Cat Health Network Feline SNP Chip Studies
Final Accomplishments

Morris Animal Foundation, the American Veterinary Medical Foundation, Winn Feline Foundation and the American Association of Feline Practitioners collaborated to form the Cat Health Network in 2011. The partners are all committed to improving feline health and recognize that combining resources may lead to major advances in cat care. Through the Cat Health Network, scientists used a gene chip containing single nucleotide polymorphisms (SNPs, pronounced "snips") to study numerous genetic predispositions to feline diseases and conditions. Following are final, lay-language status updates for all awards that have completed.

D12FE-501, *Dense Physical Linkage Map Using SNP Array for Rigorous Assembly of the Feline Genome Sequence*
Stephen J. O'Brien, PhD, National Cancer Institute
Results: Researchers Create High-Density Genetic Map of Cat Genome
The creation of a more comprehensive gene map will improve the overall status of cat genome analysis. Funded by the Cat Health Network, researchers from the National Cancer Institute improved the framework of the current assembly of the cat genome with higher-resolution mapping. This improved framework is a powerful new tool for researchers to study hereditary, infectious and chronic complex diseases in cats.

D12FE-503, ***Genetic Analysis of Hypertrophic Cardiomyopathy in Maine Coon Cats***
Gerhard Wess, Dr.med.vet., DACVIM, DECVIM-CA, University of Bern, Switzerland
Results: Hypertrophic Cardiomyopathy in Cats Is Likely Genetically Complex
Hypertrophic cardiomyopathy (HCM) is the most common cause of heart disease in cats. This condition causes thickening of the heart muscle, which impairs heart function. The cause of HCM is unknown, although certain breeds, including Maine Coons, appear to be predisposed. Funded by the Cat Health Network, researchers from the University of Bern analyzed and compared DNA from Maine Coon cats with HCM and Maine Coon cats without heart disease. Although this first-round genetic analysis did not pinpoint candidate genes for further study, continued improvements in mapping the cat genome, along with collection of more samples, may help scientists identify candidate genes in the future. The results may also indicate that HCM is genetically complex, involving the interaction of multiple genes located in several chromosomal regions. Researchers continue to collect and archive DNA samples for future study with the long-term goal of finding genetic mutations involved in HCM Maine Coons.

D12FE-504, ***Genetic Analysis of Polycystic Kidney Disease in Maine Coon Cats***
Tosso Leeb, PhD, University of Bern, Switzerland
Results: New Form of Polycystic Kidney Disease in Maine Coons Is Likely Genetically Complex
In cats with polycystic kidney disease (PKD), numerous fluid-filled cysts form within the kidneys, leading to potentially fatal kidney failure. This disease occurs most frequently in Persian cats, but a new form of PKD was recently identified in Maine Coons. However, Maine Coons with PKD do not carry the same genetic defect found in Persian cats with PKD. Funded by the Cat Health Network, researchers from the University of Bern conducted an exploratory project to identify the genetic defect in Maine Coons with PKD. Although, they were unable to localize the Maine Coon PKD mutation in the genome, the researchers continue to collect data in the hopes that additional well-defined samples will lead to identification of the genetic defect responsible for this disease. The results may also suggest that PKD in Maine Coons

could involve multiple genetic components and thus be genetically more complex than PKD in Persians.

D12FE-507, *Construction of a High-Resolution Map for Assisting Cat Genome Sequence Assembly*
Leslie A. Lyons, PhD, University of California–Davis
Results: Research Improves Map of the Cat Genome
Genetic maps determine the correct order of genes on a chromosome and the distance between those genes. These maps are valuable scientific tools that help researchers identify the genes responsible for inherited disorders. Funded by the Cat Health Network, researchers from the University of California–Davis created a radiation hybrid panel—a genetic mapping resource that will help users complete the genetic map of the cat. A more complete and accurate genetic map will help the research community locate genes and mutations of interest for traits and diseases in cats, regardless of breed.

D12FE-508, ***Genome-Wide Association Study for Hypokalemic Polymyopathy in Burmese Cats***
Leslie A. Lyons, PhD, University of California–Davis
Results: Researchers Identify Genetic Mutation Linked to Hypokalemia in Burmese Cats
Potassium is vital for muscles and nerves to function normally. Hypokalemia, a lower than normal level of potassium in the blood, has been documented in Burmese cats and is characterized by periodic muscle weakness. Funded by the Cat Health Network, researchers from the University of California–Davis identified the genetic defect responsible for hypokalemia in Burmese cats. A genetic test has been developed to screen for the mutation, which should lead to eradication of this genetic defect and improved health for Burmese cats.

