September 19, 20 and 21, 2003

St. Louis, MO

2003 AKC Canine Health Foundation
National Parent Club Canine Health Conference

Renaissance Grand Hotel, St. Louis, MO
September 19-21, 2003

Popular Sire Syndrome and Concerns of Genetic Diversity

Successful Dog Ownership

Dog chromosomes and cancer.

Caring for the Health of Your Breed

Health Surveys: Developing a Relevant, Reliable, User-friendly Survey.

Probiotics to Boost Immune System

Mechanisms Of Hypercoagulability In Dogs With Immune-Mediated Hemolytic Anemia

The Canine Health Information Center – Post Pilot Update

Mucopolysaccharidosis in Dogs: Clinical Signs to DNA Tests

A Novel Model of Canine Hemangiosarcoma: New Opportunity to Confront a Killer

Genetic Testing and Genetic Counseling (or "How Does Genetic Testing Apply to a Breeding Program?")

Advantages for Life: Purina Life Span Study

The Genetic Evaluation Of Dilated Cardiomyopathy In The Doberman Pinscher

The Genetic Evaluation Of Canine Subvalvular Aortic Stenosis
Molecular Events Leading to Cancer

Genetic Mapping and Analysis of a Canine Hereditary Renal Cancer Syndrome

High Resolution RH Mapping of the Dog Genome and Its Application to the Positional Cloning of Cancer Genes

Color Implications in Health

Vaccine Update: Controversial Issues

What Is New in Canine Reproduction and That Which Lies Ahead!!!

The Origin and Evolutionary History of the Dog

Popular Sire Syndrome and Concerns of Genetic Diversity

Jerold S. Bell, DVM, *Tufts University School of Veterinary Medicine*

There is a tendency for breeders to breed to the male who is the top-winning dog. This can also occur with a popular dog that has OFA excellent hip conformation, or has produced no epileptic offspring in matings to epileptic dams. Regardless of the popularity of the breed, if a large portion are breeding to a single stud dog, (the popular-sire syndrome), the gene pool will drift in that dog's direction and there will be a loss of genetic diversity. Too much breeding to one dog will give the gene pool an extraordinary dose of his genes, and this will include whatever detrimental recessives he may carry, to be uncovered in later generations. This can cause future breed-related genetic disease through what is known as the founder's effect.

Along with the thrill of owning a popular sire, comes your responsibility to the breed. Over time, you will find out what detrimental genes he carries. Hopefully these will cause minor faults, but occasionally they may cause genetic disorders. The true measure of a conscientious breeder is how this knowledge is disseminated to the owners of the next generation.

Purebred dog breeds have closed studbooks. No new genes are available to the breed, except from infrequent mutations that are usually not desirable. Considering a breed as a whole, genes cannot be gained through selective breeding; they can only be lost. This has lead breeders to question whether a pure breed can go though hundreds of years of selective breeding and still maintain its health and viability.

All genes come in pairs: one from the sire and one from the dam. If both genes are of the same type, the gene pair is homozygous. If the two are different, the gene pair is heterozygous. While each dog can have a maximum of two different genes in a pair, many different genes are potentially available to be part of the pair. The greater the number of genes that are available to each pair, the greater the breed diversity.

Breeders underestimate the amount of diversity that can be present in a breed; even one with a limited group of founders. A molecular genetic study of the Chinook dog breed, which was reduced to four dogs in the 1970s, showed that there was significant gene diversity and heterozygosity in the breed.

The studbook for the Thoroughbred horse has been closed for more than 300 years. However, researchers have found that on average 63 percent of the variable gene pairs are heterozygous and that 4.7 genes are potentially available to each pair. This diversity is present in spite of the fact that 95 percent of the breed traces back to a single founder male.

Some breeders express concern that inbreeding depression may affect the viability of their breed. The consequence of inbreeding depression is not due to a general effect from a high level of homozygous gene pairs. The problem that inbreeding depression causes in purebred populations, stems from the effects of deleterious recessive genes. When homozygous, they cause impaired health.

Lethal recessives place a drain on the gene pool, through smaller litter size or neonatal death. Other deleterious genes can cause disease or impair immunity. If there is no breed diversity in a gene pair, but the particular homozygote that is present is not detrimental, there is no negative effect on health. The characteristics that make a breed reproduce true to its standard are based on non-variable (homozygous) gene pairs.

The Doberman Pincher breed has a problem with von Willebrand's disease; an autosomal recessive bleeding disorder. Genetic testing has found that the defective gene is present in 77 percent of Dobermans. Doberman breeders can test and identify carrier and affected dogs. They can decrease the defective gene's frequency by breeding carriers to normal-testing dogs and selecting quality, normal-testing offspring for breeding. By not just eliminating carriers, but replacing them with their normal-testing offspring, genetic diversity will be preserved.

The perceived problem of a limited gene pool has caused some breeders to discourage linebreeding and promote outbreeding in an attempt to protect genetic diversity. However, it is a fallacy that each dog must carry the diversity of the breed. Studies in genetic conservation and rare breeds have shown that this practice actually contributes to the loss of genetic diversity.

By uniformly crossing all "lines," or families of dogs in a breed, you eliminate the differences between them, and therefore the diversity between individuals. This practice in livestock breeding has significantly reduced diversity and caused the loss of unique rare breeds. The process of maintaining separate lines, with many breeders crossing between lines and breeding back as they see fit, maintains diversity in the gene pool. It is the varied opinion of breeders as to what constitutes the ideal dog, and their selection of breeding stock that maintains breed diversity.

A basic tenet of population genetics is that gene frequencies do not change from the parental generation to the offspring. The gene frequencies will remain the same regardless of the homozygosity or heterozygosity of the parents, or whether the mating represents an instance of outbreeding, linebreeding, or inbreeding. If some breeders outbreed, and some linebreed to certain dogs that they favor while others linebreed to other dogs that they favor, then breedwide genetic diversity is maintained.

The loss of genes from a breed's gene pool occurs through selection: the use and non-use of offspring. If a popular sire is used extensively, gene frequencies, and the gene pool can shift towards his genes, limiting the breed's genetic diversity. On the other hand, dogs that are poor examples of a breed should not be used simply to maintain diversity. Related dogs with desirable qualities will maintain diversity and improve the breed.

Breeders should concentrate on selecting toward the breed standard, based on ideal temperament, performance, and conformation, and should select against the significant breed-related health issues. If breeders continually breed healthy, superior examples of their breed and avoid the popular-sire syndrome, the genetic health of the breed can be maintained.

Biographical Sketch

Jerold S. Bell, DVM is a Clinical Assistant Professor, and Director of the Clinical Veterinary Genetics Course for the Tufts University School of Veterinary Medicine. He was trained in genetics and genetic counseling at Michigan State University, and the University of Missouri. His DVM is from Cornell University. Dr. Bell lectures to all-breed and individual breed dog clubs. He is the project administrator of genetic disease control programs for national parent clubs. He performs genetic counseling through Veterinary Genetic Counseling, and practices small animal medicine at Freshwater Veterinary Hospital in Enfield, CT. He and his wife breed Gordon Setters.

Dog chromosomes and cancer.

Matthew Breen, Ph.D, *Dept. of Molecular Biomedical Sciences, College of Veterinary Medicine, North Carolina State University, 4700 Hillsborough Street, Raleigh, NC 27606*

The genome of a dog is comprised of 78 chromosomes. These chromosomes are nature's filing cabinets and contain all the genes ('files') that are required to inform cells what to do and how to behave. Many genes are associated with the regulation of cell growth, division and even death. Cancer is a term that describes a multitude of conditions with an enormous range of clinical outcomes.

One key aspect of cancer biology is the recurrent involvement of changes to chromosome structure and/or organization within the cell. These changes are referred to as chromosome aberrations. Many forms of human cancer are so closely associated with specific chromosome aberrations that the aberrations are regarded as diagnostic for the cancer. Some chromosome aberrations result in the gain or loss of chromosomal material (numerical changes), whilst others result in a reorganization of chromosomal material (structural changes). Numerical changes alter the copy number of genes in the genome and numerical changes bring together genes that are usually separated within the non-cancer genome. The interaction between these new 'neighbours' often leads to the generation of gene products that drive the cell to form a cancer. Knowledge of such gene products provides an opportunity to develop new therapies for treatment of cancers. In addition, for many human cancers there is a correlation between the presence of certain chromosome aberrations and the clinical outcome of the tumor and/or the tumor's response to therapy. For this reason many chromosome aberrations have prognostic value and this information may be used by clinicians to determine the most appropriate therapy.

Molecular cytogenetics is an exciting area of research that combines molecular biology, cytogenetics and fluorescence *in situ* hybridization (FISH). This approach, which makes use of sophisticated fluorescence microscopy techniques, allows us to look closely at the chromosomal organization of individual tumors and thus to identify cancer-associated chromosome aberrations.

Cytogenetic studies of dog cancers have be hindered by difficulties in identifying the chromosomes. We have developed a series of reagents and techniques that allow us to identify all dog chromosomes with confidence. These reagents include a set of whole chromosome paint probes and a genome-wide panel of single locus FISH probes. We have also isolated a number of canine cancer-associated genes.

We are now using our reagents to look closely at the chromosomal changes associated with a variety of canine cancers. We have conducted a detailed cytogenetic analysis of canine lymphoma and have identified chromosomal aberrations that suggest some of the mechanisms leading to pathogenetically important events are evolutionarily conserved. We have also identified chromosome aberrations that have not been reported for the corresponding human disease. These regions of the genome may thus contain novel cancer-associated genes. In addition, we have identified chromosome aberrations that appear to be correlated with increased survival and so may soon be in a position to offer prognostic aides to cancer diagnoses.

This work is supported by CHF grants 2038, 2214 and 2254.

