Bulgarian Shepherd Dog Genetic Study

Wisdom Health™ 2017

Acknowledgements:

Wisdom Health would like to thank all of the Bulgarian shepherd dog owners and breeders who have donated samples to make this study possible.

Contents

Introduction & Purpose 1
Materials and Methods 2
Similarity to Known Breeds 4
Breed Identification 6
Disease Mutation Prevalence 7
Trait Prevalence 8
Genetic Diversity Assessment 10
Conclusions 13
APPENDIX: 14

Introduction & Purpose

Between 2016-2017, Wisdom Health (formerly Mars Veterinary) received samples of Bulgarian shepherd dogs, also known as Karakachan dogs, from several owners, primarily in Bulgaria. We were interested in research on the breed as one of the indigenous breeds of Bulgaria, in order to better represent the breeds of Southeastern Europe for owners using our DNA testing services. To our knowledge, this is the first targeted investigation of SNP genotyping in the breed.

Wisdom Health has previously examined samples of 15,000+ purebred dogs of 270+ breeds and varieties from the North America, Australia, Europe and Asia for the purposes of

breed ancestry detection, disease and trait prevalence, and genetic diversity assessment. The Bulgarian shepherd dog was evaluated using a research process, the findings of which are shared below for the benefit of the study participants.

Materials and Methods

Sample processing. Nine buccal mucosal swab samples were processed by GeneSeek Inc., (Neogen Inc., Lincoln, NE). Each sample was assigned a unique sample ID and the DNA was extracted and genotyped on a custom Illumina® bead array chip. These genotypes were then sent to Wisdom Health (Vancouver, WA) for further analysis. Sample genotypes were assessed for quality based on the proportion of markers (reported as "call rates"). All samples met the quality threshold of 90% call rate required to be included in the evaluation (See Figure 1). A sample size of nine is considered inadequate to draw statistically-significant conclusions about disease and trait frequency or diversity measurements of the breed population, so these results should be considered preliminary only.

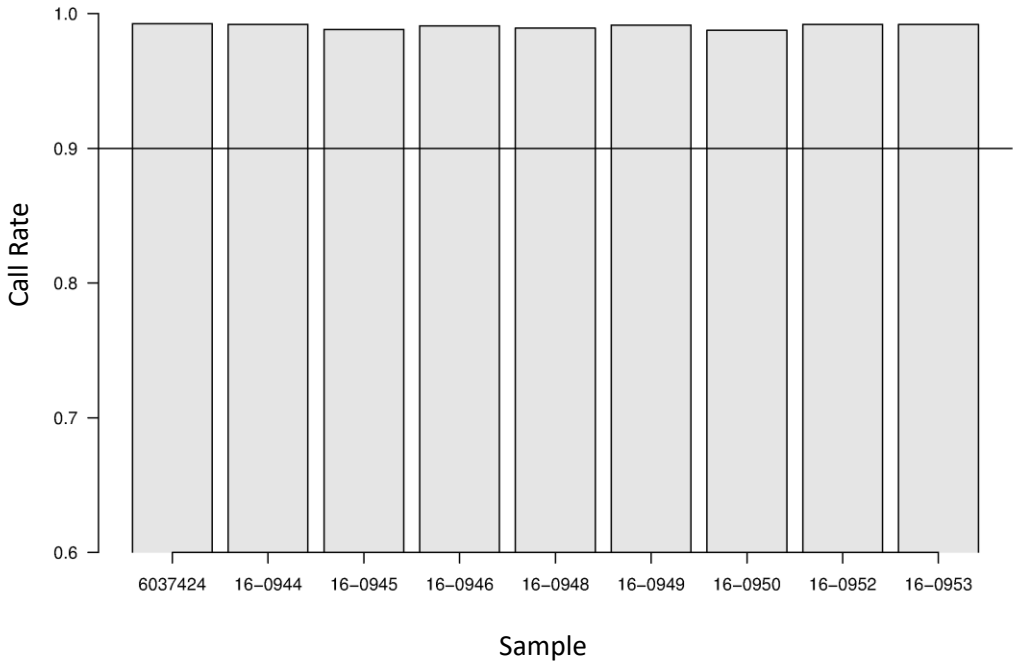


Figure 1: Call Rate of Submitted Samples

Breed similarity analysis. Assessment of how similar the genotypes of Bulgarian shepherds were to known genotypes of other breeds in our database was done with Principal Component Analysis (PCA) using the princomp package in R ver. 3.3.0 (The R Foundation, https://www.r-project.org), in addition to hierarchical clustering in the hclust package of R. This information was used to inform which breeds the Bulgarian shepherd should be compared against. Principle Component Analysis is an unsupervised clustering method of tested genotypes, and allows comparison of DNA similarity. Closely related samples, such as dogs within the same breed, will be expected to cluster together, unlike samples from other breeds. If a sample is within the cluster for the breed, this is a good indication that it is likely a pure member of this breed or species. Comparison against various groups provides further information about the sample, e.g. if clustering between the group of breed samples and a test group, this suggests genetic similarity (e.g. breed ancestry introduction) to both in that sample. Hierarchical clustering allows discrimination of different breed subgroups and helps identify where breeds might be closely related or might have originated from common ancestors.