D12FE-509, ***Genome-Wide Association Studies for Progressive Retinal Atrophies in Cats***
Leslie A. Lyons, PhD, University of California–Davis
Results: Genetic Regions Linked to Progressive Retinal Atrophy Identified in Bengal and Persian Cats
Progressive retinal atrophy (PRA), an inherited degenerative eye disease that results in blindness, is common in domestic cats. Two clinically different forms of PRA are associated with the most common breeds of cats worldwide, the Persian and the Bengal. While the Persian form of PRA is characterized by an early and rapid onset that leads to blindness by 12 to 16 weeks of age, the Bengal form progresses slowly with severe visual impairment not occurring until 1½ to 2 years of age. Funded by the Cat Health Network, researchers at the University of California–Davis identified the chromosomal locations for both of these forms of PRA. The researchers are continuing their search to identify the precise causal genes and mutations; their long-term goal is to develop a genetic test to wipe out PRA in Bengal and Persian cats, as well as other related breeds.

D12FE-513, ***Body Weight: Investigation of Genetic Aspects in an Experimental Cat Population***
Bianca Haase, Dr.med.vet, University of Sydney, Australia (approved by PI)
Results: Genetic Factors May Help Regulate Body Weight in Cats
Obesity and obesity-associated diseases are an increasing problem in household cats. In addition to food composition, increased food intake and lack of exercise, genetic factors are believed to influence the development of obesity. Funded by the Cat Health Network, researchers from the University of Sydney performed a detailed genetic comparison of overweight and lean cats. The genetic analysis uncovered differences between overweight and lean cats in three chromosomal regions that researchers believe influence body weight. One

region contains two well-known genes involved in feeding behavior, but further analyses of the three regions are needed to confirm their association with food intake and increased body weight. A better understanding of the genetic factors linked to obesity in cats may improve breeding practices and dietary management to help combat obesity in all cat breeds.

D12FE-514, ***Osteochondrodysplasia in Cats***

Bianca Haase, Dr.med.vet, University of Sydney, Australia (approved by PI)

Results: Genetic Region Identified for Folded-Ear Trait in Cats

The Scottish Fold cat breed is characterized by its unique ear shape, which results from ear cartilage malformation. There is convincing evidence that these cats have an underlying genetic defect that not only results in the characteristic folded ears but also affects the structure and function of other cartilage in the body. This defect can lead to progressive bone, joint and cartilage abnormalities that subsequently lead to severe crippling arthritis. Funded by the Cat Health Network, researchers from the University of Sydney identified a chromosomal region associated with the unique ear shape in Scottish Fold cats. The researchers' next step will be to identify the causative mutations within this region that contribute to the ear-folding trait and possibly other cartilage abnormalities. If they identify mutations, this information would help researchers develop a genetic test for cartilage abnormalities and, consequently, lead to breeding of healthier cats.

D12FE-515, ***Genome-Wide Association of Hypertrophic Cardiomyopathy in Sphynx Cats***

Kathryn M. Meurs, DVM, PhD, North Carolina State University
Approved by PI

Results: Genetic Regions Associated with Heart Disease Identified in Sphynx Cats

Hypertrophic cardiomyopathy (HCM) is the most common cause of heart disease in cats. The Sphynx breed suffers from a particularly severe form of HCM that leads to heart disease at a very young age. Although the genetic mutation responsible for HCM has been identified in other cat breeds, this same mutation is not found in Sphynx cats with HCM. Funded by the Cat Health Network, researchers from North Carolina State University performed a detailed genetic analysis of DNA from Sphynx cats with and without heart disease to try and identify the genetic mutation responsible for HCM. They identified seven chromosomal regions containing several known cardiac genes that may be associated with the development of HCM in Sphynx cats. With further study, researchers hope to identify the genetic mutations within these regions that are responsible for HCM. Identification of the causative mutations would help breeders reduce the prevalence of HCM in Sphynx cats.

D12FE-516 & D12FE-562, ***Genetic Susceptibility to Feline Infectious Peritonitis***

Niels C. Pedersen, DVM, PhD, University of California–Davis

Results: Candidate Genes Associated with Feline Infectious Peritonitis Susceptibility Identified in Birman Cats

Feline infectious peritonitis (FIP) is an almost always fatal viral disease that affects cats. Currently, there is no known effective prevention or cure for FIP. Funded by the Cat Health Network, researchers from the University of California–Davis have discovered strong evidence that susceptibility to FIP is a heritable trait. The researchers began their search for a genetic cause of susceptibility to FIP by analyzing samples from Birman cats, which are highly inbred and suffer from a high incidence of FIP. By comparing genetic samples from healthy Birman cats and Birman cats with FIP, the researchers found five candidate genes that may increase the risk of susceptibility to FIP. Each of these genes is known to play an important role in the basic viral immune response to FIP in cats. If the genetic basis for FIP susceptibility can be determined, it would open the way for the development of tests that could help to significantly reduce the overall incidence of FIP among pedigreed cats.

