UNIVERSITY *of* MISSOURI

DEPARTMENT OF VETERINARY MEDICINE & SURGERY

COLLEGE OF VETERINARY MEDICINE

Genetic Notes on the Burmese Cat Breed

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The Feline Genetics Laboratory, formerly of the University of California – Davis (UC Davis), now at the University of Missouri, has had long associations with Burmese breeders and veterinary researchers to define and identify the genetic mutations that cause various maladies in the Burmese breed. Many published studies (several listed below) have demonstrated that the Burmese breed has many genetic conditions, although the prevalence of these conditions is variable between countries. The Burmese in the USA are historically known for the autosomal recessive craniofacial defect that developed from the Contemporary lines of USA Burmese. Burmese carrying this condition have been identified in the UK, Europe and Australia due to the importation and use of the Contemporary lines. In addition, any other breed that has outcrossed to Contemporary Burmese has risk of the craniofacial defect. Recently, American Burmese breeders may be pursuing an organized project for heart disease.

In contrast, non - American Burmese are afflicted with several other conditions including GM2 gangliosidosis, hypokalemia, oral facial pain, diabetes, high triglycerides, a mid-line closure defect, and dermatosparaxis (stretchy skin, cutaneous asthenia, Ehlors-Danlos Syndrome). The genetic mutations for hypokalemia and GM2 gangliosidosis have been identified and like the craniofacial defect, the genetic test is available to assist breed management. Genetics studies regarding oral facial pain, diabetes, high triglycerides, flat-chested kittens, and dermatosparaxis are underway by our laboratory, in collaboration with other researchers, and independently by other researchers.

Our genetic studies have also included examining the population genetics of the different cat breeds and worldwide populations. In 2007, we published the first breed study that demonstrated that Singapura, Burmese and Birman had the lowest genetic diversity of the cat breeds we examined. A study between Singapura breeders and the UC Davis Veterinary Genetics Laboratory (VGL) supported our findings. Our recent studies demonstrate that the non-USA Burmese has as low genetic variation as the USA lines of Burmese. ***We strongly recommended outcrossing for all the Burmese breeds, including USA and non-USA Burmese.***

Based on genetics, the Burmese breed originated from cats of Southeast Asia. Our genetic studies group cats from Thailand, Cambodia, Vietnam, Brunei and the Philippines as Southeast Asia cats. Historically, Burmese are considered to have origins from Thailand. Thus, random bred cats from Thailand and perhaps other regions of Southeast Asia are recommended as strong genetic candidates for outcrossing. Genetic tests for colors and health conditions can assist the selection of

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cats that may be the most advantageous for outcrossing. Other breeds with Southeast origins would also be of value to the Burmese outcrossing program, including Singapura, Bombay, and Burmese from any country. Burmilla and Asian have been crossed with Persian cats, which have western origins, thus, the use of these recent crossbred breed cats would add significant diversity, but of a different "racial" origins. Other Southeast Asian breeds include Siamese (and its breed derivatives), Korat, and Birman.

Because of our various genetic projects that include Burmese from different countries, we have been able to compare the genetics of the Burmese breed groups regionally. USA Burmese have high homozygosity (0.38), implying low genetic diversity (See attached report). The non-USA Burmese, which is a mixture of UK and Australian Burmese also have low diversity and high homozygosity (0.41), as compared to random bred cats (0.04) and other breeds. When we examine the Burmese diversity by plotting the genetic differences (termed multi-dimensional scaling (MDS), we find that the USA and non-USA Burmese do not cluster together and form independent genetic groups. The USA cats have a larger spread to their cluster as it includes Contemporary and Traditional lines of Burmese. ***Thus, Burmese breeders may consider crossing the Burmese cats from different countries to help improve genetic diversity.***

Other genetic conditions in Southeast Asian cats include different forms of gangliosidosis in Korat and Siamese cats and pyruvate kinase deficiency in Singapura. Some Birman lines may have a susceptibility to FIP.

Overall, we have more genetic projects concerning Burmese than for any other breed and our various genetic studies have repeatedly demonstrated that Burmese, regardless of country, have amongst the lowest genetic diversity of all cat breeds. An organized and multi-faceted outcrossing program for the breed is highly recommended which includes the use of genetic testing and outcrossing to different populations and breeds.

