Friday, October 19, 2007

Genetics Primer

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The goal of dog breeders is to retain desirable traits while minimizing those traits that are less desirable or even deleterious. Effective breeding requires an understanding of parental contribution and the genetic transmission of traits. This talk will discuss how traits are passed down through generations, evaluation of pedigrees and assessing mode of inheritance for specific traits, making selection decisions, and various breeding approaches. Further, with the advent of tools that allow genetic testing, breeders are faced with even more information that needs to be interpreted in selecting sires and dams. How do these tests work, how they can be used, and how are they developed will also be covered along with what recourse breeders have if such tests are not yet available.

Responsible Breeding Management of Genetic Disease

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Breeders and Breeding

Breeders of dogs desire to produce the best with their matings. However, breeding has become more complicated today, and more people with intact dogs are becoming "breeders". It is up to other breeders, breed associations, and veterinarians to educate prospective breeders on understanding breed characteristics, historical selection parameters, and the continuous evolution of health testing to promote healthy breeding practices.

Adding to the complexity of breeding is the expansion of planned cross-breedings (designer breeds) to produce offspring. Therefore, the discussion is no longer between pure-bred and cross-bred, but between purposely-bred and random-bred dogs.

There is a general misconception that mixed-breed dogs are inherently free of genetic disease. This may be true for rare, breed-related disorders; but the common genetic diseases that are seen across all breeds are seen with the same frequency in mixed-breeds. A mixed-breed dog with hip arthritis has no less a case of hip dysplasia than a pure-bred dog. The only difference is that conscientious breeders test and label their dogs as dysplastic prior to the onset of clinical signs. I do not see a difference between the relative frequencies of old pure-bred dogs versus old mixed-breed dogs with hip arthritis requiring arthritis pain medication.

Testing for inherited hypothyroidism (for thyroglobulin autoantibodies by Michigan State University) shows 10.7% of 55,053 tested mixed-breed dogs to be affected. The average percentage of affected dogs for all pure breeds is 7.5%. This does not tell us that mixed-breed dogs are more prone to autoimmune thyroiditis: More mixed-breed dogs are tested based on clinical signs. However, these results show us that this hereditary disorder is seen frequently in both pure-bred and mixed-breed dogs. To those that feel that this disorder is not genetic, we look at the historical breed predilections for the disorder. Those breeds with the highest genetic propensity for autoimmune thyroiditis remain high over the years (example: 31.4% of English Setters tested), and those breeds with the lowest propensity

remain low (example: 1.1% of French Bulldogs). Selection based on thyroid testing (and in the future direct genetic tests for liability genes) should reduce the frequency of this disorder.

The most common inherited disorders for all dog breeds according to the AKC Canine Health Foundation are: cancer, eye disease, epilepsy, hip dysplasia, hypothyroidism, heart disease, autoimmune disease, allergies, patellar luxation, and renal dysplasia. With the exception of renal dysplasia, all of these genetic conditions are routinely seen in mixed-breed dogs.

There are some defective disease-causing genes that mutated so long ago, that the mutation (and its associated disease) is found in evolutionary divergent breeds. The same ancestral autosomal recessive mutation for the progressive rod cone degeneration (prcd) form of progressive retinal atrophy (PRA) is shared by over 17 diverse breeds, including the American Cocker Spaniel, Australian Cattle Dog, Chinese Crested, Kuvasz, Labrador Retriever, and Toy Poodle. The list of affected breeds continues to grow as more are discovered with the same defective gene. The question is not, "Which breeds carried this defective gene during their development", but "Which breeds did not lose this defective gene during ancestral development."

It is also not surprising that prcd-PRA affected dogs (who must receive the defective gene from both parents) have been identified in Labradoodles (Labrador x Poodle crosses), and Cockapoos (Cocker Spaniel x Poodle crosses). Labradoodles are also being diagnosed with hip dysplasia, elbow dysplasia, and inherited Addison's disease; all recognized disorders in both parent breeds.