D12FE-551, ***Genome-Wide Association Study for Heritable Lymphosarcoma in Cats***
Leslie A. Lyons, PhD, University of California–Davis
Results: Potential Genetic Region for Lymphoma Identified in Oriental-Type Cats
Lymphosarcoma, also known as lymphoma, is the most common cancer of cats worldwide. Young Siamese and Oriental cats are particularly susceptible to a novel form of lymphosarcoma. In these breeds, this cancer occurs early, generally when cats are young adults, and is located primarily within a specific location in the cat's chest. Funded by the Cat Health Network, researchers from the University of California–Davis compared DNA from affected and healthy cats and identified a chromosomal region that may harbor a candidate gene for early-onset lymphoma in Oriental Shorthair cats. Identification of genes responsible for lymphoma will help researchers develop a screening test to identify carriers and reduce disease incidence in cats. Genetic tests for lymphoma could also aid veterinarians in making a clinical diagnosis and determining prognosis for afflicted or at-risk cats.

D12FE-552, ***Genome-Wide Association Study for Autosomal Dominant Curly Hair in Cats***
Barbara Gandolfi, PhD, University of California–Davis
Results: Genetic Factors Identified for Coat Texture of Cats
The genetic bases of several cat coat colors, as well as fur length, have been characterized, but there is little data on the mechanisms involved in coat growth and curly/wooly hair. Funded by the Cat Health Network, researchers from the University of California–Davis identified two chromosomal regions involved in hair texture in two cat breeds. One region is associated with wavy coats in LaPerm cats and the other is associated with curly coats in Selkirk Rex cats. Further analysis also helped identify the genetic mutation for the curly hair trait in Selkirk Rex breed.

D12FE-553, *Genome-Wide Association Study for Rapidly Progressing Polycystic Kidney Disease in Persian Cats*
Robert A. Grahn, PhD, University of California–Davis
Results: Genes Linked to Rapidly Progressing Polycystic Kidney Disease in Humans Not Associated with Similar Disease in Cats
Polycystic kidney disease (PKD) is one of the most common inherited genetic diseases in domestic cats, and Persian-type breeds are the most widely affected. Like humans with PKD, some cats with PKD live long lives, while others die very quickly, even though all share the same genetic mutation. Funded by the Cat Health Network, researchers from University of California–Davis sought to identify a genomic region that may influence disease progression in cats. Specifically, the researchers looked at genes related to rapid PKD progression in humans. Unlike in humans, these genes were not responsible for rapid disease progression in cats. The researchers did, however, identify four genomic regions of interest and two possible candidate genes that may play a role in rapid PKD progression in cats. Further research with additional samples is needed to evaluate these genetic regions and consider the possibility that multiple genetic components, as occasionally occurs in humans, may be involved.

D12FE-555, ***Genome-Wide Association Study to Identify Type AB Blood Group in Domestic Cats***
Leslie A. Lyons, PhD, University of California–Davis
Results: Genetic Regions Responsible for Rare AB Blood Type Identified in Cats
The AB blood type is very rare in cats and is not easily distinguishable from type A. This is problematic for cats that need blood transfusions. As with humans, the blood groups of the blood donor and recipient must be matched to prevent the recipient cat's antibodies from destroying donor red blood cells that are a different type from the cat's own blood cells. Funded by the Cat Health Network, researchers from the University of California–Davis evaluated the DNA of cats in each of the blood groups and identified two significant regions

and a candidate gene associated with the AB blood type. The researchers hope to perform additional analyses that will allow them to fully characterize the genetic components of the AB blood type. With a more complete understanding of feline blood groups, veterinarians will have additional tools to help prevent possible transfusion and transplant reactions as well as neonatal deaths resulting from breeding cats with incompatible blood types.

D12FE-556, *Genome-Wide Association Study for Hypertrophic Cardiomyopathy in Siberian Cats*

Robert A. Grahn, PhD, University of California–Davis

Results: Genetic Region for HCM Identified in Siberian Cats

Hypertrophic cardiomyopathy (HCM) is the most common inherited heart disease in domestic cats. This condition causes thickening of the heart muscle, which impairs heart function. A genetic mutation for this disease has been identified in Maine Coons and Ragdolls, but although Siberian cats suffer from an inherited type of HCM, it is genetically distinct from the HCM found in these other breeds. Funded by the Cat Health Network, researchers from University of California–Davis compared DNA from Siberian cats with HCM to DNA from healthy Siberian cats and identified a genetic region that may be responsible for HCM in this breed. Although the region has no known causative genes for HCM in other species, it is linked to another form of heart disease in humans. Once a genetic mutation has been identified for HCM in Siberian cats, researchers can develop a genetic test that would help breeders reduce the prevalence of HCM in Siberian cats.

