitors of domestic cat populations,[21,40] with *Felis lybica* having the most scientific support.

Domestic cats likely participated actively in their own domestication; both humans and felines developed a symbiotic, commensal, mutual tolerance. Several independent sites of early civilizations are known to have developed between 8000 and 3000 BCE, including the Huang He River region of China; the Indus Valley in Pakistan; and the Fertile Crescent region, which extends from Iraq into Turkey, south along the Levant region of the Mediterranean coast, and, arguably, into the Nile Valley of Egypt.[8] As humans made the transition from hunter-gatherers to the more sedentary lifestyle of the farmer, and permanent settlements subsequently developed, villages produced refuse piles and grain stores, attracting mice and rats,[11] primary prey species for the small wildcat. To obtain these easy meals, bold wildcats perhaps began to tolerate humans, and humans accepted the cat because of its utility in vermin control.

Domestic Populations

Random-bred and feral cats represent the overwhelming majority of cats throughout the world, not fancy cat breed populations,[3] although most genetic studies have focused on cat breeds to date. Considering the worldwide distribution of cats, the United States likely has the highest proportion of pedigreed cats. However, the proportion of pedigreed versus random-bred cats is still fairly low; only 10% to 15% of feline patients at the University of California - Davis, Veterinary Medicine Teaching Hospital is represented by pedigreed cats.[42] A general understanding of cat breed development and a more in-depth understanding of a limited number of foundation cat breeds will help predict healthcare problems on the basis of each cat's genetic background.

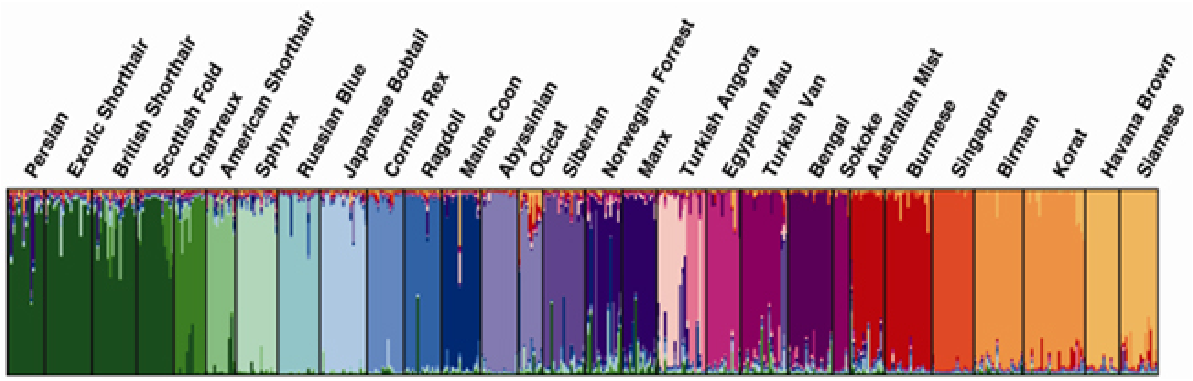
Genetic studies of over a thousand cats from worldwide populations have allowed the definition of approximately ten genetically distinct cat populations from around the world. These populations can be used as the foundation genetic pools for specific breeds. The first documented cat show that judged cats on their aesthetic value occurred in London, England, at the Crystal Palace in 1871.[1] This competition presented only a handful of breeds, including the British, Persian, Abyssinian, Angora, and Siamese. Thus, these early documented cat breeds likely represented genetically distinct populations insofar as strict breeding programs were not established at the time. However, now they are genetically distinct breeds, but their genetic origins can be traced to their foundation populations.