Breed identification. From the PCA-inferred clusters, we identified likely purebreds based on where the majority clustered and added their selected genotypes to our breed database. We can now investigate how the algorithm would behave containing the Bulgarian shepherd dogs. The foundational algorithm used in breed identification has been in commercial use for over 10 years during which time it has been used to evaluate 800,000+ dogs.

Disease mutation prevalence. The Wisdom Health genotyping array tests for over 150 disease mutations. The process to detect disease mutations using this technology has been validated and in commercial process for more than 2 years, with over 400,000+ samples analyzed by this process. This algorithm was used against all samples to identify any disease mutation markers that might be present in the Bulgarian shepherd dog.

Trait prevalence. Wisdom Health has a separate proprietary algorithm to assign phenotypic trait prevalence. The algorithm has been validated and used in our commercial process, with over 300,000+ samples analyzed by this process. This algorithm was used against all samples to identify phenotypic traits exhibited by the Bulgarian shepherd dog.

Genetic diversity assessment. In genetics, diversity of a breed can be assessed by a variety of measures, but is commonly assessed by comparing the proportion of homozygous

genotypes. A homozygous genotype is one in which the same allele or genetic marker is inherited from both sire and dam, and indicates lower genetic diversity. A higher homozygosity of the offspring indicates closer similarity of sire and dam of that offspring. Compared over breed populations, more homozygous breed populations typify less genetic diversity, which is generally considered to be a negative indicator of genetic fitness.

Similarity to Known Breeds

Based on history of the breed, the Bulgarian shepherd was assumed to be most likely related to other livestock guardian dog breeds (LGDs). Previous independent studies by Wisdom Health and others has identified many LGDs to be related to the European herding breed family, while others, such as the Anatolian shepherd dog, to be more closely related to Middle East and African breeds. The Bulgarian shepherd was compared to 278 breeds from the Wisdom Health database using hierarchical clustering with Euclidean distance to identify the most likely related breeds in the Wisdom Health database. It should be noted that Eastern and Southeastern European breeds are not well represented in the database at this time, so comparisons to these breeds are unavailable. It was found that the Bulgarian shepherd grouped most closely with the Taigan, the Anatolian shepherd dog, and the Kritikos Lagonikos, and more distantly with the Maremma sheepdog and the Saint Bernard (see Figure 2). These observations support a history of shared ancestry with Middle Eastern breeds as well as Southeastern European breeds. The Anatolian shepherd is a LGD from modern-day Turkey, the Taigan, a sighthound from Kyrgyzstan, the Kritikos Lagonikos, a sighthound from Crete (Greece), the Maremma sheepdog an LGD from Italy, and the St. Bernard, a European mountain/draft breed from the Alps of France, Switzerland, and Italy. As Bulgaria is geographically adjacent to these regions, genetic similarity to breeds from these regions is reasonable.