Biographical Sketch

Dr. Matthew Breen graduated with honours in Genetics from the University of Liverpool, U.K. in 1987. He completed his PhD, working on cytogenetics in 1990. Dr. Breen was employed as a Post Doctoral research scientist in Molecular Genetics at the Medical Research Council's Human Genetics Unit in Edinburgh, where he was responsible for developing improved fluorescence *in situ* hybridization techniques as part of the Human Genome Mapping Project. Dr. Breen then spent four years working for the Australian Thoroughbred industry, based at the University of Queensland, Brisbane Australia. In 1996 Dr. Breen returned to the U.K. where his laboratory developed molecular cytogenetics reagents, resources and techniques for application to canine genome mapping, comparative cytogenetics and cancer studies. In 1998 Dr. Breen was awarded membership of ther Institute of Biology and the title of Chartered Bioloigist.

In 2002 Dr. Breen relocated his laboratory to NCSU's College of Veterinary Medicine as part of their Genomics initiative. His research interests continue to focus on the genomics, genome mapping and the comparative aspects of canine cancer.

Health Surveys: Developing a Relevant, Reliable, User-friendly Survey.

Stan Carter, DVM

The health survey is a powerful tool for breed clubs striving to breed healthier dogs. Identifying important diseases and their relative incidence enables eradication efforts to be efficiently focused. The survey may be of a general nature or directed toward specific features of a particular disease. Many different survey types have been utilized, ranging from one-page questionnaires to lengthy, time consuming documents. It is a delicate balancing act, obtaining worthwhile information while not overwhelming the participant.

Developing a quality survey requires numerous initial considerations:

- Circulation – Internet web page, Mailings, Breed Publications, Handouts.
- Length – Short surveys may have increased participation but yield less information.
- Included disorders – Write-in areas for rare disorders; List specific types of diseases for broad categories (Mast cell cancer or Lymphosarcoma instead of "Cancer")
- Ranges to examine – Age, Time periods, # of animals
- Due Date
- Publication of results – Prompt reporting of results may encourage participation
- Anonymous?

Model surveys are available from the Canine Health Foundation. They will also send you copies of surveys from several breeds that may help with the initial design and planning. The AKC Delegates Canine Health Committee is currently working on an on-line model health survey. They hope to develop a survey that is applicable to all breeds, accessible over the Internet and directly captured into a database. Breeders, researchers and pet owners all benefit from information collected by excellent health surveys.

Biographical Sketch

Dr. Stan Carter received his DVM from the University of Missouri in 1985. He entered private practice and was owner/director of All Creatures Animal Hospital in O'Fallon, Missouri until 2000. He has a special interest in canine reproduction and founded Canine Reproductive Technologies; an AKC approved frozen semen facility, in 2000. Dr. Carter has worked for Nestle Purina since 2001, in the position of senior veterinarian in research and development.

Dr. Carter has bred and exhibited basenjis under the Silvercreek kennel name for more than thirty years. He traveled to the African Congo in 1989 with the goal of improving and broadening the current gene pool. The trip was a tremendous success, with thirteen dogs imported to the U.S. and registered as foundation stock by the AKC. The imported basenjis have been clear of the major genetic diseases affecting that breed. Dr. Carter has served as basenji health chairman and as a Basenji Club of America board member for many years.

Probiotics to Boost Immune System

G.L. Czarnecki-Maulden and J. Benyacoub. *Nestle Purina PetCare Research, St Joseph, MO*

The role of the intestinal tract in nutrient absorption is well recognized. However, the microflora that naturally inhabit the intestinal tract and their vital role in maintaining normal functioning of the gut and immune system are often overlooked. The intestinal tract is often the 'first line of defense' for the body and must be in good order for the animal to maintain a healthy immune response. Gut microflora can be divided into three broad categories: (1) potentially harmful, (2) beneficial and (3) those with apparently neutral or unknown effects. Beneficial microflora include the lactic acid bacteria (e.g., lactobacilli, bifidobacteria and enterococcus). These microflora produce short chain fatty acids that modulate the gut pH and provide a source of fuel for the cells lining the gut. This, in turn, strengthens the intestinal cells and helps enhance nutrient absorption. Microflora also produce digestive enzymes and synthesize vitamins. One of the most important roles of lactic acid bacteria is to stimulate the immune response in the gut. These microflora can directly block attachment of potential pathogens to the intestinal wall. They are also known to modulate the intestinal environment to inhibit the growth of potential pathogens and produce immune stimulating factors. Animals born into a sterile environment where they do not establish a healthy microflora balance have a weak immune system and fail to thrive.

Stress, travel, aging, changes in environment and long-term antibiotic therapy can upset the normal balance of microflora in the intestinal tract. Probiotics, live beneficial microflora ingested by the animal, can help restore and maintain microflora during these times of stress. Probiotic supplementation is often recommended in puppies being raised on milk replacer to help establish a healthy microflora balance. These probiotics are typically lactic acid bacteria such as enterococcus faecium, lactobacillus, and bifidobacteria. . Most of the research to date has been conducted with mice, humans and livestock. In these studies, probiotics have been proven to prime the mucosal immune system to be able to respond quickly and efficiently to challenges. Secretory IgA, a protective immune factor, increases in response to ingestion of some probiotics. Additionally, phagocytosis, direct destruction of invading pathogens, increases in response to ingestion of several different probiotic strains. Some probiotics also have anti-inflammatory properties and are effective in the treatment of inflammatory bowel disease and colitis in humans. For example: Probiotics have been proven to decrease illness in children attending daycare and to decrease incidence of diarrhea and viral shedding. Likewise, traveler's diarrhea and antibiotic-associated diarrhea are effectively prevented and treated with probiotics. When probiotics are consumed pre-natally, children have a lower incidence of atopic dermatitis and anti-allergenic benefits of probiotics have been demonstrated in numerous studies. As a result, the use of probiotics in human medicine, particularly in the area of pediatric medicine, is increasing.

While numerous studies have been published on immune benefits of probiotics in other species, little research has been published with pets. There are a number of potential explanations for the lack of information. Screening probiotics for potential use in pet foods is a laborious process and includes proof of safety, investigation of potential benefits in vitro, proof of survival of the strain in the intestinal tract and proof of efficacy. Probiotics are not stable under normal environmental conditions and need to be specially protected to ensure survival throughout the shelf life of the product. To determine the effect of probiotic supplementation on immune function in healthy dogs, Beagle, Labrador Retriever, Fox Terrier and Manchester Terrier puppies were fed either a control diet or the same diet supplemented with the probiotic Enterococcus faeceum (SF68). Diets were fed from weaning to one year of age. Specific canine distemper virus antibodies were measured before and at timed intervals after vaccination. While antibody titers started to decrease in puppies fed the control diet, they remained at post-vaccination levels through one year of age in puppies fed the probiotic-supplemented diet. In addition, secretory IgA levels were significantly higher in puppies fed SF68. This prolonged vaccination response and increase in secretory IgA indicates that

ingestion of the probiotic SF68 primes the puppy's immune system to better handle external challenges.

Biographical Sketch

Gail L. Czarnecki-Maulden received her BS in Animal Science from Cornell University and her MS and PhD in Animal Nutrition from the University of Illinois. In 1984, she became an Assistant Professor of companion animal nutrition in the Department of Animal Sciences at the University of Illinois and was promoted to Associate Professor 1989. In 1990, Gail joined Nestle Purina Petcare Research where she is currently a senior research nutritionist. She is a member of the University of Illinois Division of Nutritional Sciences External Advisory Panel. Gail was a member of the AAFCO Canine and Feline Nutrition Experts Subcommittees, which set nutrient standards for dog and cat foods in the US. Gail has published over 60 articles and abstracts in the area of pet nutrition.

Mechanisms Of Hypercoagulability In Dogs With Immune-Mediated Hemolytic Anemia

Donahue SM[1], Brooks M[2], Otto CM[1]
[1]Deparment of Clinical Studies, VHUP, University of Pennsylvania, Philadelphia, PA 19104
[2]Comparative Coagulation Section, Diagnostic Laboratory, College of Veterinary Medicine, Cornell University, Ithaca, NY

The formation of excessive blood clots (thrombosis), is a major cause of mortality in a variety of diseases that affect purebred and mixed breed dogs. A very common condition is immune-mediated hemolytic anemia (IMHA; a disease in which the dog's immune system destroys its own red blood cells). Once thromboses form, specialized or invasive procedures must be used to confirm their presence and define the extent of organ involvement. Even with definitive diagnosis, treatment is limited. This study was designed to test the ability of a specialized clotting test, Thromboelastography (TEG), to identify increased coagulation (hypercoagulability) in dogs with IMHA. 35 dogs were included in the study: 12 dogs with IMHA, 13 sick control dogs, and 10 normal dogs. TEG confirmed the increased tendency for dogs with IMHA to form clots (hypercoagulability). By evaluating standard coagulation studies, we have identified multiple mechanisms that contribute to hypercoagulability, including an increase in the factors that promote clots, a decrease in the factors that inhibit clots and a decrease in the factors that break down clots. Through our studies of the mechanisms of hypercoagulability in IMHA, we can now design specific treatment strategies for the prevention of the devastating syndromes of thromboembolic (inappropriate formation and migration of clots) disease in IMHA. The ability to diagnose animals at risk for the complications of hypercoagulable states is revolutionary and will change critical care practice and treatment of these potentially fatal syndromes.

Biographical Sketch

Suzanne Donahue is a 1999 graduate of the University of Pennsylvania School of Veterinary Medicine. She then completed an internship in small animal medicine and surgery along with a one year fellowship in emergency medicine at the Veterinary Hospital of the University of Pennsylvania. She has continued at the University of Pennsylvania, and is currently in the 3rd year of her residency in small animal emergency and critical care medicine. Her primary area of interest is in increased clotting tendencies in certain canine disease states.

The Canine Health Information Center – Post Pilot Update

E. Dziuk, *Orthopedic Foundation for Animals*

The Canine Health Information Center, also known as CHIC, is a centralized canine health database jointly sponsored by the AKC/Canine Health Foundation (AKC/CHF) and the Orthopedic Foundation for Animals (OFA).

Conceived in 1999, the pilot program became operational in 2001 with 8 breeds enrolled. Today, there are 26 breeds participating through their parent clubs, and over 13,000 dogs have been issued CHIC numbers.

