Closing the Gap – the Time Path

By Carmen L. Battaglia

Talent wins but it takes team work and intelligence to produce championships

Improving the conformation, health and temperament of purebred dogs should be the goal of every breeder. What makes this goal reachable began when the studbook for breeds closed. The result was the establishment of specific breeds. By definition closing the stud book means that the diversity of the genes for a breed would be restricted to those already present. Thus when a stud book closes no new genes are allowed into the breeds that were not already present in the gene pool. The exception is the occurrence of a few infrequent mutations. By closing a gene pool the pedigrees of each breed became dependable and reliable as a tool for improving breed type, health and temperament. Further refinements occurred as breeders began to use breed standards as their guide for breeding and selection. The result produced a large number (N=170) of desirable breeds with verifiable ancestries. Over time these closely monitored populations have become especially suitable for the study of diseases. Most of the major advances have occurred during the past two decades. With the advancement of DNA tests more improvements became possible at a faster pace. Other notable advancements included those in the area of digital radiographs, laboratory tests, nutrition and better breeding methods. Today, breeders can use these protocols to breed by direction rather than by chance.

When the canine genome sequencing project was first undertaken the American Kennel Club, Canine Health Foundation (AKC/CHF) became one of its largest non-profit supporters. Once it was completed the canine genome joined four other completed sequences, including one for the human and another for the chimpanzee. Many benefits were quickly realized. The breakthrough discovery on Neuronal Ceroid Lipofuscinosis (Tibetan Terriers) led to landmark stem cell replacement therapy in a California boy who was suffering with a disorder called Batten Disease. Other useful advancements quickly followed. For example, a test was developed for copper toxicosis (CT) in Bedlington Terriers where 25% are affected, 50% are carriers and only 25% are clear (Bell). Other was discoveries included a test for juvenile cataracts in Boston Terriers along with the mechanism involved in the transmission of the tick-borne disease, Rocky Mountain Spotted Fever (Brewer). Genetic markers for illnesses in Basenjis, Standard Poodles and English Cocker Spaniels followed. These technological advancements demonstrate what can be accomplished when breeders, clubs and research efforts are combined.

The key to this kind of success involves cooperation and sufficient funding. Perhaps the best example was the collaborative effort between the AKC/CHF and the Orthopedic Foundation for Animals (OFA) which resulted in the development of the Canine Health Information Center (CHIC) (www.caninehealthinfo.org). CHIC is an online registry that works with parent clubs to establish a panel of testable disorders for specific breeds. The CHIC concept is that dogs achieve a CHIC certification by

completing the health-checks identified by their breed club. Passing each health test is not a requirement for certification. CHIC is about being health conscious, not about being faultless. For those not ready to share in an open database CHIC offers a way to protect the privacy of their information. CHIC enters all test information into their database. Breeders who chose to restrict their test results participate in the aggregate because summary data is useful for research and statistical reporting.

CHIC functions not only as a tool for breeders and their clubs but as a resource for health information that can be shared in various ways. In this respect, every breeder can participate even if they are only willing to share limited amounts of information. Restricted data has value because it can be used for general searches about diseases and traits. This is often useful for research and the calculation of statistical averages. For example, summary data is useful to breeders who wish to compare their results to their breed's average.

Since its inception the AKC/CHF has funded more than 340 studies. Many of the top ten diseases found in purebred dogs are being studied at 74 veterinary schools and research institutions worldwide including those located in Argentina, Great Britain, France, Germany, Australia, and the Netherlands. Because of the many new methods and technological breakthroughs that have occurred there are more than 60 DNA tests now available for screening breeding stock.

THE TIME PATH

One of the major obstacles in bringing new DNA tests forward is called the time-path. This is the amount of time and effort required to identify a problem, characterize it, call it by its proper name, and secure funding. If the researcher is successful and discovers a solution, a protocol is developed for use by veterinarians and breeders. Unfortunately, the time-path is often longer than most expect. For example, once a project has been indentified and funded, blood samples and pedigrees must be collected. If the researcher is successful and a marker found, the next step is to make the information available in an easy to use and understandable manner. The time-path for the total process can be as short as a few years or as long as a decade. Each time a new test or new method is developed a new learning curve begins. Veterinarians and breeders must learn what laboratories can administer the test, how the results can be used and interpreted and what mechanism is available to identity and mange the carriers. With this kind of information and technology the genes that took years to collect can be saved while diseases and disorders can be controlled and eliminated.