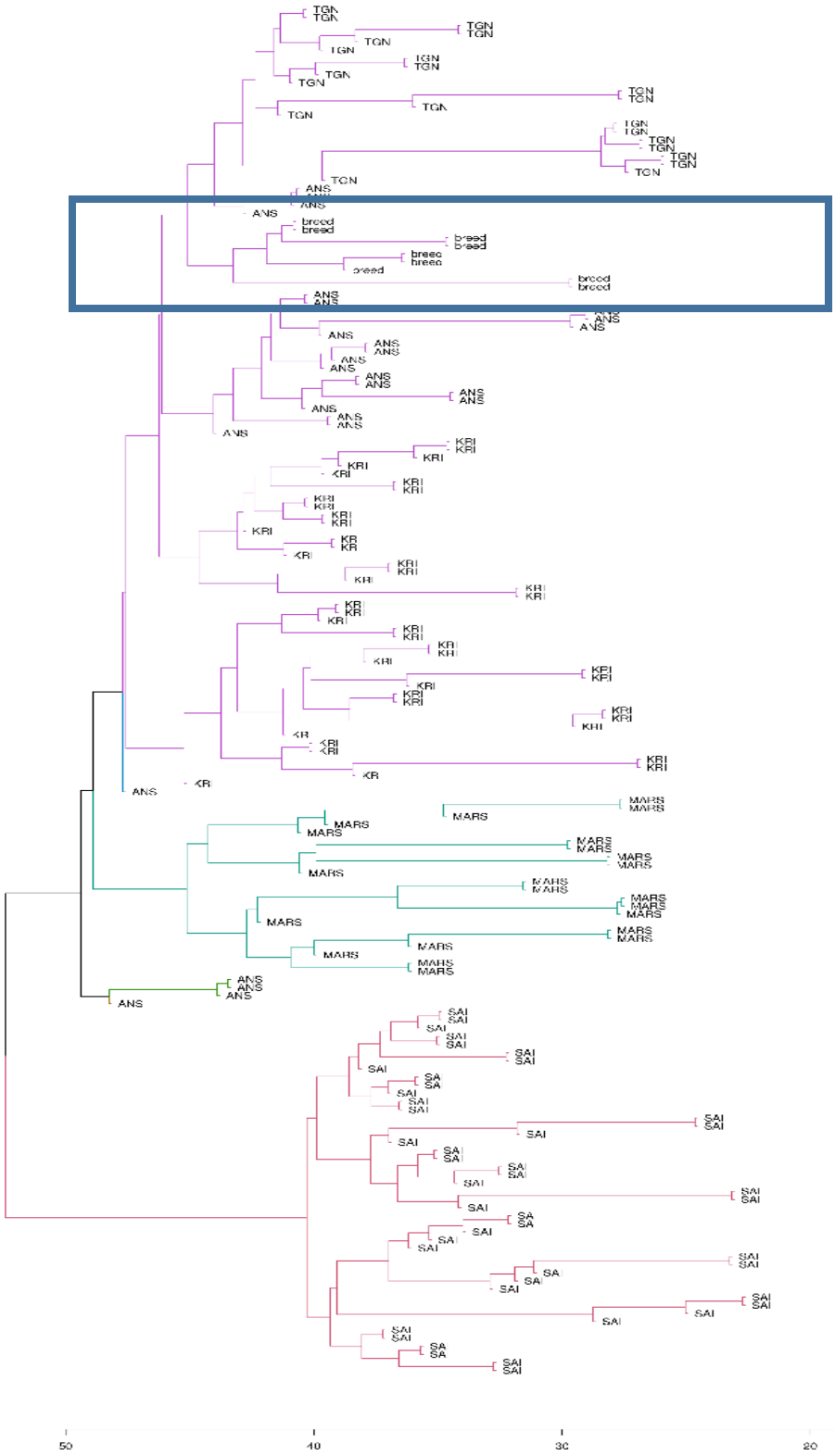


Figure 2: Hierarchical Clustering of Bulgarian Shepherd (breed) against related breeds Taigan (TGN), Anatolian Shepherd (ANS), Kritikos Lagonikos (KRI), Maremma sheepdog (MARS), and St. Bernard (SAI).

Breed Identification

The 9 submitted samples clustered tightly and were moderately distinct when compared to existing canid signatures in the database (Figure 3). The “All Breeds Outgroup” represents a single sample of each breed extant in our database, and functions as a control group. Comparison against next-closest breeds also supported genetic distinction from this breed (Figure 4). These findings suggest that the breed signature is likely to be successful and allow for detection of this breed in submitted dogs of unknown ancestry.

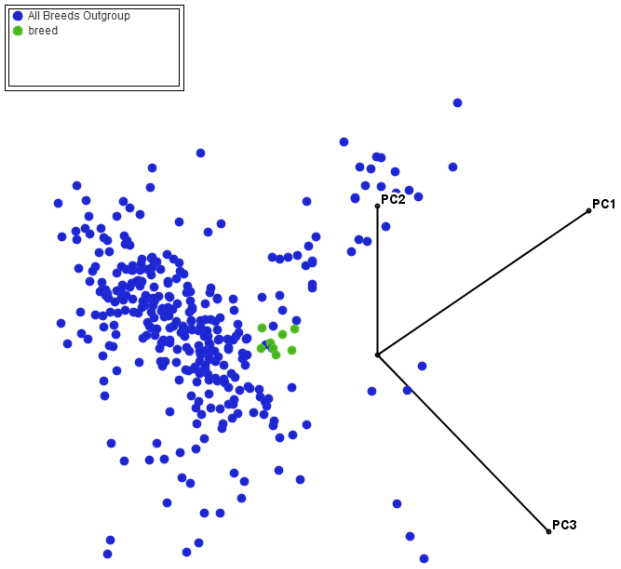


Figure 3: PCA Comparison of Bulgarian Shepherd (breed) against All Breeds Outgroup

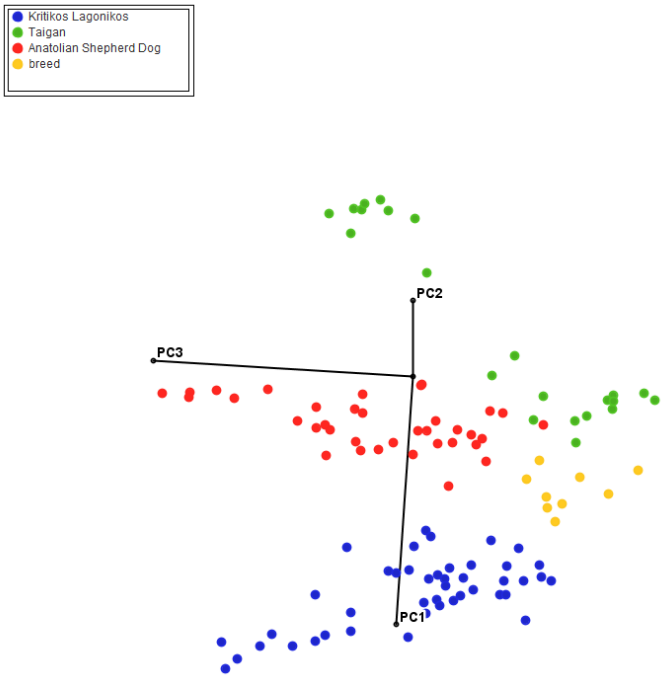


Figure 4: Comparison of Bulgarian shepherd (breed) against closest related breeds (Anatolian Shepherd, Kritikos Lagonikos, and Taigan)