CHIC Mission Statement

To provide a source of health information for owners, breeders, and scientists, that will assist in breeding healthy dogs.

CHIC Goals

- To work with parent clubs in the identification of health issues for which a central information system should be established.
- To establish and maintain a central health information system in a manner that will support research into canine disease and provide health information to owners and breeders.
- To establish scientifically valid diagnostic criteria for the acceptance of information into the database.
- To base the availability of information on individually identified dogs at the consent of the owner.

CHIC Overview

The CHIC database is a tool that collects health information on individual animals from multiple sources. This centralized pool of data is maintained to assist breeders in making more informed breeding decisions and for scientists in conducting research. In order for data to be included in CHIC, test results must be based on scientifically valid diagnostic criteria.

Core to the CHIC philosophy is the realization that each breed has different health concerns. Not all diseases have known modes of inheritance, nor do all diseases have screening tests. Some screening tests are based on phenotypic evaluation, others on genetic testing. With all these variables, a key element of CHIC is to customize or tailor the CHIC requirements to the needs of each breed. These unique requirements are established through input from the parent club prior to the breed's entry into the CHIC program. Breed specific requirements typically consist of the inherited diseases that are of the greatest concern and for which some screening test is available.

Regardless of breed, each dog must be permanently identified in order to have test results included in CHIC. Permanent identification may be in the form of microchip, or tattoo.

A CHIC number and CHIC report are issued when test results are entered into the database satisfying each breed specific requirement, and when the owner of the dog has opted to release the results into the public domain. The CHIC number by itself does not imply normal test results, rather, it indicates that all the required breed specific tests were performed and the results made publicly available. The CHIC report is a consolidated listing of the tests

performed, the age of the dog at the time of the test, and the corresponding test results.

As new results are recorded, updated CHIC reports reflecting the additional information are generated.

Once included in the CHIC program, the breed specific requirements are dynamic. As health priorities within a breed change, or as new screening tests become available, the breed specific requirements can be modified to reflect the current environment. If the breed specific requirements are modified, existing CHIC numbers are not revoked. The CHIC number is issued to a dog completing all required tests at a given point in time.

CHIC provides each participating parent club quarterly reports consisting of both aggregate numbers and specific dogs that have been issued CHIC numbers.

CHIC Website

The CHIC website is located at www.caninehealthinfo.org. The website contains basic information on CHIC such as its mission and goals, and maintains a listing of the participating breeds and specific breed requirements. The CHIC website also provides a search engine to identify dogs that have been issued CHIC numbers. The CHIC website also provides direct hotlinks to the OFA website so users can take advantage of the expanded health screening information available on the dog's sire, dam, offspring, and siblings.

Participating Breeds/Test Requirements (as of Aug '03)

Akita - Hips, Eyes, Thyroid
American Water Spaniel – Hips, Eyes, Cardiac
Basenji – Hips, Eyes, Pyruvate Kinase Deficiency
Bearded Collie – Hips, Eyes, Thyroid
Belgian Sheepdog – Hips, Eyes, Elbows
Belgian Tervuren – Hips, Eyes, Elbows, Thyroid
Borzoi – Eyes, Thyroid, Cardiac
Boston Terrier – Eyes, Patellas, Deafness
Bull Terrier – Cardiac, Patellas, Kidney Function, Deafness
Clumber Spaniel – Hips, Eyes, Elbows
Golden Retriever – Hips, Eyes, Elbows, Cardiac
Great Dane – Hips, Eyes, Thyroid, Cardiac
Greater Swiss Mountain Dog – Hips, Eyes, Elbows
Havanese – Hips, Eyes, Patellas, Deafness
Irish Setter – Hips, PRA, Thyroid
Italian Greyhound – Hips, Eyes, Thyroid, Patellas
Japanese Chin – Eyes, Patellas, Cardiac
Labrador Retriever – Hips, Eyes, Elbows
Mastiff – Hips, Eyes, Elbows, Cardiac
Newfoundland – Hips, Elbows, Cardiac, Cystinuria
Papillon – Eyes, Cardiac, Patellas
Rhodesian Ridgeback – Hips, Eyes, Elbows, Thyroid
Rottweiler – Hips, Eyes, Elbows, Cardiac
Tibetan Terrier – Hips, Eyes, Deafness
Welsh Springer Spaniel – Hips, Eyes, Thyroid

Biographical Sketch

Eddie Dziuk earned a BS degree in Economics from Mount Saint Mary's College. He spent the next 16 years with the Fortune 100 IT firm, Electronic Data Systems (EDS). In August of 2001, Eddie left EDS to become the Chief Operating Officer of the Orthopedic Foundation for Animals (OFA). In this position, he has a unique opportunity to combine his years of business and management experience with his love of animals and concern over canine health issues. Eddie has been an active participant in the sport of purebred dogs for over twenty five years. As a breeder and exhibitor of beagles, he finished his first champion at the age of thirteen, and has owner-handled four different beagles to all breed best in show wins, including the breed's record holder for BIS and National Specialty wins.

Mucopolysaccharidosis in Dogs: Clinical Signs to DNA Tests

U. Giger, P. Foureman, N.M. Ellinwood, L. Berman, M. Van Hoeven, P. Wang, A. Seng, L.G. Sarvas, T. O'Malley, P. O'Donnell, K.J. Cullen, M.L. Casal, P.S. Henthorn, ME. Haskins. *Section of Medical Genetics University of Pennsylvania*, 3900 Spruce Street, Philadelphia, PA.19104-6010; 215 898 8894; fax 215 573 2162; penngen@mail.vet.upenn.edu; www.vet.upenn.edu/penngen.

The University of Pennsylvania's Section of Medical Genetics has been involved in the discovery of hereditary diseases of companion animals for several decades and has developed and established diagnostic laboratory tests to accurately detect affected animals as well as carriers. A particular area of interest and expertise at Penn is the study of lysosomal storage diseases, including mucopolysaccharidosis (MPS). With support from the National Institutes of Health, the National MPS Society, Inc., and most recently the AKC Canine Health Foundation, these storage diseases have been characterized from the clinical signs to the molecular defect and carrier tests have been developed.

In mucopolysaccharidosis, long-chain sugars of the body are not properly broken down. The ensuing cellular accumulation is systemic and can result to varying degrees in skeletal deformities, including defects in the sternum, vertebrae, and joints, corneal cloudiness, facial dysmorphia, and neurological signs. The skeletal malformations are generally recognized within the first few days to months of life, whereas the neurologic signs do not appear until adulthood in some forms of MPS. Typically the MPS storage material can be found in the urine. In humans, each MPS disorder occurs relatively rarely but all together represent a large and important group (1 in 5,000 births). Some MPS disorders have been described in several animal species including cats, mice, goats, and emus, and several have been identified in different canine breeds. Some appear to occur rarely, whereas, others have been found to be prevalent in a breed. MPS should be suspected with the typical multisystemic clinical signs and positive urine MPS spot test. A definitive diagnosis is reached by demonstrating deficient activity of a specific enzyme in blood or tissue, or by DNA testing, if the disease-causing mutation in a breed has been documented.

The first canine MPS disorder identified was MPS VII in a mixed breed dog at the University of Pennsylvania 25 years ago. The study of this and other MPS subtypes led to better understanding of the disease process and also to the first successful treatment of a multisystemic disorder with gene therapy. The same mutation causing MPS VII in the original mixed breed dog has now been identified to cause MPS VII in German Shepherds. MPS I was first recognized in the Plott hound, and has since also been identified as an isolated case in a Rottweiler. All MPS disorders are autosomal recessively inherited, except for MPS II seen in Labrador Retrievers, which is inherited as an x-linked recessive trait. MPS III, also known as Sanfilippo syndrome, is unique in that this is the only MPS disorder with primarily neurologic signs such as ataxia and tremors. MPS IIIA occurs in the Wirehaired Dachshund and the New Zealand Huntaway dog. Most recently MPS IIIB has been found in Schipperkes, which do not exhibit clinical signs until they are two years of age. The disease is slowly progressing resulting in the need for euthanasia by 5 years of age. The disease-causing mutation has recently been identified, and the results from screening 1000 Schipperkes indicated that the mutant allele is very prevalent in the breed.

MPS VI was first seen in Miniature Pinschers with stunted growth and skeletal abnormalities mostly involving the hips, and were misdiagnosed with hip dysplasia or femoral head necrosis. The molecular defect in this breed has just been identified and screening of Miniature Pinschers for carriers and affected dogs is now possible. Further studies are in progress to define the MPS VI mutation in Chesapeake Bay Retrievers and Miniature Schnauzers (as they

do not have the same mutation as the Miniature Pinschers).

The DNA tests for MPS disorders require cheek swabs or an EDTA blood sample and are being offered through the Josephine Deubler Genetic Disease Testing Laboratory at the University of Pennsylvania (www.vet.upenn.edu/penngen).

We are also interested in determining if the common occurrence of Legge-Calves-Perthes (LCP) disease in Miniature Pinschers and other small breeds is related to MPS disorders. LCP is a devastating hip disease with necrosis of the femoral head due to an unknown cause. Although LCP is different from hip dysplasia and MPS, similar bone changes are observed and, therefore, MPS and LCP disease may be related in these breeds. To receive further information contact us at www.vet.upenn.edu/penngen or by email penngen@mail.vet.upenn.edu or by fax to 215 573 2162.

Biographical Sketch

Urs Giger received his veterinary degree from the University of Zürich, Switzerland, where he also pursued his initial clinical training in small animal medicine and surgery and a doctoral thesis on the orthopedic correction of canine hip dysplasia. In 1981, he moved as a postdoctoral fellow to the United States where he subsequently completed a residency in small animal medicine at the University of Florida.
He then joined the faculty of the School of Veterinary Medicine at the University of Pennsylvania in Philadelphia and has been over the years a clinician in the Medicine, Oncology and Pediatrics/Genetics Service. He is currently the Charlotte Newton Sheppard Professor of Medicine and Chief of Medical Genetics and has a secondary appointment at the University of Zürich. He is a diplomate of the American and European College of the Veterinary Internal Medicine and is heading the Pediatrics and Genetics Clinic, the Metabolic Genetics Laboratory, the Josephine Deubler Genetic Disease Testing Laboratory and the Transfusion Medicine Center at the University of Pennsylvania. His clinical and research expertise and interests are in hereditary and hematologic disorders of small animals and are reflected in over 140 original publications as well as many more reviews and abstracts. He was last year's recipient of the International Scientific Lifetime Achievement Award from the World Small Animal Veterinary Association.