With DNA technology and new breeding protocols the problems of the breeder can be addressed more directly. In the past the popular approach was to simply eliminate all of the carriers and affected dogs from a breeding program. Unfortunately, this approach quickly affected the diversity of a breed's gene pool. Others took a different approach and conducted test-matings to identify carriers, affected and normals. This did not prove to be a desirable method because the undesirable genes are either present or not and test breedings often produced

affected dogs that had to be carefully placed or euthanized. More recently better methods have become available that can reduce many of the problems of the past. For example, DNA testing can be used to eliminate problems because it allows breeders to manage carriers while saving the genes needed to maintain breed type and temperament. The screening of breeding stock followed by the selection of quality offspring offers a significant improvement over test-matings.

It has been well established that DNA tests will help breeders decrease the frequency of defective genes. If no test is available carriers can be carefully bred. The approach recommended is to breed carriers to those that appear normal when evaluated. The assumption is that the breeder will follow-up on the offspring produced. Using this approach breeders can select normal offspring for future breedings. This is a slower and less certain approach and it will not eliminate all of the carriers but it will reduce their frequency.

Because of the increased awareness of diagnostic tests better decisions can be made with positive results. The following tests and laboratories that administer tests for genetic disorders and some conformation traits are listed.

CANINE GENETIC TESTS – 2008

DISORDER	BREED	TEST TYPE	TEST ORG.	
Canine Leukocyte Adhesion Deficiency (CLAD)	**Irish Red & White Setter Irish Setter**	**Direct**	**Optigen**	

Cataract, juvenile (Early onset Hereditary Cataract – EHD)	**Boston Terrier** **French Bulldog** **Staffordshire Bull Terrier**	**Direct**	**Optigen**	
Ceroid lipofuscinosis	**Border Collie**	**Direct**	**Optigen**	
Ceroid lipofuscinosis	**American Bulldog** **Dachshund** **England Setter**	**Direct**	**U Missouri**	
Coat Color and Nose Color variations	**Australian Shepherd** **Border Collie** **Brittany** **Belgian Shepherd** **Belgian Tervuren** **Cardigan Welsh Corgi** **Collie (Rough, Smooth)** **Cocker Spaniel** **Curly-Coated Retriever** **Belgian Malinois** **Dachshund** **Dalmatian** **Doberman Pinscher** **English Cocker Spaniel** **Engish Setter** **English Springer Spaniel** **Field Spaniel** **Flat-coated Retriever** **French Bulldog** **German Shepherd Dog** **German long haired Pointer** **German Wirehaired Pointer** **Great Dane** **Greyhound** **Groenendael** **Labrador Retriever** **Laekenois** **Large Munsteriander** **Lowchen** **Newfoundland** **Pointer** **Pomeranian** **Poodle** **Portuguese Water Dog** **Pudelpointer** **Shetland Sheepdog** **Staffordshire Bull Terrier** **Whippet** **Wirehaired Pointing Griffon**	**Direct**	**HealthGene**	
Coat Color Gene Variations	**Alaskan Klee Kai** **American Cocker Spaniel** **Australian Cattle Dog** **Border Collie** **Curly Coated Retriever** **Dalmatian** **Doberman Pinscher** **English Cocker Spaniel**	**Direct**		

	English Springer Spaniel **Flat Coated Retriever** **Gordon Setter** **Labrador Retriever** **Newfoundland** **Pointer** **Poodle** **Schipperke** **Scottish Terrier** **Stumpy Tail Cattle Dog**			
Coat Length (FGF 5)	**Weimeraner**	**Direct**	**Animal Health Trust**	
Cobalamin Malabsorption (Methylmalonic Aciduria)	**Australian Shepherd** **Giant Schnauzer**	**Direct**	**PennGen**	
Collie Eye Anomaly (Choroidal Hypoplasia)	**Australian Shepherd** **Border Collie** **Lancashire Heeler** **Nova Scotia Duck Tolling Retriever** **Rough Coated Collie** **Shetland Sheepdog** **Smooth Coated Collie** **Whippet Longhair**	**Direct**	**Optigen**	
Cobalamin Malabsorption (Methylmalonic Aciduria)	**Beagle** **Border Collie** **DSH** **Shar Pei**	**Phenotypic**	**Penn Gen**	
Cone (Retinal) Degeneration	**German Shorthaired pointer**	**Direct**	**Optigen**	
Congenital Hopothyroidism With Goiter (CHG)	**Rat Terrier** **Toy Fox Terrier**	**Direct**	**Michigan State U. Fyfe Lab** **PennGen**	
Congenital Stationary Night Blindness (RPE65-CSNB)	**Briard**	**Direct**	**Optigen** **Animal Health Trust**	
Cystinuria	**Newfoundland** **Labrador Retriever**	**Direct**	**Optigen (Newf only)** **PennGen** **VetGen (Newf only)**	
Degenerative myelopathy (DM)	**German Shepherd Dog (Flash test)** **Boxer (RAPD)** **Pembroke Welsh Corgi (RAPD)** **Rhodesian Ridgeback (RAPD)**	**Direct Susceptibility loci)**	**U-Florida – Neuro Service**	
Factor VII Deficiency	**Alaskan Klee Kai** **Beale** **Scottish Deerhound**	**Direct**	**PennGen**	
Factor IX Deficiency	**Kerry Blue Terrier**	**Direct**	**PennGen**	
Fanconi Syndrome	**Basenji**	**Linked Marker**	**U-Missouri**	

