PRESENTATION OF THE MEMBERS OF THE WORKING GROUP (WG)

Helle Friis Proschowsky, DK Veterinarian with a Ph.D. in genetics. Until 2010 associate professor at the department of Animal Genetics at Copenhagen University. From 2010 veterinary consultant at the Danish Kennel Club with responsibility for genetic counselling of breeders and breed clubs, breeder education and general health communication in the DKC magazine, on the webpage and on social medias. Secretary of the Health Board of the DKC and member of the Scientific Committee of the NKU.

Birgitte Schjøth, DK DVM with a special focus on reproduction. Long term owner of the Danish semen bank "Canicold" and author of a reproduction book for breeders. Breeder of Old English Sheepdogs with the prefix "*Danish Delight*" since 1970 and show judge for a number of breeds. Teacher in reproduction on the Danish Kennel Club (DKC) breeder's education courses. Member of the DKC Health Board, the NKU Scientific Committee and the FCI Breeding Committee.

Åke Hedhammar, SE DVM, M Sc, PhD is now a senior Professor in Internal Medicine – Small Animals and Dipl. in Internal Medicine –Companion Animals still involved in research mainly on the genomics of spontaneously occurring complex traits in dogs (diseases and behavior) serving as models also for their human counterparts. He also keeps on serving as scientific advisor and veterinary consultant to the Swedish Kennel Club. These tasks also include being a member of the Scientific Commission of the FCI and he is also serving on WSAVA hereditary defect committee. Initiator of the 1st International Workshop on Enhancement of Genetic Health in Pedigree Dogs, (The Dog Health workshop) held in Stockholm 2012. Have bred boxers with the prefix *Facit* and served as judge in working trials.

Renée Sporre-Willes, SE Former president of the FCI Standards Commission, present of the Swedish ditto, Cynological expert at the Sw. KC for 30 years, co-editor in chief of the Sw. KC magazine *Hundsport* for 30 years, all-round judge, breeder since 1969 of champions in Pugs, Pekingese, Norwich Terriers and Lagotto under the prefix of *Cobby's*. Initiated the Sw. Pug Dog Club in 1977 and named it Mops Orden. Author of encyclopedia's and breed books on dogs in Swedish and English.

Christine Sonberg, N Breeder of Welsh Corgi, Boston Terrier and Pug, President of the Norwegian Pug Club, FCI judge, and an international lecturer.

Kristin Wear Prestrud, N DVM, PhD is veterinary advisor in the Norwegian Kennel Club (NKC) since 2008, after several years of as clinician and researcher at the Norwegian School of Veterinary Science. Her main focus areas in the NKC are healthy breeding, BSI and exaggerated conformation, DNA testing, research, breed club advisory, breeders' education and teaching veterinary and vet nurse students about ethics, sound breeding, behavior and animal welfare. KWP has been member of the in health/breeding committee of several breed clubs, and has bred some litters and competed at dog shows and in obedience in earlier years. Nowadays she

spends all spare time on search and rescue dogs, as dog handler, instructor and judge of search dog certification tests.

Kirsi Sainio, FIN, chair, is an associate professor of developmental biology in the University of Helsinki. Chair of the FCI Scientific Commission, former member of the Finnish Kennel Club Board (2008- 2016) and chair of the Finnish Kennel Club Scientific Committee (2008-2016).

Tiina Taulos, FIN Longtime Poodle breeder of all sizes awarded by the Finnish Kennel Club of Lauri Vuolasvirta prize for the highest recognition of Dog breeding in Finland. Succesful Boston Terrier and Pug breeder as well as long time experience of French Bulldogs and first Finnish breed specialist. Finnish Poodle Club representative at the Finnish Kennel Club Counsil. Board member at the Finnish Toy Dog Club and in charge of educating and testing new toy breed judges as well as new Poodle judges. Silver medal from the Finnish Poodle Club and Finnish Dog Breeder's Club. Dog show judge in FCI groups 3, 4, 5, 8, 9 and 10.

Katariina Mäki, FIN, secretary, is a breeding expert in the Finnish Kennel Club since 2012. Member of the FKC Scientific Committee since 2002. PhD in animal breeding 2004 (University of Helsinki), thesis “Breeding against hip and elbow dysplasia in dogs”. Her research interests are small populations and inbreeding as well as breeding value estimation for health and longevity traits.

Enclosure 13

REFERENCES ON BRACHYCEPHALIC AIRWAY SYNDROME

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Wykes PM[1]. [1]Reference Surgical Veterinary Practice, Englewood, Colorado 80110.
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Abstract
This is a complex condition, recognized primarily in brachycephalic breeds, that results in varying degrees of upper airway obstruction. The signs consist of respiratory distress, stridor, reduced exercise tolerance, and in more severe cases, cyanosis and collapse. The inherent anatomy of the brachycephalic skull contributes to the development of these signs. Such anatomic features include: a shortened and distorted nasopharynx, stenotic nares, an elongated soft palate, and everted laryngeal saccules. The increased negative pressure created in the pharyngolaryngeal region, as a result of these obstructing structures, ultimately results in distortion and collapse of the arytenoid cartilages of the larynx.