Best regards,

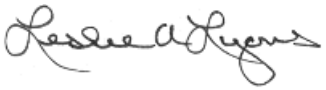

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Table 1 The phenotypic traits of the domestic cat **– special interest for Burmese**

Disease / Trait (alleles) OMIA Entry	MOI‡	Phenotype	Gene	Gene Name	Mutation
Agouti (A^+, a, A^{Pbe})[1, 2] 000201-9685	AR	Banded fur to solid	*ASIP*	*Agouti-signaling protein*	c.122_123delCA; Pbe haplotype
Brown (B^+, b, b^l)[3, 4] 001249-9685	AR	Brown, light brown color variants	*TYRP1*	*Tyrosinase related protein*	b = -5IVS6, b^l = c.298C>T
Color (C^+, C^b, C^s, c)[4-6] 000202-9685	AR	Burmese, Siamese color pattern, full albino	*TYR*	*Tyrosinase*	c^b = c.715G>T, c^s = c.940G>A, c = c.975delC
Dilution (D^+, d)[7] 000206-9685	AR	Black to grey / blue, Orange to cream	*MLPH*	*Melanophilin*	c.83delT
Extension (E^+, e, e^r) – *Amber*[8] 001199-9685	AR	Brown/red color variant	*MC1R*	*Melanocortin receptor 1*	c.250G>A; c.439TCT
Japanese Bobtail (J, j^+)[9]	AD	*Kinked tail*	*HES7*	*Hairy and Enhancer of Split family, transcription factor 7*	c.5A>G
Longhair (L^+, l)[10, 11] 000439-9685	AR	Long fur	*FGF5*	*Fibroblast growth factor 5*	c.356_367insT, c.406C>T, c.474delT, c.475A>C
Orange (O, o^+)	X linked	Change in pigment hue	*unknown*	*unknown*	*unknown*
Tabby(T^M, t^b)[12] 001429-9685	AR	Blotched/classic pattern	*TAQPEP*	*Transmembrane aminopeptidase Q*	S59X, T139N, D228N, W841X
Ticked (T^a, t) 001484-9685	AD	No Tabby pattern	*unknown*	*unknown*	*unknown*
White (W, w^+)[13] 000209-9685	AD	Loss of pigmentation	*KIT*	*KIT*	FERV1 LTR ins
Wide-band	AR?	Length of pheomelanin band in hair	*unknown*	*unknown*	*unknown*

‡ Mode of inheritance of the non-wild type variant. A "+" implies the wild type allele when known. In reference to the mutant allele, AD implies autosomal dominant, AR implies autosomal recessive, co-D implies co-dominant. OMIA: Online Mendelian Inheritance in Animals (http://omia.angis.org.au/home/) entries provides links to citations and clinical descriptions of the phenotypes and the diseases. Presented citations are for the causative variant discovery.

Table 2 Inherited diseases of domestic cats for which a commercial DNA test is available **– special interest for Burmese**