Most worldwide cat fancy associations, such as the Cat Fanciers' Association (CFA),[16,17] The International Cat Association (TICA),[61] the Governing Council of the Cat Fancy (GCCF),[2] and the Fédération Internationale Féline (FIFe),[22] recognize approximately 35 to 41 cat breeds, although only a few breeds overwhelmingly dominate the census of the registries. Persian cats and related breeds (e.g., Exotics, a shorthaired Persian variety) are among the most popular cat breeds worldwide and represent an overwhelming majority of pedigreed cats. Although not all cats produced by breeders are registered - perhaps only 20% to 30% - the CFA, one of the largest cat registries worldwide, generally registers approximately 40,000 pedigreed cats annually.[18] Approximately 16,000 to 20,000 are Persians, and approximately 3000 are Exotics; thus, the Persian group of cats represents more than 50% of the cat fancy population. Common breeds that generally have at least 1000 annual registrants are Abyssinians, Maine Coons, and Siamese. Other popular breeds include the Birman and Burmese, which are more prevalent in other areas, such as the United Kingdom. Most of these popular breeds also represent the oldest and most established cat breeds worldwide. However, because of different breeding standards in different registries and population sub-structuring, not all cats identified as the same breed are genetically alike. Disease frequencies may be different for breeds in different parts of the world. For example, polycystic kidney disease has been shown to have about the same prevalence in Persian cats around the world,[5,6,10,15] but hypokalemia in the Burmese is more limited to cats in the United Kingdom and Australia[9,36] and is not found in populations in the United States. Some lines of Burmese in the United States segregate for a craniofacial defect, which is not commonly found in Burmese cats outside the United States.[50] The breed sub-structuring may be partially due to rabies control measures that reduce migration of cats among countries, but it is also likely that the known health concerns in the breeds have led to strong restrictions of imports and exports of fancy-breed cats.

A more recently developed cat breed, the Bengal,[31] which is a hybrid between the Asian Leopard cat, *Prionailurus bengalensis*, and the domestic cat, has gained significant popularity throughout the world, even though some registries currently do not recognize the breed. Because of limited wildcat founders, the hybrid cats may have decreased genetic variation. These hybrid cats may also have allelic incompatibilities for a given gene; the genes between the two species, leopard cat and domestic cat, have millions of years of evolutionary divergence, which allows differences at the DNA sequence level of a gene. Hence, an accumulation of different genetic variants that are functional within the species, but nonfunctional across the felid species, are likely present in some Bengal cats. Thus, hybrid cat breeds may have unexpected health problems and infertility, creating a challenge for both genetic studies and primary healthcare.

Many modern cat breeds derived from an older "foundation" breed, thereby forming breed families or groups. Approximately 22 breeds can be considered foundation or "natural" breeds. Genetic studies have also shown that the foundation breeds have either significantly different genetic pools or sufficient selection and inbreeding that created significant genetic distinction (Figure 1). Cat breeds derived from the foundation breeds are often based on single gene variants, such as longhaired and shorthaired varieties, or even a hairless variety, as found in the Devon Rex and Sphynx grouping. Color variants also tend to demarcate breeds, such as the "pointed" variety of the Persian, known as the Himalayan by many cat enthusiasts and as a separate breed by some associations, such as TICA.[61] These derived breeds are not genetically significantly different and therefore share health concerns. Selkirk Rex, American Shorthair, and British Shorthair all use Persians to help define their structure; thus, these breeds also suffer from polycystic kidney disease,[43] and their genetic signatures are very similar to that of Persians, nearly obscuring their original population foundations of U.S. and UK cats.

Figure 1. Genetic distinction of domestic cat breeds



Different colors represent genetically distinct groups of cats. Different breeds of the same color imply they form a breed "family" in that these breeds are not genetically distinct from one another.

A Population Case Study: Turkish Cats

The Lyons' Feline Genetics Laboratory has a standing interest in the dynamics of cat populations and domestic cat breeds. Through interactions with cat breeders, both in the United States and abroad, and also with collaborators from Turkish universities and animal shelters, the laboratory performed **three** studies on the genetics of cats reportedly and documented to be from Turkey.

Round 1

The first study was published in a scientific journal in 2007 and analyzed 14 Turkish Angora and 21 Turkish Van. These cats were primarily from breeders within the United States, and cats were selected to have no grandparents in common. Contributions from as many different breeders was attempted to properly survey the gene pool and genetic structure of the Turkish Angora and Turkish Van breeds in comparison to a variety of other breed cats from the USA. Random-bred cats from collaborators at Turkish universities were also analyzed.