Fanconi Syndrome	**Basenji** **Norwegian Elkhound**	**Phenotypic**	**PennGen**	
Fucosidosis	**English Springer Spaniel**	**Direct**	**PennGen** **Animal Health Trust**	
Glanzmann's Thrombasthenia (Type I)	**Great Pyrenees** **Otterhound**	**Direct**	**Auburn U – Boudreaux Lab**	
Globoid cell leukodystrophy	**Cairn Terrier** **West highland White Terrier**	**Direct**	**Jefferson Medical College**	
Glycogenosis (GSD) Type IIIa	**Curly Coated Retriever**	**Direct**	**Mich. State U Fyfe Lab**	
Glycogenosis (GSD) Type IV	**Norwegian Forest Cat**	**Direct**	**PennGen**	
GM1-Gangliosidosis	**Portuguese Water Dog**	**Direct**	**NY U, Neurogenetics Lab**	
Hypertrophic Cardiomyopathy	**Maine Coon Cat** **Ragdoll**	**Direct**	**Washington State U., Meurs Lab**	
Ivermectin Sensitivity (MDR-1)	**Australian Shepherd** **Collie** **Old English Sheepdog** **Shetland Sheepdog**	**Direct**	**Washington State U., Pharm Lab**	
L-2-HGA (L-2-hydroxyglutaric aciduria)	**Staffordshire Bull Terrier**	**Direct**	**Animal Health Trust**	
Mannosidosis	**DSH** **Persian**	**Direct**	**PennGen**	
Merle Gene (SILV)	**Australian Shepherds** **Beauceron Shepherd** **Border Collie** **CArdian Welsh Corgi** **Catahoula Leopard Dog** **Chihuahua** **Cocker Spaniel Collie** **Dachshund** **Great Danes** **Norwegian Hound** **Pitt Bull** **Pomeranian** **Pyrenean Shepherd** **Shetland Sheepdogs**	**Direct**	**GenMark**	
Mucolipidosis II (I-Cell Disease)	**DSH**	**Direct**	**PennGen**	
Mucopolysaccaharidosis (MPS)	**DSH** **German Shepherd Dog** **Miniature Pinscher** **Miniature Schnauzer** **Schipperke** **Siamese**	**Direct**	**PennGen**	
Muscular Myopathy (Centronuculear Myopathy)	**Labrador Retriever**	**Direct**	**Alfort School of Vet Medicine, France**	
Myotonia Congenita	**Miniature Schnauzer**	**Direct**	**Optigen** **PennGen**	

Narcolepsy	**Dachshund** **Doberman Pinscher** **Labrador Retriever**	**Direct**	**Optigen**	
Neonatal Encephalopathy	**Standard Poodle**	**Direct**	**U Missouri**	
Neophropathy (Hereditary N., Familial N.)	**English Cocker Spaniel**	**Direct**	**Optigen**	
Phosphofructokinase Deficiency (PFK)	**American Cocker Spaniel** **English Springer Spaniel**	**Direct**	**Optigen** **PennGen** **VetGen** **Animal Health Trust**	
Polycystic Kidney Disease (PKD)	**American Shorthair** **Himalayan** **Persian** **Scottish Fold**	**Direct**	**UC-Davis – Lyons Lab.** **Animal Health Trust**	
Primary Hyperparathyroidism	**Keeshond**	**Linkage**	**Cornell – Goldstein Lab.**	
Progressive Retinal Atrophy (cord1)	**Dachshund, Miniature Longhaired** **English Springer Spaniel**	**Direct**	**Animal Health Trust** **U Missouri**	
Progressive Retinal Atrophy Dominant	**Bullmastiff** **English Mastiff**	**Direct**	**Optigen**	
Progressive Retinal Atrophy (prcd)	**American Cocker Spaniel** **American Eskimo Dog** **Australian Cattle Dog** **Chesapeake Bay Retriever** **Chinese Crested** **Cockapoo** **English Cocker Spaniel** **Entelbucher Mt. Dog** **Finnish Lapphund** **Golden Retriever** **Kuvasz** **Labradoodle** **Labrador retriever** **Lapponian Herder** **Nova Scotia Duck Trolling Retriever** **Poodle (miniature, toy)** **Portuguese Water Dog** **Spanish Water Dog** **Stumpy Tail Cattle Dog** **Swedish Lapphund**	**Direct**	**Optigen**	
Progressive Retinal Atrophy (rcd1)	**Irish Red & White Setter** **Irish Setter**	**Direct**	**Optigen** **Animal Health Trust**	
Progressive Retinal Atrophy (rcd3)	**Cardigan Welsh Corgi**	**Direct**	**Mich. State U. - Peterson-Jones Lab. Optigen** **VetGen**	