D12FE-557, *Genome-Wide Association Study for Deafness in Dominant White Coat Cats*

Barbara Gandolfi, PhD, University of California–Davis

Results: Genetic Region Associated with Dominant White Coat Color Identified in Cats

Dominant white coat color is a common trait of several fancy cat breeds as well as random-bred cats. Unfortunately, cats with white coats, particularly those with blue eyes, have a high risk for deafness. Funded by the Cat Health Network, researchers from the University of California–Davis sought to determine whether the genes involved in dominant white coat color are also associated with deafness in white cats. Their analysis revealed a chromosomal region highly correlated with the dominant white coat color, but this region did not show a high association with deafness in white cats. Because several mutations may be responsible for the lack of hearing in white cats, additional research is needed to fully identify the mutation in the gene or genes responsible for deafness. The identification of the genetic mutation that results in deafness in white cats would help researchers develop a genetic test to help breeders to remove animals carrying this trait from their breeding programs.

D12FE-558, *Genome-Wide Association Study for Catnip Response in Domestic Cats*

Leslie A. Lyons, PhD, University of California–Davis

Results: No Significant Genetic Region Identified for Catnip Response in Cats

About 50 percent of cats respond to catnip. Funded by the Cat Health Network, researchers from the University of California–Davis tested 192 shelter cats for catnip response in controlled settings. DNA was collected from cats responding to catnip and compared to DNA of nonresponding cats. Genetic analysis of these samples did not reveal a causative gene associated with catnip response. Identification of genes responsible for catnip response may provide clues to the mechanisms involved in olfactory responses to drugs and chemicals in cats.

D12FE-559, Genome-Wide Association Study for Heritable Feline Orofacial Pain Syndrome in Burmese Cats

Clare Rusbridge, BVMS, DECVN, PhD, MRCVS, Neurovet Ltd, Stone Lion Veterinary Hospital (Approved by PI)

Results: Genetic Regions Associated with Feline Orofacial Pain Identified in Burmese Cats

Feline orofacial pain syndrome (FOPS) is a disorder in cats that is characterized by signs of severe oral discomfort and frequently leads to self-mutilation. FOPS is especially prevalent in Burmese cats, which suggests that genetic heritability may play a role. Funded by the Cat Health Network, researchers from Stone Lion Veterinary Hospital, University of California–Davis and the University of Sydney compared the DNA of Burmese cats affected by FOPS with the DNA of unaffected Burmese cats and identified two significant chromosomal regions that may be associated with FOPS in this breed. One region contains a candidate gene responsible for a protein that has been implicated in other pain syndromes, including migraines. Further analysis is needed to confirm the association of this gene with FOPS in Burmese cats. Once the genetic mutation is identified, this information will help researchers develop a genetic test that would not only allow for a more targeted and effective treatment of FOPS but would also would help breeders screen their cats.

D12FE-502: Mapping Feline Disease Phenotypes Using Interspecies Hybrids, 9/1/2011-4/30/2013

William J. Murphy, PhD, Texas A&M AgriLife Research, Final Report due 06/01/2013

D12FE-505: Genetic Estimation of Introgression Between Domestic Cat and Wildcat Populations, 8/1/2011-7/31/2013

Leslie A. Lyons, Ph.D., University of California/Davis, Final Report due 09/01/2013

D12FE-506: Genome-wide Association Studies of Brachycephaly in Domestic Cats, 8/1/2011-7/31/2013

Leslie A. Lyons, Ph.D., University of California/Davis, Final Report due 09/01/2013

D12FE-510: Genome-wide Association Study for Congenital Muscular Dystrophy in Sphynx and Devon Rex Cats., 8/1/2011-6/1/2013

Robert A. Grahn, Ph.D., University of California/Davis, Final Report due 06/01/2013

D12FE-511: Identification of a Novel Gene for a Familial Reflux Nephropathy in Ragdoll Cats, 9/1/2011-2/28/2013

Hannes T Lohi, PhD, University of Helsinki, Final Report pending

D12FE-512: Genome-Wide Association Study to Identify Susceptibility Genes for Diabetes Mellitus in Cats, 11/1/2011-11/1/2013

Yaiza Forcada, DVM Dip. ECVI, University of London, Final Report due 12/01/2013

D12FE-550: Identification of SNP Markers to Distinguish Scottish Wildcats, Domestic Cats and their Hybrids, 5/1/2011-5/1/2012

Paul O'Donoghue, PhD, The University of Chester, Final Report pending

D12FE-560: Genome-wide Characterization of Recombination and Recombination Hotspots in Cats, 2/1/2012-1/31/2014

Leslie A. Lyons, Ph.D., University of California/Davis, Final Report due 03/01/2014

D12FE-564: Identification of SNP Markers to Distinguish Scottish Wildcats, Domestic Cats and Their Hybrids. 6/1/2012-5/31/2013

Paul O'Donoghue, PhD, The University of Chester, Final Report due 07/01/2013