The major outcomes of the first analyses of these breeds indicated:

1. Cats from the Mediterranean area, including Turkey, Israel, Cairo, Egypt, and Italy are genetically distinct from cats of Western Europe, Asia, and the Eastern coast of Kenya, forming four major and distinct populations (races) of cats in the world.
2. Three cat breeds appear to have their ancient origins in the Mediterranean, including Turkish Angora, Turkish Van, and potentially the Egyptian Mau.
3. The Turkish Van and Turkish Angora are genetically distinct breeds.
4. The Turkish Angora had more genetic diversity and a lower inbreeding level in comparison to Turkish Vans, suggesting they are slightly more genetically healthy.
5. Both Turkish Angora and Turkish Van were at the higher end of the spectrum of inbreeding levels amongst the cats evaluated, suggesting minimal outcrossing may be warranted.
6. The genetic variation of the random-bred Turkish cats was amongst the highest of all cat populations, suggesting the region was the origin of cat domestication.

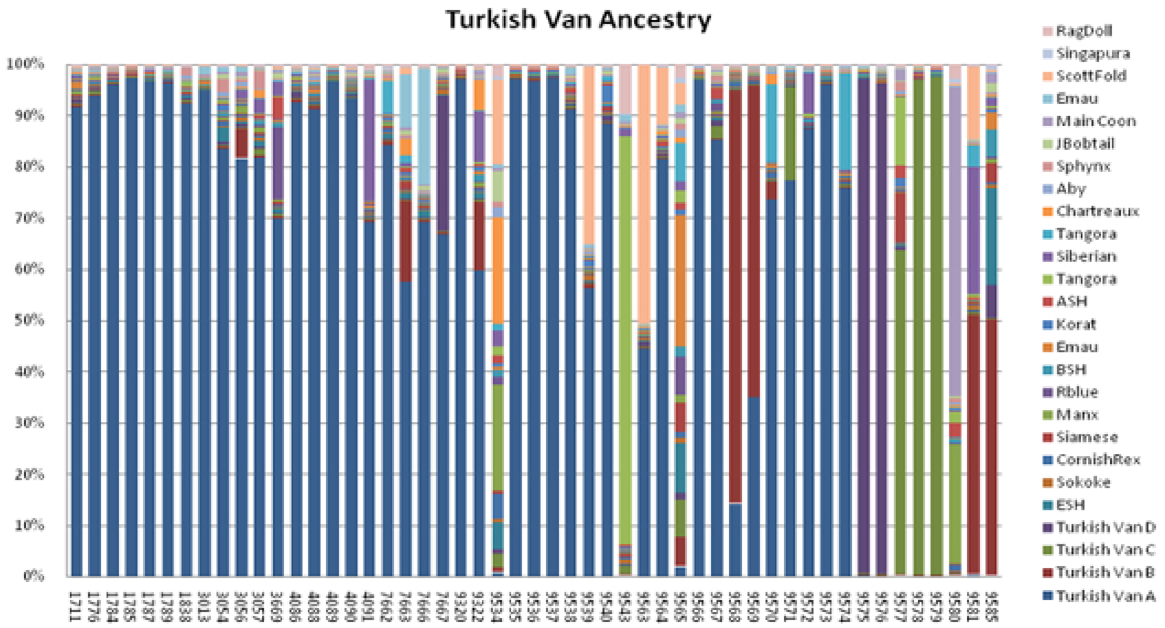
Round 2 (Figure 2)

At the request of various Turkish Van breeders and because of the interest to add genetic diversity to the Van breed by using cats from Turkey, the study was extended and analyzed an additional 30 cats. These cats represented individuals supplied by several different breeders from the USA, The Netherlands, Sweden, and Turkey. Four cats were included that were listed as crosses with cats noted as Van Kedisi. These cats were genetically compared to the original 21 cats of the breed-diversity study.