So, if breeders desire to produce the best with their matings, the basic question becomes; "Who is a reputable breeder?" For purposely-bred dogs, it is those breeders who perform genetic testing for breed-susceptible disorders. Official test results should be made available to prospective breeders, and the pet and breeding-stock purchasing public. It doesn't matter whether a breeder is a large commercial breeder, or only breeds once. In today's environment, not testing for documented breed-related hereditary diseases is irresponsible breeding.

Responsible breeding also involves knowledge of how best to use the results of genetic testing. For pure-breeds there are concerns about the breadth of the available gene pool and genetic diversity. Genetic test results should be used to benefit the overall health of breeds, not to limit it. A discussion of these issues, and breeding recommendations for genetic disorders based on different modes of inheritance are included in the proceedings of the 2007 Tufts' Canine & Feline Breeding and Genetics Conference: www.vin.com/tufts/2007.

Genetic Test Results and Genetic Registries

For direct genetic tests, official test results of the parents, and/or the offspring (tested prior to placement) should be made available to prospective breeders or purchasers of pet or breeding dogs. For some breed associations, the results of genetic testing are available in on-line, publicly accessible databases.

For disorders where there is no direct genetic test available, the knowledge of phenotypic test results (for affected, or carrier status if possible) should be made available in open health database registries. For most of these disorders, it is only through the open reporting of affected dogs that knowledge of

disease risk can be identified through the test results or health status of close relatives.

The Orthopedic Foundation for Animals (OFA: www.offa.org) maintains semi-open health registries for testable genetic disorders. Applications for all of the hereditary disorders in their databases include a check-off to openly report ALL test results; both normal and abnormal. For many breeds of dogs tracking hip dysplasia for example, over one-third of the applicants check the box for open reporting. **It is important that as breeders and veterinarians we encourage open reporting of health results.** The days of stigmatizing conscientious, health-testing breeders who have produced dogs with hereditary disease are gone. No one wants to produce affected offspring from their matings, and no one should be blamed if this occurs (unless the breeder is not doing the recommended health testing). It should be everyone's goal to produce healthy offspring, but this is not possible if the only available health information is about normal dogs, but not abnormal dogs. Once the majority of owners are initialing the box for open reporting, the OFA can change it to a check-off box for not reporting abnormal test results.

The Canine Health Information Center (CHIC: www.caninehealthinfo.org) was established by the AKC Canine Health Foundation and the OFA to assist breeds with managing breed-specific genetic disorders. The AKC national breed clubs determine the recommended testable disorders for the breed (whether tests of the phenotype or the genotype). If an owner is contemplating breeding their dog, they can look up the recommended genetic tests to perform in their breed. Veterinarians can also assist prospective breeders by looking up and discussing the recommended genetic tests for the breed. Prospective breeding dogs can be researched, and their genetic test results, as well as that of their close relatives can be studied.

The benefit of the CHIC system is that dogs gain CHIC certification by completing their health testing, regardless of their test results. **CHIC is about health consciousness, not health perfection.** As more tests for defective genes are developed, every individual is likely to carry some deleterious genes.

Veterinarians should ask for pedigrees and results of parental or early age health testing of pure-bred and cross-bred puppies on first presentation to their clinics. If the test results were not provided to the owner, many can be immediately searched in on-line databases like OFA or CHIC. **A lack of available test results shows that the puppy was not purchased from a health conscious breeder, and it may be liable to develop genetic disease.** The general public must be educated to become informed "consumers" when purchasing puppies. They should spend as much time researching the purchase of what will become a member of their family for 10+ years, as they do purchasing home appliances. Breeder health guarantees that provide for replacement of puppies with genetic disease are often worthless; as few pet owners will be willing to give up a member of their family once an emotional bond has been established.

Example: Cerebellar Abiotrophy (Ataxia) in Scottish Terriers
The Scottish Terrier Club of America (STCA) has provided all of the tools necessary to determine genetic risk of carrying the defective gene causing the autosomal recessive genetic disorder cerebellar abiotrophy (CA), or for producing affected puppies. CA is a degenerative neurological disease that causes slowly progressive incoordination from several months to several years of age. The defective

gene is old, and widespread in the Scottish Terrier gene pool worldwide.