A Novel Model of Canine Hemangiosarcoma: New Opportunity to Confront a Killer

N Akhtar[1], ML Padilla[1], EB Dickerson[1], H Steinberg[2], M Breen[3], R Auerbach[4,5], **SC Helfand[1,5]**
[1]Departments of Medical Sciences and [2]Pathobiological Sciences, School of Veterinary Medicine, University of Wisconsin-Madison, Madison, WI; [3]Department of Molecular Biomedical Sciences, College of Veterinary Medicine, North Carolina State University, Raleigh, NC; [4]Laboratory of Developmental Biology, University of Wisconsin-Madison; [5]University of Wisconsin Comprehensive Cancer Center, Madison, WI

Increasingly, it has become more important to develop models of naturally occurring canine cancer that can be systematically examined in the laboratory. These efforts help us to better understand fundamental cellular derangements, identify potential therapeutic targets, and test novel therapies. Hemangiosarcoma (HSA) arises from transformed vascular endothelial (blood vessel) cells. This tumor represents ≥7% of all canine malignancies, and it is more commonly seen in male dogs between 8 and 10 years old. German shepherd dogs are at greatest risk for HSA, but Golden Retrievers, Great Danes, boxers, English setters, and pointers are also over represented breeds. The spleen, right atrium, and subcutis are the most common sites for primary HSA in dogs. Local infiltration and systemic metastases are the common growth patterns. Metastatic sites are widespread with the lung and liver being the most frequently affected organs. Splenic rupture results in tumor implants throughout the abdomen. Morbidity and mortality is often due to acute internal hemorrhage secondary to tumor rupture. Despite surgery and intensive chemotherapy, the median survival time for dogs diagnosed with HSA is little more than six months.

We established a canine hemangiosarcoma cell line derived from malignant endothelial cells comprising a spontaneous tumor in a dog to provide a renewable source of endothelial cells for studies of angiogenesis, the formation of new blood vessels, in malignancy. Pieces of the hemangiosarcoma biopsy were engrafted subcutaneously in a bg/nu/XID (immunodeficient) mouse allowing the tumor cells to expand in vivo. A cell line, SB-HSA, was derived from the xenograft. SB-HSA cells expressed vascular endothelial growth factor (VEGF) receptors-1 and –2, CD31, CD146, $\alpha_v\beta_3$ integrin, and produced several growth factors and cytokines, including VEGF, basic fibroblast growth factor, and interleukin (IL) –8 that are stimulatory to endothelial cell growth. These results indicated that the cells recapitulated features of mitotically activated endothelia. In vivo, SB-HSA cells stimulated robust angiogenic responses in mice and formed tumor masses composed of aberrant vascular channels in immunocompromised mice that mimicked canine HSA, providing novel opportunities for investigating the effectiveness of antiangiogenic agents. Using this model, we determined that IL-12, a cytokine with both immunostimulatory and antiangiogenic effects, suppressed angiogenesis induced by and tumor growth of SB-HSA cells. The endothelial cell model we have described offers unique opportunities to pursue further investigations with IL-12, as well as other antiangiogenic approaches in cancer therapy, with special emphasis on canine HSA.

Biographical Sketch

Dr. Stuart Helfand is an Associate Professor of oncology at the University of Wisconsin School of Veterinary Medicine. In addition to providing care to pet dogs and cats with cancer in the oncology clinic, Dr. Helfand conducts laboratory research focused on cancer immunotherapy and targeted approaches to inhibit blood vessel growth within tumors. To this end, his laboratory has developed several models to study canine cancer and is conducting research into discovering vulnerable features ("targets") in canine cancer. These efforts are providing opportunities to investigate exciting new approaches for the treatment of a variety of canine cancers such as hemangiosarcoma, osteosarcoma, and melanoma.

Genetic Testing and Genetic Counseling
(or "How Does Genetic Testing Apply to a Breeding Program?")

Paula Henthorn, Ph.D, *University of Pennsylvania School of Veterinary Medicine*

Fueled by an increased awareness of genetic diseases in dogs, and by the Human and Canine Genome Projects, we have entered a time of significant advances in the study of dog genetic diseases. An increased understanding, by breeders and by veterinarians, of how genetic diseases are recognized and studied is critical for efficient progress to be made. Awareness of genetic disorders and their distinguishing characteristics is the foundation of their control. With enough information, including accurate diagnosis, knowledge of the mode of inheritance, and identification of asymptomatic carriers of recessively inherited disease, the risks of producing genetically defective offspring can be determined, and appropriate breeding decisions can be made. Our burgeoning knowledge of the gene content of the canine genome will have a dramatic impact our ability to identify these carriers of genetic diseases by dramatically increasing the rate at which DNA-based genetic tests are developed.

DNA-based genetic tests identify differences in DNA sequences and are of two different varieties. One type of test, referred to as a mutation-based test, recognizes disease-causing mutations while a second type of test, the linked-polymorphism test, recognizes DNA differences that are near the disease-causing gene and are used to track normal and mutant alleles of that gene through pedigrees. While there are differences in how these two types of tests are developed and how they are used, both involve the same basic techniques, based on the availability of the dog's DNA and on the use of the polymerase chain reaction (PCR).

Mutation based tests recognize the specific DNA mutation that causes the genetic disease. Mutation-based genetic tests:

- require knowledge of the specific mutation (which itself requires that the normal gene sequence also be known)
- can be used for carrier detection as well as to detect affected animals
- may be breed specific, so different tests may be necessary to test for the same genetic disease in different breeds
- do not require DNA samples from additional members of a pedigree

Tests that recognize variations in DNA sequence outside, but closely linked to the gene involved in the disease are known as linked polymorphism tests. In other words, a linked polymorphism-based test does not involve the disease gene itself, but relies on the ability to detect a normal variation in DNA sequence (polymorphism) on the same chromosome and near the disease gene. Therefore, it is not even necessary to understand what gene is involved in the disease in order to perform the test. This type of test:

- requires the identification of a specific polymorphism, which itself requires the cloning and usually sequencing of a particular piece of DNA and the preliminary gene mapping studies that demonstrate that the polymorphism is linked to the disease. DNA from many individuals within pedigrees in which the disease segregates is necessary. However it is not necessary to know the exact mutation, or even the disease-causing gene.

- is most accurate for use in families in which the parents of the animal in question are informative and DNA is available from an affected full sibling of the animal to be tested. For an animal to be informative, it must be heterozygous (have two different alleles) at the linked marker locus. These are not necessities, but additional research is needed to make the tests accurate for use on individual animals and often for use in different breeds.

- will be in error a small proportion of the time, which can be predicted if the distance between the disease gene and linked polymorphic locus is known. An error in the test occurs if there is recombination between the linked polymorphic locus and the disease-causing gene. Many informative pedigrees which contain animals segregating both the disease (or a polymorphism at the disease gene locus) and the linked polymorphism are necessary to get a good estimate of the frequency of recombination between the two loci and thus the likelihood that the test will give an erroneous result.

  Which type of test is best, mutation-based or linked polymorphism-bases?

  It is not a question of which is best, but rather is any test available. For the vast majority of diseases with a linked-polymorphism based test, a mutation-based test will eventually be developed. The important issue is to understand the differences between the two types of tests and the resulting differences in how the test results should be used to advise breeders.

  The practicality and success of a genetic screening program depends on the following requisites (after Jolly et al, 1981, Adv. Vet. Sci. & Comp. Med. 25:245):

  a. The disease occurs with sufficient frequency to be of economic or social importance.

  b. The test for the heterozygote is accurate and affordable.

  c. Culling of heterozygotes does not deplete key genetic resources.

  d. Test and control program should be acceptable to breeders (precede by educational and public relations programs).

  e. Genetic counseling is available to breeders.

  f. Breed societies have rules to insure control is based on test results.

  Cooperation between veterinary medicine professionals (veterinarians and researchers) and breeders and breed organizations are essential and rewarding components of the genetic screening programs that allow us to effectively control the incidence of genetic disease.

Biographical Sketch

Dr. Paula Henthorn received her Ph.D. in genetics from the University of Wisconsin and continued her work in human genetics as a postdoctoral fellow at the University of Pennsylvania, in the School of Medicine. She joined the faculty at the School of Veterinary Medicine, also at the University of Pennsylvania, in 1990. Her activities at the Veterinary School include studies of the molecular basis of genetic diseases and the development of genetic tests for companion animals, as well as teaching genetics to veterinarians and veterinary students.

Advantages for Life: Purina Life Span Study

M.R. Kelly, Ph.D, B. Larson, D. Lawler, R.D. Kealy, *Nestlé Purina PetCare Research*

The Purina Life Span Study evaluated the effects of 25% diet restriction on joint development and subsequent osteoarthritis, several potential markers of aging, and longevity in Labrador Retrievers. Forty-eight 8-week-old Labrador Retriever puppies from 7 litters were paired by gender and weight and randomly assigned to a control [control] group or restricted [lean-fed] group. The control group had ad libitum access to food for 15 minutes per day, and the lean-fed littermate was fed 25% less food than the control puppy. At 3.25 years, the formulation and amount fed to both groups of dogs was changed. The control-fed group was offered 62.1 Kcal of metabolizable energy (ME)/kg of estimated ideal body weight for the rest of their lives. Each dog in the lean-fed group continued to receive 25% less food than its pair-mate consumed the previous day. All dogs received the same dry, extruded 100 percent nutritionally complete and balanced diet, just the amount fed to the control-fed and lean-fed groups differed. Dogs were weighed weekly as puppies, periodically as adolescents and weekly as adults. Beginning at 6 years of age, they were evaluated annually for body condition using the Purina Body Condition System™, a validated standard used by veterinarians to evaluate body physique in pets. Other health indicators, including annual radiographs, body fat, lean body mass and bone mass, effective glucose and insulin use, serum cholesterol and triglyceride levels, cardiac parameters, immune and antioxidant variables, were measured annually. Health-related events, as well as time and cause of death, also were recorded.