The outcomes of this second study suggested:

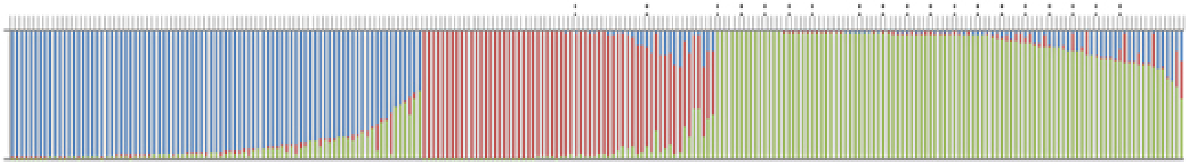
1. Sixteen (16) of the 30 cats were highly significantly similar genetically to the Turkish Vans from the USA, suggesting these cats constitute the same breed. These cats were designated Type A Turkish Vans (Figure 2, red in Figure 3).The three of four cats noted as crosses with Van Kedisi cats were in this grouping.
2. One cat was significantly similar to a Turkish Angora (Type C in Figure 2, blue in Figure 3).
3. Thirteen (13) cats had genetics that were significantly different from Turkish Vans, potentially from three different genetic sources designated as Type B, C and D.

Figure 2. Genetic analysis of Turkish cats



Genetic profiles of Turkish Van cats analyzed in the Turkish cat study. Colors indicate different genetic profiles. Each line is a different cat. Cats to the left are registered Turkish Vans in the USA.

Figure 3. Genetic analysis of Turkish cats in comparison to street cats from Cyprus and Turkey



Genetic profiles of cats analyzed in the Turkish cat study. Colors indicate different genetic profiles. Each line is a different cat. Blue = Turkish street cats and Turkish Angoras; red = Turkish Vans; and green = cats from Cyprus. Three genetic groupings were statistically significant.

Round 3

After debate and complaints that breeders did not get to fairly contribute to the second study, even though submissions were accepted for over a year, an additional 130 cats were considered that were submitted by many different breeders. The breeders were asked to prioritize cats again. Ninety-three (93) had sufficient DNA for the analysis. In addition, random-bred cats from Cyprus, which were collected from the Malcolm Cat Sanctuary as part of a study with National Geographic, were available for comparison. A larger analysis was performed that included Turkish Angoras, random-bred cats from Turkey and Cyprus, all cats submitted for the previous studies, and the new 93 cats, for a **database of 248 cats**. All cats were considered in one large analysis. The analysis partitioned the cats based solely on genetic variation, **not by any other identification**. Three major genetic groupings of cats were observed. A cutoff value of 50% similarity was used to assign a cat to a group. The groupings were then inspected to see what cats they contained.

The overall summary of the Turkish cat study suggested:

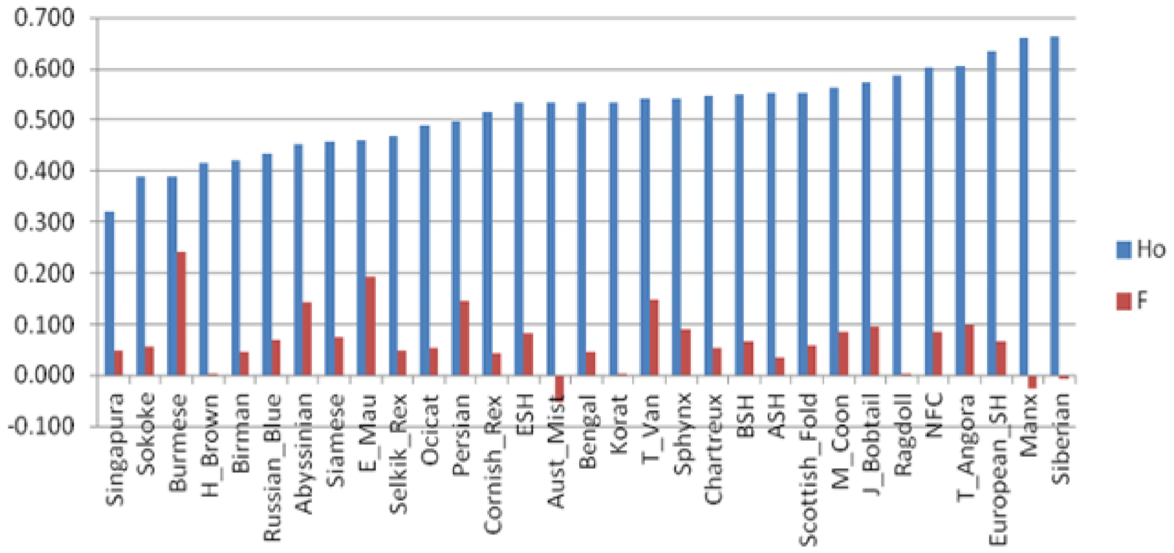
1. Results from the previous two studies are upheld and consistent.
2. Turkish Angora is a distinct breed and with significant contribution from Turkish random-bred cats. **The Turkish Angora breed contains the most representative cats of Turkey.**