The STCA has an area on their website entitled CA Central (www.stca.biz/GrandCentral/) where a list of all confirmed CA affected dogs and their pedigrees is listed. The club maintains an online searchable pedigree database (www.stca.biz/pedigrees/) that includes identification of all dogs with obligate CA risk. They also have a relative risk analysis calculator in CA Central that allows breeders to calculate the CA carrier and affected risk of dogs and of proposed matings.

The STCA has funded several studies to identify the autosomal recessive defective gene causing CA, and its members and breeders hope to some day have a genetic test for carriers. However, CA Central allows their breeders to minimize their current risk of producing Scottish Terriers affected with cerebellar abiotrophy, and reduce the frequency of the defective gene now, while waiting for a genetic test to be developed.

Health testing and the knowledgeable use of test results is now an important requirement for responsible breeding. Breeders, veterinarians, and breed organizations must educate the general public of the need to check for health testing in their dog purchases. As this happens, the overall genetic health of purposely-bred dogs will improve.

Biographical Profile

Dr. Anita M. Oberbauer is Professor and Vice-Chair in the Department of Animal Science at the University of California, Davis. She earned a B.S. at the University of California, Davis in zoology, a Ph.D. degree from Cornell University in animal physiology minoring in statistics and pathology, and then conducted postdoctoral research in growth factors and gene regulation at Loma Linda University and in Biological Chemistry at University of California, Los Angeles. She has received the Jim Corbin Award in Companion Animal Biology offered by the American Society of Animal Science and distinguished teaching awards from UC Davis and the Western Section of the American Society of Animal Science. She serves on the Board of Directors of the Orthopedic Foundation for Animals. Her research program emphasizes growth and development focusing on the relationship between skeletal size and overall body composition, as well characterizing the genetic basis for health disorders in dogs. She is the current health education chair of for the American Belgian Tervuren Club, and actively competes with her Belgian Tervuren which she shows in all AKC venues open to the herding group.

Dr. Jerold S. Bell is a Clinical Associate Professor, and Director of the Clinical Veterinary Genetics Course for the Tufts Cummings 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 is a lecturer to all-breed and individual breed dog clubs. He has published numerous articles on breeding and genetics in the AKC Gazette. He is the project administrator of genetic disease control programs for national parent clubs, and practices small animal medicine at Freshwater Veterinary Hospital in Enfield, CT. He and his wife breed Gordon Setters.

Dr. Oberbauer's research has been supported by the following grants:

1613: Development of a Genetic Marker for Idiopathic Epilepsy in the Belgian Tervuren and Belgian Sheepdog
1657T.- Identification and Inheritance of DNA Markers for Addison's Disease
2015: Development of a Genetic Marker for Idiopathic Epilepsy in the Belgian Tervuren and Belgian Sheepdog
2104: Defining Inheritance of Idiopathic Epilepsy in the Mastiff, Poodle and Giant Schnauzer
2226: Characterizing the Inheritance of Addison's Disease and Linked DNA Markers
2227: Defining the Mode of Inheritance for Primary Lens Luxation and Juvenile Cataracts in the Jack Russell Terrier
224: Characterizing Idiopathic Epilepsy in the Poodle, Giant Schnauzer, English Mastiff: An Assessment of Inheritance
225: Establishing a Genetic Linkage Between Addison's Disease and DNA Markers
2614: Refining the Genetic Linkage For Idiopathic Epilepsy in the Belgian Tervuren and Sheepdog
351-A: Identifying the Mode of Inheritance for Primary Lens Luxation and Juvenile Cataracts in the Parson Russell Terrier
668-A: Inheritance of Addison's Disease in Nova Scotia Duck Tolling Retrievers
958: Idiopathic Epilepsy in the Poodle: Identifying Genomic Risk Factors