Earlier results published from this same study showed that hip joint laxity was significantly less among dogs given reduced food intake. The severity of osteoarthritis (OA) was less in lean-fed dogs as well. By age 5, moderate-to-severe coxofemoral OA was present in 43% of the control-fed dogs, compared to only 9% among the lean-fed dogs. By 8 years of age, OA was found in multiple joints (hip, stifle, shoulder, elbow) with greater frequency and severity among the control-fed dogs. Osteoarthritis was identified radiographically in two (45%) or three (32%) different joints in 77% of the control-fed dogs but only 10% of the lean-fed dogs at 8 years of age. Another indicator reflecting the delayed development of OA in the lean-fed dogs is the age at which 50% of the dogs (the median) in each group required regular medical treatment for OA. Among the control-fed dogs, this occurred at 10.3 years of age, but was delayed by almost 3 years (13.3 years of age) in the lean-fed group, a statistically ($P< 0.001$) and clinically significant difference. The need for treatment of any health condition was also delayed in the lean-fed dogs. The age when 50 percent of the dogs required treatment for a chronic condition was 12.0 years among the lean-fed dogs, compared to 9.9 years for the control-fed dogs. Between the two groups, age at mortality differed more significantly than causes. Median life span was increased by 1.8 years, or 15 percent, in the lean-fed dogs compared to the control-fed dogs ($P<0.001$, Figure 1). Median life span (age at which 50 percent of the dogs in the group had died) was 11.2 years in the control-fed group compared to 13.0 years in the lean-fed group. By age 10, only three lean-fed dogs had died, compared to seven control-fed dogs. At the end of the twelfth year, 11 lean-fed dogs were alive, with only one control-fed dog surviving. Twenty-five percent of the lean-fed group survived to 13.5 years, while none of the dogs from the control-fed group lived to that age. Throughout the study, the lean-fed group had a significantly ($P<0.01$) greater mean percentage of lean body mass. The lean-fed group also experienced a two-year delay in loss of lean body mass (the average onset of decline was 11 years vs. 9 years) compared to control-fed dogs, and maintained significantly ($P<0.01$) lower body condition scores. The average BCS (from age 6 through 12 years) for the lean-fed and control-fed dogs was 4.6 ± 0.2 and 6.7 ± 0.2, respectively (Figure 2). Thus, the control-fed dogs were only slightly to moderately overweight and the lean-fed dogs were well within the ideal body condition of 4 to 5 on Nestlé Purina's 9-point scale. Despite this, the correlation between BCS at middle age and longevity was impressive.

As can be seen in Figure 2, dogs with a BCS of 5 or less at middle age (6 through 8 years of age) were more likely to live beyond 12 years of age compared to those with a higher BCS. The lean-fed group had lower serum triglycerides and triiodothyronine, as well as improved insulin and glucose utilization. The Purina Life Span Study demonstrated that feeding to ideal body condition (BCS of 4 to 5 on 9-point scale) increased the median life span and delayed the onset of signs of chronic disease in this group of Labrador Retrievers.

Biographical Sketch

Dr. Melissa Kelly received her PhD in Nutrition Science from The University of North Carolina at Greensboro. During her tenure, she conducted nutritional cell biology research using a cell culture model to study the effects of antioxidants on free radical-induced DNA damage and apoptosis. After finishing her dissertation, Dr. Kelly accepted a position as a Research Scientist at Nestlé Purina PetCare Research in the Technical Communications team. There, she is responsible for developing and implementing global communication programs that assist in the enhancement of the perception, image and understanding of Nestle Purina's nutrition science and technology among external contacts in the scientific, veterinary and breeder communities. In addition, Dr. Kelly develops and delivers internally-focused training to NP staff in relevant areas of pet nutrition. Dr. Kelly's special areas of interest include weight management, protein and antioxidants.

Caring for the Health of Your Breed

Asa Mays, DVM, Dr. J. Charles Garvin and Susan LaCroix Hamil

Breeding dogs carries with it an enormous responsibility. Not just for the health of the sire and/or dam or for the litter, but a lifetime of commitment for each resulting generation, dependent upon your good choices today.

Inherited diseases can be devastating. There is more at risk than simply the health of the animal. The breeder's reputation is also at stake, not to mention the financial and legal risks. And let's not forget about the years of planning a pedigree to improve the breed and attain that ever-distant goal, the breed standard.

So what can you do? Recognize the health issues that tend to affect your breed. Keep an eye out for affected animals in the pedigree; perform all possible tests to determine that your animal is as healthy as possible. Of course, the first step to fixing the problem is admitting you have a problem in the first place! There is no shame in admitting there is a health problem in your breed, or even in your line! Though this may be the toughest step, it is by far the most important, and the only way to begin to combat genetic disease.

The final step is to DO SOMETHING ABOUT IT! Remove affected animals from the breeding pool. But take care not to throw the baby out with the bathwater! Proven carriers can be carefully integrated into the breeding program. And be sure to share your information with others.

We know the attendees at this conference are dedicated to improving canine health, and we need your help to educate others!

Biographical Profiles

Asa Mays received his DVM from the Ohio State University, then went on to obtain a Masters of Medical Science in Immunology from Tulane University in New Orleans. He spent fifteen years as the Associate Editor of the Merck Veterinary Manual, and just recently retired from Merial Ltd. Dr. Mays obtained his first AKC registered dog in 1958, and began exhibiting in 1968. Dr. Mays has bred, exhibited and handled Beagles, Borzoi, Dachshunds and Salukis, having produced approximately 40 champions over 13 years, including a Borzoi that was a top producer in the breed, including having produced a Best In Show Winner. A past president of Borzoi Club of America and active in several all breed clubs and specialty clubs, Dr. Mays currently serves on the Boards of Directors for both the American Kennel Club and the AKC Canine Health Foundation.

Since his first dog show in 1965, **Dr. J. Charles Garvin** has been continuously involved in the sport, first in obedience, then Junior Showmanship and conformation. With his mother Betty (AKC Delegate 1979-1993) and his wife Lynn, his Korcula Kennels, Reg. has produced 85 Dalmatian Champions, the majority he personally handled. He has bred and owned 5 BIS winners and several of the top winners and producers in the breed. He won the Junior Showmanship finals at Westminster in 1969, the only person ever to win that honor with a Dalmatian.

First approved as an AKC Judge in 1980, he has judged at the Dalmatian national specialty five times, including at the 1984 AKC Centennial Show. An AKC Delegate from the Marion Ohio KC since 1990, he is the only Delegate whose mother was also an AKC Delegate.

He has served on the Board of the Dalmatian Club of America for 22 years, seven as President and 11 as Vice-President.

He now is serving his first term on the Board of Directors of the American Kennel Club.

Born in Columbus, Ohio, he graduated from Ohio Wesleyan University, received his medical degree from the University of Southern California, and completed his specialty training at Ohio State University Hospitals.

He is an Ophthalmic Surgeon and physician executive, and president of a 65 physician medical group practice. He has taken extensive training in business and management, is certified by the American Board of Medical Management, and is a Certified Physician Executive.

In the community, he has been active in many other volunteer and professional boards and committees, frequently as chair. On the personal side, he and his wife of 29 years have a son, John, in graduate school in Computer Science; Chad, a college freshman; and daughter Laura in high school.

Susan LaCroix Hamil graduated from Louisiana State University with a Bachelor of Science degree in 1972 and received a Master degree in Library Science from California State University in 1975. She has bred Bloodhounds under the Quick Creek prefix since 1970. In that time, Quick Creek has finished or produced more than 40 champions, including specialty and all breed Best In Show winners as well as obedience title holders and titled man-trailers.

Mrs. Hamil is the past president of the American Bloodhound Club and currently serves as their delegate to the AKC. She also serves on the Delegate's Canine Health Committee, and is on the Board of Directors of the AKC Canine Health Foundation. As a breeder, veterinary technician and veterinary hospital manager she is interested in the health and welfare of all dogs and most particularly in the challenges presented to the fancy and the sport of purebred dogs.

The Genetic Evaluation Of Dilated Cardiomyopathy In The Doberman Pinscher

K.M. Muers, Ph.D, *The Ohio State University College of Veterinary Medicine*

Dilated cardiomyopathy (DCM), a primary heart muscle disorder characterized by poor cardiac function, is inherited in the Doberman Pinscher. Therapy for DCM does not cure or even successfully control the clinical signs. The inability to control the disease has led to increased interest in disease prevention through careful selection of unaffected dogs for breeding. However, since DCM is often not apparent until later in the adult life of the dog, many dogs are selected for breeding before they are found to be affected. A blood test that could identify affected animals before they are used for breeding would greatly decrease the prevalence of DCM.

Careful evaluation of a 4 generation, 39 member family has provided an explanation of the pattern of inheritance of the disease. A genome wide scan is being performed to identify informative canine markers associated with DCM in the Doberman Pinscher. Genetic markers from the canine genetic map are evaluated by polymerase chain reaction (PCR) and linkage analysis and evaluated for genetic linkage with MLINK. The highest linkage score we have identified so far is 1.9. A canine marker with a score of 3 or greater is considered a significant lead in the identification of the genetic cause of this disease. The eventual identification of an informative marker will be the first step in the development of a DNA screening test for this disease.

Biographical Sketch

Dr. Kathryn Meurs is currently an Associate Professor in the Department of Veterinary Clinical Sciences at The Ohio State University-College of Veterinary Medicine. She completed her DVM in 1990 at the University of Wisconsin – Madison and completed a small animal internship at North Carolina State University in 1991. She completed a Cardiology residency at Texas A&M University and is board certified from the American College of Veterinary Internal Medicine (Cardiology).