3. Turkish Vans are a distinct breed and show significantly less influence from Turkish random-bred cats.
4. Cyprus cats are a distinct population within the Mediterranean.
5. Some limited migration of cats occurs between Cyprus and Turkey.
6. Types B, C and D cats from Round 2 were cats from Cyprus.
7. The Turkish Van is genetically similar to the four cats submitted as Van Kedisi.

Conclusions

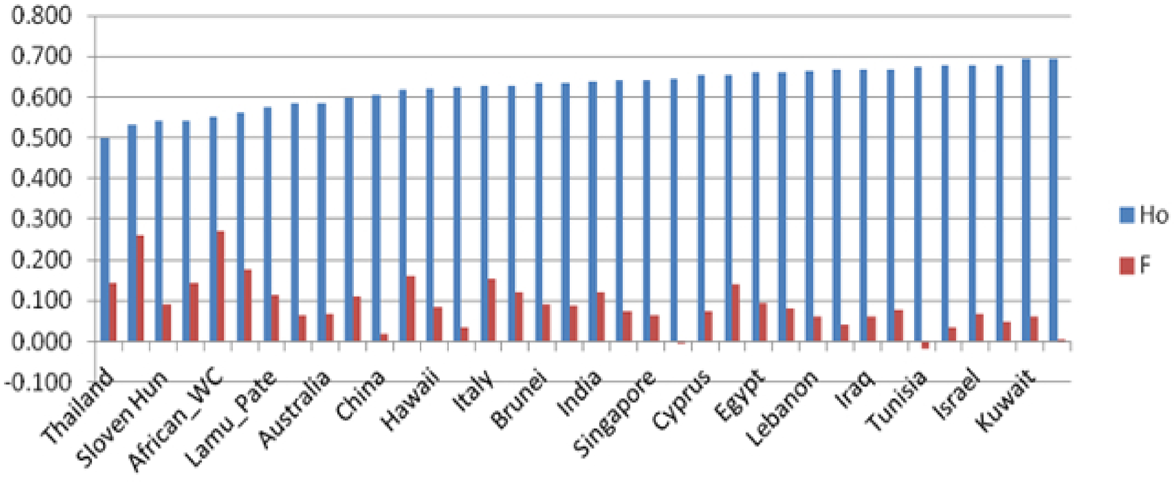
The analysis of cat populations supports several aspects of genetic research but importantly also the management of cat breeds. Breeds that are genetically related all share the same health concerns. These breed "families" would be starting candidates for discussions of outcrossing to increase genetic diversity (Figure 4). In addition, by knowing the populations of origin, the health concerns of the foundation populations could be at risk and need to be considered for specific diseases and vice versa. Foundation, random-bred cats could be used in outcrossing programs to increase gene pools but likewise need to be monitored for unwanted genetic traits.

Figure 4a. Estimating cat breed health with genetics: genetic variation in cat breeds



Ho is average heterozygosity; F is the fixation index.

Figure 4b. Estimating cat breed health with genetics: genetic variation in random-bred cats



Ho is average heterozygosity; F is the fixation index.

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