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Aron DN, Crowe DT.
Abstract
This article presents an overview of the clinical features of upper airway obstructive disorders. It includes more detailed discussions of certain common conditions such as brachycephalic airway syndrome, laryngeal paralysis, and upper airway obstruction due to trauma, foreign bodies, extraluminal masses, and tumours of the larynx and trachea.

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Localization of canine brachycephaly using an across breed mapping approach.
Bannasch D[1], Young A, Myers J, Truvé K, Dickinson P, Gregg J, Davis R, Bongcam-Rudloff E, Webster MT, Lindblad-Toh K, Pedersen N.
Author information
Abstract
The domestic dog, Canis familiaris, exhibits profound phenotypic diversity and is an ideal model organism for the genetic dissection of simple and complex traits.

However, some of the most interesting phenotypes are fixed in particular breeds and are therefore less tractable to genetic analysis using classical segregation-based mapping approaches. We implemented an across breed mapping approach using a moderately dense SNP array, a low number of animals and breeds carefully selected for the phenotypes of interest to identify genetic variants responsible for breed-defining characteristics. Using a modest number of affected (10-30) and control (20-60) samples from multiple breeds, the correct chromosomal assignment was identified in a proof of concept experiment using three previously defined loci; hyperuricosuria, white spotting and chondrodysplasia. Genome-wide association was performed in a similar manner for one of the most striking morphological traits in dogs: brachycephalic head type. Although candidate gene approaches based on comparable phenotypes in mice and humans have been utilized for this trait, the causative gene has remained elusive using this method. Samples from nine affected breeds and thirteen control breeds identified strong genome-wide associations for brachycephalic head type on Cfa 1. Two independent datasets identified the same genomic region. Levels of relative heterozygosity in the associated region indicate that it has been subjected to a selective sweep, consistent with it being a breed defining morphological characteristic. Genotyping additional dogs in the region confirmed the association. To date, the genetic structure of dog breeds has primarily been exploited for genome wide association for segregating traits. These results demonstrate that non-segregating traits under strong selection are equally tractable to genetic analysis using small sample numbers.
Abstract

PLoS Genet. 2016 May 12;12(5):e1006000. doi: 10.1371/journal.pgen.1006000. eCollection 2016.

Utilizing the Dog Genome in the Search for Novel Candidate Genes Involved in Glioma Development-Genome Wide Association Mapping followed by Targeted Massive Parallel Sequencing Identifies a Strongly Associated Locus.

Truvé K[1,2], Dickinson P[3], Xiong A[4], York D[3], Jayashankar K[5], Pielberg G[6], Koltookian M[7], Murén E[6], Fuxelius HH[1], Weishaupt H[4], Swartling FJ[4], Andersson G[1], Hedhammar Å[8], Bongcam-Rudloff E[1], Forsberg-Nilsson K[4], Bannasch D[5], Lindblad-Toh K[6,7].

Author information

Abstract

Gliomas are the most common form of malignant primary brain tumors in humans and second most common in dogs, occurring with similar frequencies in both species. Dogs are valuable spontaneous models of human complex diseases including cancers and may provide insight into disease susceptibility and oncogenesis. Several brachycephalic breeds such as Boxer, Bulldog and Boston Terrier have an elevated risk of developing glioma, but others, including Pug and Pekingese, are not at higher risk. To identify glioma-associated genetic susceptibility factors, an across-breed genome-wide association study (GWAS) was performed on 39 dog glioma cases and 141 controls from 25 dog breeds, identifying a genome-wide significant locus on canine chromosome (CFA) 26 (p = 2.8 x 10-8). Targeted re-sequencing of the 3.4 Mb candidate region was performed, followed by genotyping of the 56 SNVs that best fit the association pattern between the re-sequenced cases and controls. We identified three candidate genes that were highly associated with glioma susceptibility: CAMKK2, P2RX7 and DENR. CAMKK2 showed reduced expression in both canine and human brain tumors, and a non-synonymous variant in P2RX7, previously

demonstrated to have a 50% decrease in receptor function, was also associated with disease. Thus, one or more of these genes appear to affect glioma susceptibility