Disease Mutation Prevalence

All samples were screened for 150+ genetic mutations. Of these tests, only one mutation was found positively detected in the Bulgarian shepherd samples: von Willebrand type 2, a mutation associated with type 2 von Willebrand disease (vWD), a moderate to severe clotting disorder. The particular mutation found has thus far only been associated with vWD type 2 in the German shorthaired and Wirehaired pointer. Other breeds have demonstrated type 2 vWD, but it does not appear to be associated with this mutation. Additionally, several breeds are known to be positive for this particular mutation but show no clinical signs of vWD type 2, so the significance of this finding in the Bulgarian shepherd samples is unknown at this time. Of the dogs tested, only one was found to be a carrier (having one copy of the mutation). The mutation is recessive in behavior, so no potentially affected individuals were identified in the tested population. The owner of this carrier will be notified privately for his/her consideration. See Table 2 in the Appendix for a complete listing of disease results in this study.

Type 2 von Willebrand disease is a moderate to severe clotting disorder. Typical symptoms include mucosal bleeding, such as nose bleeds (epistaxis), bleeding from the gums, gastrointestinal bleeding, and blood in the urine. Exceptionally excessive and prolonged bleeding may be observed after trauma or surgery, and spontaneous bleeding may also be encountered. This condition can lead to death if untreated.

Trait Prevalence

All samples were assessed for various traits governing physical phenotype, including coat color, coat length, and morphology. Few coat color traits were fixed (homozygous) in the breed. Please note that the allelic frequency may be related to presence or the inverse (absence) of the trait, depending on allele mapping assignments. A result of "1" refers to a heterozygote (single copy), "0" and "2" to homozygotes (no copies or two copies inherited). Summary of results are found in Table 1. Table 2 describes basic effect of various color pattern loci. Based on these data, it appears that the Bulgarian shepherd breed carries the alleles for sable (A^y), tan points (a^t), liver/brown (b^s), melanistic mask (E^m), clear red/yellow (e), piebald or white spotting (s^p), dominant black and/or brindle (absence of k^y allele) and non-dominant black (k^y), one of the alleles responsible for the saddle tan pattern, and one of the alleles responsible for prick or erect ear carriage. Other traits may become apparent on testing additional dogs.

Table 1: Trait Allelic Frequencies in Bulgarian Shepherd

Gene Name	Description	Allele Name	# of Copies of the Allele			Allele Frequency
			0	1	2	
ASIP	Sable	A^y	5	2	2	0.333333333
ASIP	Tan points	a^t	3	4	2	0.444444444
ASIP	Recessive black	a	9	0	0	0
TYRP1	Liver	b^c	9	0	0	0
TYRP2	Liver	b^s	7	1	1	0.166666667
MC1R	Melanistic mask	E^m	3	5	1	0.388888889
MC1R	Grizzle/domino	E^g	9	0	0	0
MC1R	Clear red/yellow	e	8	1	0	0.055555556
MITF	Piebald	s^p	2	3	4	0.611111111
CBD103	Non-dominant black	k^y	3	6	0	0.333333333
PSMB7	Harlequin	H	9	0	0	0
RSPO2 SNP4	Furnishings	F	0	0	9	1

RSPO2 SNP7	Furnishings	F	9	0	0	0
FGF4	Chondrodysplasia		0	0	9	1
T-box transcription factor	Bobtail		9	0	0	0
KRT71	Curly coat		0	1	8	0.944444444
FGF5	Long coat		9	0	0	0
RALY	Saddle		1	6	2	0.555555556
IGF1	Small size		0	0	9	1
Ear morphology	Ear carriage		2	5	2	0.5
IGF1R	Small size (<10")		0	0	9	1
Skull shape	Brachycephaly		0	0	9	1

Table 2: Subset of Genes Responsible for Coat Colors and Patterns and Their Dominance Hierarchies

Trait	Variants dominant → recessive	Description
Extension (E Locus)	$E^m>E^g>E>e$	Determines extent of phaeomelanin (cream/yellow/red) vs. eumelanin (black/liver)
Dominant Black (K Locus)	$K^B>K^{br}>k^y$	Determines presence (k^y or K^{br}) or absence (K^B) of phaeomelanin (red) coat patterns. Currently, testing does not distinguish between K^B (dominant black) and K^{br} (brindle).
Agouti (A Locus)	$A^y>a^w>a^t>a$	Determines most types of phaeomelanin (red) coat patterns
Black/Brown (B Locus)	$B>b^c$, b^s, b^d	Determines if eumelanin is black or liver/brown/chocolate. Currently cannot test for b^d.
White Spotting (S Locus)	$S>s^p$	A common gene governing production of pigment vs. no pigment (white). In some breeds, s^p behaves co-dominantly, in others, recessively.
Harlequin (H Locus)	H>h	Modifies merle gene expression
Saddle Tan Pattern (RALY gene)	Present/Absent	If present, allows for saddle-tan pattern expression instead of tan pointing. Operates in conjunction with other genes.