Dr. Meurs has a Ph.D. in Genetics from Texas A&M University and her areas of interest include familial aspects of cardiovascular disease, especially cardiomyopathy.

The Genetic Evaluation Of Canine Subvalvular Aortic Stenosis

K.M.Meurs, Ph.D, *The Ohio State University College of Veterinary Medicine*

Subvalvular Aortic Stenosis (SAS) is a congenital heart disease characterized by a fibrous ridge located below the aortic valve. Affected dogs are at risk of developing heart valve infections, congestive heart failure or sudden death. Although mildly affected dogs can live a normal lifespan, severely affected dogs live an average of 19 months. The defect has been shown to be inherited in the Newfoundland breed, and is likely to be inherited in the Golden Retriever, Boxer and Rottweiler, among others. Since this is a familial defect in at least some breeds, affected dogs should not be bred. However, mildly affected dogs can be difficult to diagnose without Doppler echocardiography, an expensive test with limited availability. Therefore, there is significant interest in developing a blood test to screen for SAS.

The objectives of our studies are to define the clinical (phenotypic) and genotypic characteristics of SAS in various breeds of dogs. A genome wide scan is being performed to identify informative canine markers associated with SAS in individual breeds of dogs. In the Newfoundland, 3 close families of dogs are being studied to identify a genetic marker linked to SAS. Genetic markers from the canine genetic map are evaluated by polymerase chain reaction (PCR) and linkage analysis and evaluated for genetic linkage with MLINK. This will be the first step in the development of a DNA screening test for this disease.

Biographical Sketch

Dr. Kathryn Meurs is currently an Associate Professor in the Department of Veterinary Clinical Sciences at The Ohio State University-College of Veterinary Medicine. She completed her DVM in 1990 at the University of Wisconsin – Madison and completed a small animal internship at North Carolina State University in 1991. She completed a Cardiology residency at Texas A&M University and is board certified from the American College of Veterinary Internal Medicine (Cardiology).

Dr. Meurs has a Ph.D. in Genetics from Texas A&M University and her areas of interest include familial aspects of cardiovascular disease, especially cardiomyopathy.

Molecular Events Leading to Cancer

Jaime F. Modiano, Ph.D, *Integrated Department of Immunology; AMC Cancer Research Center of the University of Colorado Cancer Center; University of Colorado Health Sciences Center, Denver, CO*

The last three decades have produced significant advances in our understanding of why cancer arises. The initial discoveries of viral genes that could transform cells and cause tumors (hence called oncogenes) were followed by the recognition that these genes had cellular counterparts that regulated growth and proliferation (called proto-oncogenes). Shortly thereafter, it became clear that to the "yin" of oncogenes there was a "yang", that is, there were genes that prevented growth and proliferation of normal cells, and that their dysfunction could also lead to tumors. These were called "tumor suppressor genes", and much work has been devoted to understand their roles in sporadic (non-heritable) cancers as well as in heritable cancer syndromes.

Several dozen-tumor suppressor genes have been identified in humans and laboratory animals, and results from our lab and others show that the function of every tumor suppressor analyzed to date is evolutionarily conserved in dogs. However, various important and intriguing questions remain regarding the role of tumor suppressor genes in cancer, such as why does a deficiency in a given gene that is a global regulator of cell proliferation lead to very specific kinds of tumors, and also how can individuals who share the same risk exhibit much different disease incidence and outcomes? The answers to these questions are likely to be multifactorial. An obvious component is the interaction with environment. But, just as the similarities between humans and dogs allow us to use data from the disease in one species to understand the disease in the other, some of the differences among these species, for example, the relative prevalence of carcinomas versus sarcomas, indicate that environmental factors are unlikely to account for the observed tumor specificity or the differences in relative risk.

In hindsight, part of the problem we have faced is that, by focusing on individual genes we tended to lose the forest for the trees. The recognition that the products of proto-oncogenes and tumor suppressor genes are members of non-linear, interactive biochemical cascades or pathways has offered glimpses into the nature of specificity and risk. Thus, a single protein can interact in different ways in different cells to achieve different functional outcomes, so loss of a tumor suppressor protein may increase the probability of transformation in one cell type, but not in another. Yet, if we focus on the pathway rather than the gene, we find that most or all tumors share common functional (if not genetic) lesions. More importantly, identifying the genes within a pathway that account for specificity may help us outline those genes that underlie the relative risk in individuals (or in breeds of dogs). This presentation will show various examples of how different canine tumors achieve inactivation of two central tumor suppressor gene pathways, and offer insights into future work that will allow us to design better strategies for treatment and prevention.

Biographical Sketch

Dr. Jaime Modiano completed his veterinary training and PhD in Immunology at the University of Pennsylvania, a residency in Veterinary Clinical Pathology at Colorado State University, and a post-doctoral fellowship at the National Jewish Center for Immunology and Respiratory Medicine. He was appointed to the faculty in the Department of Veterinary Pathobiology at Texas A&M University as Assistant Professor between 1995 and 1999. Currently, Dr. Modiano is Associate Professor in the Integrated Department of Immunology and the AMC Cancer Research Center, and a Full Member of the Comprehensive Cancer Center of the University of Colorado Health Sciences Center in Denver, CO. His research program is supported through federal and private sources. Dr. Modiano has co-authored more than 35 peer-reviewed scientific manuscripts, and over 70 abstracts, presentations, and book chapters focused on various aspects of cancer biology, including the genetic basis of cancer and applications of genetic immunotherapy to treat metastatic tumors. Dr. Modiano is married to Dr. Michelle G. Ritt, a board certified specialist in Veterinary Internal Medicine. They share their home with 2 dogs ("Logan", a Gordon Setter and "Kira", a "Malamutt").

Genetic Mapping and Analysis of a Canine Hereditary Renal Cancer Syndrome

Frode Lingaas* [a], Kenine E. Comstock* [b], Ewen F. Kirkness[c], Anita Sørensen [a], Tone Aarskaug[a], Christophe Hitte[f], Michael L. Nickerson[d], Lars Moe [a], Laura S. Schmidt[g], Rachael Thomas[h], Matthew Breen[e], Francis Galibert[f], Berton Zbar[d] and **Elaine A. Ostrander**
[a]Norwegian School of Veterinary Science, P.O. Box 8146 N-0033 Oslo, Norway
[b] Clinical and Human Biology Divisions, Fred Hutchinson Cancer Research Center, P.O. Box 19024, D4-100, Seattle, WA 98109-1024 USA [c]The Institute for Genomic Research, 9712 Medical Center Drive, Rockville, MD 20850 USA; [d] Laboratory of Immunobiology, Center for Cancer Research, National Cancer Institute, Frederick, MD 21702 USA; [e]Dept. of Molecular Biomedical Sciences, College of Veterinary Medicine, North Carolina State University, Raleigh, NC 27606 USA; [f]UMR 6061 CNRS, Génétique et Développement, Faculté de Médecine, 35043 Rennes Cédex, France; [g]Basic Research Program, SAIC-Frederick, Inc., National Cancer Institute Frederick, Frederick, MD, 21702 USA; [h]Oncology Research, Animal Health Trust, Lanwades Park, Kentford, Newmarket, Suffolk, CB8 7UU United Kingdom

We have proposed previously that mapping cancer susceptibility genes in the domestic dog can circumvent many of the difficulties associated with mapping human cancer susceptibility genes. To this end we describe our progress toward the localization of a gene for a rare canine kidney cancer syndrome termed Hereditary Multifocal Renal Cystadenocarcinoma and Nodular Dermatofibrosis (RCND). RCND is a rare, naturally occurring syndrome characterized by bilateral, multifocal tumors in kidneys and numerous firm nodules in the skin consisting of dense collagen fibers, that was originally described in German Shepherds. We previously mapped RCND to canine chromosome 5 (CFA5) with a highly significant Lod score of 16.7 (theta = 0.016). We have now narrowed the RCND interval, following selection and RH mapping of canine genes from the 1x canine genome sequence, to a small portion of CFA5 that corresponds to human chromosome 17p11.2. Using comparative genomics, we evaluated potential candidate genes in the region and undertaken mutation screening in those considered most likely. This work underscores the emerging power of canine genomics to aid in the pursuit of genes causing mammalian disease. Towards that end, we present data on a likely candidate gene.

Biographical Sketch

Dr. Elaine A. Ostrander is Member of the Divisions of Clinical Research and Human Biology at the Fred Hutchinson Cancer Research Center, Affiliate Professor in the departments of Biology and Genome Sciences at the University of Washington, and Head of the Interdisciplinary program in Genetics/Genomics at the Fred Hutchinson Cancer Research Center. Dr. Ostrander's research interests are in the area of genetic mapping and genomics. She oversees a large research lab aimed at mapping and cloning genes that, when mutated, increase the risk of breast and prostate cancer in humans. In addition, she oversees an international effort aimed at mapping the canine genome, and finding cancer susceptibility genes in dogs. Her most recent interests include understanding population genetic structure of modern domestic dogs.

High Resolution RH Mapping of the Dog Genome and Its Application to the Positional Cloning of Cancer Genes

Elaine A. Ostrander [1], Richard Guyon[2], Ewen F. Kirkness[3], Christophe Hitte[2], Kenine Comstock[1], Edouard Cadieu[2], Heidi G. Parker[1], Pascale Quignon[2], Travis Lorentzen[1], Corinne Renier[2], Jennifer K, Lowe[1], Stephanie Gloux[2] , Françoise Vignaux[2], Lisa Kim[1] , Catherine André[2], Francis Galibert[1]

[1]Clinical and Human Biology Divisions, Fred Hutchinson Cancer Research Center, Seattle WA USA, [2]UMR 6061 CNRS, Génétique et développement, Faculté de Médecine, 35043 Rennes Cédex, France, [3]The Institute for Genome Research, Rockville, MD.