Demography and health of **Pugs** under primary veterinary care in England.
O'Neill DG, Darwent EC, Church DB, Brodbelt DC.
Canine Genet Epidemiol. 2016 Jun 10;3:5. doi: 10.1186/s40575-016-0035-z. eCollection 2016.
Free PMC Article
Abstract
BACKGROUND:
The Pug is an ancient dog breed and was the fifth most commonly registered UK pedigree breed in 2014. However, the breed has been reported to be predisposed to several disorders including ocular, respiratory and dermatological problems. The VetCompass Programme collates de-identified clinical data from primary-care veterinary practices in the UK for epidemiological research. Using VetCompass clinical data, this study aimed to characterise the demography and common disorders of the general population of Pugs under veterinary care in England.
RESULTS:
Pugs comprised 2709 (1.03 %) of 264,260 study dogs under veterinary care from September 1(st), 2009 to 30(th) April, 2015. Annual proportional birth rates showed that Pugs rose from less than 1 % of annual birth cohorts before 2008 to comprise 2.8 % of the 2013 annual birth cohort. The most common colours of Pugs were fawn (63.1 %), black (27.7 %), apricot (7.6 %) and silver (2.1 %). Of the 1009 pugs under veterinary care in the study during 2013, 688 (68.19 %) had at least one disorder recorded. The most prevalent disorders recorded overall were overweight/obesity (number of events: 133, prevalence: 13.18 %, 95 % CI: 11.12-15.43), corneal disorder (88, 8.72 %, 95 % CI: 7.05-10.63) and otitis externa (76, 7.53 %, 95 % CI: 5.98-9.34). The most prevalent disorder groups were ophthalmological (n = 164, prevalence: 16.25 %, 95 % CI: 14.03-18.68), dermatological (157, 15.60 %, 95 % CI: 13.38-17.95) and aural (152, 15.06 %, 95 % CI: 12.91-17.42). The most prevalent body locations affected were the head-and-neck (n = 439, prevalence = 43.51 %, 95 % CI: 40.42-46.63) and abdomen (195, 19.33 %, 95 % CI: 16.93-21.90). The most prevalent organ systems affected were the integument (321, 31.81 %, 95 % CI: 28.15-35.72) and digestive (257, 25.47 %, 95 % CI: 22.54-28.65). The most prevalent pathophysiologic processes recorded were inflammation (386, 38.26 %, 95 % CI: 34.39-42.27) and congenital/developmental (153, 15.16 %, 95 % CI: 12.61-18.13).
CONCLUSIONS:
Ownership of Pugs in England is rising steeply. Overweight/obesity, corneal disorder and otitis externa are the most common disorders in Pugs. Identification of health priorities based on VetComapss data can support evidence-based reforms to improve health and welfare within the breed.

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Impact of Facial Conformation on Canine Health: Brachycephalic Obstructive Airway Syndrome.
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Abstract

The domestic dog may be the most morphologically diverse terrestrial mammalian species known to man; pedigree dogs are artificially selected for extreme aesthetics dictated by formal Breed Standards, and breed-related disorders linked to conformation are ubiquitous and diverse. Brachycephaly--foreshortening of the facial skeleton--is a discrete mutation that has been selected for in many popular dog breeds e.g. the Bulldog, Pug, and French Bulldog. A chronic, debilitating respiratory syndrome, whereby soft tissue blocks the airways, predominantly affects dogs with this conformation, and thus is labelled Brachycephalic Obstructive Airway Syndrome (BOAS). Despite the name of the syndrome, scientific evidence quantitatively linking brachycephaly with BOAS is lacking, but it could aid efforts to select for healthier conformations. Here we show, in (1) an exploratory study of 700 dogs of diverse breeds and conformations, and (2) a confirmatory study of 154 brachycephalic dogs, that BOAS risk increases sharply in a non-linear manner as relative muzzle length shortens. BOAS only occurred in dogs whose muzzles comprised less than half their cranial lengths. Thicker neck girths also increased BOAS risk in both populations: a risk factor for human sleep apnoea and not previously realised in dogs; and obesity was found to further increase BOAS risk. This study provides evidence that breeding for brachycephaly leads to an increased risk of BOAS in dogs, with risk increasing as the morphology becomes more exaggerated. As such, dog breeders and buyers should be aware of this risk when selecting dogs, and breeding organisations should actively discourage exaggeration of this high-risk conformation in breed standards and the show ring.

If society wanted to reduce BOAS risk, but not ban any existing breeds, then an even more moderate strategy could be adopted. Several approaches could be used towards breeding towards more moderate, lower-risk morphologies, each of which may have strengths and weaknesses and may be differentially supported by stakeholders involved in this issue [37]:

1. Selecting only those dogs with more moderate, lower-risk morphologies for breeding. The further amendment of breed standards to promote lower-risk morphologies and penalise high-risk, extreme morphologies (potentially including quantitative limits) may aid this approach,
2. Health screening of morphologically extreme dogs to help select only those that are free of BOAS for breeding,
3. Developing genetic tests to highlight high and low risk animals e.g. individuals within high risk breeds with or without elongated soft palates. Genetically testing for the anatomical abnormalities of BOAS may not be the optimal solution as these features may be strongly linked with skull morphology, and thus this may not be feasible strategy
   and/or
4. For breeds lacking sufficient individuals with moderate morphologies, judicious out-crossing to increase health and phenotypic diversity. This approach would require the necessary cooperation from kennel clubs.