Genetic Diversity Assessment

We investigated the diversity of individuals using genotype homozygosity. This metric is defined as the ratio of markers that are homozygous (identical) for both copies of the allele, inherited from sire and dam. Homozygosity is also sometimes called internal diversity, as it is a measure of the degree of similarity of the lineage of sire and dam as inherited by their offspring when a large number of genetic markers are considered. Low homozygosity represents high diversity of individuals and vice versa.

The histogram below shows homozygosity on the horizontal axis, with relative number of individuals of this diversity level on vertical axis. For informational purposes, Anatolian Shepherd was included as the closest genetic relative, as well as all breeds from the Wisdom Health database. The more diverse the dog, the farther left on the X axis the dog will fall (see Figure 5).

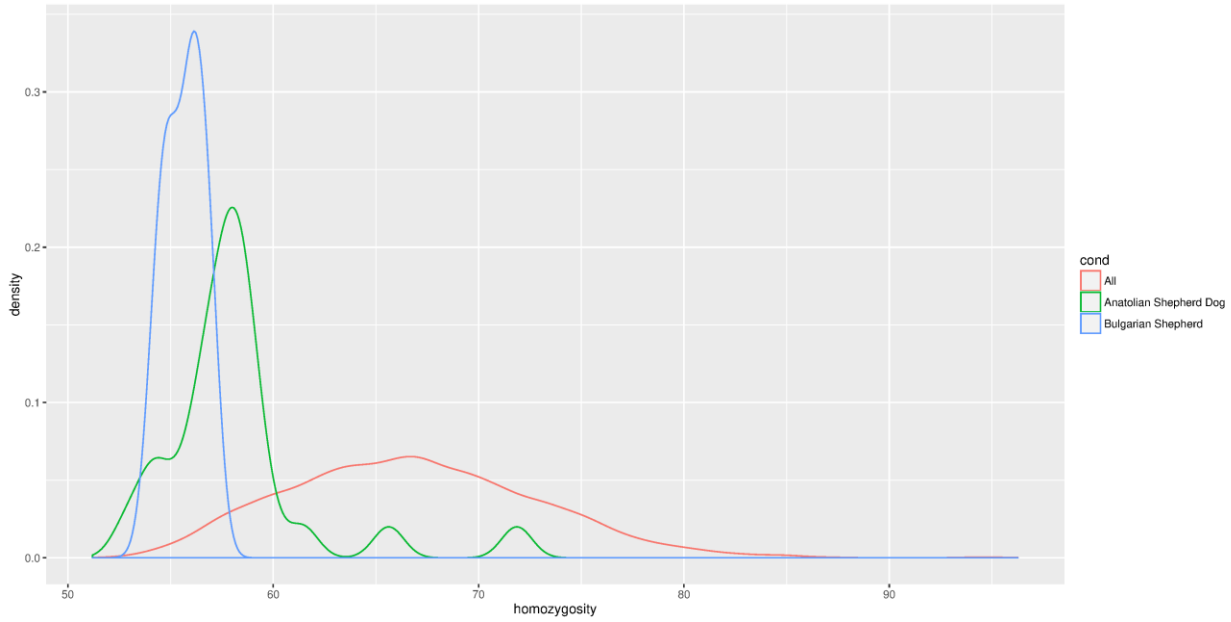


Figure 5: Diversity of Individual Bulgarian Shepherds, Anatolian Shepherds, and All Breeds (Density= percentage exhibiting the diversity score)

The Bulgarian shepherd dogs were found to have a much lower distribution of homozygosity (higher diversity) than nearly all other breeds in the Wisdom Health database (Figure 6). Median homozygosity was 55.6% for the group. This is an excellent diversity level, desirable for breed longevity.

This places the Bulgarian shepherd within the most diverse 10% of breeds in the Wisdom Health database, but may also be artefactual due to low sample count.