The purebred dog population consists of over 300 partially inbred genetic isolates termed breeds. Restriction of gene flow between breeds, together with strong selection for behavioral and physiologic traits, has led to the establishment of a unique resource for dissecting the genetic basis of both simple and complex mammalian traits. Of particular interest are genes responsible for complex human diseases such as cancer, heart disease, and blindness. Towards this end, we present a comprehensive radiation hybrid (RH) map of the canine genome composed of 3400 markers, including 1,700 microsatellites, 1,000 cloned gene sequences and ESTs, and 700 canine-specific BAC-ends. The 3400 markers map to 3130 unique positions and define an average inter-marker distance of 10cR5000, corresponding to 1Mbase. The map provides nearly complete coverage of the canine genome. The inclusion of 1000 dog genes and ESTs allows refined mapping of breakpoints between conserved segments of human and dog chromosomes, and suggests some 85 evolutionarily conserved segments between the dog and human genomes. Approximately 800 of the 1,700 mapped microsatellites have HET or PIC values ≥0.5, providing a well characterized resource for genome wide scans in purebred pedigrees. The 700 mapped BAC-ends constitute an initial framework of clones for anchoring the physical map and provide a format for positional cloning studies. We describe the utilization of this map for the positional cloning of several genes of interest.

Biographical Sketch

Dr. Elaine A. Ostrander is Member of the Divisions of Clinical Research and Human Biology at the Fred Hutchinson Cancer Research Center, Affiliate Professor in the departments of Biology and Genome Sciences at the University of Washington, and Head of the Interdisciplinary program in Genetics/Genomics at the Fred Hutchinson Cancer Research Center. Dr. Ostrander's research interests are in the area of genetic mapping and genomics. She oversees a large research lab aimed at mapping and cloning genes that, when mutated, increase the risk of breast and prostate cancer in humans. In addition, she oversees an international effort aimed at mapping the canine genome, and finding cancer susceptibility genes in dogs. Her most recent interests include understanding population genetic structure of modern domestic dogs.

Color Implications in Health

Sheila M. Schmutz and Tom G. Berryere *University of Saskatchewan, Saskatoon Canada*
schmutz@sask.usask.ca

Coat color has been of considerable interest to dog breeders for many years. In 1957, C.C. Little provided a comprehensive hypothesis with many genes and alleles to explain most of the colors and patterns in dogs, based on breeding records. For the past few years we have studied genes involved in the pigmentation pathway at the DNA level (http://skyway.usask.ca/~schmutz/dogcolors.html). Many of Little's predictions have held true but some have not.

We found DNA polymorphisms in several genes in the pigmentation pathway. We used these polymorphisms or markers to map genes named *EDNRB* and *DCT* to chromosome number 22, *KITLG* to chromosome number 15, *TYR* to chromosome number 21 and *TYRP1* to chromosome number 11. These markers have also been used in family studies to follow whether the same variant of the marker always was inherited with a particular coat color, pattern, or associated health problem.

We have identified multiple mutations in some genes such as *TYRP1* that cause brown color, none of which have ill effects on health. Whereas other coat color genes have multiple effects, including some on health. For example merle, which when homozygous, usually causes deafness and sometimes also serious eye problems. We have conducted a family study using Australian Shepherds and have excluded several genes as the cause of merle: *EDNRB, KITLG, MITF, ASIP, TYR, PAX3.* We are currently studying Harlequin and merle in Great Danes using the polymorphisms in these same genes. Family and data collection are still ongoing but results thus far are more optimistic. (Harlequin Great Danes are thought to be HhMm, or heterozygous at both the Harl and merle causing genes and so finding which gene causes the Harlequin pattern may also lead us to find the gene that causes merle.

It was suggested that "albino" Dobermans may have a mutation in tyrosinase, since that is the cause of many types of albinism in humans and mice. However, in a recently completed study, the entire coding sequence of *TYR* was normal in such Dobermans (GenBankAY336053) and also in blue and Isabella Doberman Pinschers. These results suggest that the *P* gene may be the cause of this albinism. We did find that these same Isabella and red Dobermans were both homozygous for the *TYRP1* proline deletion mutation indicating both are actually brown in base color.

Black Hair Follicular Dysplasia is a disorder that has occurred in my own kennel in Large Munsterlanders. Areas of the coat that are normally black in color are grey at birth and then these weak hairs break and fall out. The underlying darkly pignmented skin is also wrinkled and sometimes pimply. Using this litter we have shown that neither *MC1R, DCT, TYRP1, KITLG*, nor *TYR* are the genes causing this disease. Colleagues at the University of Pennsylvania plan to continue studies of this disease and samples were also sent to other collaborators in Germany.

Currently, we are also studying *MITF* in microphthalmicied multipe forms of this gene in the dog (GenBank AY2400952). Alternate start codons and some differential splicing of exon 1 and 6 result in different forms in different tissues. Thereby a mutation in exon 1 may lead to an effect on the eye and not on coat color, whereas a mutation in exon 7 could affect both tissues.

We have recently identifed the mutation in *MC1R* that causes melanistic mask. At amino acid 264, methionine is replaced by valine. Some dogs with melanistic mask have premature greying of the muzzle but this does not seem to be correlated with whether they are homozygous or heterozygous for mask.

Some coat patterns such as Harlequin, merle and Irish spotting can make it impossible to see the mask. Likewise dogs that are black or brown or blue do not show their mask against their similar body color. This further confirms that dogs in breeds where mask is part of the standard such as Bullmastiffs and Boxers, the reddish coat colors are due to the agouti alleles and not an ee genotype at *MC1R*.

In the course of this same study we were able to show conclusively that brindle is not caused by an *MC1R* allele, as Little had predicted . Several dog owners had found that the prediction of an E^{br} allele did not fit their breeding data either.

We thank the many dog owners who have contributed DNA samples from their dogs or complete litters to our study. In addition we are particularly grateful to C.A. Sharp (Australian Shepherds), J.P. Yousha (Great Danes), and Ione Smith (Doberman Pinschers) who coordinated collection of groups of animals in particular breeds for family studies.

Key to Gene Abbreviations

Gene Abbreviation	Gene Name	C. C. Little's Locus
ASIP	agouti signalling protein	A locus
TYRP1	tryrosinase related protein 1	B locus
TYR	tyrosinase	C locus?
MC1R	melanocortin 1 receptor	E locus
DCT	dopachrome tautomerase	
EDNRB	endothelin receptor B	
KITLG	KIT ligand	
MITF	microphthalmia transcription factor	
PAX3	paired box 3 protein	

Biographical Sketch

Sheila Schmutz has been a professor at the University of Saskatchewan since 1986 where she teaches animal genetics to agriculture and veterinary students. Most of her research is done using DNA to studies traits in cattle, including coat color, which has expanded in the past few years to include dogs (http://skyway.usask.ca/~schmutz/dogcolors.html). Sheila and her husband have had and bred Large Munsterlanders for the past 25 years. Her dogs "volunteer" for her DNA studies regularly but many dog owners participate by sending in cheek brushes for DNA from their litters.

Vaccine Update: Controversial Issues

Saralyn Smith-Carr, DVM, PhD, DACVIM; Jim Wright, DVM, PhD, DACVPM

Many controversial issues surround the use of vaccines in the dog and cat. New vaccine technology has let to an increase in the number of vaccines available for prevention of infectious disease in susceptible pets. However, risk of disease rather than availability should be considered when determining which vaccines are used in a vaccination program. Uncertainty arises concerning the designation of vaccines that should be used in a vaccine program and the method of individualizing the vaccine program for each pet. The American Veterinary Medical Association has designated core and non-core vaccines for dogs and cats to provide guidance to the veterinary practitioner. Core vaccines are those needed by all cats and dogs while non-core vaccines are recommended based on increased risk of exposure to an infectious agent.

An assortment of vaccines are available that are in both core and non-core vaccine categories. Therefore, the type4 of vaccine that is administered is also an issue of divergence. The types of vaccines available are modified live virus, killed virus or bacteria, subunit, and recombinant virus. Veterinarians as health-care givers must be conscious of when to choose modified live, subunit, killed or recombinant vaccines for incorporation into the vaccine program for each individual pet. Reasons for choice of a particular vaccine are efficacy, availability and avoidance of predictable adverse vaccine reactions such as abortion caused by administering live virus vaccines to pregnant animals.

Unpredictable adverse reactions to vaccines are another problem that both pet owners and veterinarians face today. Most adverse reactions such as hypersensitivity reactions can be successfully treated or minor reactions such as soreness, fever and lethargy disappear within a day without treatment. More severe adverse reactions occur that are linked to recent vaccination of the pet. Injection-site sarcomas and autoimmune disease are two such adverse reactions linked to vaccine administration that may lead to the death of the animal. Injection-site sarcomas in cats became a problem with the advent of feline leukemia virus vaccine, a subunit vaccine, and rabies vaccine, a killed virus vaccine that contain an aluminum-based adjuvant. Adjuvants are used in vaccine formulation to boost the immune response to the vaccine proteins (antigens). Hypersensitivity reactions leading to urticaria and wheal formation have been associated with the leptospira bacterin. Therefore adverse reactions are an important consideration in vaccine selection.

Vaccine programs along with improved sanitation have been very beneficial in the prevention of transmission and spread of severe infectious diseases. Therefore the abandonment of these programs would be neither wise nor advised. A better approach would be to evaluate how often a vaccine should be administered. This would decrease the frequency of vaccines that potentially lead to adverse reactions. Yearly vaccinations have been the standard of health in the past; however, with the development of the; more advanced vaccines, protection may last longer. Therefore the issue of controversy is duration of immunity of core vaccines. Reports from the veterinary investigators have indicated that the duration of immunity of the core vaccines are longer than one year. These same investigators have expressed the view that all canine core vaccines except rabies should be administered every three years instead of yearly. We decided to conduct our own investigation into the duration of immunity of three of the core vaccines recommended for dogs, canine adenovirus, canine distemper virus, and canine parvovirus vaccines.