Progressive Retinal Atrophy (rcd1a	**Sloughi**	**Direct**	**VetGen (Irish Setter)**	
Progressive Retinal Atrophy – Type A	**Miniature Schnauzer**	**Direct**	**Optigen**	
Progressive Retinal Atrophy – X-Linked	**Samoyed** **Siberian Husky**	**Direct**	**Optigen**	
Pyruvate Dehydrogenase Phosphatase Deficiency (PDH or PDP 1)	**Clumber Spaniel** **Sussex Spaniel**	**Direct**	**U Missouri Animal Health Trust**	
Pyruvate Kinase Deficiency (PK)	**Abyssinian** **American Eskimo Dog Basenji** **Beagle** **Cairn Terrier** **Chihuahua** **Dachshund** **DSH** **Somali** **West highland White Terrier**	**Direct**	**Optigen (Basenji)** **PennGen (All)** **VetGen (Basenji)** **Animal Health Trust (Westies)**	
Renal Dysplasia	**Lhasa Apso** **Shih Tzu** **Soft Coated Wheaten Terrier**	**Linkage**	**VetGen**	
Retinal Dysplasia – Canine Multi-focal retinopathy (CMR)	**Bullmastiff** **Coton de Tulear** **Dogue de Bordeaux** **Great Pyrenees** **Mastiff (English & French)**	**Direct**	**Optigen**	
Severe Dysplasia – Canine Multi-focal Retinopahty (CMR)	**Bullmastiff** **Coton de Tulear** **Dogue de Bordeaux** **Great Pyrenees** **Mastiff (English & French)**	**Direct**	**PennGen**	
Severe Muscular Atrophy	**Maine Coon Cat**	**Direct**	**Michigan State U – Fyfe Lab.**	
Thrombopathia	**Bassett Hound** **Landseer** **Sptiz**	**Direct**	**Auburn U – Boudreaux Lab.**	
Trapped Neutrophil Syndrome (TNS)	**Border Collie**	**Linkage**	**U. New South Wales**	
Von Willibrand's Diesase	**Bernese Mt Dog** **Doberman Pinscher** **Drentsche Patrijshound** **German Pinscher** **Kerry Blue Terrier** **Manchester Terrier** **Papillion** **Pembroke Welsh Corgi** **Poodle** **Scottish Terrier** **Shetland Sheepdog**	**Direct**	**VetGen**	
Von Willibrand's Diesase	**Irish Red & White Setter**	**Direct**	**Animal Health Trust**	

CONTACT LABORATORY SOURCES:

Alfort School of Veterinary Medicine: France, http://www.labradorcnm.com/
Animal Helath Trust: (England): http://www.aht.org.uk/sci_disc_genetics_dna.html#canine
Auburn University – Boudreaux Lab:
http://www.vetmed.auburn.edu/index.pl/Boudreaux_mk (334) 844 2692
Cornell – Goldstein Lab.: http://www.vet.cornell.edu/labgoldstein/ (607) 253 4480
Cornell Univ. Comparative Coagulation Lab.
http://www.diaglab.vet.cornell.edu/coag/test/hemopwh.asp (607) 275 0622
GenMark: http://www.genmarkag.com/home_companion.php (877) 766 3446
Health Gene: www.hearthgene.com (877) 371 1551
Jefferson Medical College: David.wenger@mail.tju.edu
Michigan State University – Peterson-Jones Lab:
http://www.cardigancorgis.com/PraPressRelease.aspx (517) 353 3278
New York University Neurogenetics lab: http://pwdca.org/GM1app.html (212) 263 2943
Optigen: www.optigen.com (607) 257 0301
PennGen: www.vet.upenn.edu/penngen (215) 898 8894
UC Davis – Lyons Lab: http://www.vgl.ucdavis.edu/service/catPKD.html (530) 752 2211
U Missouri – Johnson Lab: http://www.caninegeneticsdiseases.net/ (573) 884 3712
U New South Wales- Wilton Lab: a.wilton@unsw.edu.au
U Florida – Neuro Service: http://www.neuro.vetmeded.ufl.edu/dm_flash_test_web/index.html
(352) 392 4700 x 4700
VetGen: www.vetgen.com (800) 483 8436
Washington State U – Meurs Lab: http://www.vetmed.wsu.edu.edu/deptsVCGL/
(509) 335 6038
Washington State U – Pham Lab:
http://www.vetmed.wsu.edu.edu/annonements/invermectin/ownerinfo.asp (509) 335 3745

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