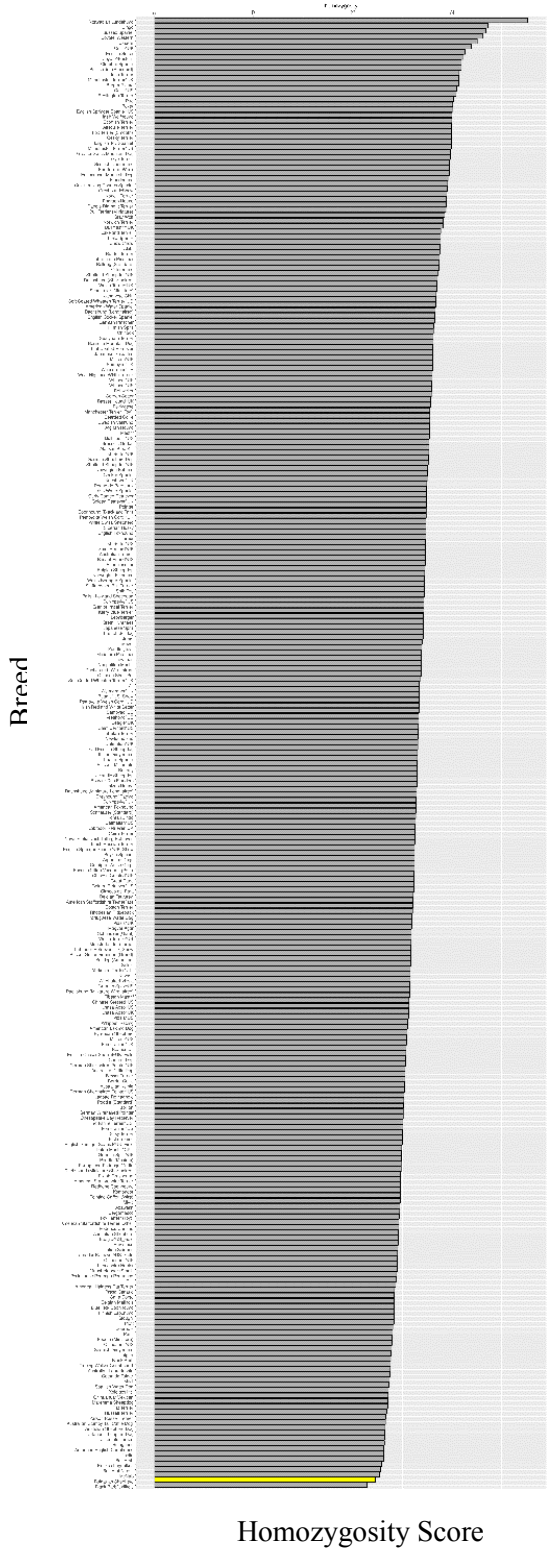


Figure 6: Average Homozygosity Levels of Various Breeds (Bulgarian Shepherd highlighted in yellow)

Conclusions

Our initial analysis of Bulgarian shepherd dogs suggests that this is a breed distinct from all other breeds in the current Wisdom Health database. The breed genotype is a unique genetic blend of Southeastern European and Middle Eastern genotypes, and shows the greatest resemblance to the Anatolian shepherd dog, Kritikos Lagonikos, and Taigan, but is distinct from these breeds. The breed sampling was found to carry a single detectable disease mutation, vWD2, associated with von Willebrand disease only in the German wirehaired and shorthaired pointers, and therefore of unknown significance in this breed. Trait genotyping indicates that the breed is heterozygous for many coat color patterns and some morphological traits. Initial scores of genetic diversity in the breed are high, suggesting a landrace rather than a breed from a closed, traditional registry. As this was a small sample size, additional samples of unique Bulgarian shepherd dogs must be tested to form statistically-significant conclusions as to disease and trait prevalence and diversity. Additional research into other breeds of Bulgaria, and adjacent countries, especially Southeastern Europe are recommended to determine if additional genetic relatives are present.

Appendix:

Table 2: Disease Test Results

Disease Name	Samples Positive
Alaskan Husky Encephalopathy, (AHE)	0
Amelogenesis Imperfecta, (AI)	0
Autosomal Recessive Severe Combined Immunodeficiency, (ARSCID)	0
Bandera's Neonatal Ataxia, (BNAt)	0
Benign Familial Juvenile Epilepsy or Remitting Focal Epilepsy	0
Bleeding disorder due to P2RY12 defect	0
Bobtail	0
Canine Cyclic Neutropenia (CN), Cyclic Hematopoiesis, Gray Collie Syndrome	0
Canine Multifocal Retinopathy 1, (CMR1); mutation originall found in Mastiff-related breeds	0
Canine Multifocal Retinopathy 2, (CMR2); mutation originally found in Coton de Tulear	0
Canine Multifocal Retinopathy 3, (CMR3); mutation originally found in Lapponian Herder	0
Canine Scott Syndrome	0
Cavalier King Charles Spaniel Muscular Dystrophy, (CKCS-MD)	0
Centronuclear Myopathy, (CNM); mutation originally found in Great Dane	0
Centronuclear Myopathy, (CNM); mutation originally found in Labrador Retriever	0
Cerebellar Hypoplasia; mutation originally found in Eurasier	0
Cerebral Dysfunction; mutation originally found in Friesian Stabyhoun	0
Chondrodysplasia; mutation originally found in Norwegian Elkhound and Karelian Bear Dog	0
Cleft Lip and Palate with Syndactyly; ADAMTS20 gene mutation originally found in Nova Scotia Duck Tolling Retriever	0
Cleft Palate; DLX6 gene mutation originally found in Nova Scotia Duck Tolling Retriever	0
Color Locus H (PSMB7 gene): Harlequin (H allele)	0
Complement 3 (C3) Deficiency	0
Cone Degeneration, (CD) or Achromatopsia	0
Cone Degeneration, (CD) or Achromatopsia; mutation originally found in German Shepherd	0
Cone Degeneration, (CD) or Achromatopsia; mutation originally found in German Shorthaired Pointer	0
Cone-Rod Dystrophy 1, (crd1); mutation originally found in American Staffordshire Terrier	0
Cone-Rod Dystrophy 2, (crd2); mutation originally found in American Pit Bull Terrier	0
Cone-Rod Dystrophy, Standard Wirehaired Dachshund, (crd SWD)	0
Congenital Hypothyroidism; mutation originally found in Tenterfield Terrier	0
Congenital Hypothyroidism; mutation originally found in Toy Fox and Rat Terrier	0
Congenital Keratoconjunctivitis Sicca and Ichthyosiform Dermatosis, (CKCSID)	0
Congenital Myasthenic Syndrome, (CMS); mutation originally found in Jack Russell Terrier	0
Congenital Myasthenic Syndrome, (CMS); mutation originally found in Labrador Retriever	0
Congenital Myasthenic Syndrome, (CMS); mutation originally found in Old Danish Pointing Dog	0
Craniomandibular Osteopathy, (CMO); mutation associated with terrier breeds	0
Cystinuria Type I-A; mutation originally found in Newfoundland Dog	0