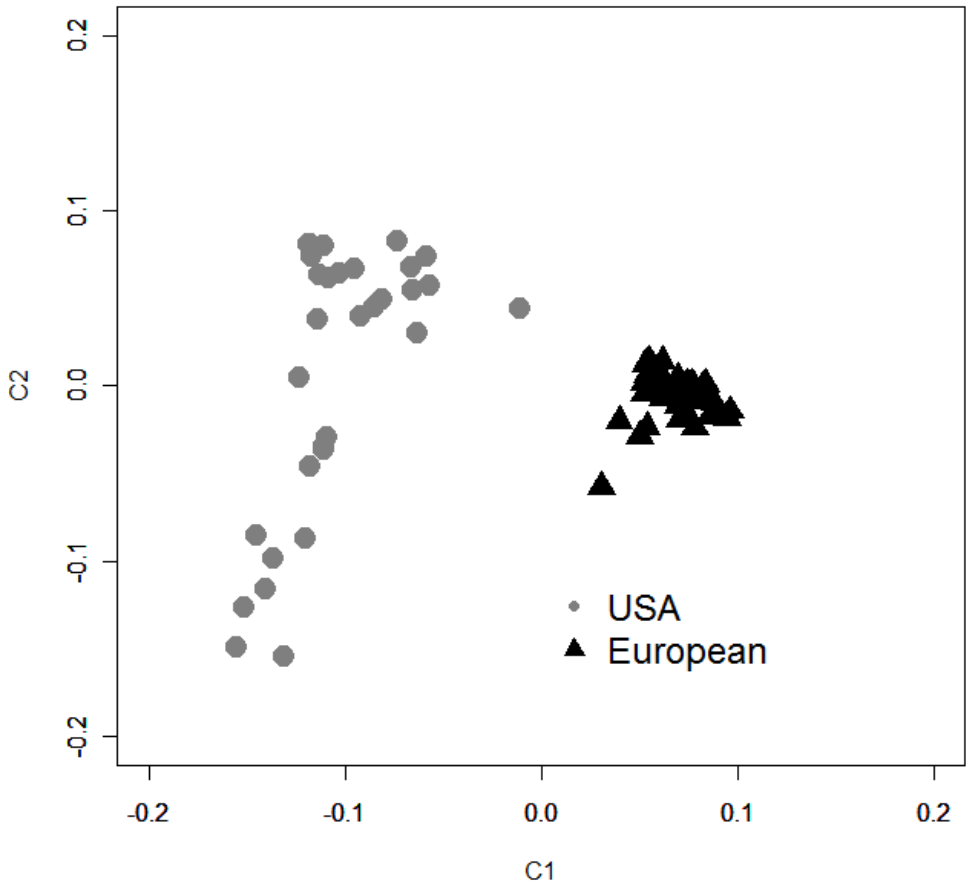
Disease / Trait (alleles) OMIA Entry	MOI‡	Phenotype	Gene	Gene Name	Mutation
AB Blood Type (A^+, AB, b)[14, 15] 000119-9685	AR	Determines Type B	*CMAH*	*cytidine monophospho-N-acetylneuraminic acid hydroxylase*	c.1del-53_70, c.139G>A
Craniofacial Defect[16]	AR	Craniofacial Defect	*ALX1*	*Aristaless-Like Homeobox 1*	c.496delCTCTCAGGACTG
Gangliosidosis 1[17] 000402-9685	AR	Lipid storage disorder (GM1)	*GLB1*	*Galactosidase, beta 1*	c.1457G>C
Gangliosidosis 2[18] 01462-0985	AR	Lipid storage disorder (GM2)	*HEXB*	*Hexominidase B*	c.1356del-1_8, c.1356_1362delGTTCTCA
Gangliosidosis 2[19] 01462-0985	AR	Lipid storage disorder (GM2)	*HEXB*	*Hexominidase B*	c.39delC
Hypokalemia[20] 001759-9685	AR	Potassium deficiency (HK)	*WNK4*	*WNK lysine deficient protein kinase 4*	c.2899C>T
Pyruvate Kinase Def.[21] 000844-9685	AR	Hemopathy (PK Deficiency)	*PKLR*	*pyruvate kinase, liver, RBC*	c.693+304G>A

‡ Mode of inheritance of the non-wild type variant. Not all transcripts for a given gene may have been discovered or well documented in the cat, mutations presented as interpreted from original publication. A "+" implies the wild type allele when known. In reference to the mutant allele, AD implies autosomal dominant, AR implies autosomal recessive, co-D implies co-dominant. OMIA: Online Mendelian Inheritance in Animals (http://omia.angis.org.au/home/) entries provides links to citations and clinical descriptions of the phenotypes and the diseases. Presented citations are for the causative variant discovery.

Inbreeding coefficient based on the observed versus expected number of homozygous genotypes in each sample.

USA Burmese 0.38
European Burmese 0.41
Random bred 0.04
LaPerm 0.07
Selkirk rex 0.15
Bengal 0.19
American curl 0.11
Japanese bobtail 0.14

MDS American vs European Burmese:



European Burmese cluster very tightly, while American Burmese are more interspersed, this is an indication of higher genetic diversity within the American Burmese.