Deafness risk in the Dalmatian is maintained by balancing selection

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Introduction: Congenital sensironeural deafness affects a significant proportion of Dalmatian pups that is predicted to range from 8-20% and includes both unilateral (one ear) and bilateral (both ears) forms. Genomic analyses have uncovered alleles that affect deafness risk in a complex manner. One major risk haplotype occurs in the vicinity of the gene Micropthalmia-Associated Transcription Factor (MITF) : a gene that impacts melanocyte migration and proliferation. Population-based allele frequency could not be ascertained from our mapping population as our sample cohort for genomic analysis was subject to ascertainment biases.

Objective: The aim of the study was to assess the frequency of the MITF risk allele in the potential Dalmatian breeding population by assaying dogs exhibited at a conformation show.

Materials & Methods: DNA was collected by buccal swab sampling from Dalmatians exhibited at a regional breed specialty event. Forty dogs participated in the sampling. All dogs demonstrated acceptable phenotypes according to the breed standard according to assessors. Five judges participated in offering an external evaluation of the dog considering pigmentation and markings as well as ear-phenotype. Dog samples were later assayed for the risk haplotype by a marker SNP using allele-specific amplification for genotyping. Deafness status for the participating dogs was unknown at assessment but might have been either normal hearing or unilateral deaf based on standard selection practices in the breed.

Results:

Risk-allele frequency in the assayed dogs demonstrated strong deviation from Hardy-Weinberg expectation ($P=7.09e^{-07}$). Of the forty dogs assayed, thirty-six (90%) were heterozygous for the risk allele, while expectation was 50%. Two dogs each were homozygous for the high-risk and low-risk alleles respectively. Analysis of the visual inspection data of the animals showed that dogs homozygous for the low risk alleles had significantly less pigmentation on their nose and lips.

Conclusions:

Preliminary work suggests that deafness risk alleles at MITF demonstrate overdominance. This in turn implies some selective advantage to heterozygosity. It is likely that there is active selection against the risk allele via the application of Brain-Auditory-Evoked-Response (BAER) testing of pups for deafness. The avenue for selection against the low-risk allele is harder to explain but may be affected by external patterning, with breeders favouring dogs with greater pigmentation in the belief that this might reduce deafness risk. Because the low-risk homozygous dogs were siblings, further work is required to test this hypothesis.