Cystinuria Type II-A; mutation originally found in Australian Cattle Dog	0
Degenerative Myelopathy, (DM)	0
Dental Hypomineralization; mutation originally found in Border Collie	0
Dilated Cardiomyopathy, (DCM); mutation originally found in Doberman Pinscher (USA)	0
Duchenne or Dystrophin Muscular Dystrophy, (DMD); mutation originally found in Golden Retriever	0
Duchenne or Dystrophin Muscular Dystrophy, (DMD); mutation originally found in Norfolk Terrier	0
Dystrophic Epidermolysis Bullosa; mutation originally found in Central Asian Ovcharka	0
Dystrophic Epidermolysis Bullosa; mutation originally found in Golden Retriever	0
Early-Onset Progressive Polyneuropathy; mutation originally found in Alaskan Malamute	0
Early-Onset Progressive Polyneuropathy; mutation originally found in Greyhound	0
Episodic Falling Syndrome, (EFS)	0
Exercise-Induced Collapse, (EIC)	0
Factor IX Deficiency or Hemophilia B; mutation Gly379Glu	0
Factor IX Deficiency or Hemophilia B; mutation originally found in Airedale Terrier	0
Factor IX Deficiency or Hemophilia B; mutation originally found in Lhasa Apso	0
Factor VII Deficiency	0
Factor VIII Deficiency or Hemophilia A; mutation originally found in Boxer	0
Factor VIII Deficiency or Hemophilia A; mutation originally found in German Shepherd Dog	0
Factor VIII Deficiency or Hemophilia A; mutation originally found in Havanese	0
Factor VIII Deficiency or Hemophilia A; p.Cys548Tyr mutation originally found in German Shepherd	0
Factor XI Deficiency	0
Fanconi Syndrome	0
Fetal Onset Neuroaxonal Dystrophy, (FNAD)	0
Glanzmann Thrombasthenia Type I, (GT); mutation originally found in Great Pyrenees	0
Globoid Cell Leukodystrophy, (GLD) or Krabbe Disease; mutation originally found in Irish Setter	0
Globoid Cell Leukodystrophy, (GLD) or Krabbe Disease; mutation originally found in Terriers	0
Glycogen Storage Disease Type II or Pompe Disease, (GSD II)	0
Glycogen Storage Disease Type IIIa, (GSD IIIa)	0
GM2 Gangliosidosis; mutation originally found in Japanese Chin	0
GM2 Gangliosidosis; mutation originally found in Toy Poodle	0
Golden Retriever Progressive Retinal Atrophy 2, (GR_PRA 2)	0
Hereditary Ataxia or Cerebellar Ataxia; mutation originally found in Old English Sheepdog and Gordon Setter	0
Hereditary Elliptocytosis	0
Hereditary Footpad Hyperkeratosis, (HFH)	0
Hereditary Vitamin D-Resistant Rickets, (HVDRR) Type II	0
Hyperekplexia or Startle Disease	0
Hyperuricosuria, (HUU)	0
Hypocatalasia or Acatalasemia	0
Hypomyelination; mutation originally found in Weimaraner	0
Ichthyosis; mutation originally found in Great Dane	0
Intestinal Cobalamin Malabsorption or Imerslund-Gräsbeck Syndrome, (IGS); mutation originally found in Beagle	0