Biographical Sketch

Saralyn Smith-Carr, DVM, PhD, DACVIM, completed her DVM at Tuskegee University School of Veterinary Medicine in 1978. She completed an internship program in Small Animal Medicine, Surgery and Radiology at Tuskegee University School of Veterinary Medicine from 1978-1979. Afterwards, Dr. Smith-Carr spent one year in practice as a staff veterinarian at the Atlanta Humane Society, followed by an internship program in Small Animal Medicine and Surgery and immediately afterwards a combined residency and masters program in Small Animal Internal Medicine at Washington State University College of Veterinary Medicine. Her PhD from WSU was in immunology of retroviruses, particularly immune subsets observed by flow cytometry during Bovine Leukemia Virus Infection. She returned to Tuskegee University School of Veterinary Medicine as an assistant professor in the Department of Small Animal Medicine and Surgery in 1987. Dr. Smith-Carr achieved tenure and promotion to associate professor and also the Norden's Teacher of the Year Award in 1990. She is presently an associate professor in the Department of Clinical Science at Auburn College of Veterinary Medicine and achieved board certification in the American College of Veterinary Medicine in 2000. Clinical interests include internal medicine, diseases of the liver, lower urinary system, reproductive tract and infectious diseases. Research interests are in using immunology techniques, particularly flow cytometry, to determine the immune responses to infectious disease.

Successful Dog Ownership

Keith Benson, President and Chief Operating Officer of Triple Crown Dog Academy, Inc.
Jessy Gabriel, Co-Director of Training and certified professional dog trainer and animal care specialist,Triple Crown Dog Academy, Inc.

Pet education, including socialization and training, is a fundamental element in successful dog ownership. Early socialization and imprinting will affect the dog's confidence and how it reacts to its environment, including other people and animals. Training improves the quality of life for dogs of all ages; however, effective education programs should begin at an early age and extend beyond the training classes and into the homes where dogs live. Training also allows owners to effectively communicate with their pets, promoting a well adjusted companion and life lasting bond. Genetics, nutrition and training are all vital elements in the lifecycle of successful dog ownership. Successful training programs require an understanding of the basic science behind how dogs learn. One of many techniques that combine the principles of classical and operant conditioning is clicker training. With this technique, dogs are conditioned to associate the sound of the click to a positive outcome, or reward. For most dog owners this is a good first step towards imprinting desirable behaviors and the experience provides a better understanding of how dogs learn. Solvable training and behavior problems are the primary reason that owners become unhappy with their dogs. Unfortunately, this leads to millions of unwanted dogs in shelters each year. Providing educational resources on breeds, behavior, and training will help to keep pets in the home where they belong. As responsible breeders and pet care providers, it is our responsibility to promote training and education for the life of the dog.

Biographical Sketch

Keith Benson received his degree in Psychology and spent several years conducting neuropsychological and personality testing in the behavioral and forensic field. A long time passion for dogs led him to a career change of working with people and their pets. Keith became a certified professional dog trainer and behavior specialist, and for the past ten years he has been helping people strengthen the special bond that lies within all of our canine companions. During this time, he has offered behavioral consulting, competed in AKC obedience, conformation, and the European sport of Schutzhund. He has also participated in training demonstrations around the country, as well as being featured in numerous national publications.

Keith is currently the President and Chief Operating Officer of Triple Crown Dog Academy, Inc., the largest training and behavior center for dogs in the world. This 350 acre complex hosts dog shows of all kinds from around the United States and is also the campus for Triple Crown Academy for professional dog trainers, Inc., where he is the Educational Director. Along with 7 other Academy instructors, Keith teaches pet obedience theory and application, business development and behavior modification to students from around the world. Triple Crown's Pet Products Development Committee, for which he is Executive Director, strives to design and create pet products that will enhance the relationship between owners and their pets. Triple Crown's dedication to bettering the people-pet relationship shows in their efforts to educate people on how dogs learn and how to effectively communicate with their pets.

Jessy Gabriel, Co-Director of Training and certified professional dog trainer and animal care specialist, has been with Triple Crown Dog Academy, Inc. since its inception. She has worked with thousands of dogs and owners to reach their training goals through private lessons, group classes, and In-Kennel Training. She has also trained and certified several police dogs. As Head Instructor of Triple Crown Academy for Professional Dog Trainers Inc., Jessy has helped many people realize their dream of becoming a professional dog trainer. Her knowledge of how dogs learn and experience in working with thousands of dogs is utilized as an inventor for Triple Crown's Pet Products Division. Jessy has successfully competed and shown at Regional and National shows in many areas of dog sports including: AKC Obedience, Agility, and Hunt Tests; SAR; and Schutzhund. She has represented the United States in WUSV World Schutzhund Championship in Germany, as well as the FCI World Schutzhund Championship in Switzerland.

What is New in Canine Reproduction and That Which Lies Ahead!!!

Dr. William C. Truesdale

Since the 1980s there has been increased scientific awareness and availability of Technology for the Canine Breeder.

An explosive veterinary and breeder interest in centers for the collection, storage and use of canine semen is at a rapid growth. Many are individually owned, as well as franchised facilities, within the US and worldwide (Clone, Symbiotics, ICSB). Other purposes are geared in the direction of genetic counseling and health testing (OFA, Cardiac monitoring, OD, CHIC) at this point monitoring physical health, physical exam, CBC and profiles, fecal and urine, *Brucella canis*, culture for other bacteria, when indicated. There has also been a focus on reproductive health (gonads, semen evaluation, exam of prostate, etc.).

Utilization of Frozen Semen

I. Types of Breeding with Frozen Semen

a. Standard AI

b. Transcervical Scandinavian and Endoscopic Transcervical

c. Surgical Standard, and Laproscopic Technique

II. Timing the Bitch for Frozen Semen

a. Behavior of Bitch

b. Vaginal Smears and their use

c. Vaginoscopy Changes and the cycle

d. LH Testing

e. Progesterone (The Gold Standard); RIA, Illuminescence In-House Testing, etc.

III. DNA Testing: Paternity, and as a Vehicle to ID Dual Sired Progeny

IV. Pregnancy Determination

a. Palpation

b. X-ray

c. Relaxin Test

d. Ultrasound

e. Vaginal Cytology and Clumping Effect (Dr. E. Mason ongoing study in Norfolk, VA)

V. Whelping Date

a. Estimate by Breeding/The Whelping Chart

b. LH Peak due 65 + One Day

c. Progesterone = Ovulation due 63 days conception 2-3 days post ovulation

d. Ultrasound and software to determine whelping date

e. Fetal Size

f. Progesterone less than 2 nanograms, when ready to whelp if ovulation not determined

VI. Whelpwise: A Prenatal Care Service involved Fetal Ultrasound and Uterine Contraction Monitoring

VII. Discussion and Slides: What Lies Ahead for Canine Reproduction

a. Improved Freezing Techniques for easier use

b. Invitro Fertilaztion

c. Introcytoplasmic Sperm Injection

d. Gender Selection based on physical properties of X/Y sperm and time of breeding and ovulation

e. Lazaron-Cloning/Cryopreservation slides to show first litter due in 1-5 years.

i. What are the ethics of this?

ii. Will it be welcome by breeders and its registry?

f. Weak Point: Is cultivating the Ova for Canine Cloning and Synchronizing Estrous for Implanting of the Surrogate Dam, Cloned Embryo Not Suitable for Freezing/ VERY FRAGILE; LSU and Texas A&M lead the way

There is a need for research on canine fertility; both the maintenance of and treatment for, and the funding for educating dog breeders.

Much has been said that priority one is to get our canine supporters "breeder wise." Much myth surrounds the dog breeding world. Only through science and education can this be resolved.

Biographical Sketch

Dr. William C. Truesdale is a graduate of Michigan State University (School of Veterinary Medicine, Class of 1972). He is a past intern of the Rowley Memorial Hospital in Springfield, MA.

Dr. Truesdale has been in private practice for Small Animals since 1977. Although he categorizes himself as a general practitioner, his special interest is in reproductive issues. He has lectured at numerous dog clubs on the subject, to include the Doberman Pinscher Club of America, Ladies Dog Club, Newfoundland Club of America, New England Terrier Club, New England Rottweiler Club and the Middlesex Boxer Club, to mention a few. In October 2000, Dr. Truesdale was selected by the AKC/Breeders Education Committee to officiate as a Key speaker at the First AKC Breeders Education Seminar.

One of Dr. Truesdale's passions is breeding successive Champion Boxers. To date he has bred and/or owned over 90 Champions, to include six generations of All Breed Best In Show Winners, and National Specialty Winners, and the Number One Stud Dog (Boxer) for the past four years. As a breeder he advocates health testing, this he feels is a must to assure the future of any breed. He is currently the President of the American Boxer Charitable Foundation and an advisor to the ABC Health Committee. Dr. Truesdale is also a Director of the AKC Canine Health Foundation.

The Origin and Evolutionary History of the Dog

Robert K. Wayne, *Department of Biology, University of California at Lost Angeles, Los Angeles, CA 90095-1606*

The domestic dog is a remarkably diverse species, so different in size and proportion that Darwin suggested it must have originated from several wild canine species. However, archeological evidence indicates that all dogs may have originated from a single population of gray wolves about 14,000 years ago. This event was coincident with the shift from hunter-gatherer to more sedentary agricultural societies. We have surveyed genetic diversity of the domestic dog and other canines to understand their evolutionary history. The dog family, *Canidae*, represents a very early divergence in the history of carnivores and is not closely related to any other carnivore family. Within *Canidae*, three distinct groups are apparent including the fox0like, wolf-like and South American canids. We found a surprising amount of genetic diversity in the domestic dog suggesting a more ancient and diverse origin, perhaps over 100,000 years ago, and which involved several populations of gray wolves. The discrepancy between archaeological and genetic dates implies a dramatically different relationship between dog and human may have existed in more ancient times. Finally, dogs and wolves continue to interact genetically through the production of natural and artificial of dog-wolf hybrids. Such hybrids cause legal and conservation problems.

Biographical Profile

Dr. Robert Wayne received his PhD from Johns Hopkins University. He is currently in the Department of Organismic Biology, Ecology and Evolution at the University of California at Los Angeles. Dr. Wayne's research interests include application of molecular genetic techniques to questions in systematics, population genetics, sociobiology and conservation.