Intestinal Cobalamin Malabsorption or Imerslund-Gräsbeck Syndrome, (IGS); mutation originally found in Border Collie	0
L-2-Hydroxyglutaric aciduria, (L2HGA); mutation originally found in Staffordshire Bull Terrier	0
Lagotto Storage Disease, (LSD)	0
Lamellar Ichthyosis	0
Ligneous Membranitis	0
Macrothrombocytopenia; disease-linked variant originally found in Norfolk and Cairn Terrier	0
May-Hegglin Anomaly, (MHA)	0
Mucopolysaccharidosis Type 3A, (MPS IIIA); mutation originally found in Dachshund	0
Mucopolysaccharidosis Type VII, (MPS VII); mutation originally found in Brazilian Terrier	0
Multi-Drug Resistance 1, (MDR1)	0
Muscular Dystrophy, Ullrich-type; mutation originally found in Landseer	0
Muscular Hypertrophy (Double Muscling)	0
Musladin-Lueke Syndrome, (MLS)	0
Myotonia Congenita; mutation originally found in Australian Cattle Dog	0
Myotubular Myopathy; mutation originally found in Rottweiler	0
Narcolepsy; mutation originally found in Dachshund	0
Narcolepsy; mutation originally found in Doberman Pinscher	0
Narcolepsy; mutation originally found in Labrador Retriever	0
Neonatal Cerebellar Cortical Degeneration or Cerebellar Abiotrophy, (NCCD)	0
Neonatal Encephalopathy with Seizures, (NEWS)	0
Neuronal Ceroid Lipofuscinosis 1, (NCL1); mutation originally found in Dachshund	0
Neuronal Ceroid Lipofuscinosis 7, (NCL7); mutation originally found in Chinese Crested Dog and Chihuahua	0
Neuronal Ceroid Lipofuscinosis 8, (NCL8); mutation originally found in English Setter	0
Neuronal Ceroid Lipofuscinosis 10, (NCL10); mutation originally found in American Bulldog	0
Neuronal Ceroid Lipofuscinosis 12, (NCL12); mutation originally found in Tibetan terrier	0
Osteochondrodysplasia; mutation originally found in Miniature Poodle	0
Osteogenesis Imperfecta, (OI); mutation originally found in Beagle	0
Osteogenesis Imperfecta, (OI); mutation originally found in Dachshund	0
Persistent Müllerian Duct Syndrome, (PMDS); mutation originally found in Miniature Schnauzer	0
Phosphofructokinase (PFK) Deficiency or Glycogen Storage Disease Type VII	0
Polycystic Kidney Disease, (PKD); mutation originally found in Bull Terrier	0
Prekallikrein Deficiency	0
Primary Ciliary Dyskinesia, (PCD)	0
Primary Hereditary Cataract (PHC); mutation originally found in Australian Shepherd	0
Primary Hyperoxaluria, (PH); mutation originally found in Coton de Tulear	0
Primary Lens Luxation, (PLL)	0
Primary Open Angle Glaucoma, (POAG); mutation originally found in Beagle	0
Primary Open Angle Glaucoma, (POAG); mutation originally found in Norwegian Elkhound	0
Progressive Early-Onset Cerebellar Ataxia; mutation originally found in Finnish Hound	0
Progressive Retinal Atrophy Cone-Rod Dystrophy, (cord1-PRA / crd4)	0
Progressive Retinal Atrophy Type III, (PRA type III); mutation originally found in Tibetan Spaniel and Tibetan Terrier	0

Progressive Retinal Atrophy, (CNGA1-PRA); mutation originally found in Shetland Sheepdog	0
Progressive Retinal Atrophy, (PAP1_PRA); mutation originally found in Papillon and Phalene	0
Progressive Retinal Atrophy, (PRA); mutation originally found in Basenji	0
Progressive Retinal Atrophy; Swedish Vallhund marker test	0
Protein Losing Nephropathy, (PLN); NPHS1 gene variant	0
Pyruvate Dehydrogenase Phosphatase 1 (PDP1) Deficiency	0
Pyruvate Kinase Deficiency; mutation originally found in Beagle	0
Pyruvate Kinase Deficiency; mutation originally found in Pug	0
Pyruvate Kinase Deficiency; mutation originally found in West Highland White Terrier	0
QT Syndrome	0
Renal Cystadenocarcinoma and Nodular Dermatofibrosis, (RCND)	0
Rod-Cone Dysplasia 1, (rcd1); mutation originally found in Irish Setter	0
Rod-Cone Dysplasia 1a, (rcd1a); mutation originally found in Sloughi	0
Rod-Cone Dysplasia 3, (rcd3)	0
Sensory Ataxic Neuropathy, (SAN)	0
Severe Combined Immunodeficiency in Frisian Water Dogs, (SCID)	0
Skeletal Dysplasia 2, (SD2)	0
Spinal Dysraphism	0
Spinocerebellar Ataxia or Late-Onset Ataxia (SCA, LOA)	0
Spinocerebellar Ataxia with Myokymia and/or Seizures, (SAMS)	0
Spondylocostal Dysostosis	0
Trapped Neutrophil Syndrome, (TNS)	0
Van den Ende-Gupta Syndrome, (VDEGS)	0
Von Willebrand Disease (vWD) Type 1; mutation originally found in the Doberman Pinscher	0
Von Willebrand Disease (vWD) Type 2; mutation originally found in German Wirehaired Pointer	1
Von Willebrand Disease (vWD) Type 3; Kooikerhondje, Scottish terrier, and Shetland sheepdog variants	0
X-Linked Ectodermal Dysplasia, (XHED) or Anhidrotic Ectodermal Dysplasia	0
X-Linked Hereditary Nephropathy, (XLHN)	0
X-Linked Hereditary Nephropathy, (XLHN); mutation originally found in Navasota Dog	0
X-Linked Progressive Retinal Atrophy 1, (XLPRA1)	0
X-Linked Progressive Retinal Atrophy 2, (XLPRA2)	0
X-linked Severe Combined Immunodeficiency (XSCID); mutation originally found in Basset Hound	0
X-linked Severe Combined Immunodeficiency (XSCID); mutation originally found in Cardigan Welsh Corgi	0
X-Linked Tremors; mutation originally found in English Springer Spaniel	0